Appendix J: Forest plots

J.1 Diagnostic tools for psoriatic arthritis

Diagnostic tools for Psoriatic Arthritis

Figure 1: ToPAS vs clinical diagnosis by rheumatologist

Study	TP	FP	FN	TN	Sensitivity	Specificity
Gladman 2009	146	13	18	80	0.89 [0.83, 0.93]	0.86 [0.77, 0.92]

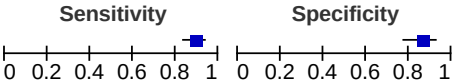
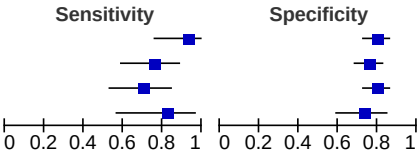


Figure 2: PASE vs clinical diagnosis by rheumatologist

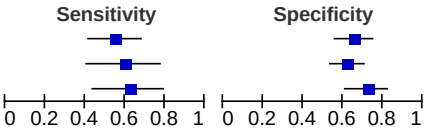
Study	TP	FP	FN	TN	Sensitivity	Specificity
Dominguez 2009 (active)	25	31	2	122	0.93 [0.76, 0.99]	0.80 [0.72, 0.86]
Dominguez 2009 (TH:44)	28	37	9	116	0.76 [0.59, 0.88]	0.76 [0.68, 0.82]
Dominguez 2009 (TH:47)	26	31	11	122	0.70 [0.53, 0.84]	0.80 [0.72, 0.86]
Husini 2007	14	14	3	38	0.82 [0.57, 0.96]	0.73 [0.59, 0.84]



Note: all of the Dominguez data is from the same population

Figure 3: PAQ vs clinical diagnosis by rheumatologist

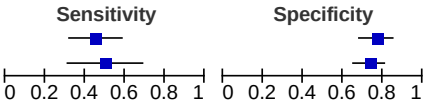
Study	TP	FP	FN	TN	Sensitivity	Specificity
Alenius2002 any arthritis	33	36	27	69	0.55 [0.42, 0.68]	0.66 [0.56, 0.75]
Alenius2002 periph/axial	18	51	12	84	0.60 [0.41, 0.77]	0.62 [0.53, 0.70]
Ibrahim 2009	20	21	12	55	0.63 [0.44, 0.79]	0.72 [0.61, 0.82]



Note: all of the Alenius data is from the same population

Figure 4: mPAQ vs clinical diagnosis by rheumatologist

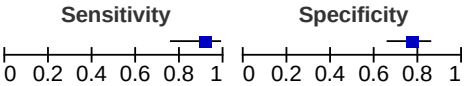
Study	TP	FP	FN	TN	Sensitivity	Specificity
Alenius2002 any arthritis	27	24	33	81	0.45 [0.32, 0.58]	0.77 [0.68, 0.85]
Alenius2002 periph/axial	15	36	15	99	0.50 [0.31, 0.69]	0.73 [0.65, 0.81]



Note: all of the Alenius data is from the same population

Figure 5: PEST vs clinical diagnosis by rheumatologist

Study	TP	FP	FN	TN	Sensitivity	Specificity
Ibrahim 2009	30	19	3	62	0.91 [0.76, 0.98]	0.77 [0.66, 0.85]



J.2 Topicals – trunk and limbs

J.2.1 Vitamin D analogue vs placebo

Figure 6: Investigator's assessment (clear/nearly clear) at 4-10 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Calcipotriol OD						
Barker 1999	13	28	1	26	0.9%	12.07 [1.70, 85.93]
Fleming2010A	9	79	0	40	0.5%	9.74 [0.58, 163.17]
Kaufmann 2002	107	480	16	157	19.9%	2.19 [1.34, 3.58]
Subtotal (95% CI)		**587**		**223**	**21.4%**	**2.78 [1.75, 4.41]**
Total events	129		17			
Heterogeneity: Chi² = 3.81, df = 2 (P = 0.15); I² = 48%						
Test for overall effect: Z = 4.34 (P < 0.0001)						
1.1.2 Calcipotriol BD						
Dubertret 1992	46	62	11	62	9.1%	4.18 [2.40, 7.29]
Guenther 2002	115	227	19	206	16.5%	5.49 [3.51, 8.59]
Highton 1995	87	124	23	123	19.1%	3.75 [2.55, 5.52]
Papp 2003	103	308	8	107	9.8%	4.47 [2.25, 8.87]
Subtotal (95% CI)		**721**		**498**	**54.5%**	**4.48 [3.50, 5.73]**
Total events	351		61			
Heterogeneity: Chi² = 1.67, df = 3 (P = 0.64); I² = 0%						
Test for overall effect: Z = 11.90 (P < 0.00001)						
1.1.3 Calcitriol OD						
Perez 1996	37	84	0	84	0.4%	75.00 [4.68, 1201.67]
Subtotal (95% CI)		**84**		**84**	**0.4%**	**75.00 [4.68, 1201.67]**
Total events	37		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.05 (P = 0.002)						
1.1.4 Calcitriol BD						
Langner 1992	21	29	9	29	7.4%	2.33 [1.30, 4.20]
Langner 1993	24	32	13	32	10.8%	1.85 [1.16, 2.94]
Subtotal (95% CI)		**61**		**61**	**18.2%**	**2.05 [1.42, 2.95]**
Total events	45		22			
Heterogeneity: Chi² = 0.38, df = 1 (P = 0.54); I² = 0%						
Test for overall effect: Z = 3.84 (P = 0.0001)						
1.1.5 Taclacitol (OD)						
Langley2011A	33	184	5	91	5.5%	3.26 [1.32, 8.08]
Subtotal (95% CI)		**184**		**91**	**5.5%**	**3.26 [1.32, 8.08]**
Total events	33		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.56 (P = 0.01)						
Total (95% CI)		**1637**		**957**	**100.0%**	**3.90 [3.24, 4.70]**
Total events	595		105			
Heterogeneity: Chi² = 26.86, df = 10 (P = 0.003); I² = 63%						
Test for overall effect: Z = 14.32 (P < 0.00001)						
Test for subgroup differences: Chi² = 17.73, df = 4 (P = 0.001), I² = 77.4%						

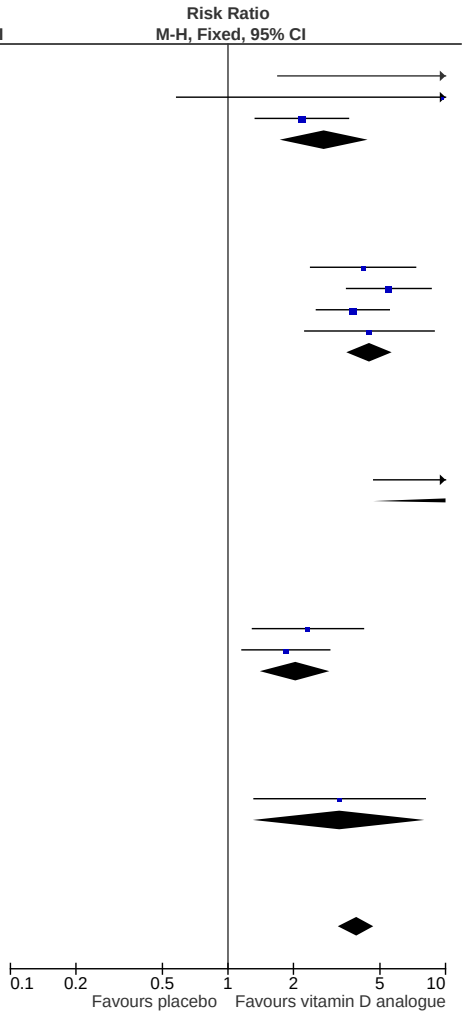


Figure 7: Patient's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Calcipotriol OD or BD						
Guenther 2002	117	227	26	206	30.0%	4.08 [2.79, 5.98]
Harrington 1996	148	291	13	71	23.0%	2.78 [1.68, 4.60]
Kaufmann 2002	137	480	15	157	24.9%	2.99 [1.81, 4.93]
Subtotal (95% CI)		**998**		**434**	**77.9%**	**3.35 [2.58, 4.34]**
Total events	402		54			
Heterogeneity: Chi² = 1.77, df = 2 (P = 0.41); I² = 0%						
Test for overall effect: Z = 9.11 (P < 0.00001)						
1.2.5 Tacalcitol (OD)						
Langley2011A	35	163	14	64	22.1%	0.98 [0.57, 1.70]
Subtotal (95% CI)		**163**		**64**	**22.1%**	**0.98 [0.57, 1.70]**
Total events	35		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.07 (P = 0.95)						
Total (95% CI)		**1161**		**498**	**100.0%**	**2.82 [2.24, 3.56]**
Total events	437		68			
Heterogeneity: Chi² = 17.93, df = 3 (P = 0.0005); I² = 83%						
Test for overall effect: Z = 8.78 (P < 0.00001)						
Test for subgroup differences: Chi² = 15.71, df = 1 (P < 0.0001), I² = 93.6%						

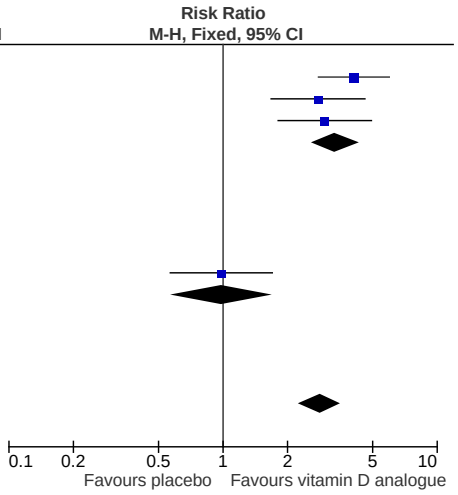


Figure 8: % change in PASI at 4 weeks

Study or Subgroup	Vitamin D analogue Mean	Vitamin D analogue SD	Vitamin D analogue Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 Calcipotriol BD								
Dubertret 1992	-58.6	31.7	60	-35.4	37.2	60	100.0%	-23.20 [-35.57, -10.83]
Subtotal (95% CI)			**60**			**60**	**100.0%**	**-23.20 [-35.57, -10.83]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.68 (P = 0.0002)								
Total (95% CI)			**60**			**60**	**100.0%**	**-23.20 [-35.57, -10.83]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.68 (P = 0.0002)								
Test for subgroup differences: Not applicable								

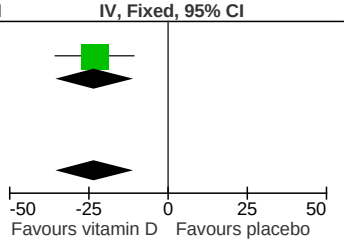


Figure 9: Withdrawals due to adverse events at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Calcipotriol OD						
Barker 1999	0	30	1	30	3.4%	0.33 [0.01, 7.87]
Kaufmann 2002	15	456	12	144	41.8%	0.39 [0.19, 0.82]
Subtotal (95% CI)		**486**		**174**	**45.3%**	**0.39 [0.19, 0.80]**
Total events	15		13			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.92); I² = 0%						
Test for overall effect: Z = 2.57 (P = 0.01)						
1.4.2 Calcipotriol BD						
Guenther 2002	4	216	2	177	5.0%	1.64 [0.30, 8.84]
Harrington 1996	8	304	4	74	14.8%	0.49 [0.15, 1.57]
Highton 1995	6	139	8	138	18.4%	0.74 [0.27, 2.09]
Subtotal (95% CI)		**659**		**389**	**38.2%**	**0.76 [0.38, 1.52]**
Total events	18		14			
Heterogeneity: Chi² = 1.36, df = 2 (P = 0.51); I² = 0%						
Test for overall effect: Z = 0.77 (P = 0.44)						
1.4.3 Calcitriol OD						
Perez 1996	0	84	0	84		Not estimable
Subtotal (95% CI)		**84**		**84**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.4.4 Calcitriol BD						
Langner 1992	0	29	0	29		Not estimable
Langner 1993	1	32	0	32	1.1%	3.00 [0.13, 71.00]
Subtotal (95% CI)		**32**		**32**	**1.1%**	**3.00 [0.13, 71.00]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
1.4.5 Tacalcitol OD						
Langley2011A	4	167	4	68	13.0%	0.41 [0.10, 1.58]
Scarpa 1997	1	157	0	157	1.1%	3.00 [0.12, 73.08]
van de Kerkhof 1996	1	122	0	122	1.1%	3.00 [0.12, 72.93]
Subtotal (95% CI)		**446**		**347**	**15.3%**	**0.80 [0.28, 2.28]**
Total events	6		4			
Heterogeneity: Chi² = 2.26, df = 2 (P = 0.32); I² = 12%						
Test for overall effect: Z = 0.43 (P = 0.67)						
Total (95% CI)		**1707**		**1026**	**100.0%**	**0.62 [0.40, 0.97]**
Total events	40		31			
Heterogeneity: Chi² = 6.37, df = 8 (P = 0.61); I² = 0%						
Test for overall effect: Z = 2.11 (P = 0.03)						
Test for subgroup differences: Chi² = 3.10, df = 3 (P = 0.38), I² = 3.4%						

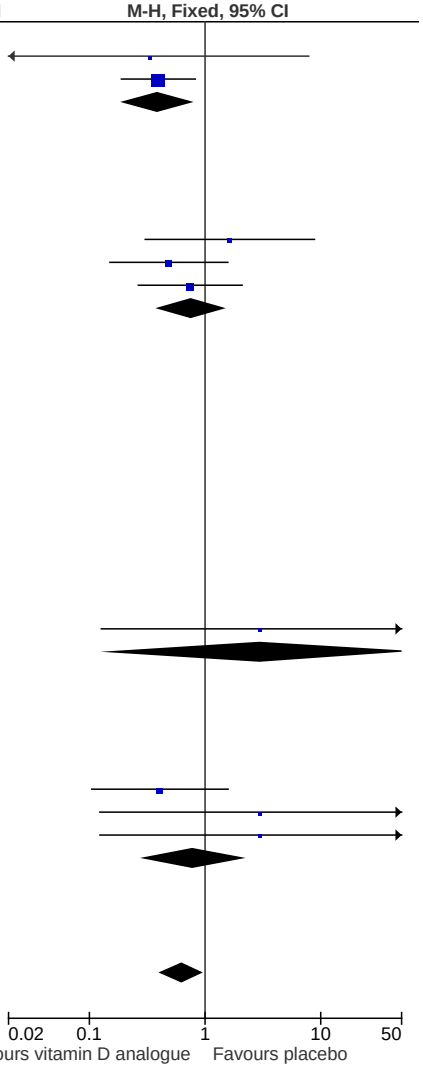


Figure 10: Withdrawals due to lack of efficacy at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 Calcipotriol OD						
Barker 1999	0	30	1	30	6.1%	0.33 [0.01, 7.87]
Subtotal (95% CI)		**30**		**30**	**6.1%**	**0.33 [0.01, 7.87]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
1.5.2 Calcipotriol BD						
Guenther 2002	2	227	19	208	80.2%	0.10 [0.02, 0.41]
Harrington 1996	0	304	1	74	9.7%	0.08 [0.00, 1.99]
Subtotal (95% CI)		**531**		**282**	**89.9%**	**0.09 [0.02, 0.36]**
Total events	2		20			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%						
Test for overall effect: Z = 3.45 (P = 0.0006)						
1.5.3 Calcitriol OD						
Perez 1996	0	84	0	84		Not estimable
Subtotal (95% CI)		**84**		**84**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.5.4 Calcitriol BD						
Langner 1992	0	29	0	29		Not estimable
Langner 1993	1	32	1	32	4.0%	1.00 [0.07, 15.30]
Subtotal (95% CI)		**61**		**61**	**4.0%**	**1.00 [0.07, 15.30]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
1.5.5 Tacalcitol OD						
Scarpa 1997	0	157	0	157		Not estimable
Subtotal (95% CI)		**157**		**157**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**863**		**614**	**100.0%**	**0.15 [0.05, 0.42]**
Total events	3		22			
Heterogeneity: Chi² = 2.62, df = 3 (P = 0.45); I² = 0%						
Test for overall effect: Z = 3.58 (P = 0.0003)						
Test for subgroup differences: Chi² = 2.52, df = 2 (P = 0.28), I² = 20.7%						

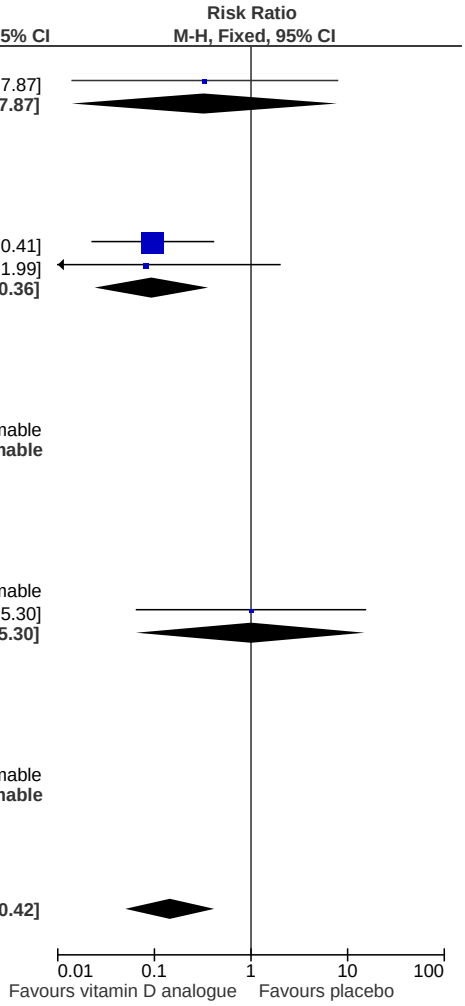


Figure 11: Skin atrophy at 4 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 Calcipotriol BD						
Guenther 2002	1	227	1	208	100.0%	0.92 [0.06, 14.56]
Papp 2003	0	308	0	108		Not estimable
Subtotal (95% CI)		**535**		**316**	**100.0%**	**0.92 [0.06, 14.56]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.95)						
Test for subgroup differences: Not applicable						

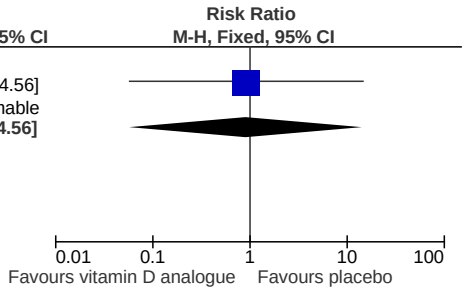
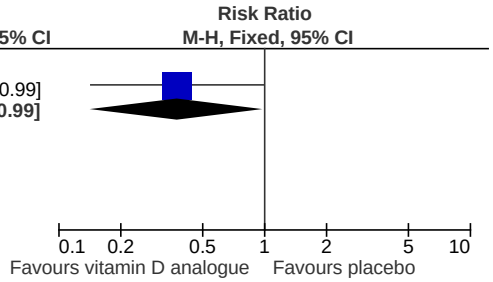


Figure 12: Relapse rate (8 weeks post treatment)

Study or Subgroup	Vitamin D Events	Vitamin D Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.4 Tacalcitol OD vs. placebo						
Langley2011A	7	31	3	5	100.0%	0.38 [0.14, 0.99]
Subtotal (95% CI)		**31**		**5**	**100.0%**	**0.38 [0.14, 0.99]**
Total events	7		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.98 (P = 0.05)						

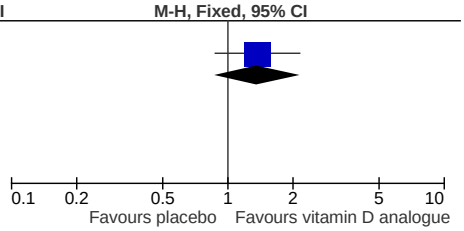


Test for subgroup differences: Not applicable

J.2.2 Vitamin D or vitamin D analogue vs placebo (children)

Figure 13: Investigator's assessment (clear/nearly clear) at 8 weeks

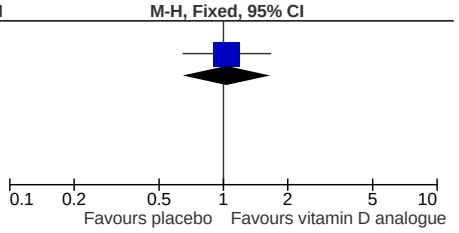
Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.2 Calcipotriol BD						
Oranje 1997	26	43	15	34	100.0%	1.37 [0.87, 2.15]
Subtotal (95% CI)		**43**		**34**	**100.0%**	**1.37 [0.87, 2.15]**
Total events	26		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						



Test for subgroup differences: Not applicable

Figure 1: Patient's assessment (clear/nearly clear) at 8 weeks

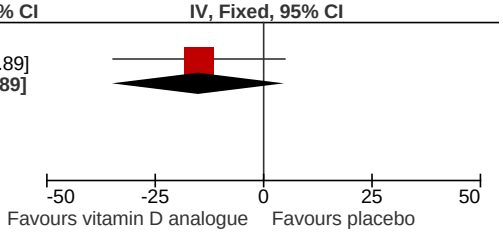
Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Calcipotriol BD						
Oranje 1997	21	43	16	34	100.0%	1.04 [0.65, 1.66]
Subtotal (95% CI)		**43**		**34**	**100.0%**	**1.04 [0.65, 1.66]**
Total events	21		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.15 (P = 0.88)						



Test for subgroup differences: Not applicable

Figure 2: % change in PASI at 8 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
2.5.1 Calcipotriol BD				
Oranje 1997	-14.9	10.0963	100.0%	-14.90 [-34.69, 4.89]
Subtotal (95% CI)			**100.0%**	**-14.90 [-34.69, 4.89]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.48 (P = 0.14)				



Test for subgroup differences: Not applicable

J.2.3 Potent corticosteroid vs placebo

Figure 16: Investigator's assessment (clear/nearly clear) at 3-8 weeks

Note: different scale

Study or Subgroup	Potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Betamethasone dipropionate (OD)						
Fleming2010A	14	83	0	40	1.4%	14.15 [0.87, 231.46]
Kaufmann 2002	176	476	16	157	49.0%	3.63 [2.25, 5.86]
Subtotal (95% CI)		**559**		**197**	**50.4%**	**3.91 [2.44, 6.27]**
Total events	190		16			
Heterogeneity: Chi² = 0.91, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 5.68 (P < 0.00001)						
3.1.2 Betamethasone dipropionate (BD)						
Papp 2003	174	312	8	107	24.3%	7.46 [3.80, 14.63]
Wortzel 1975	15	39	4	37	8.4%	3.56 [1.30, 9.74]
Subtotal (95% CI)		**351**		**144**	**32.6%**	**6.46 [3.65, 11.44]**
Total events	189		12			
Heterogeneity: Chi² = 1.52, df = 1 (P = 0.22); I² = 34%						
Test for overall effect: Z = 6.40 (P < 0.00001)						
3.1.3 Mometasone furoate (OD)						
Medansky 1987	18	50	7	45	15.0%	2.31 [1.07, 5.02]
Subtotal (95% CI)		**50**		**45**	**15.0%**	**2.31 [1.07, 5.02]**
Total events	18		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.12 (P = 0.03)						
3.1.4 Hydrocortisone butyrate (BD)						
Sears 1997	12	78	1	83	2.0%	12.77 [1.70, 95.92]
Subtotal (95% CI)		**78**		**83**	**2.0%**	**12.77 [1.70, 95.92]**
Total events	12		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.48 (P = 0.01)						
Total (95% CI)		**1038**		**469**	**100.0%**	**4.68 [3.38, 6.48]**
Total events	409		36			
Heterogeneity: Chi² = 7.94, df = 5 (P = 0.16); I² = 37%						
Test for overall effect: Z = 9.28 (P < 0.00001)						
Test for subgroup differences: Chi² = 5.67, df = 3 (P = 0.13), I² = 47.1%						

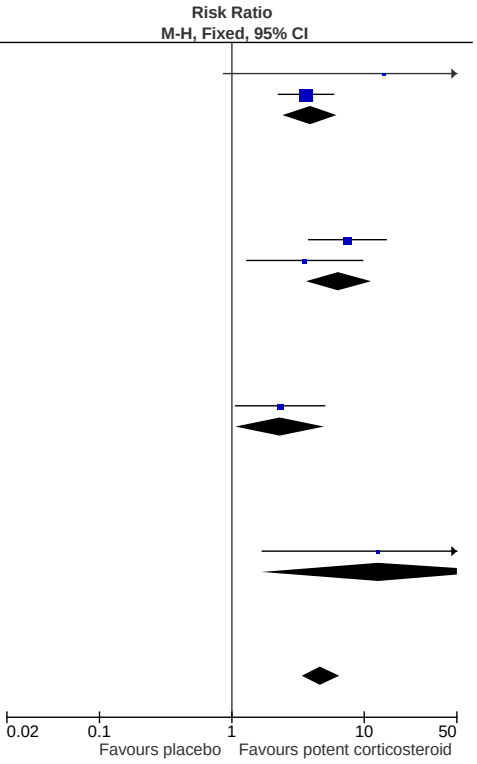


Figure 3: Patient's assessment (clear/nearly clear) at 3-4 weeks

Study or Subgroup	Potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 Betamethasone dipropionate (OD)						
Kaufmann 2002	216	476	15	157	92.1%	4.75 [2.91, 7.76]
Subtotal (95% CI)		**476**		**157**	**92.1%**	**4.75 [2.91, 7.76]**
Total events	216		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 6.22 (P < 0.00001)						
3.3.4 Hydrocortisone butyrate (BD)						
Sears 1997	12	78	2	83	7.9%	6.38 [1.48, 27.62]
Subtotal (95% CI)		**78**		**83**	**7.9%**	**6.38 [1.48, 27.62]**
Total events	12		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.48 (P = 0.01)						
Total (95% CI)		**554**		**240**	**100.0%**	**4.88 [3.06, 7.77]**
Total events	228		17			
Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%						
Test for overall effect: Z = 6.67 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%						

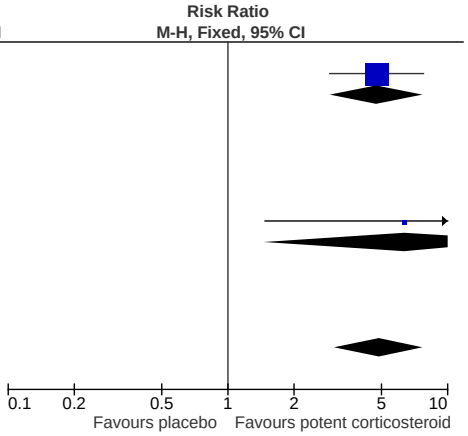


Figure 4: Withdrawals due to adverse events at 3-12 weeks

Note: different scale

Study or Subgroup	Corticosteroid (potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.8.2 Once daily potent corticosteroid						
Kaufmann 2002	5	452	12	144	79.8%	0.13 [0.05, 0.37]
Medansky 1987	0	50	3	47	15.8%	0.13 [0.01, 2.54]
Subtotal (95% CI)		**502**		**191**	**95.6%**	**0.13 [0.05, 0.36]**
Total events	5		15			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.99); I² = 0%						
Test for overall effect: Z = 4.01 (P < 0.0001)						
3.8.6 Twice daily potent corticosteroid						
Sears 1997	1	84	0	85	2.2%	3.04 [0.13, 73.47]
Stein 2001	3	40	0	40	2.2%	7.00 [0.37, 131.28]
Wortzel 1975	0	39	0	37		Not estimable
Subtotal (95% CI)		**163**		**162**	**4.4%**	**5.02 [0.60, 42.26]**
Total events	4		0			
Heterogeneity: Chi² = 0.15, df = 1 (P = 0.70); I² = 0%						
Test for overall effect: Z = 1.49 (P = 0.14)						
Total (95% CI)		**665**		**353**	**100.0%**	**0.35 [0.18, 0.69]**
Total events	9		15			
Heterogeneity: Chi² = 9.58, df = 3 (P = 0.02); I² = 69%						
Test for overall effect: Z = 3.04 (P = 0.002)						
Test for subgroup differences: Chi² = 9.20, df = 1 (P = 0.002), I² = 89.1%						

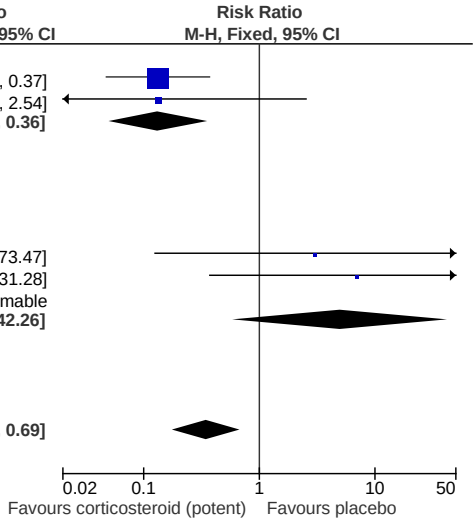
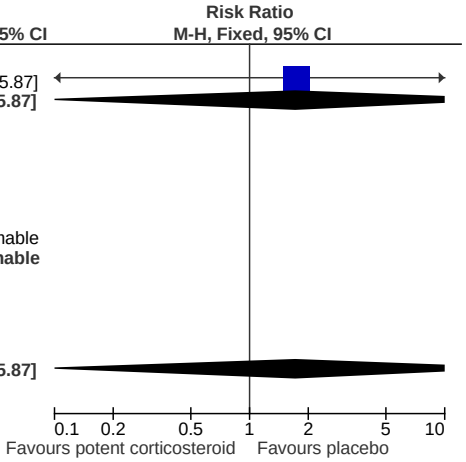


Figure 5: Skin atrophy at 3-4 weeks

Study or Subgroup	Potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.8.1 Betamethasone dipropionate (BD)						
Papp 2003	2	313	0	108	100.0%	1.74 [0.08, 35.87]
Subtotal (95% CI)		**313**		**108**	**100.0%**	**1.74 [0.08, 35.87]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.36 (P = 0.72)						
3.8.3 Mometasone furoate (OD)						
Medansky 1987	0	50	0	45		Not estimable
Subtotal (95% CI)		**50**		**45**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**363**		**153**	**100.0%**	**1.74 [0.08, 35.87]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.36 (P = 0.72)						
Test for subgroup differences: Not applicable						



J.2.4 Very potent corticosteroid vs placebo

Figure 6: Investigator's assessment (clear/nearly clear) at 2-4 weeks

Note: different scale

Study or Subgroup	Very potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
4.1.1 Clobetasol propionate OD						
Decroix 2004	144	189	5	33	27.0%	5.03 [2.23, 11.32]
Subtotal (95% CI)		**189**		**33**	**27.0%**	**5.03 [2.23, 11.32]**
Total events	144		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.90 (P < 0.0001)						
4.1.2 Clobetasol propionate BD						
Gottlieb 2003C	85	120	27	125	32.9%	3.28 [2.30, 4.67]
Jarratt 2006	47	60	2	60	19.2%	23.50 [5.98, 92.40]
Lebwohl 2002	10	61	1	20	12.8%	3.28 [0.45, 24.05]
Lowe 2005	84	162	0	29	8.1%	31.10 [1.98, 487.82]
Subtotal (95% CI)		**403**		**234**	**73.0%**	**8.07 [1.81, 35.96]**
Total events	226		30			
Heterogeneity: Tau² = 1.64; Chi² = 13.69, df = 3 (P = 0.003); I² = 78%						
Test for overall effect: Z = 2.74 (P = 0.006)						
Total (95% CI)		**592**		**267**	**100.0%**	**6.45 [2.63, 15.81]**
Total events	370		35			
Heterogeneity: Tau² = 0.60; Chi² = 13.40, df = 4 (P = 0.009); I² = 70%						
Test for overall effect: Z = 4.07 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.30, df = 1 (P = 0.59), I² = 0%						

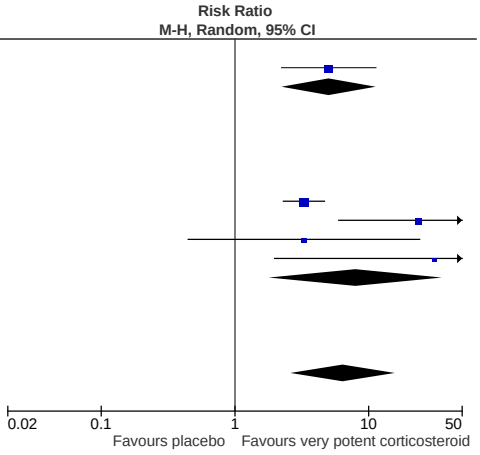


Figure 7: Patient's assessment (clear/nearly clear) at 2 weeks

Study or Subgroup	Very potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.3.2 Clobetasol propionate BD						
Gottlieb 2003C	79	139	36	140	96.0%	2.21 [1.61, 3.03]
Lebwohl 2002	8	61	1	20	4.0%	2.62 [0.35, 19.71]
Subtotal (95% CI)		**200**		**160**	**100.0%**	**2.23 [1.62, 3.05]**
Total events	87		37			
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 4.98 (P < 0.00001)						
Test for subgroup differences: Not applicable						

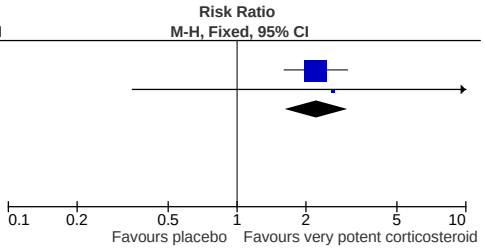


Figure 23: Withdrawals due to adverse events at 2-4 weeks

Note: different scale

Study or Subgroup	Corticosteroid (v potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.6.1 Clobetasol propionate OD						
Decroix 2004	1	184	0	30	20.5%	0.50 [0.02, 12.06]
Subtotal (95% CI)		**184**		**30**	**20.5%**	**0.50 [0.02, 12.06]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.42 (P = 0.67)						
4.6.2 Clobetasol propionate BD						
Beutner 2006	0	25	0	25		Not estimable
Gottlieb 2003C	0	135	1	137	35.6%	0.34 [0.01, 8.23]
Jarratt 2006	0	60	0	60		Not estimable
Jorizzo 1997	1	36	1	39	23.0%	1.08 [0.07, 16.69]
Lebwohl 2002	0	58	0	19		Not estimable
Lowe 2005	1	155	0	21	21.0%	0.42 [0.02, 10.07]
Subtotal (95% CI)		**469**		**301**	**79.5%**	**0.58 [0.11, 3.15]**
Total events	2		2			
Heterogeneity: Chi² = 0.35, df = 2 (P = 0.84); I² = 0%						
Test for overall effect: Z = 0.64 (P = 0.52)						
Total (95% CI)		**653**		**331**	**100.0%**	**0.56 [0.12, 2.52]**
Total events	3		2			
Heterogeneity: Chi² = 0.35, df = 3 (P = 0.95); I² = 0%						
Test for overall effect: Z = 0.76 (P = 0.45)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%						

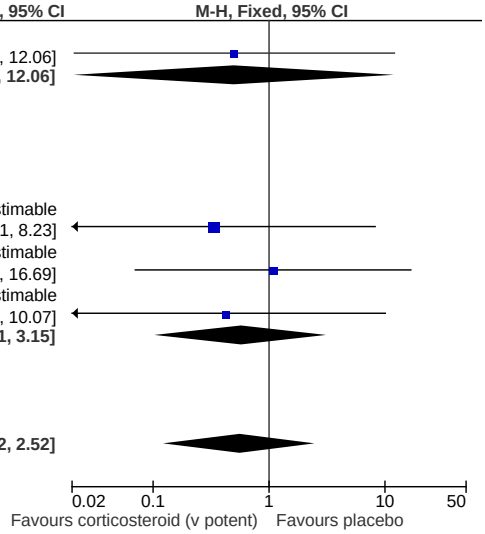


Figure 8: Withdrawals due to lack of efficacy at 4 weeks

Note: different scale

Study or Subgroup	Corticosteroid (very potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.7.1 Clobetasol propionate OD						
Decroix 2004	0	183	1	32	100.0%	0.06 [0.00, 1.44]
Subtotal (95% CI)		**183**		**32**	**100.0%**	**0.06 [0.00, 1.44]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.74 (P = 0.08)						
4.7.2 Clobetasol propionate BD						
Jarratt 2006	0	60	0	60		Not estimable
Beutner 2006	0	25	0	25		Not estimable
Subtotal (95% CI)		**85**		**85**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**268**		**117**	**100.0%**	**0.06 [0.00, 1.44]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.74 (P = 0.08)						
Test for subgroup differences: Not applicable						

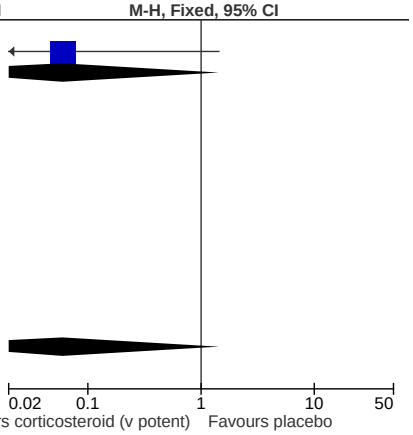
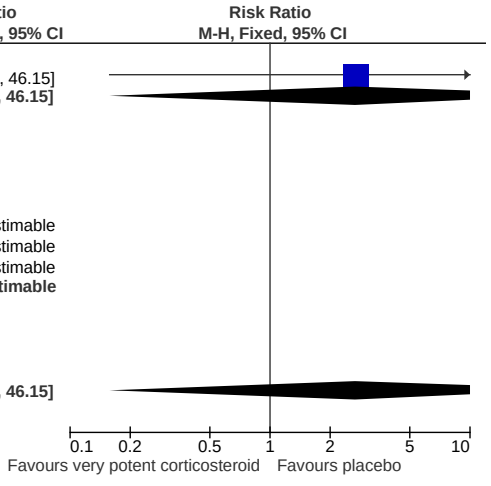


Figure 95: Skin atrophy at 4 weeks

Study or Subgroup	Very potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.8.1 Clobetasol propionate OD						
Decroix 2004	7	188	0	33	100.0%	2.70 [0.16, 46.15]
Subtotal (95% CI)		**188**		**33**	**100.0%**	**2.70 [0.16, 46.15]**
Total events	7		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
4.8.2 Clobetasol propionate BD						
Beutner 2006	0	25	0	25		Not estimable
Jarratt 2006	0	60	0	60		Not estimable
Jorizzo 1997	0	35	0	38		Not estimable
Subtotal (95% CI)		**120**		**123**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**308**		**156**	**100.0%**	**2.70 [0.16, 46.15]**
Total events	7		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Test for subgroup differences: Not applicable						

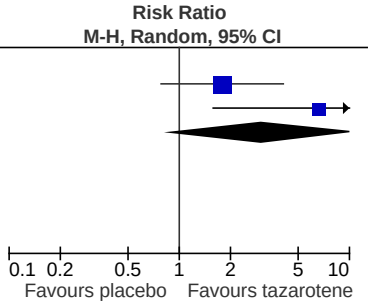


J.2.5 Tazarotene vs placebo

Figure 26: Investigator's assessment (clear/nearly clear) at 12 weeks

Study or Subgroup	Tazarotene Events	Tazarotene Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.1.1 Tazarotene						
Weinstein 2003 - study A	24	439	7	229	59.7%	1.79 [0.78, 4.09]
Weinstein 2003 - study B	26	421	2	214	40.3%	6.61 [1.58, 27.58]
Subtotal (95% CI)		**860**		**443**	**100.0%**	**3.03 [0.83, 11.07]**
Total events	50		9			

Heterogeneity: Tau² = 0.55; Chi² = 2.56, df = 1 (P = 0.11); I² = 61%
Test for overall effect: Z = 1.67 (P = 0.09)

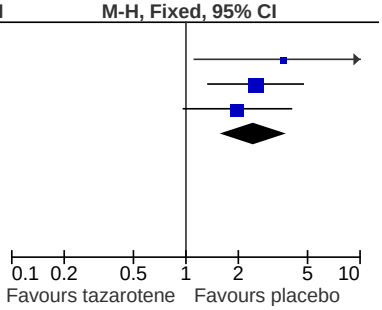


Test for subgroup differences: Not applicable

Figure 27: Withdrawals due to adverse events at 12 weeks

Study or Subgroup	Tazarotene Events	Tazarotene Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.2.1 Tazarotene						
Weinstein 1996	24	186	3	84	13.5%	3.61 [1.12, 11.67]
Weinstein 2003 - study A	53	439	11	229	47.4%	2.51 [1.34, 4.72]
Weinstein 2003 - study B	35	421	9	214	39.1%	1.98 [0.97, 4.04]
Subtotal (95% CI)		**1046**		**527**	**100.0%**	**2.45 [1.58, 3.80]**
Total events	112		23			

Heterogeneity: Chi² = 0.78, df = 2 (P = 0.68); I² = 0%
Test for overall effect: Z = 4.02 (P < 0.0001)

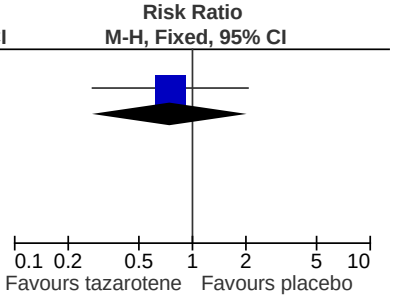


Test for subgroup differences: Not applicable

Figure 10: Withdrawal due to lack of efficacy at 12 weeks

Study or Subgroup	Tazarotene Events	Tazarotene Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.3.1 Tazarotene						
Weinstein 1996	9	216	6	108	100.0%	0.75 [0.27, 2.05]
Subtotal (95% CI)		**216**		**108**	**100.0%**	**0.75 [0.27, 2.05]**
Total events	9		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)

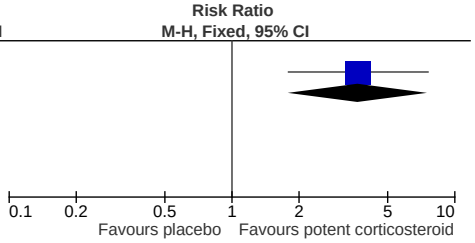


Test for subgroup differences: Not applicable

J.2.6 Potent corticosteroid vs placebo (for maintenance of remission)

Figure 30: Investigator's assessment (clear/slight at 24 weeks)

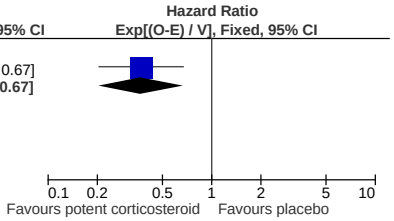
Study or Subgroup	Potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.1.2 Betamethasone dipropionate (BD)						
Katz 1991	27	46	7	44	100.0%	3.69 [1.79, 7.59]
Subtotal (95% CI)		**46**		**44**	**100.0%**	**3.69 [1.79, 7.59]**
Total events	27		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.55 (P = 0.0004)						



Test for subgroup differences: Not applicable

Figure 11: Time-to-relapse after a maximum of 24 weeks

Study or Subgroup	Potent corticosteroid Events	Total	Placebo Events	Total	O-E	Variance	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI
6.2.1 Betamethasone dipropionate (BD)								
Katz 1991	16	46	35	44	-10.9	10.98	100.0%	0.37 [0.21, 0.67]
Subtotal (95% CI)		**46**		**44**			**100.0%**	**0.37 [0.21, 0.67]**
Total events	16		35					
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.29 (P = 0.001)								



Test for subgroup differences: Not applicable

J.2.7 Vitamin D or vitamin D analogue vs potent corticosteroid

Figure 12: Investigator's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Vitamin D analogues Events	Total	Corticosteroid (potent) Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
7.1.1 Calcipotriol OD vs betamethasone dipropionate OD						
Fleming2010A	9	79	14	83	5.3%	0.68 [0.31, 1.47]
Kaufmann 2002	107	480	176	476	18.4%	0.60 [0.49, 0.74]
Subtotal (95% CI)		**559**		**559**	**23.7%**	**0.61 [0.50, 0.74]**
Total events	116		190			
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%						
Test for overall effect: Z = 4.95 (P < 0.00001)						
7.1.2 Calcipotriol BD vs betamethasone dipropionate BD						
Douglas 2002	142	365	169	363	19.5%	0.84 [0.71, 0.99]
Papp 2003	103	308	174	312	19.0%	0.60 [0.50, 0.72]
Subtotal (95% CI)		**673**		**675**	**38.6%**	**0.71 [0.51, 0.98]**
Total events	245		343			
Heterogeneity: Tau² = 0.05; Chi² = 6.69, df = 1 (P = 0.010); I² = 85%						
Test for overall effect: Z = 2.07 (P = 0.04)						
7.1.3 Calcipotriol BD vs betamethasone valerate BD						
Molin 1997	119	205	116	207	19.6%	1.04 [0.88, 1.22]
Subtotal (95% CI)		**205**		**207**	**19.6%**	**1.04 [0.88, 1.22]**
Total events	119		116			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						
7.1.4 Calcitriol BD vs betamethasone dipropionate BD						
Camarasa 2003	67	128	81	130	18.1%	0.84 [0.68, 1.04]
Subtotal (95% CI)		**128**		**130**	**18.1%**	**0.84 [0.68, 1.04]**
Total events	67		81			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.61 (P = 0.11)						
Total (95% CI)		**1565**		**1571**	**100.0%**	**0.76 [0.62, 0.94]**
Total events	547		730			
Heterogeneity: Tau² = 0.05; Chi² = 26.80, df = 5 (P < 0.0001); I² = 81%						
Test for overall effect: Z = 2.59 (P = 0.009)						
Test for subgroup differences: Chi² = 17.16, df = 3 (P = 0.0007), I² = 82.5%						

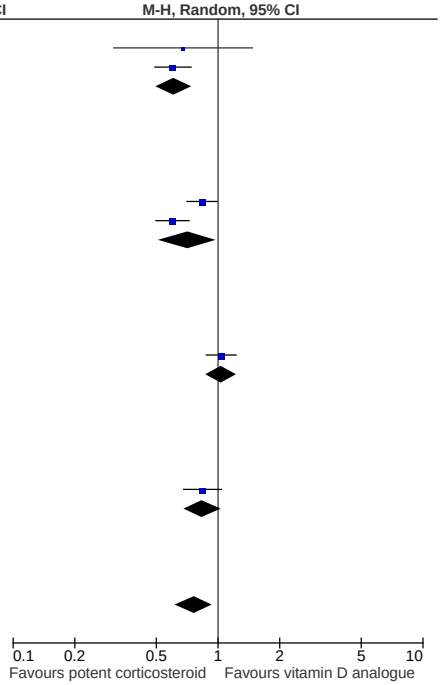


Figure 13: Patient's assessment (clear/nearly clear) at 4-6 weeks

Study or Subgroup	Vitamin D analogues Events	Vitamin D analogues Total	Corticosteroid (potent) Events	Corticosteroid (potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.2.2 Calcipotriol OD vs betamethasone dipropionate OD						
Kaufmann 2002	137	480	216	476	29.4%	0.63 [0.53, 0.75]
Subtotal (95% CI)		**480**		**476**	**29.4%**	**0.63 [0.53, 0.75]**
Total events	137		216			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.27 (P < 0.00001)						
7.2.3 Calcipotriol BD vs betamethasone dipropionate BD						
Douglas 2002	140	365	183	363	24.8%	0.76 [0.64, 0.90]
Subtotal (95% CI)		**365**		**363**	**24.8%**	**0.76 [0.64, 0.90]**
Total events	140		183			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.24 (P = 0.001)						
7.2.4 Calcipotriol BD vs betamethasone valerate BD						
Cunliffe 1992	123	201	101	200	13.7%	1.21 [1.02, 1.44]
Kragballe 1991	280	342	237	342	32.1%	1.18 [1.08, 1.29]
Subtotal (95% CI)		**543**		**542**	**45.8%**	**1.19 [1.10, 1.29]**
Total events	403		338			
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						
Test for overall effect: Z = 4.25 (P < 0.0001)						
Total (95% CI)		**1388**		**1381**	**100.0%**	**0.92 [0.86, 0.99]**
Total events	680		737			
Heterogeneity: Chi² = 65.58, df = 3 (P < 0.00001); I² = 95%						
Test for overall effect: Z = 2.37 (P = 0.02)						
Test for subgroup differences: Chi² = 56.32, df = 2 (P < 0.00001), I² = 96.4%						

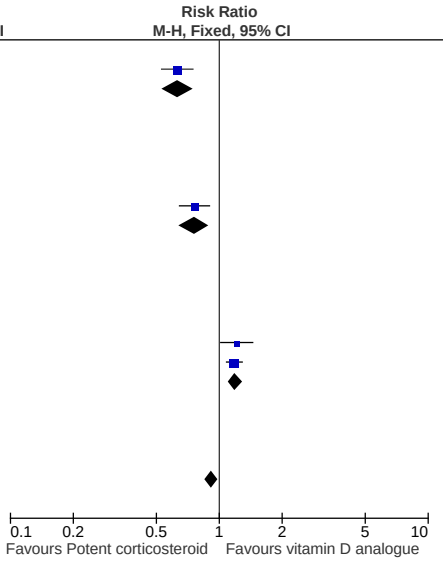


Figure 14: % change in PASI at 6-8 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
7.3.1 Calcipotriol (BD) vs betamethasone valerate (BD)				
Kragballe 1991	7.2	2.169141	73.8%	7.20 [2.95, 11.45]
Molin 1997	2.4	3.642779	26.2%	2.40 [-4.74, 9.54]
Subtotal (95% CI)			**100.0%**	**5.94 [2.29, 9.60]**
Heterogeneity: Chi² = 1.28, df = 1 (P = 0.26); I² = 22%				
Test for overall effect: Z = 3.19 (P = 0.001)				
Test for subgroup differences: Not applicable				

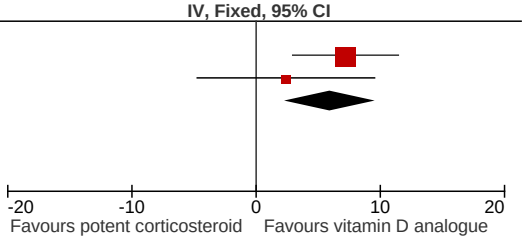


Figure 15: Relapse rate (8 weeks post-treatment)

Study or Subgroup	Vitamin D analogues Events	Vitamin D analogues Total	Corticosteroid (potent) Events	Corticosteroid (potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.4.1 Calcitriol BD vs betamethasone dipropionate BD						
Camarasa 2003	30	58	55	73	100.0%	0.69 [0.52, 0.91]
Subtotal (95% CI)		**58**		**73**	**100.0%**	**0.69 [0.52, 0.91]**
Total events	30		55			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.62 (P = 0.009)						
Test for subgroup differences: Not applicable						

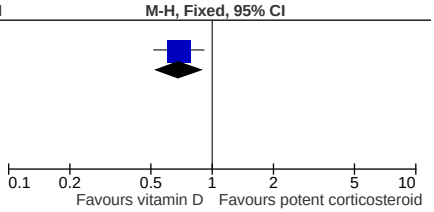


Figure 37: Withdrawals due to adverse events at 4-8 weeks

Study or Subgroup	Vitamin D analogues Events	Vitamin D analogues Total	Corticosteroid (potent) Events	Corticosteroid (potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.5.1 Calcipotriol OD vs betamethasone dipropionate OD						
Kaufmann 2002	15	456	5	452	34.6%	2.97 [1.09, 8.11]
Subtotal (95% CI)		**456**		**452**	**34.6%**	**2.97 [1.09, 8.11]**
Total events	15		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.13 (P = 0.03)						
7.5.2 Calcipotriol BD vs betamethasone dipropionate BD						
Douglas 2002	0	332	0	344		Not estimable
Subtotal (95% CI)		**332**		**344**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
7.5.3 Calcipotriol BD vs betamethasone valerate BD						
Cunliffe 1992	5	188	3	189	20.6%	1.68 [0.41, 6.91]
Kragballe 1991	2	345	1	345	6.9%	2.00 [0.18, 21.95]
Molin 1997	6	207	3	210	20.5%	2.03 [0.51, 8.01]
Subtotal (95% CI)		**740**		**744**	**48.0%**	**1.87 [0.75, 4.66]**
Total events	13		7			
Heterogeneity: Chi² = 0.04, df = 2 (P = 0.98); I² = 0%						
Test for overall effect: Z = 1.35 (P = 0.18)						
7.5.4 Calcipotriol (BD) vs fluocinonide (BD)						
Bruce 1994	0	57	1	56	10.4%	0.33 [0.01, 7.87]
Subtotal (95% CI)		**57**		**56**	**10.4%**	**0.33 [0.01, 7.87]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
7.5.9 Calcitriol BD vs. betamethasone dipropionate BD						
Camarasa 2003	2	124	1	122	6.9%	1.97 [0.18, 21.42]
Subtotal (95% CI)		**124**		**122**	**6.9%**	**1.97 [0.18, 21.42]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.56 (P = 0.58)						
Total (95% CI)		**1709**		**1718**	**100.0%**	**2.10 [1.13, 3.90]**
Total events	30		14			
Heterogeneity: Chi² = 1.88, df = 5 (P = 0.87); I² = 0%						
Test for overall effect: Z = 2.34 (P = 0.02)						
Test for subgroup differences: Chi² = 1.84, df = 3 (P = 0.61), I² = 0%						

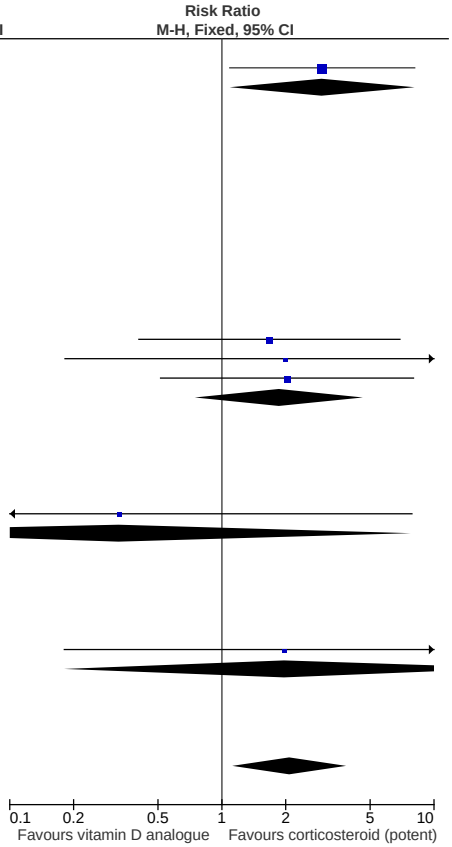


Figure 16: Withdrawal due to lack of efficacy at 6 weeks

Study or Subgroup	Vitamin D analogues Events	Vitamin D analogues Total	Corticosteroid (potent) Events	Corticosteroid (potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.6.2 Calcipotriol BD vs betamethasone valerate BD						
Cunliffe 1992	6	190	6	193	54.1%	1.02 [0.33, 3.09]
Kragballe 1991	1	345	2	345	18.2%	0.50 [0.05, 5.49]
Subtotal (95% CI)		**535**		**538**	**72.3%**	**0.89 [0.33, 2.41]**
Total events	7		8			
Heterogeneity: Chi² = 0.28, df = 1 (P = 0.60); I² = 0%						
Test for overall effect: Z = 0.24 (P = 0.81)						
7.6.3 Calcitriol BD vs. betamethasone dipropionate BD						
Camarasa 2003	4	126	3	122	27.7%	1.29 [0.30, 5.65]
Subtotal (95% CI)		**126**		**122**	**27.7%**	**1.29 [0.30, 5.65]**
Total events	4		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.73)						
Total (95% CI)		**661**		**660**	**100.0%**	**1.00 [0.44, 2.28]**
Total events	11		11			
Heterogeneity: Chi² = 0.44, df = 2 (P = 0.80); I² = 0%						
Test for overall effect: Z = 0.00 (P = 1.00)						
Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0%						

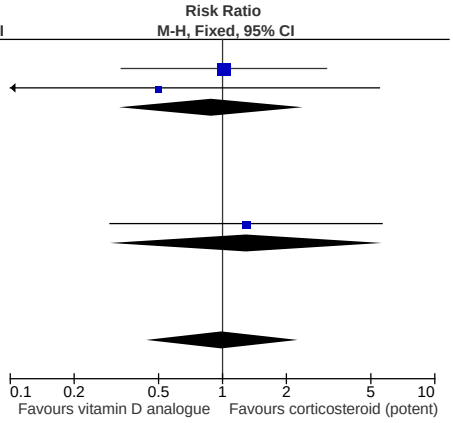
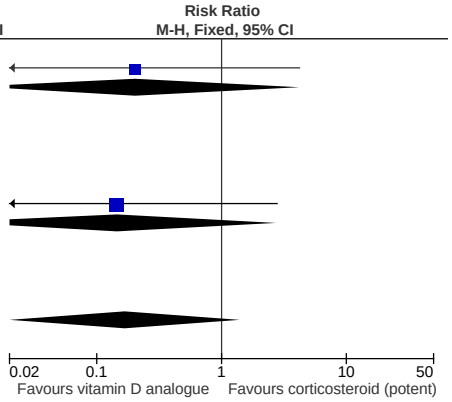


Figure 17: Skin atrophy at 4-8 weeks

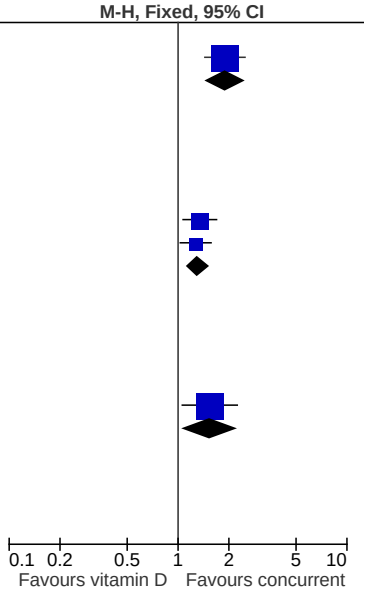
Study or Subgroup	Vitamin D analogues Events	Vitamin D analogues Total	Corticosteroid (potent) Events	Corticosteroid (potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.7.1 Calcipotriol BD vs. betamethasone dipropionate BD						
Papp 2003	0	308	2	313	41.6%	0.20 [0.01, 4.22]
Subtotal (95% CI)		**308**		**313**	**41.6%**	**0.20 [0.01, 4.22]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.03 (P = 0.30)						
7.7.2 Calcipotriol BD vs betamethasone valerate BD						
Molin 1997	0	207	3	210	58.4%	0.14 [0.01, 2.79]
Subtotal (95% CI)		**207**		**210**	**58.4%**	**0.14 [0.01, 2.79]**
Total events	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.28 (P = 0.20)						
Total (95% CI)		**515**		**523**	**100.0%**	**0.17 [0.02, 1.40]**
Total events	0		5			
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.88); I² = 0%						
Test for overall effect: Z = 1.65 (P = 0.10)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.88), I² = 0%						



J.2.8 Concurrent vitamin D or vitamin D analogue and potent corticosteroid (one applied in the morning and one in the evening) vs vitamin D or vitamin D analogue alone

Figure 18: Investigator's assessment (clear/nearly clear) at 6-8 weeks

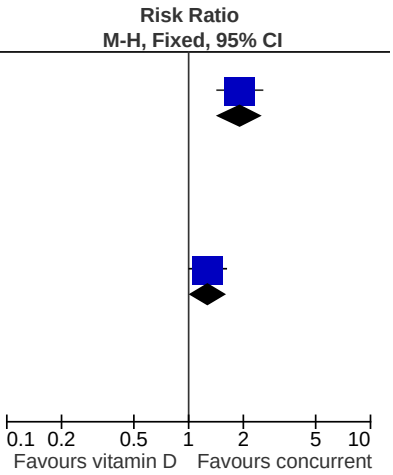
Study or Subgroup	Concurrent Events	Concurrent Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.1.1 Calcipotriol and betamethasone valerate vs calcipotriol OD						
Kragballe 1998	94	174	49	172	100.0%	1.90 [1.44, 2.49]
Subtotal (95% CI)		**174**		**172**	**100.0%**	**1.90 [1.44, 2.49]**
Total events	94		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.58 (P < 0.00001)						
11.1.2 Calcipotriol and betamethasone valerate vs calcipotriol BD						
Kragballe 1998	94	174	69	172	58.4%	1.35 [1.07, 1.69]
Ruzicka 1998	60	78	52	86	41.6%	1.27 [1.03, 1.57]
Subtotal (95% CI)		**252**		**258**	**100.0%**	**1.32 [1.12, 1.54]**
Total events	154		121			
Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%						
Test for overall effect: Z = 3.36 (P = 0.0008)						
11.1.3 Calcipotriol and betamethasone valerate vs calcipotriol BD - no response at 2 weeks						
Ruzicka 1998	27	39	22	49	100.0%	1.54 [1.06, 2.24]
Subtotal (95% CI)		**39**		**49**	**100.0%**	**1.54 [1.06, 2.24]**
Total events	27		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.27 (P = 0.02)						



Test for subgroup differences: Chi² = 5.22, df = 2 (P = 0.07), I² = 61.7%

Figure 41: Patient's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Concurrent Events	Concurrent Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.2.1 Calcipotriol and betamethasone valerate vs calcipotriol OD						
Kragballe 1998	89	174	46	172	100.0%	1.91 [1.44, 2.55]
Subtotal (95% CI)		**174**		**172**	**100.0%**	**1.91 [1.44, 2.55]**
Total events	89		46			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.43 (P < 0.00001)						
11.2.2 Calcipotriol and betamethasone valerate vs calcipotriol BD						
Kragballe 1998	89	174	69	172	100.0%	1.28 [1.01, 1.61]
Subtotal (95% CI)		**174**		**172**	**100.0%**	**1.28 [1.01, 1.61]**
Total events	89		69			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.04 (P = 0.04)						



Test for subgroup differences: Chi² = 4.62, df = 1 (P = 0.03), I² = 78.4%

Figure 42: Withdrawals due to adverse events at 4-8 weeks

Note: different scale

Study or Subgroup	Concurrent Events	Concurrent Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.4.1 Calcipotriol and potent corticosteroid vs calcipotriol OD						
Kragballe 1998	3	168	8	163	48.6%	0.36 [0.10, 1.35]
Subtotal (95% CI)		**168**		**163**	**48.6%**	**0.36 [0.10, 1.35]**
Total events	3		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						
11.4.2 Calcipotriol and potent corticosteroid vs calcipotriol BD						
Kragballe 1998	3	168	6	163	36.4%	0.49 [0.12, 1.91]
Ruzicka 1998	1	77	1	77	6.0%	1.00 [0.06, 15.70]
Salmhofer 2000	0	63	1	63	9.0%	0.33 [0.01, 8.03]
Subtotal (95% CI)		**308**		**303**	**51.4%**	**0.52 [0.17, 1.61]**
Total events	4		8			
Heterogeneity: Chi² = 0.30, df = 2 (P = 0.86); I² = 0%						
Test for overall effect: Z = 1.14 (P = 0.25)						
Total (95% CI)		**476**		**466**	**100.0%**	**0.44 [0.19, 1.04]**
Total events	7		16			
Heterogeneity: Chi² = 0.47, df = 3 (P = 0.93); I² = 0%						
Test for overall effect: Z = 1.87 (P = 0.06)						
Test for subgroup differences: Chi² = 0.16, df = 1 (P = 0.69), I² = 0%						

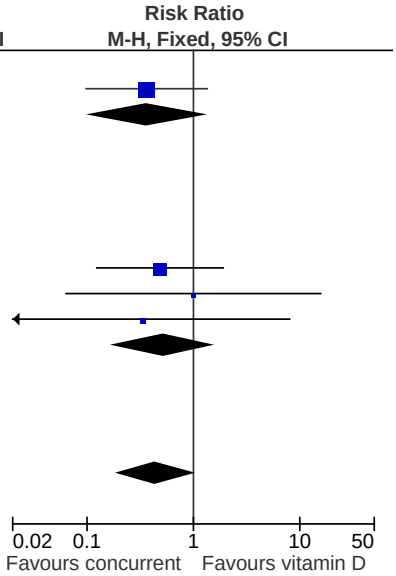
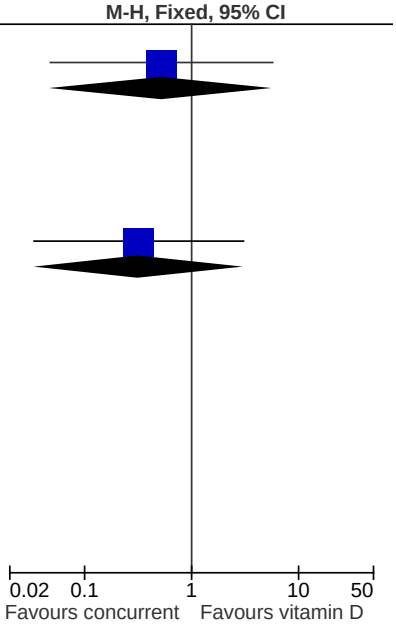


Figure 19: Withdrawal due to lack of efficacy at 4-8 weeks

Note: different scale

Study or Subgroup	Concurrent Events	Concurrent Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.5.3 Calcipotriol and betamethasone valerate vs calcipotriol OD						
Kragballe 1998	1	166	2	174	100.0%	0.52 [0.05, 5.73]
Subtotal (95% CI)		**166**		**174**	**100.0%**	**0.52 [0.05, 5.73]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.60)						
11.5.4 Calcipotriol and betamethasone valerate vs calcipotriol BD						
Kragballe 1998	1	166	3	160	100.0%	0.32 [0.03, 3.06]
Subtotal (95% CI)		**166**		**160**	**100.0%**	**0.32 [0.03, 3.06]**
Total events	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.99 (P = 0.32)						
11.5.5 Calcipotriol + diflucortolone valerate vs calcipotriol (BD)						
Salmhofer 2000	0	63	0	63		Not estimable
Subtotal (95% CI)		**63**		**63**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Chi² = 0.09, df = 1 (P = 0.77), I² = 0%						



J.2.9 Combined product containing potent corticosteroid and vitamin D analogue vs vitamin D or vitamin D analogue

Figure 20: Investigator's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.2.1 Combination vs. vitamin D OD						
Fleming2010A	44	162	9	79	2.9%	2.38 [1.23, 4.63]
Kaufmann 2002	276	490	107	480	25.8%	2.53 [2.10, 3.04]
Langley2011A	73	183	33	184	7.8%	2.22 [1.56, 3.18]
Ortonne 2004	143	249	43	252	10.2%	3.37 [2.51, 4.51]
Subtotal (95% CI)		**1084**		**995**	**46.7%**	**2.65 [2.30, 3.05]**
Total events	536		192			
Heterogeneity: Chi² = 3.85, df = 3 (P = 0.28); I² = 22%						
Test for overall effect: Z = 13.65 (P < 0.00001)						
8.2.2 Combination vs. vitamin D BD						
Guenther 2002	95	150	115	227	21.8%	1.25 [1.05, 1.49]
Kragballe 2004	178	322	133	327	31.5%	1.36 [1.15, 1.60]
Subtotal (95% CI)		**472**		**554**	**53.3%**	**1.31 [1.16, 1.48]**
Total events	273		248			
Heterogeneity: Chi² = 0.47, df = 1 (P = 0.49); I² = 0%						
Test for overall effect: Z = 4.43 (P < 0.00001)						
Total (95% CI)		**1556**		**1549**	**100.0%**	**1.94 [1.77, 2.13]**
Total events	809		440			
Heterogeneity: Chi² = 64.24, df = 5 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 13.94 (P < 0.00001)						
Test for subgroup differences: Chi² = 55.19, df = 1 (P < 0.00001), I² = 98.2%						

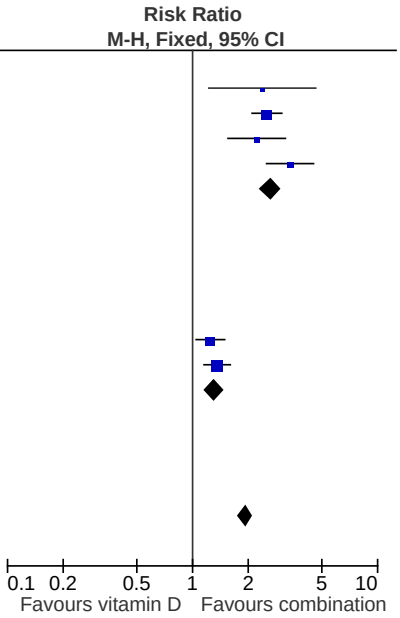


Figure 21: Patient's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Random, 95% CI
8.3.1 Calcipotriol + betamethasone dipropionate vs. calcipotriol OD						
Kaufmann 2002	316	490	137	480	26.4%	2.26 [1.93, 2.64]
Subtotal (95% CI)		**490**		**480**	**26.4%**	**2.26 [1.93, 2.64]**
Total events	316		137			
Heterogeneity: Not applicable						
Test for overall effect: Z = 10.24 (P < 0.00001)						
8.3.2 Calcipotriol + betamethasone dipropionate vs. calcipotriol BD						
Guenther 2002	98	150	117	227	26.2%	1.27 [1.07, 1.51]
Subtotal (95% CI)		**150**		**227**	**26.2%**	**1.27 [1.07, 1.51]**
Total events	98		117			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.71 (P = 0.007)						
8.3.3 Calcipotriol + betamethasone dipropionate vs. tacalcitol OD						
Langley2011A	69	171	35	163	23.1%	1.88 [1.33, 2.65]
Ortonne 2004	145	249	44	252	24.3%	3.34 [2.50, 4.45]
Subtotal (95% CI)		**420**		**415**	**47.4%**	**2.52 [1.44, 4.43]**
Total events	214		79			
Heterogeneity: Tau² = 0.14; Chi² = 6.26, df = 1 (P = 0.01); I² = 84%						
Test for overall effect: Z = 3.22 (P = 0.001)						
Total (95% CI)		**1060**		**1122**	**100.0%**	**2.05 [1.35, 3.11]**
Total events	628		333			
Heterogeneity: Tau² = 0.17; Chi² = 43.35, df = 3 (P < 0.00001); I² = 93%						
Test for overall effect: Z = 3.36 (P = 0.0008)						
Test for subgroup differences: Chi² = 25.44, df = 2 (P < 0.00001), I² = 92.1%						

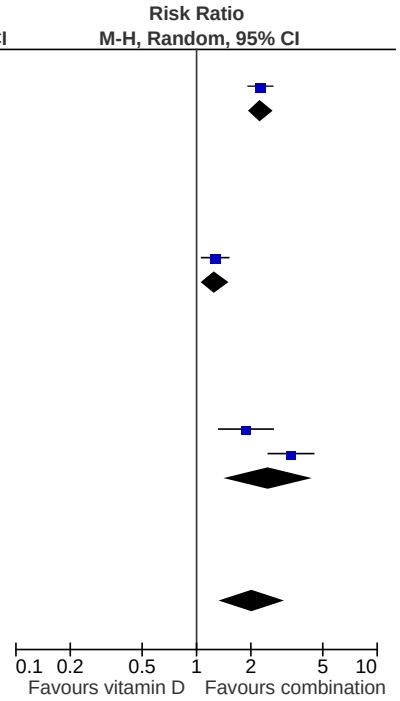


Figure 22: % change in PASI at 4-8 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
8.4.1 Calcipotriol + betamethasone dipropionate vs. calcipotriol OD				
Fleming2010A	-13.9	4.22425	15.4%	-13.90 [-22.18, -5.62]
Kaufmann 2002	-25.3	7.68874	4.7%	-25.30 [-40.37, -10.23]
Subtotal (95% CI)			**20.1%**	**-16.54 [-23.80, -9.29]**
Heterogeneity: Chi² = 1.69, df = 1 (P = 0.19); I² = 41%				
Test for overall effect: Z = 4.47 (P < 0.00001)				
8.4.2 Calcipotriol + betamethasone dipropionate vs. calcipotriol BD				
Guenther 2002	-9.8	2.97825	31.0%	-9.80 [-15.64, -3.96]
Kragballe 2004	-9.2	2.7959	35.2%	-9.20 [-14.68, -3.72]
Subtotal (95% CI)			**66.2%**	**-9.48 [-13.48, -5.49]**
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.88); I² = 0%				
Test for overall effect: Z = 4.65 (P < 0.00001)				
8.4.3 Calcipotriol + betamethasone dipropionate vs. tacalcitol OD				
Langley2011A	-14.7	4.46737	13.8%	-14.70 [-23.46, -5.94]
Subtotal (95% CI)			**13.8%**	**-14.70 [-23.46, -5.94]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 3.29 (P = 0.001)				
Total (95% CI)			**100.0%**	**-11.62 [-14.87, -8.37]**
Heterogeneity: Chi² = 5.05, df = 4 (P = 0.28); I² = 21%				
Test for overall effect: Z = 7.01 (P < 0.00001)				
Test for subgroup differences: Chi² = 3.34, df = 2 (P = 0.19), I² = 40.2%				

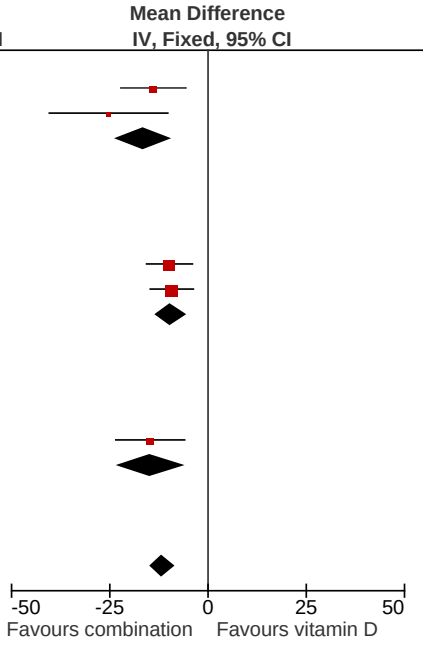


Figure 23: Relapse rate at 8 weeks post-treatment

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.5.4 Calcipotriol + betamethasone dipropionate vs. tacalcitol OD						
Langley2011A	28	67	7	31	100.0%	1.85 [0.91, 3.77]
Subtotal (95% CI)		**67**		**31**	**100.0%**	**1.85 [0.91, 3.77]**
Total events	28		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.70 (P = 0.09)						
Test for subgroup differences: Not applicable						

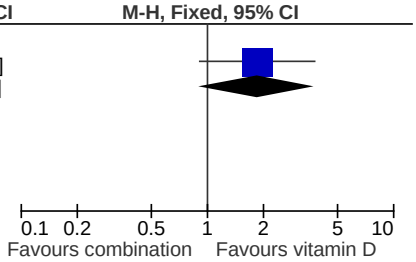


Figure 24: Withdrawal due to adverse events at 4-8 weeks

Note: different scale

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.6.1 Calcipotriol + betamethasone dipropionate vs. calcipotriol OD						
Kaufmann 2002	3	480	15	456	66.7%	0.19 [0.06, 0.65]
Subtotal (95% CI)		**480**		**456**	**66.7%**	**0.19 [0.06, 0.65]**
Total events	3		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.64 (P = 0.008)						
8.6.2 Calcipotriol + betamethasone dipropionate vs. calcipotriol BD						
Guenther 2002	0	143	4	216	15.6%	0.17 [0.01, 3.09]
Subtotal (95% CI)		**143**		**216**	**15.6%**	**0.17 [0.01, 3.09]**
Total events	0		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.20 (P = 0.23)						
8.6.3 Calcipotriol + betamethasone dipropionate vs. tacalcitol OD						
Langley2011A	3	174	4	167	17.7%	0.72 [0.16, 3.17]
Subtotal (95% CI)		**174**		**167**	**17.7%**	**0.72 [0.16, 3.17]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.43 (P = 0.66)						
Total (95% CI)		**797**		**839**	**100.0%**	**0.28 [0.12, 0.67]**
Total events	6		23			
Heterogeneity: Chi² = 2.06, df = 2 (P = 0.36); I² = 3%						
Test for overall effect: Z = 2.86 (P = 0.004)						
Test for subgroup differences: Chi² = 2.02, df = 2 (P = 0.36), I² = 0.9%						

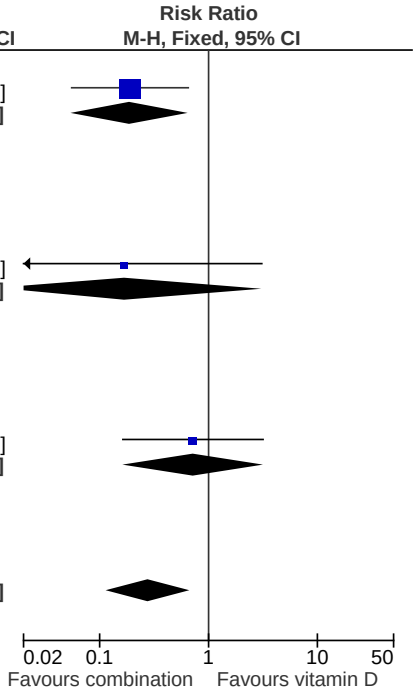


Figure 25: Withdrawal due to lack of efficacy at 4 weeks

Note: different scale

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.9.3 Calcipotriol + betamethasone dipropionate vs. calcipotriol BD						
Guenther 2002	0	151	2	227	100.0%	0.30 [0.01, 6.21]
Subtotal (95% CI)		**151**		**227**	**100.0%**	**0.30 [0.01, 6.21]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.44)						
Test for subgroup differences: Not applicable						

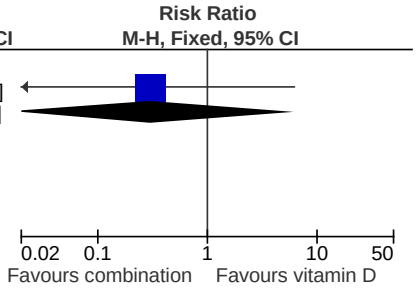
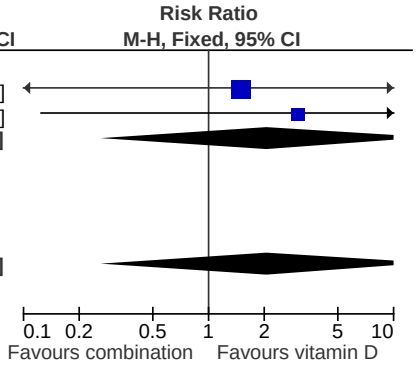


Figure 26: Skin atrophy at 4-12 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.10.1 Calcipotriol + betamethasone dipropionate vs. calcipotriol BD						
Guenther 2002	1	151	1	227	61.7%	1.50 [0.09, 23.85]
Kragballe 2004	1	322	0	327	38.3%	3.05 [0.12, 74.51]
Subtotal (95% CI)		**473**		**554**	**100.0%**	**2.09 [0.27, 16.53]**
Total events	2		1			
Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%						
Test for overall effect: Z = 0.70 (P = 0.48)						
Total (95% CI)		**473**		**554**	**100.0%**	**2.09 [0.27, 16.53]**
Total events	2		1			
Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%						
Test for overall effect: Z = 0.70 (P = 0.48)						
Test for subgroup differences: Not applicable						



J.2.10 Combined product containing vitamin D analogue and potent corticosteroid vs potent corticosteroid

Figure 27: Investigator's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Combination Events	Combination Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.1.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate OD						
Fleming2010A	44	162	14	83	9.4%	1.61 [0.94, 2.76]
Kaufmann 2002	276	490	176	476	90.6%	1.52 [1.32, 1.75]
Subtotal (95% CI)		**652**		**559**	**100.0%**	**1.53 [1.33, 1.76]**
Total events	320		190			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%						
Test for overall effect: Z = 6.08 (P < 0.00001)						
Test for subgroup differences: Not applicable						

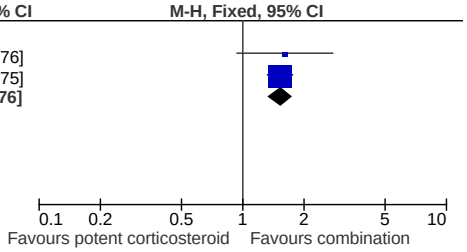


Figure 28: Patient's assessment (clear/nearly clear) at 4 weeks

Study or Subgroup	Combination Events	Combination Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.2.2 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate OD						
Kaufmann 2002	316	490	216	476	100.0%	1.42 [1.26, 1.60]
Subtotal (95% CI)		**490**		**476**	**100.0%**	**1.42 [1.26, 1.60]**
Total events	316		216			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.82 (P < 0.00001)						
Test for subgroup differences: Not applicable						

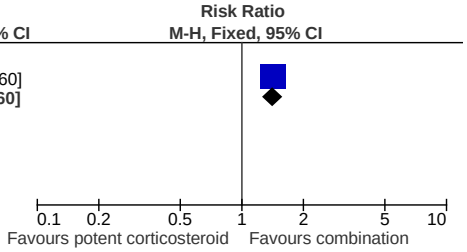


Figure 29: % change in PASI at 4-8 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
10.3.1 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate OD				
Fleming2010A	-6.16	4.06842	52.9%	-6.16 [-14.13, 1.81]
Kaufmann 2002	-14.2	4.31542	47.1%	-14.20 [-22.66, -5.74]
Subtotal (95% CI)			**100.0%**	**-9.94 [-15.75, -4.14]**
Heterogeneity: Chi² = 1.84, df = 1 (P = 0.18); I² = 46%				
Test for overall effect: Z = 3.36 (P = 0.0008)				
Test for subgroup differences: Not applicable				

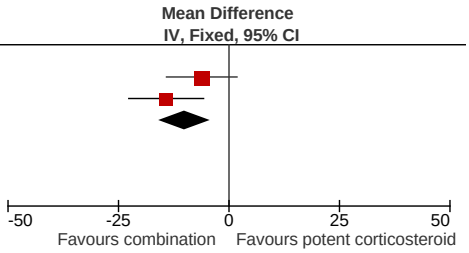
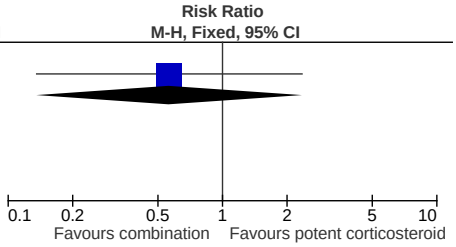


Figure 30: Withdrawals due to adverse events at 4 weeks

Study or Subgroup	Combination Events	Combination Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.4.2 Calcipotriol + betamethasone dipropionate vs. betamethasone dipropionate OD						
Kaufmann 2002	3	480	5	452	100.0%	0.56 [0.14, 2.35]
Subtotal (95% CI)		**480**		**452**	**100.0%**	**0.56 [0.14, 2.35]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.43)						

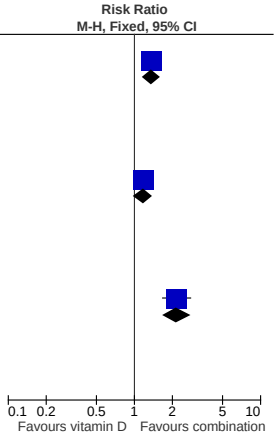


Test for subgroup differences: Not applicable

1.1.1 Combined product containing vitamin D analogue and potent corticosteroid *then* vitamin D or vitamin D analogue vs vitamin D or vitamin D analogue

Figure 31: Investigator's assessment (clear/nearly clear) at 8-12 weeks

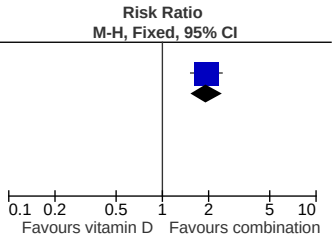
Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
12.1.1 Calcipotriol + betamethasone dipropionate (8 wk) then vitamin D OD (4 wk) vs. calcipotriol BD (12 wk)						
Kragballe 2004	178	322	133	327	100.0%	1.36 [1.15, 1.60]
Subtotal (95% CI)		**322**		**327**	**100.0%**	**1.36 [1.15, 1.60]**
Total events	178		133			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.67 (P = 0.0002)						
12.1.2 Calcipotriol + betamethasone dipropionate (4 wk) then vitamin D OD weekdays/ Dovobet weekends (8 wks) vs. calcipotriol BD (12 wk)						
Kragballe 2004	154	323	133	327	100.0%	1.17 [0.99, 1.39]
Subtotal (95% CI)		**323**		**327**	**100.0%**	**1.17 [0.99, 1.39]**
Total events	154		133			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.79 (P = 0.07)						
12.1.3 Calcipotriol + betamethasone dipropionate (4 wk) then calcipotriol OD (4 wks) vs. tacalcitol OD (8 wk)						
Ortonne 2004	126	249	59	252	100.0%	2.16 [1.68, 2.79]
Subtotal (95% CI)		**249**		**252**	**100.0%**	**2.16 [1.68, 2.79]**
Total events	126		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.93 (P < 0.00001)						



Test for subgroup differences: Chi² = 15.29, df = 2 (P = 0.0005), I² = 86.9%

Figure 32: Patient's assessment (clear/nearly clear) at 8 weeks

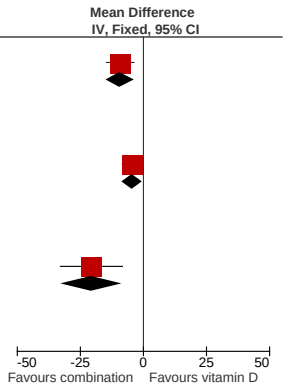
Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
12.2.2 Calcipotriol + betamethasone dipropionate (4 wk) then calcipotriol OD (4 wks) vs. tacalcitol OD (8 wk)						
Ortonne 2004	130	249	68	252	100.0%	1.93 [1.53, 2.45]
Subtotal (95% CI)		**249**		**252**	**100.0%**	**1.93 [1.53, 2.45]**
Total events	130		68			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.50 (P < 0.00001)						



Test for subgroup differences: Not applicable

Figure 33: % change in PASI at 8-12 weeks

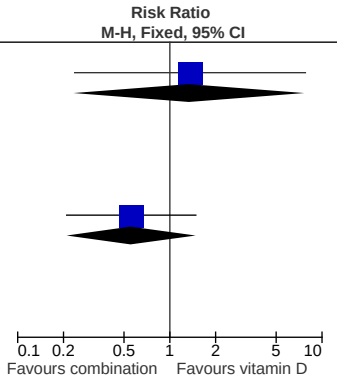
Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
12.3.1 Calcipotriol + betamethasone dipropionate (8 wk) then vitamin D OD (4 wk) vs. calcipotriol BD (12 wk)				
Kragballe 2004	-9.2	2.7959	100.0%	-9.20 [-14.68, -3.72]
Subtotal (95% CI)			**100.0%**	**-9.20 [-14.68, -3.72]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 3.29 (P = 0.0010)				
12.3.2 Calcipotriol + betamethasone dipropionate (4 wk) then vitamin D OD weekdays/ Dovobet weekends (8 wks) vs. calcipotriol BD (12 wk)				
Kragballe 2004	-4.4	2.01513	100.0%	-4.40 [-8.35, -0.45]
Subtotal (95% CI)			**100.0%**	**-4.40 [-8.35, -0.45]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.18 (P = 0.03)				
12.3.3 Calcipotriol + betamethasone dipropionate (4 wk) then calcipotriol OD (4 wks) vs. tacalcitol OD (8 wk)				
Ortonne 2004	-20.6	6.2604	100.0%	-20.60 [-32.87, -8.33]
Subtotal (95% CI)			**100.0%**	**-20.60 [-32.87, -8.33]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 3.29 (P = 0.001)				



Test for subgroup differences: Chi² = 7.00, df = 2 (P = 0.03), I² = 71.4%

Figure 58: Withdrawal due to adverse events at 8-12 weeks

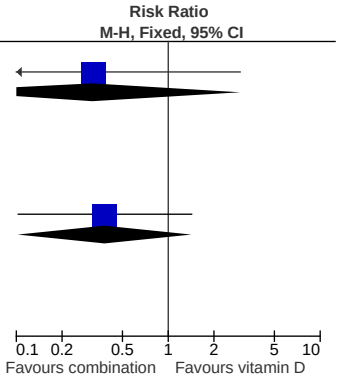
Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
12.4.1 Calcipotriol + betamethasone dipropionate (4 wk) then calcipotriol BD (8 wk) vs calcipotriol BD (12 wk)						
Saraceno 2007	3	53	2	48	100.0%	1.36 [0.24, 7.79]
Subtotal (95% CI)		**53**		**48**	**100.0%**	**1.36 [0.24, 7.79]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.73)						
12.4.2 Calcipotriol + betamethasone dipropionate (4 wk) then calcipotriol OD (4 wks) vs. tacalcitol OD (8 wk)						
Ortonne 2004	6	223	11	228	100.0%	0.56 [0.21, 1.48]
Subtotal (95% CI)		**223**		**228**	**100.0%**	**0.56 [0.21, 1.48]**
Total events	6		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.17 (P = 0.24)						



Test for subgroup differences: Chi² = 0.76, df = 1 (P = 0.38), I² = 0%

Figure 59: Withdrawal due to lack of efficacy at 8-12 weeks

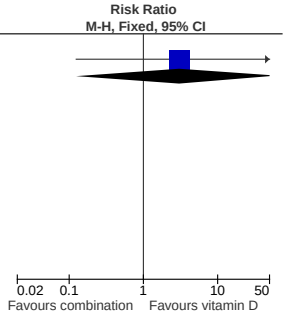
Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
12.6.1 Calcipotriol + betamethasone dipropionate (4 wk) then calcipotriol BD (8 wk) vs calcipotriol BD (12 wk)						
Saraceno 2007	1	51	3	49	100.0%	0.32 [0.03, 2.98]
Subtotal (95% CI)		**51**		**49**	**100.0%**	**0.32 [0.03, 2.98]**
Total events	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						
12.6.2 Calcipotriol + betamethasone dipropionate (4 wk) then calcipotriol OD (4 wks) vs. tacalcitol OD (8 wk)						
Ortonne 2004	3	220	8	225	100.0%	0.38 [0.10, 1.43]
Subtotal (95% CI)		**220**		**225**	**100.0%**	**0.38 [0.10, 1.43]**
Total events	3		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.43 (P = 0.15)						



Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.89), I² = 0%

Figure 34: Skin atrophy at 12 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
12.9.1 Calcipotriol + betamethasone dipropionate (8 wk) then vitamin D OD (4 wk) vs. calcipotriol BD (12 wk)						
Kragballe 2004	1	322	0	327	100.0%	3.05 [0.12, 74.51]
Subtotal (95% CI)		**322**		**327**	**100.0%**	**3.05 [0.12, 74.51]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
12.9.2 Calcipotriol + betamethasone dipropionate (4 wk) then vitamin D OD weekdays/ Dovobet weekends (8 wks) vs. calcipotriol BD (12 wk)						
Kragballe 2004	0	322	0	327		Not estimable
Subtotal (95% CI)		**322**		**327**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

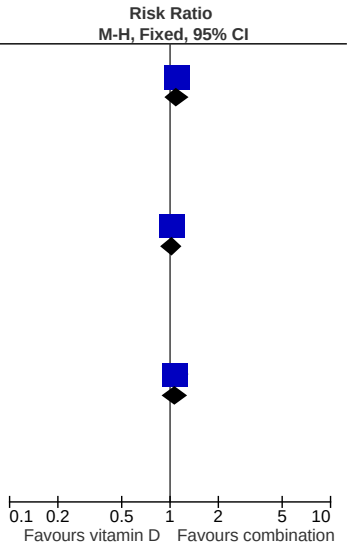


Test for subgroup differences: Not applicable

J.2.11 Combined product containing potent corticosteroid and vitamin D analogue vs vitamin D or vitamin D analogue (for maintenance of remission)

Figure 35: Investigator's assessment (clear/nearly clear) at 52 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
13.2.1 Combination (52 wk) vs. combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	80	104	62	89	100.0%	1.10 [0.93, 1.31]
Subtotal (95% CI)		**104**		**89**	**100.0%**	**1.10 [0.93, 1.31]**
Total events	80		62			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.12 (P = 0.26)						
13.2.2 Combination (52 wk) vs. alternating combination and calcipotriol (52 wk)						
Kragballe 2006(A)	80	104	78	104	100.0%	1.03 [0.88, 1.20]
Subtotal (95% CI)		**104**		**104**	**100.0%**	**1.03 [0.88, 1.20]**
Total events	80		78			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						
13.2.3 Alternating combination and calcipotriol (52 wk) vs combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	78	104	62	89	100.0%	1.08 [0.90, 1.28]
Subtotal (95% CI)		**104**		**89**	**100.0%**	**1.08 [0.90, 1.28]**
Total events	78		62			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.82 (P = 0.41)						

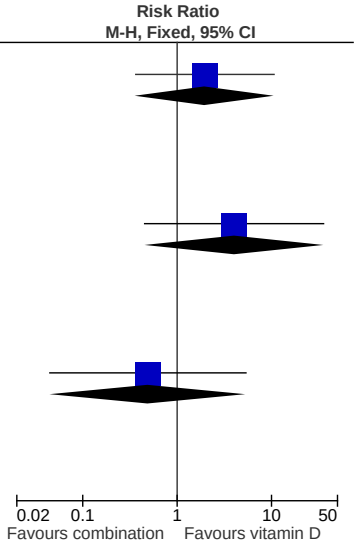


Test for subgroup differences: $Chi^2 = 0.42$, df = 2 (P = 0.81), $I^2 = 0\%$

Figure 36: Skin atrophy at 52 weeks

Note: different scale

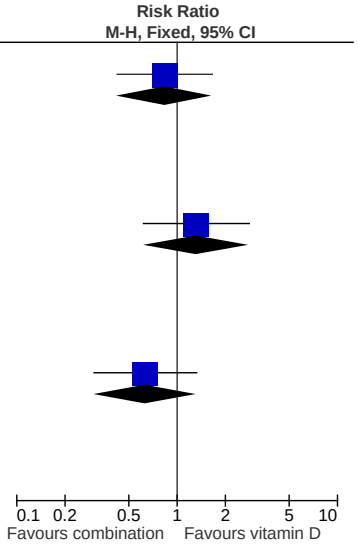
Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
13.3.1 Combination (52 wk) vs. combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	4	212	2	209	100.0%	1.97 [0.37, 10.65]
Subtotal (95% CI)		**212**		**209**	**100.0%**	**1.97 [0.37, 10.65]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
13.3.2 Combination (52 wk) vs. alternating combination and calcipotriol (52 wk)						
Kragballe 2006(A)	4	212	1	213	100.0%	4.02 [0.45, 35.66]
Subtotal (95% CI)		**212**		**213**	**100.0%**	**4.02 [0.45, 35.66]**
Total events	4		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.25 (P = 0.21)						
13.3.3 Alternating combination and calcipotriol (52 wk) vs combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	1	213	2	209	100.0%	0.49 [0.04, 5.37]
Subtotal (95% CI)		**213**		**209**	**100.0%**	**0.49 [0.04, 5.37]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.58 (P = 0.56)						



Test for subgroup differences: Chi² = 1.66, df = 2 (P = 0.44), I² = 0%

Figure 63: Withdrawal due to adverse events at 52 weeks

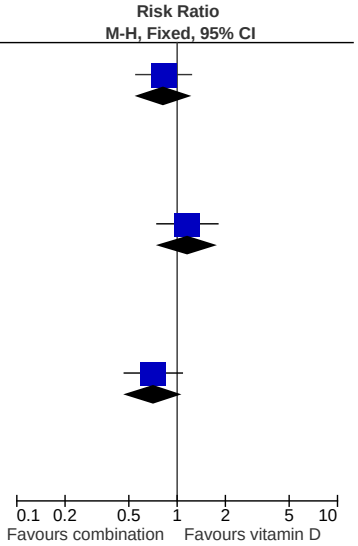
Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
13.4.1 Combination (52 wk) vs. combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	14	162	16	155	100.0%	0.84 [0.42, 1.66]
Subtotal (95% CI)		**162**		**155**	**100.0%**	**0.84 [0.42, 1.66]**
Total events	14		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						
13.4.2 Combination (52 wk) vs. alternating combination and calcipotriol (52 wk)						
Kragballe 2006(A)	14	162	11	168	100.0%	1.32 [0.62, 2.82]
Subtotal (95% CI)		**162**		**168**	**100.0%**	**1.32 [0.62, 2.82]**
Total events	14		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.72 (P = 0.47)						
13.4.3 Alternating combination and calcipotriol (52 wk) vs combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	11	168	16	155	100.0%	0.63 [0.30, 1.32]
Subtotal (95% CI)		**168**		**155**	**100.0%**	**0.63 [0.30, 1.32]**
Total events	11		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.21 (P = 0.23)						



Test for subgroup differences: Chi² = 1.87, df = 2 (P = 0.39), I² = 0%

Figure 64: Withdrawal due to lack of efficacy at 52 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
13.6.1 Combination (52 wk) vs. combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	35	183	42	181	100.0%	0.82 [0.55, 1.23]
Subtotal (95% CI)		**183**		**181**	**100.0%**	**0.82 [0.55, 1.23]**
Total events	35		42			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
13.6.2 Combination (52 wk) vs. alternating combination and calcipotriol (52 wk)						
Kragballe 2006(A)	35	183	31	188	100.0%	1.16 [0.75, 1.80]
Subtotal (95% CI)		**183**		**188**	**100.0%**	**1.16 [0.75, 1.80]**
Total events	35		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						
13.6.3 Alternating combination and calcipotriol (52 wk) vs combination (4 wk) then calcipotriol (48 wk)						
Kragballe 2006(A)	31	188	42	181	100.0%	0.71 [0.47, 1.08]
Subtotal (95% CI)		**188**		**181**	**100.0%**	**0.71 [0.47, 1.08]**
Total events	31		42			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.61 (P = 0.11)						



Test for subgroup differences: Chi² = 2.63, df = 2 (P = 0.27), I² = 23.9%

J.2.12 Vitamin D or vitamin D analogue vs dithranol

Figure 37: Investigator's assessment (clear/nearly clear) at 8-12 weeks - calcipotriol

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Dithranol Events	Dithranol Total	Weight	Risk Ratio M-H, Random, 95% CI
14.1.1 Calcipotriol BD vs. dithranol OD						
Berth Jones 1992	180	231	116	227	54.5%	1.52 [1.32, 1.76]
Christensen 1999	6	89	4	77	2.9%	1.30 [0.38, 4.43]
Wall 1998	92	153	67	131	42.5%	1.18 [0.95, 1.45]
Subtotal (95% CI)		**473**		**435**	**100.0%**	**1.36 [1.10, 1.68]**
Total events	278		187			
Heterogeneity: Tau² = 0.02; Chi² = 4.00, df = 2 (P = 0.14); I² = 50%						
Test for overall effect: Z = 2.80 (P = 0.005)						
Total (95% CI)		**473**		**435**	**100.0%**	**1.36 [1.10, 1.68]**
Total events	278		187			
Heterogeneity: Tau² = 0.02; Chi² = 4.00, df = 2 (P = 0.14); I² = 50%						
Test for overall effect: Z = 2.80 (P = 0.005)						
Test for subgroup differences: Not applicable						

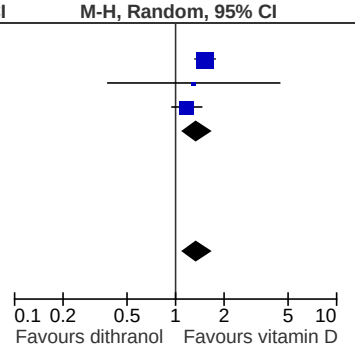
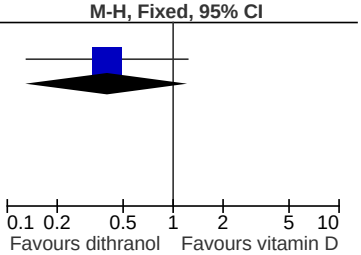


Figure 38: Investigator's assessment (clear/nearly clear) at 8 weeks - calcitriol

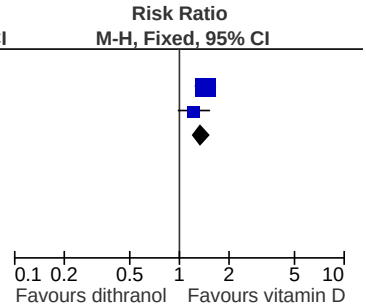
Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Dithranol Events	Dithranol Total	Weight	Risk Ratio M-H, Fixed, 95% CI
14.2.3 Calcitriol BD vs. dithranol OD						
Hutchinson 2000	4	60	9	54	100.0%	0.40 [0.13, 1.22]
Subtotal (95% CI)		**60**		**54**	**100.0%**	**0.40 [0.13, 1.22]**
Total events	4		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.60 (P = 0.11)						



Test for subgroup differences: Not applicable

Figure 39: Patient's assessment (clear/nearly clear) at 8-12 weeks

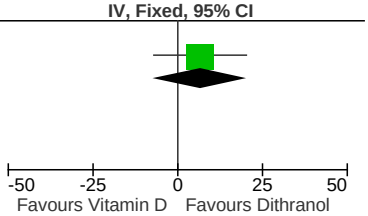
Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Dithranol Events	Dithranol Total	Weight	Risk Ratio M-H, Fixed, 95% CI
14.3.1 Calcipotriol BD vs. dithranol OD						
Berth Jones 1992	180	231	123	227	63.9%	1.44 [1.25, 1.65]
Wall 1998	93	153	65	131	36.1%	1.23 [0.99, 1.52]
Subtotal (95% CI)		**384**		**358**	**100.0%**	**1.36 [1.21, 1.53]**
Total events	273		188			
Heterogeneity: Chi² = 1.54, df = 1 (P = 0.21); I² = 35%						
Test for overall effect: Z = 5.18 (P < 0.00001)						



Test for subgroup differences: Not applicable

Figure 40: % change in PASI at 8 weeks

Study or Subgroup	Vitamin D analogue Mean	Vitamin D analogue SD	Vitamin D analogue Total	Dithranol Mean	Dithranol SD	Dithranol Total	Weight	Mean Difference IV, Fixed, 95% CI
14.4.2 Calcipotrol BD vs. dithranol OD								
van der kerkhof 2006	-57	35.4	46	-63.6	29.1	40	100.0%	6.60 [-7.04, 20.24]
Subtotal (95% CI)			**46**			**40**	**100.0%**	**6.60 [-7.04, 20.24]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.95 (P = 0.34)								



Test for subgroup differences: Not applicable

Figure 41: Withdrawal due to adverse events at 8-12 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Dithranol Events	Dithranol Total	Weight	Risk Ratio M-H, Fixed, 95% CI
14.5.1 Calcipotriol BD vs. dithranol OD						
Berth Jones 1992	4	216	12	211	26.9%	0.33 [0.11, 0.99]
Christensen 1999	2	89	6	82	13.8%	0.31 [0.06, 1.48]
van der kerkhof 2006	7	47	3	48	6.6%	2.38 [0.66, 8.67]
Wall 1998	9	161	20	145	46.6%	0.41 [0.19, 0.86]
Subtotal (95% CI)		**513**		**486**	**93.8%**	**0.51 [0.31, 0.83]**
Total events	22		41			
Heterogeneity: Chi² = 6.85, df = 3 (P = 0.08); I² = 56%						
Test for overall effect: Z = 2.67 (P = 0.007)						
14.5.2 Calcitriol BD vs. dithranol OD						
Hutchinson 2000	0	48	2	38	6.2%	0.16 [0.01, 3.22]
Subtotal (95% CI)		**48**		**38**	**6.2%**	**0.16 [0.01, 3.22]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.20 (P = 0.23)						
Total (95% CI)		**561**		**524**	**100.0%**	**0.49 [0.30, 0.79]**
Total events	22		43			
Heterogeneity: Chi² = 7.40, df = 4 (P = 0.12); I² = 46%						
Test for overall effect: Z = 2.90 (P = 0.004)						
Test for subgroup differences: Chi² = 0.55, df = 1 (P = 0.46), I² = 0%						

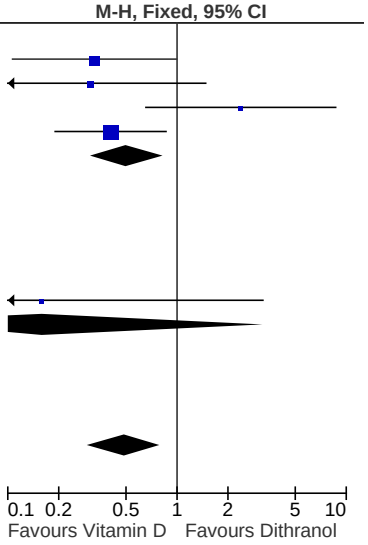
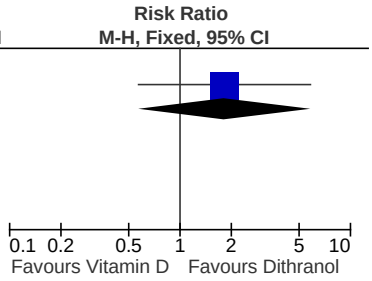


Figure 68: Withdrawal due to lack of efficacy at 8 weeks

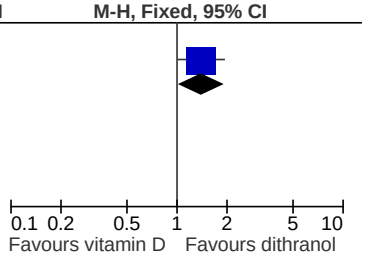
Study or Subgroup	Vitamin D analogue Events	Total	Dithranol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
14.6.2 Calcipotrol BD vs. dithranol OD						
van der kerkhof 2006	7	47	4	49	100.0%	1.82 [0.57, 5.83]
Subtotal (95% CI)		**47**		**49**	**100.0%**	**1.82 [0.57, 5.83]**
Total events	7		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.01 (P = 0.31)						



Test for subgroup differences: Not applicable

Figure 42: Relapse rate (8 weeks post-treatment)

Study or Subgroup	Vitamin D analogue Events	Total	Dithranol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
14.7.2 Calcipotriol BD vs. dithranol OD						
Christensen 1999	50	62	19	33	100.0%	1.40 [1.02, 1.92]
Subtotal (95% CI)		**62**		**33**	**100.0%**	**1.40 [1.02, 1.92]**
Total events	50		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.08 (P = 0.04)						

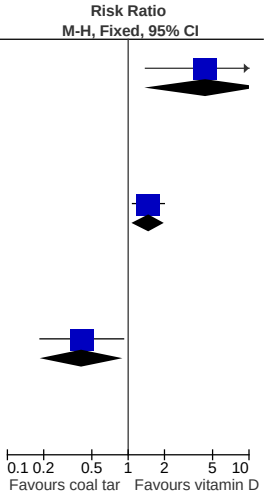


Test for subgroup differences: Not applicable

J.2.13 Vitamin D or vitamin D analogue vs coal tar

Figure 43: Investigator's assessment (clear/nearly clear) at 6-12 weeks

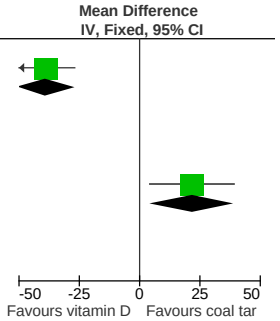
Study or Subgroup	Vitamin D analogue Events	Total	Coal tar Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
15.1.1 Calcipotriol BD vs 15% coal tar solution in aqueous cream OD for 6 weeks						
Tham 1994	13	27	3	27	100.0%	4.33 [1.39, 13.50]
Subtotal (95% CI)		**27**		**27**	**100.0%**	**4.33 [1.39, 13.50]**
Total events	13		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.53 (P = 0.01)						
15.1.2 Calcipotriol BD vs. coal tar polytherapy (coal tar 5%/allantoin 2%/hydrocortisone cream 0.5%) BD for 8 weeks						
Pinheiro 1997	47	65	28	57	100.0%	1.47 [1.09, 1.99]
Subtotal (95% CI)		**65**		**57**	**100.0%**	**1.47 [1.09, 1.99]**
Total events	47		28			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.49 (P = 0.01)						
15.1.3 Calcipotriol BD vs. coal tar solution (liquor carbonis distillate (LCD 15%, equivalent to 2.3% coal tar) BD for 12 weeks						
Alorapalli 2010	6	28	14	27	100.0%	0.41 [0.19, 0.92]
Subtotal (95% CI)		**28**		**27**	**100.0%**	**0.41 [0.19, 0.92]**
Total events	6		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.17 (P = 0.03)						



Test for subgroup differences: $Chi^2 = 12.83$, df = 2 (P = 0.002), $I^2 = 84.4\%$

Figure 44: % change in PASI at 6-12 weeks

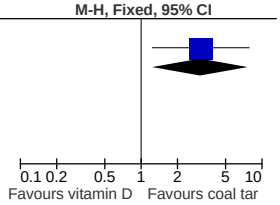
Study or Subgroup	Vitamin D analogue Mean	SD	Total	Coal tar Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
15.2.1 Calcipotriol BD vs 15% coal tar solution in aqueous cream OD for 6 weeks								
Tham 1994	-69.8	20.4	27	-30.9	24.6	27	100.0%	-38.90 [-50.95, -26.85]
Subtotal (95% CI)			**27**			**27**	**100.0%**	**-38.90 [-50.95, -26.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 6.32 (P < 0.00001)								
15.2.2 Calcipotriol BD vs. coal tar solution (liquor carbonis distillate (LCD 15%, equivalent to 2.3% coal tar) BD for 12 weeks								
Alorapalli 2010	-36.5	33.1079	28	-58.2	33.1079	27	100.0%	21.70 [4.20, 39.20]
Subtotal (95% CI)			**28**			**27**	**100.0%**	**21.70 [4.20, 39.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.43 (P = 0.02)								



Test for subgroup differences: Chi² = 31.24, df = 1 (P < 0.00001), I² = 96.8%

Figure 45: Relapse rate (6 weeks post treatment)

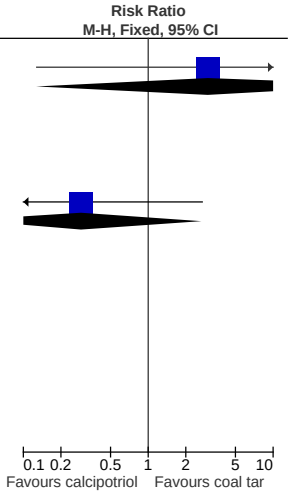
Study or Subgroup	Vitamin D analogue Events	Total	Coal tar Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
15.3.2 Calcipotriol BD vs. coal tar solution (liquor carbonis distillate (LCD 15%, equivalent to 2.3% coal tar) BD for 12 weeks						
Alorapalli 2010	7	9	4	16	100.0%	3.11 [1.24, 7.79]
Subtotal (95% CI)		**9**		**16**	**100.0%**	**3.11 [1.24, 7.79]**
Total events	7		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.42 (P = 0.02)						



Test for subgroup differences: Not applicable

Figure 46: Withdrawal due to adverse events at 6-12 weeks

Study or Subgroup	Vitamin D analogue Events	Total	Coal tar Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
15.4.1 Calcipotriol BD vs 15% coal tar solution in aqueous cream OD for 6 weeks						
Tham 1994	1	25	0	25	100.0%	3.00 [0.13, 70.30]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**3.00 [0.13, 70.30]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
15.4.2 Calcipotriol BD vs. coal tar polytherapy (coal tar 5%/allantoin 2%/hydrocortisone cream 0.5%) BD for 8 weeks						
Pinheiro 1997	1	62	3	54	100.0%	0.29 [0.03, 2.71]
Subtotal (95% CI)		**62**		**54**	**100.0%**	**0.29 [0.03, 2.71]**
Total events	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.28)						
15.4.3 Calcipotriol BD vs. coal tar solution (liquor carbonis distillate (LCD 15%, equivalent to 2.3% coal tar) BD for 12 weeks						
Alorapalli 2010	0	28	0	27		Not estimable
Subtotal (95% CI)		**28**		**27**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



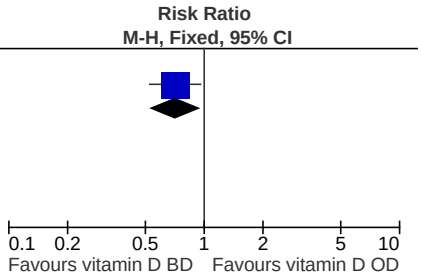
Test for subgroup differences: Chi² = 1.40, df = 1 (P = 0.24), I² = 28.7%

J.2.14 Vitamin D or vitamin D analogue once daily vs vitamin D or vitamin D analogue twice daily

Figure 47: Investigator's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Vitamin D OD Events	Vitamin D OD Total	Vitamin D BD Events	Vitamin D BD Total	Weight	Risk Ratio M-H, Fixed, 95% CI
18.1.5 Calcipotriol OD vs BD						
Kragballe 1998	49	172	69	172	100.0%	0.71 [0.53, 0.96]
Subtotal (95% CI)		**172**		**172**	**100.0%**	**0.71 [0.53, 0.96]**
Total events	49		69			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.24 (P = 0.02)

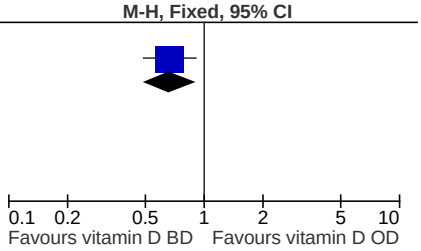


Test for subgroup differences: Not applicable

Figure 48: Patient's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Vitamin D OD Events	Vitamin D OD Total	Vitamin D BD Events	Vitamin D BD Total	Weight	Risk Ratio M-H, Fixed, 95% CI
18.2.5 Calcipotriol OD vs BD						
Kragballe 1998	46	172	69	172	100.0%	0.67 [0.49, 0.91]
Subtotal (95% CI)		**172**		**172**	**100.0%**	**0.67 [0.49, 0.91]**
Total events	46		69			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.58 (P = 0.010)

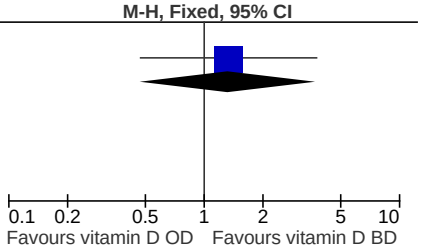


Test for subgroup differences: Not applicable

Figure 49: Withdrawal due to adverse events at 8 weeks

Study or Subgroup	Vitamin D OD Events	Vitamin D OD Total	Vitamin D BD Events	Vitamin D BD Total	Weight	Risk Ratio M-H, Fixed, 95% CI
18.5.5 Calcipotriol OD vs BD						
Kragballe 1998	8	174	6	174	100.0%	1.33 [0.47, 3.76]
Subtotal (95% CI)		**174**		**174**	**100.0%**	**1.33 [0.47, 3.76]**
Total events	8		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)

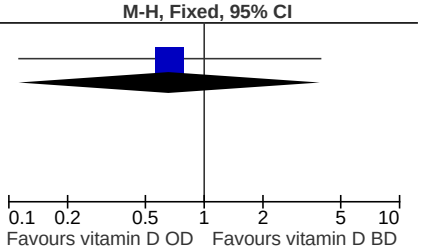


Test for subgroup differences: Not applicable

Figure 50: Withdrawal due to lack of efficacy at 8 weeks

Study or Subgroup	Vitamin D OD Events	Vitamin D OD Total	Vitamin D BD Events	Vitamin D BD Total	Weight	Risk Ratio M-H, Fixed, 95% CI
18.8.5 Calcipotriol OD vs BD						
Kragballe 1998	2	174	3	174	100.0%	0.67 [0.11, 3.94]
Subtotal (95% CI)		**174**		**174**	**100.0%**	**0.67 [0.11, 3.94]**
Total events	2		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.45 (P = 0.65)



Test for subgroup differences: Not applicable

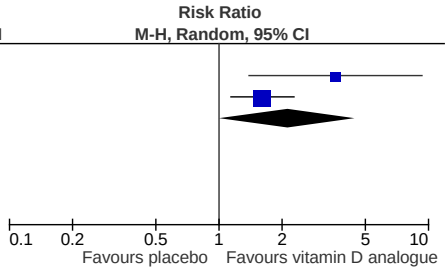
J.3 Topicals – difficult to treat sites (face, flexures and scalp)

J.3.1 Scalp: Vitamin D or vitamin D analogue vs placebo

Figure 78: Investigator's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Calcipotriol OD						
Green 1994	15	25	4	24	34.2%	3.60 [1.39, 9.31]
Jemec 2008	100	272	31	136	65.8%	1.61 [1.14, 2.28]
Subtotal (95% CI)		**297**		**160**	**100.0%**	**2.12 [1.01, 4.48]**
Total events	115		35			

Heterogeneity: Tau² = 0.19; Chi² = 2.43, df = 1 (P = 0.12); I² = 59%
Test for overall effect: Z = 1.97 (P = 0.05)

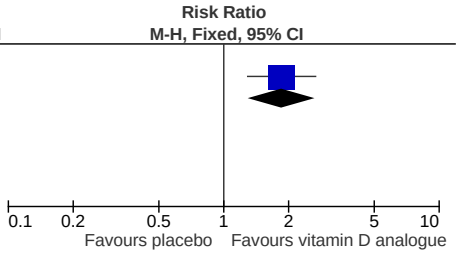


Test for subgroup differences: Not applicable

Figure 51: Patient's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Vitamin D analogue Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Calcipotriol OD						
Jemec 2008	104	272	28	136	100.0%	1.86 [1.29, 2.67]
Subtotal (95% CI)		**272**		**136**	**100.0%**	**1.86 [1.29, 2.67]**
Total events	104		28			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.34 (P = 0.0008)

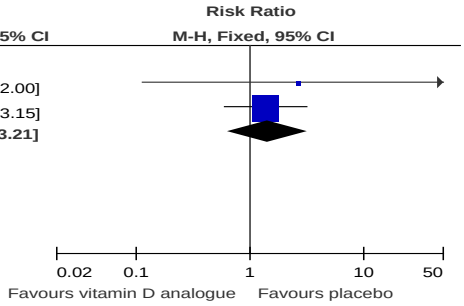


Test for subgroup differences: Not applicable

Figure 80: Withdrawals due to adverse events at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Calcipotriol OD						
Green 1994	1	25	0	22	5.3%	2.65 [0.11, 62.00]
Jemec 2008	20	235	7	113	94.7%	1.37 [0.60, 3.15]
Subtotal (95% CI)		**260**		**135**	**100.0%**	**1.44 [0.65, 3.21]**
Total events	21		7			

Heterogeneity: Chi² = 0.16, df = 1 (P = 0.69); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)

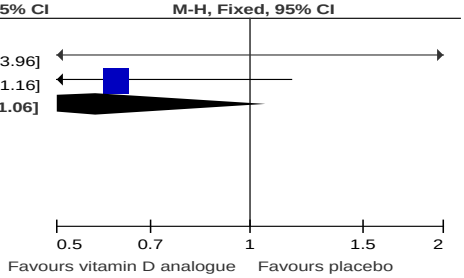


Test for subgroup differences: Not applicable

Figure 81: Withdrawals due to lack of efficacy at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Calcipotriol OD						
Green 1994	0	24	2	24	10.6%	0.20 [0.01, 3.96]
Jemec 2008	19	234	16	122	89.4%	0.62 [0.33, 1.16]
Subtotal (95% CI)		**258**		**146**	**100.0%**	**0.57 [0.31, 1.06]**
Total events	19		18			

Heterogeneity: Chi² = 0.53, df = 1 (P = 0.46); I² = 0%
Test for overall effect: Z = 1.77 (P = 0.08)



Test for subgroup differences: Not applicable

J.3.2 Scalp: Potent corticosteroid vs placebo

Figure 82: Investigator's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Betamethasone dipropionate (OD)						
Jemec 2008	356	556	31	136	75.6%	2.81 [2.05, 3.85]
Subtotal (95% CI)		**556**		**136**	**75.6%**	**2.81 [2.05, 3.85]**
Total events	356		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 6.42 (P < 0.00001)						
2.1.2 Betamethasone valerate (BD)						
Franz 1999	68	115	12	57	24.4%	2.81 [1.66, 4.75]
Subtotal (95% CI)		**115**		**57**	**24.4%**	**2.81 [1.66, 4.75]**
Total events	68		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.85 (P = 0.0001)						
Total (95% CI)		**671**		**193**	**100.0%**	**2.81 [2.14, 3.68]**
Total events	424		43			
Heterogeneity: Chi² = 0.00, df = 1 (P = 1.00); I² = 0%						
Test for overall effect: Z = 7.48 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 1.00), I² = 0%						

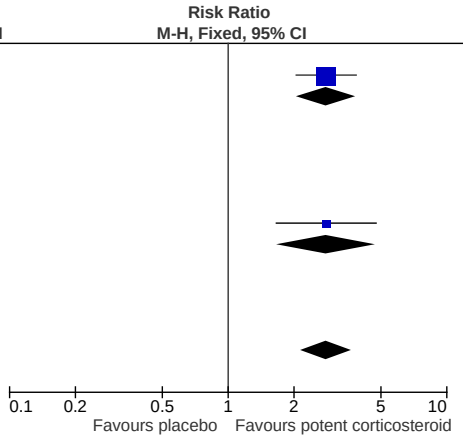


Figure 52: Patient's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Betamethasone dipropionate (OD)						
Jemec 2008	348	556	28	136	77.1%	3.04 [2.17, 4.26]
Subtotal (95% CI)		**556**		**136**	**77.1%**	**3.04 [2.17, 4.26]**
Total events	348		28			
Heterogeneity: Not applicable						
Test for overall effect: Z = 6.48 (P < 0.00001)						
2.2.2 Betamethasone valerate (BD)						
Franz 1999	71	115	10	57	22.9%	3.52 [1.97, 6.29]
Subtotal (95% CI)		**115**		**57**	**22.9%**	**3.52 [1.97, 6.29]**
Total events	71		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.25 (P < 0.0001)						
Total (95% CI)		**671**		**193**	**100.0%**	**3.15 [2.35, 4.21]**
Total events	419		38			
Heterogeneity: Chi² = 0.18, df = 1 (P = 0.67); I² = 0%						
Test for overall effect: Z = 7.73 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%						

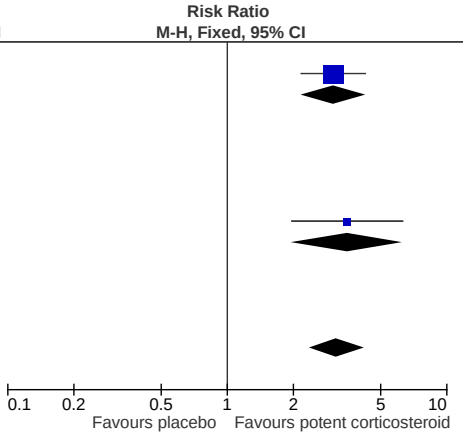


Figure 53: Withdrawals due to adverse events at 4-8 weeks

Study or Subgroup	Corticosteroid (potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.2 Betamethasone dipropionate OD						
Jemec 2008	6	515	7	113	100.0%	0.19 [0.06, 0.55]
Subtotal (95% CI)		**515**		**113**	**100.0%**	**0.19 [0.06, 0.55]**
Total events	6		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.06 (P = 0.002)						
2.3.4 Betamethasone valerate BD						
Franz 1999	0	115	0	57		Not estimable
Subtotal (95% CI)		**115**		**57**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**630**		**170**	**100.0%**	**0.19 [0.06, 0.55]**
Total events	6		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.06 (P = 0.002)						
Test for subgroup differences: Not applicable						

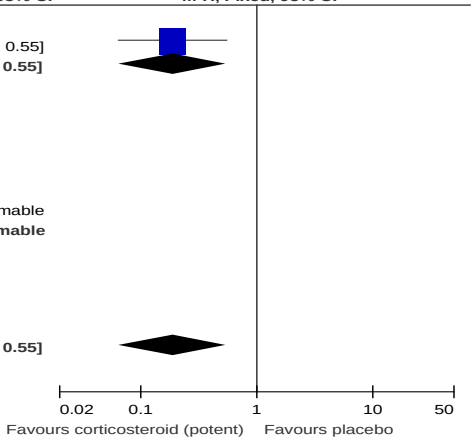
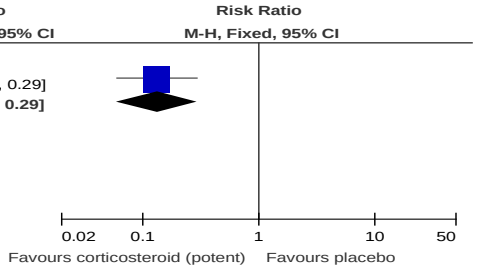


Figure 54: Withdrawals due to treatment failure at 8 weeks

Study or Subgroup	Corticosteroid (potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.2 Betamethasone dipropionate OD						
Jemec 2008	9	518	16	122	100.0%	0.13 [0.06, 0.29]
Subtotal (95% CI)		**518**		**122**	**100.0%**	**0.13 [0.06, 0.29]**
Total events	9		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.00 (P < 0.00001)						



J.3.3 Scalp: Very potent corticosteroid vs placebo

Figure 86: Investigator's assessment (clear/nearly clear) at 2-4 weeks

Note: different scale

Study or Subgroup	Very potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Clobetasol propionate BD						
Franz 2000	86	125	5	63	22.9%	8.67 [3.71, 20.27]
Olsen 1991	129	188	16	189	55.0%	8.11 [5.02, 13.08]
Sofen 2011	35	41	5	40	17.5%	6.83 [2.98, 15.66]
Subtotal (95% CI)		**354**		**292**	**95.4%**	**8.01 [5.49, 11.67]**
Total events	250		26			
Heterogeneity: Chi² = 0.18, df = 2 (P = 0.92); I² = 0%						
Test for overall effect: Z = 10.82 (P < 0.00001)						
3.1.2 Clobetasol propionate OD						
Jarratt 2004	40	95	1	47	4.6%	19.79 [2.81, 139.55]
Subtotal (95% CI)		**95**		**47**	**4.6%**	**19.79 [2.81, 139.55]**
Total events	40		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.00 (P = 0.003)						
Total (95% CI)		**449**		**339**	**100.0%**	**8.55 [5.88, 12.43]**
Total events	290		27			
Heterogeneity: Chi² = 1.04, df = 3 (P = 0.79); I² = 0%						
Test for overall effect: Z = 11.25 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.79, df = 1 (P = 0.37), I² = 0%						

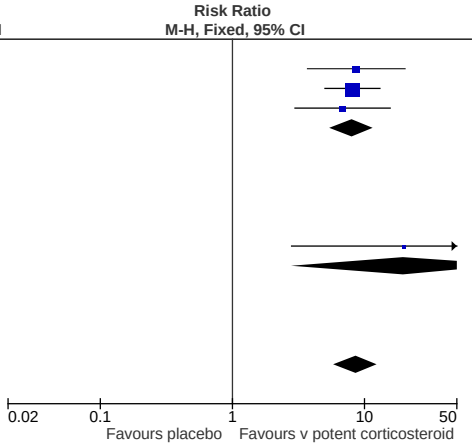


Figure 55: Patient's assessment (clear/nearly clear) at 2 weeks

Note: different scale

Study or Subgroup	Very potent steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.2.2 Clobetasol propionate BD						
Franz 2000	77	125	4	63	100.0%	9.70 [3.72, 25.30]
Subtotal (95% CI)		**125**		**63**	**100.0%**	**9.70 [3.72, 25.30]**
Total events	77		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.65 (P < 0.00001)						
Test for subgroup differences: Not applicable						

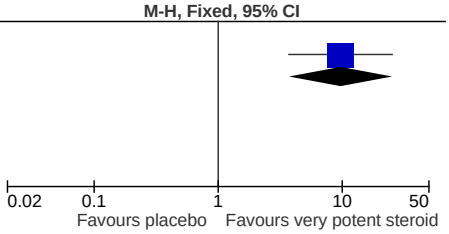


Figure 88: Skin atrophy at 4 weeks

Study or Subgroup	Very potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 Clobetasol propionate OD						
Jarratt 2004	0	94	0	47		Not estimable
Subtotal (95% CI)		**94**		**47**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.3.2 Clobetasol propionate BD						
Sofen 2011	0	41	1	40	100.0%	0.33 [0.01, 7.76]
Subtotal (95% CI)		**41**		**40**	**100.0%**	**0.33 [0.01, 7.76]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Total (95% CI)		**135**		**87**	**100.0%**	**0.33 [0.01, 7.76]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Test for subgroup differences: Not applicable						

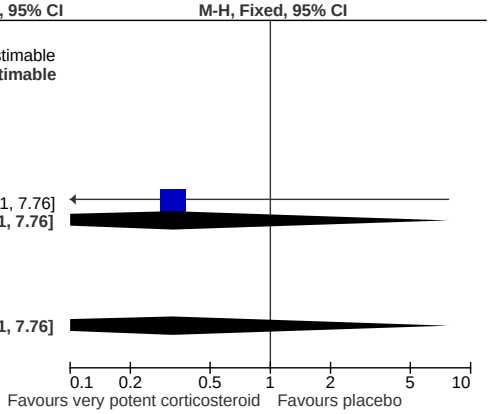


Figure 56: Withdrawals due to adverse events at 2-4 weeks

Note: different scale

Study or Subgroup	Corticosteroid (very potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.5.1 Clobetasol propionate BD						
Franz 2000	0	125	0	63		Not estimable
Olsen 1991	0	188	1	189	50.6%	0.34 [0.01, 8.17]
Sofen 2011	0	37	1	39	49.4%	0.35 [0.01, 8.35]
Subtotal (95% CI)		**350**		**291**	**100.0%**	**0.34 [0.04, 3.25]**
Total events	0		2			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%						
Test for overall effect: Z = 0.93 (P = 0.35)						
3.5.2 Clobetasol propionate OD						
Jarratt 2004	0	95	0	47		Not estimable
Subtotal (95% CI)		**95**		**47**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**445**		**338**	**100.0%**	**0.34 [0.04, 3.25]**
Total events	0		2			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%						
Test for overall effect: Z = 0.93 (P = 0.35)						
Test for subgroup differences: Not applicable						

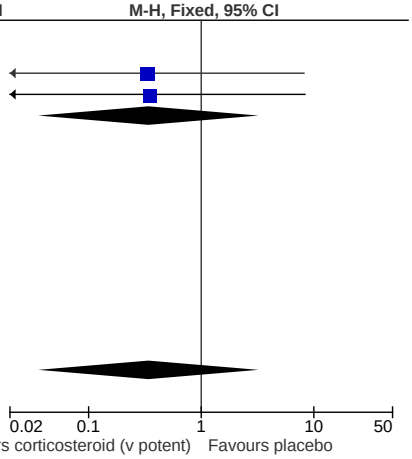
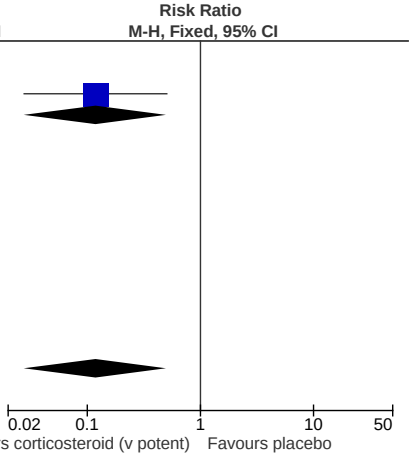


Figure 90: Withdrawals due to lack of efficacy at 2-4 weeks

Note: different scale

Study or Subgroup	Corticosteroid (very potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.5.1 Clobetasol propionate BD						
Franz 2000	0	125	0	63		Not estimable
Olsen 1991	2	188	17	189	100.0%	0.12 [0.03, 0.50]
Subtotal (95% CI)		**313**		**252**	**100.0%**	**0.12 [0.03, 0.50]**
Total events	2		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.88 (P = 0.004)						
3.5.2 Clobetasol propionate OD						
Jarratt 2004	0	95	0	47		Not estimable
Subtotal (95% CI)		**95**		**47**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**408**		**299**	**100.0%**	**0.12 [0.03, 0.50]**
Total events	2		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.88 (P = 0.004)						
Test for subgroup differences: Not applicable						



J.3.4 Scalp: Combined product containing potent corticosteroid and vitamin D analogue vs placebo

Figure 91: Investigator's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.3 Combination (OD) - Black/African-American						
Tyring 2010	48	60	9	18	53.3%	1.60 [0.99, 2.58]
Subtotal (95% CI)		**60**		**18**	**53.3%**	**1.60 [0.99, 2.58]**
Total events	48		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.92 (P = 0.05)						
4.2.4 Combination (OD) - Hispanic/Latino						
Tyring 2010	49	75	8	24	46.7%	1.96 [1.09, 3.53]
Subtotal (95% CI)		**75**		**24**	**46.7%**	**1.96 [1.09, 3.53]**
Total events	49		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.24 (P = 0.03)						
Total (95% CI)		**135**		**42**	**100.0%**	**1.77 [1.21, 2.58]**
Total events	97		17			
Heterogeneity: Chi² = 0.28, df = 1 (P = 0.59); I² = 0%						
Test for overall effect: Z = 2.95 (P = 0.003)						
Test for subgroup differences: Chi² = 0.27, df = 1 (P = 0.60), I² = 0%						

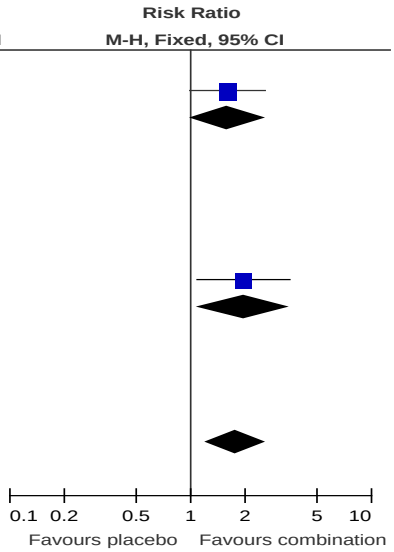


Figure 57: Patient's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.3.1 Combination (OD)						
Tyring 2010	84	135	15	42	100.0%	1.74 [1.14, 2.67]
Subtotal (95% CI)		**135**		**42**	**100.0%**	**1.74 [1.14, 2.67]**
Total events	84		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.55 (P = 0.01)						
Test for subgroup differences: Not applicable						

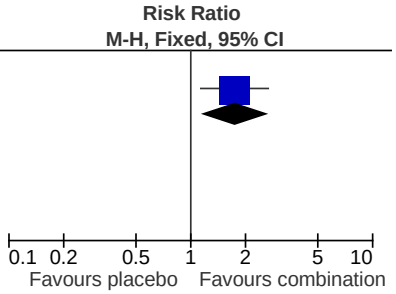
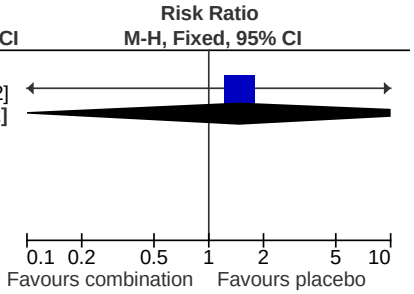


Figure 58: Withdrawal due to adverse events at 8 weeks

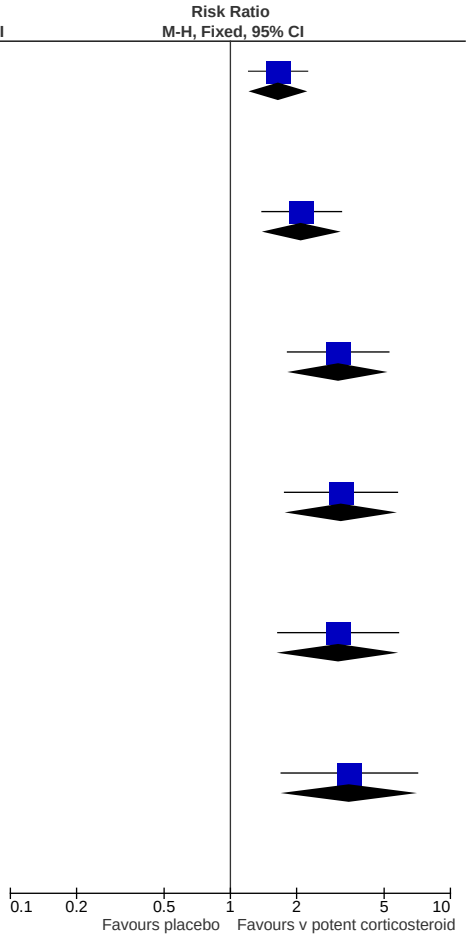
Study or Subgroup	Combination Events	Combination Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.4.1 Combination (OD)						
Tyring 2010	2	118	0	34	100.0%	1.47 [0.07, 29.92]
Subtotal (95% CI)		**118**		**34**	**100.0%**	**1.47 [0.07, 29.92]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.25 (P = 0.80)						
Test for subgroup differences: Not applicable						



J.3.5 Scalp: Very potent corticosteroid vs placebo for maintenance of remission

Figure 59: Duration of remission (N still in remission)

Study or Subgroup	Very potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.1.1 1 month						
Poulin 2010	48	67	30	69	100.0%	1.65 [1.21, 2.24]
Subtotal (95% CI)		**67**		**69**	**100.0%**	**1.65 [1.21, 2.24]**
Total events	48		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.17 (P = 0.002)						
5.1.2 2 months						
Poulin 2010	41	67	20	69	100.0%	2.11 [1.39, 3.20]
Subtotal (95% CI)		**67**		**69**	**100.0%**	**2.11 [1.39, 3.20]**
Total events	41		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.52 (P = 0.0004)						
5.1.3 3 months						
Poulin 2010	39	67	13	69	100.0%	3.09 [1.82, 5.25]
Subtotal (95% CI)		**67**		**69**	**100.0%**	**3.09 [1.82, 5.25]**
Total events	39		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.17 (P < 0.0001)						
5.1.4 4 months						
Poulin 2010	34	67	11	69	100.0%	3.18 [1.76, 5.75]
Subtotal (95% CI)		**67**		**69**	**100.0%**	**3.18 [1.76, 5.75]**
Total events	34		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.84 (P = 0.0001)						
5.1.5 5 months						
Poulin 2010	30	67	10	69	100.0%	3.09 [1.64, 5.81]
Subtotal (95% CI)		**67**		**69**	**100.0%**	**3.09 [1.64, 5.81]**
Total events	30		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.50 (P = 0.0005)						
5.1.6 6 months						
Poulin 2010	27	67	8	69	100.0%	3.48 [1.70, 7.10]
Subtotal (95% CI)		**67**		**69**	**100.0%**	**3.48 [1.70, 7.10]**
Total events	27		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.42 (P = 0.0006)						



Test for subgroup differences: Chi² = 9.10, df = 5 (P = 0.11), I² = 45.1%

Figure 60: Skin atrophy at 6 months

Study or Subgroup	Very potent corticosteroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poulin 2010	1	67	0	69	100.0%	3.09 [0.13, 74.50]
Total (95% CI)		**67**		**69**	**100.0%**	**3.09 [0.13, 74.50]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						

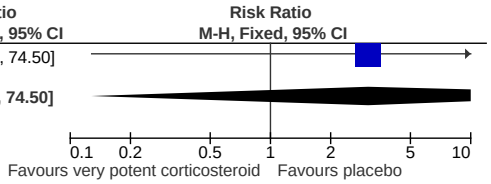
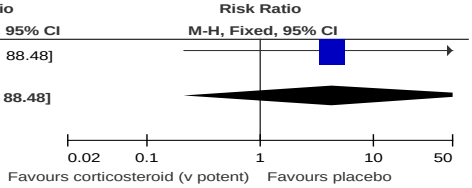


Figure 61: Withdrawals due to adverse events at 6 months

Note: different scale

Study or Subgroup	Corticosteroid (very potent) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poulin 2010	2	60	0	52	100.0%	4.34 [0.21, 88.48]
Total (95% CI)		**60**		**52**	**100.0%**	**4.34 [0.21, 88.48]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.96 (P = 0.34)						



J.3.6 Scalp: Vitamin D or vitamin D analogue vs potent corticosteroid

Figure 62: Investigator's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Random, 95% CI
6.1.1 Calcipotriol OD vs betamethasone dipropionate OD						
Jemec 2008	100	272	356	556	31.2%	0.57 [0.49, 0.68]
van de Kerkhof 2009	124	286	343	562	33.4%	0.71 [0.61, 0.82]
Subtotal (95% CI)		**558**		**1118**	**64.6%**	**0.64 [0.52, 0.79]**
Total events	224		699			
Heterogeneity: Tau² = 0.02; Chi² = 3.50, df = 1 (P = 0.06); I² = 71%						
Test for overall effect: Z = 4.17 (P < 0.0001)						
6.1.2 Calcipotriol BD vs betamethasone valerate BD						
Klaber 1994	138	236	175	232	35.4%	0.78 [0.68, 0.88]
Subtotal (95% CI)		**236**		**232**	**35.4%**	**0.78 [0.68, 0.88]**
Total events	138		175			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.83 (P = 0.0001)						
Total (95% CI)		**794**		**1350**	**100.0%**	**0.69 [0.58, 0.82]**
Total events	362		874			
Heterogeneity: Tau² = 0.02; Chi² = 8.19, df = 2 (P = 0.02); I² = 76%						
Test for overall effect: Z = 4.28 (P < 0.0001)						
Test for subgroup differences: Chi² = 2.28, df = 1 (P = 0.13), I² = 56.2%						

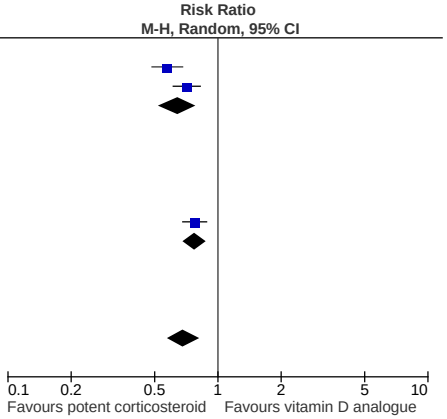


Figure 63: Patient's assessment (clear/nearly clear) at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Random, 95% CI
6.2.1 Calcipotriol OD vs betamethasone dipropionate OD						
Jemec 2008	104	272	348	556	30.8%	0.61 [0.52, 0.72]
van de Kerkhof 2009	128	286	337	562	33.7%	0.75 [0.65, 0.86]
Subtotal (95% CI)		**558**		**1118**	**64.5%**	**0.68 [0.56, 0.83]**
Total events	232		685			
Heterogeneity: Tau² = 0.01; Chi² = 3.22, df = 1 (P = 0.07); I² = 69%						
Test for overall effect: Z = 3.88 (P = 0.0001)						
6.2.2 Calcipotriol BD vs betamethasone valerate BD						
Klaber 1994	136	236	171	232	35.5%	0.78 [0.68, 0.89]
Subtotal (95% CI)		**236**		**232**	**35.5%**	**0.78 [0.68, 0.89]**
Total events	136		171			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.61 (P = 0.0003)						
Total (95% CI)		**794**		**1350**	**100.0%**	**0.71 [0.62, 0.82]**
Total events	368		856			
Heterogeneity: Tau² = 0.01; Chi² = 5.76, df = 2 (P = 0.06); I² = 65%						
Test for overall effect: Z = 4.59 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.39, df = 1 (P = 0.24), I² = 27.8%						

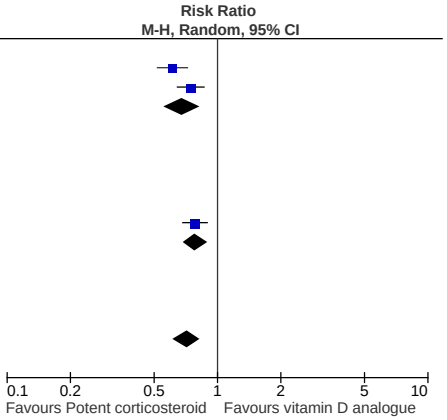


Figure 64: Relapse rate after 4 weeks

Study or Subgroup	Favours vitamin D analogue Events	Favours vitamin D analogue Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.3.1 Calcipotriol BD vs betamethasone valerate BD						
Klaber 1994	75	99	102	129	100.0%	0.96 [0.83, 1.10]
Subtotal (95% CI)		**99**		**129**	**100.0%**	**0.96 [0.83, 1.10]**
Total events	75		102			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
Test for subgroup differences: Not applicable						

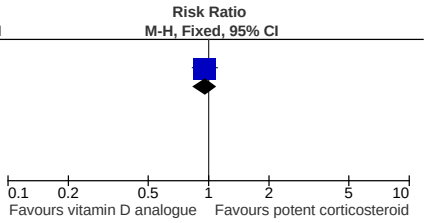


Figure 100: Withdrawal due to adverse events at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Corticosteroid (potent) Events	Corticosteroid (potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.4.1 Calcipotriol OD vs. betamethasone dipropionate OD						
Jemec 2008	20	235	6	515	35.8%	7.30 [2.97, 17.95]
van de Kerkhof 2009	8	256	7	504	44.9%	2.25 [0.83, 6.14]
Subtotal (95% CI)		**491**		**1019**	**80.8%**	**4.49 [2.36, 8.55]**
Total events	28		13			
Heterogeneity: Chi² = 2.95, df = 1 (P = 0.09); I² = 66%						
Test for overall effect: Z = 4.57 (P < 0.00001)						
6.4.9 Calcipotriol BD vs betamethasone valerate BD						
Klaber 1994	11	231	2	227	19.2%	5.40 [1.21, 24.11]
Subtotal (95% CI)		**231**		**227**	**19.2%**	**5.40 [1.21, 24.11]**
Total events	11		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						
Total (95% CI)		**722**		**1246**	**100.0%**	**4.67 [2.57, 8.48]**
Total events	39		15			
Heterogeneity: Chi² = 3.02, df = 2 (P = 0.22); I² = 34%						
Test for overall effect: Z = 5.06 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.82), I² = 0%						

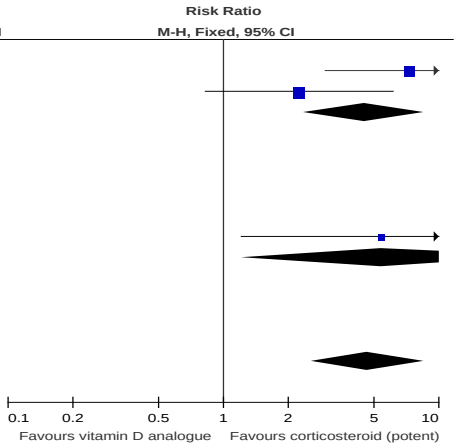
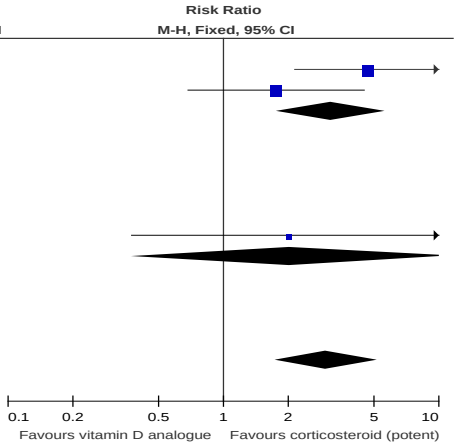


Figure 65: Withdrawal due to lack of effiacy at 4-8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Corticosteroid (potent) Events	Corticosteroid (potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.5.1 Calcipotriol OD vs. betamethasone dipropionate OD						
Jemec 2008	19	234	9	518	41.1%	4.67 [2.15, 10.17]
van de Kerkhof 2009	8	256	9	506	44.4%	1.76 [0.69, 4.50]
Subtotal (95% CI)		**490**		**1024**	**85.4%**	**3.16 [1.76, 5.66]**
Total events	27		18			
Heterogeneity: Chi² = 2.47, df = 1 (P = 0.12); I² = 59%						
Test for overall effect: Z = 3.87 (P = 0.0001)						
6.5.2 Calcipotriol BD vs betamethasone valerate BD						
Klaber 1994	4	224	2	227	14.6%	2.03 [0.37, 10.95]
Subtotal (95% CI)		**224**		**227**	**14.6%**	**2.03 [0.37, 10.95]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.82 (P = 0.41)						
Total (95% CI)		**714**		**1251**	**100.0%**	**2.99 [1.73, 5.19]**
Total events	31		20			
Heterogeneity: Chi² = 2.70, df = 2 (P = 0.26); I² = 26%						
Test for overall effect: Z = 3.91 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.24, df = 1 (P = 0.63), I² = 0%						



J.3.7 Scalp: Vitamin D or vitamin D analogue vs very potent corticosteroid

Figure 102: Investigator's assessment (clear/nearly clear) at 4 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Very potent corticosteroid Events	Very potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.1.1 Calcipotriol (BD) vs clobetasol propionate (OD)						
Reygagne 2005	21	75	38	76	100.0%	0.56 [0.37, 0.86]
Subtotal (95% CI)		**75**		**76**	**100.0%**	**0.56 [0.37, 0.86]**
Total events	21		38			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.66 (P = 0.008)						
Test for subgroup differences: Not applicable						

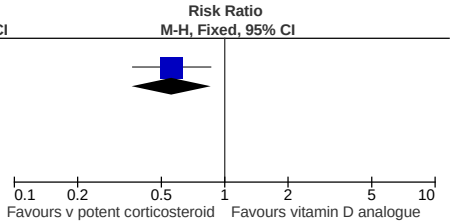


Figure 66: Patient's assessment (clear/nearly clear) at 4 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Very potent corticosteroid Events	Very potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.2.1 Calcipotriol (BD) vs clobetasol propionate (OD)						
Reygagne 2005	23	75	36	76	100.0%	0.65 [0.43, 0.98]
Subtotal (95% CI)		**75**		**76**	**100.0%**	**0.65 [0.43, 0.98]**
Total events	23		36			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.05 (P = 0.04)						
Test for subgroup differences: Not applicable						

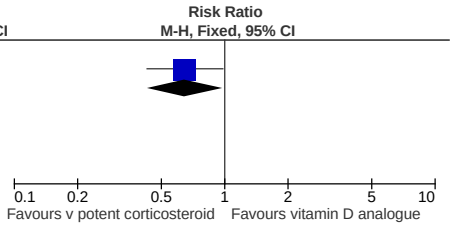
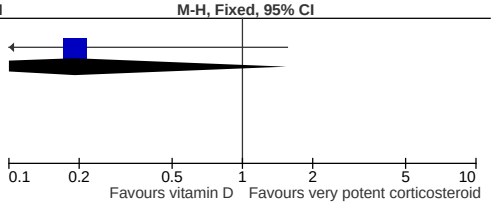


Figure 67: Skin atrophy at 4 weeks

Study or Subgroup	Vitamin D Events	Vitamin D Total	Very potent corticosteroid Events	Very potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.3.1 Calcipotriol (BD) vs clobetasol propionate (OD)						
Reygagne 2005	1	64	6	74	100.0%	0.19 [0.02, 1.56]
Subtotal (95% CI)		**64**		**74**	**100.0%**	**0.19 [0.02, 1.56]**
Total events	1		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						

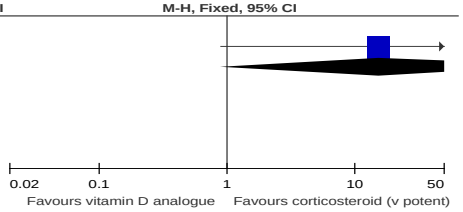


Test for subgroup differences: Not applicable

Figure 68: Withdrawal due to adverse events at 4 weeks

Note: different scale

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Corticosteroid (v potent) Events	Corticosteroid (v potent) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.4.1 Calcipotriol (BD) vs clobetasol propionate (OD)						
Reygagne 2005	7	71	0	73	100.0%	15.42 [0.90, 265.00]
Subtotal (95% CI)		**71**		**73**	**100.0%**	**15.42 [0.90, 265.00]**
Total events	7		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.88 (P = 0.06)						

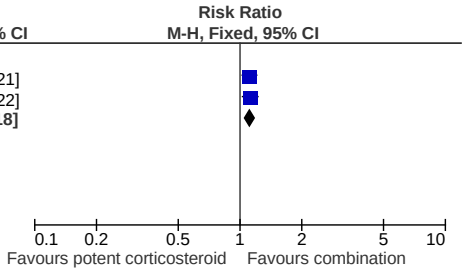


Test for subgroup differences: Not applicable

J.3.8 Scalp: Combined product containing vitamin D analogue and potent corticosteroid vs potent corticosteroid

Figure 69: Investigator's assessment (clear/nearly clear) at 8 weeks

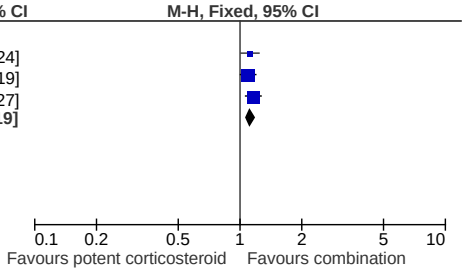
Study or Subgroup	Combination Events	Combination Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.1.1 Combination OD vs. betamethasone dipropionate OD						
Jemec 2008	385	541	356	556	50.5%	1.11 [1.02, 1.21]
van de Kerkhof 2009	388	567	343	562	49.5%	1.12 [1.03, 1.22]
Subtotal (95% CI)		**1108**		**1118**	**100.0%**	**1.12 [1.05, 1.18]**
Total events	773		699			
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%						
Test for overall effect: Z = 3.61 (P = 0.0003)						



Test for subgroup differences: Not applicable

Figure 70: Patient's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.2.1 Combination OD vs. betamethasone dipropionate OD						
Buckley 2008	100	108	91	110	11.7%	1.12 [1.01, 1.24]
Jemec 2008	371	541	348	556	44.5%	1.10 [1.01, 1.19]
van de Kerkhof 2009	395	567	337	562	43.9%	1.16 [1.07, 1.27]
Subtotal (95% CI)		**1216**		**1228**	**100.0%**	**1.13 [1.07, 1.19]**
Total events	866		776			
Heterogeneity: Chi² = 0.91, df = 2 (P = 0.64); I² = 0%						
Test for overall effect: Z = 4.26 (P < 0.0001)						

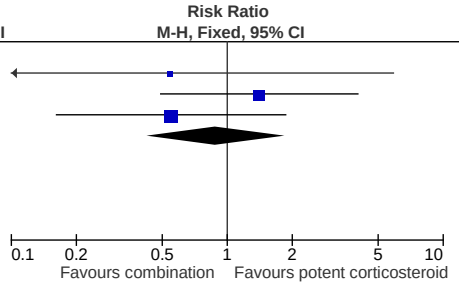


Test for subgroup differences: Not applicable

Figure 71: Withdrawal due to adverse events at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.4.1 Combination OD vs. betamethasone dipropionate OD						
Buckley 2008	1	95	2	103	12.9%	0.54 [0.05, 5.88]
Jemec 2008	8	488	6	515	39.2%	1.41 [0.49, 4.03]
van de Kerkhof 2009	4	524	7	504	47.9%	0.55 [0.16, 1.87]
Subtotal (95% CI)		**1107**		**1122**	**100.0%**	**0.88 [0.42, 1.85]**
Total events	13		15			

Heterogeneity: Chi² = 1.49, df = 2 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.33 (P = 0.74)

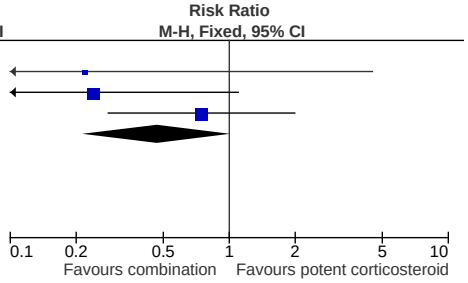


Test for subgroup differences: Not applicable

Figure 72: Withdrawal due to lack of effiacy at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Potent corticosteroid Events	Potent corticosteroid Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.5.1 Combination OD vs. betamethasone dipropionate OD						
Buckley 2008	0	94	2	103	11.8%	0.22 [0.01, 4.50]
Jemec 2008	2	482	9	518	42.9%	0.24 [0.05, 1.10]
van de Kerkhof 2009	7	527	9	506	45.4%	0.75 [0.28, 1.99]
Subtotal (95% CI)		**1103**		**1127**	**100.0%**	**0.47 [0.22, 1.01]**
Total events	9		20			

Heterogeneity: Chi² = 1.86, df = 2 (P = 0.39); I² = 0%
Test for overall effect: Z = 1.94 (P = 0.05)



Test for subgroup differences: Not applicable

J.3.9 Scalp: Conbined product containing potent corticosteroid and vitamin D analogue vs vitamin D or vitamin D analogue

Figure 110: Investigator's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Random, 95% CI
9.1.1 Combination OD vs calcipotriol BD						
Kragballe 2009	142	207	33	105	22.2%	2.18 [1.62, 2.94]
Subtotal (95% CI)		**207**		**105**	**22.2%**	**2.18 [1.62, 2.94]**
Total events	142		33			

Heterogeneity: Not applicable
Test for overall effect: Z = 5.15 (P < 0.00001)

9.1.10 Combination OD vs calcipotriol OD						
Jemec 2008	385	541	100	272	37.4%	1.94 [1.64, 2.28]
van de Kerkhof 2009	388	567	124	286	40.4%	1.58 [1.37, 1.82]
Subtotal (95% CI)		**1108**		**558**	**77.8%**	**1.74 [1.42, 2.13]**
Total events	773		224			

Heterogeneity: Tau² = 0.01; Chi² = 3.37, df = 1 (P = 0.07); I² = 70%
Test for overall effect: Z = 5.42 (P < 0.00001)

Total (95% CI)		**1315**		**663**	**100.0%**	**1.83 [1.52, 2.20]**
Total events	915		257			

Heterogeneity: Tau² = 0.02; Chi² = 5.54, df = 2 (P = 0.06); I² = 64%
Test for overall effect: Z = 6.48 (P < 0.00001)
Test for subgroup differences: Chi² = 1.53, df = 1 (P = 0.22), I² = 34.7%

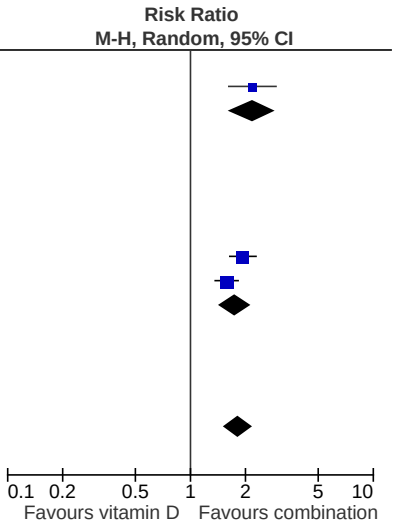


Figure 73: Patient's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.2.1 Combination (OD) vs calcipotriol OD						
Jemec 2008	371	541	104	272	38.8%	1.79 [1.53, 2.11]
van de Kerkhof 2009	395	567	128	286	47.8%	1.56 [1.35, 1.79]
Subtotal (95% CI)		**1108**		**558**	**86.6%**	**1.66 [1.50, 1.85]**
Total events	766		232			
Heterogeneity: Chi² = 1.70, df = 1 (P = 0.19); I² = 41%						
Test for overall effect: Z = 9.41 (P < 0.00001)						
9.2.2 Combination OD vs calcipotriol BD						
Kragballe 2009	170	207	36	105	13.4%	2.40 [1.82, 3.15]
Subtotal (95% CI)		**207**		**105**	**13.4%**	**2.40 [1.82, 3.15]**
Total events	170		36			
Heterogeneity: Not applicable						
Test for overall effect: Z = 6.29 (P < 0.00001)						
Total (95% CI)		**1315**		**663**	**100.0%**	**1.76 [1.60, 1.94]**
Total events	936		268			
Heterogeneity: Chi² = 7.95, df = 2 (P = 0.02); I² = 75%						
Test for overall effect: Z = 11.23 (P < 0.00001)						
Test for subgroup differences: Chi² = 5.99, df = 1 (P = 0.01), I² = 83.3%						

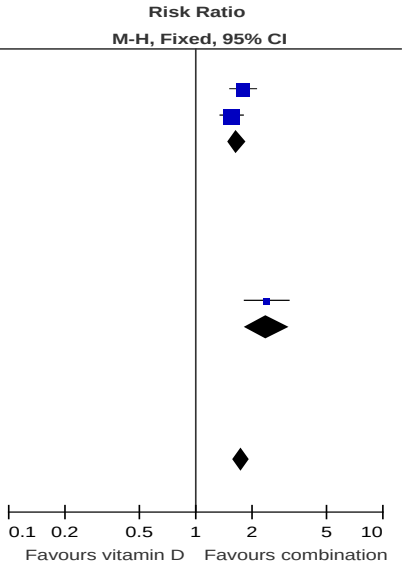


Figure 74: Relapse rate at 8 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.4.1 Combination (OD) vs calcipotriol (BD)						
Kragballe 2009	73	135	10	29	100.0%	1.57 [0.93, 2.65]
Subtotal (95% CI)		**135**		**29**	**100.0%**	**1.57 [0.93, 2.65]**
Total events	73		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.68 (P = 0.09)						
Test for subgroup differences: Not applicable						

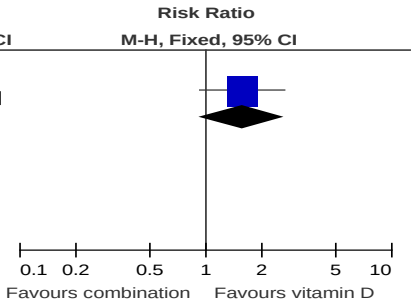


Figure 75: Withdrawal due to adverse events at 8 weeks

Note: different scale

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.5.1 Combination (OD) vs calcipotriol OD						
Jemec 2008	8	488	20	235	54.0%	0.19 [0.09, 0.43]
van de Kerkhof 2009	4	524	8	256	21.5%	0.24 [0.07, 0.80]
Subtotal (95% CI)		**1012**		**491**	**75.6%**	**0.21 [0.11, 0.40]**
Total events	12		28			
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 4.63 (P < 0.00001)						
9.5.2 Combination (OD) vs calcipotriol (BD)						
Kragballe 2009	2	192	9	91	24.4%	0.11 [0.02, 0.48]
Subtotal (95% CI)		**192**		**91**	**24.4%**	**0.11 [0.02, 0.48]**
Total events	2		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.92 (P = 0.004)						
Total (95% CI)		**1204**		**582**	**100.0%**	**0.18 [0.10, 0.33]**
Total events	14		37			
Heterogeneity: Chi² = 0.76, df = 2 (P = 0.69); I² = 0%						
Test for overall effect: Z = 5.51 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.65, df = 1 (P = 0.42), I² = 0%						

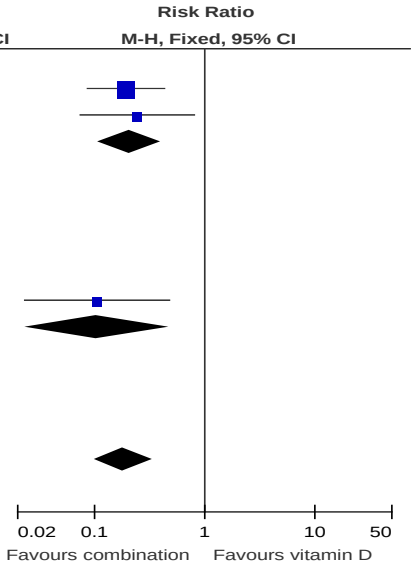


Figure 76: Withdrawal due to adverse events at 52 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.7.1 Combination (OD) vs calcipotriol OD						
Luger 2008	9	346	44	309	100.0%	0.18 [0.09, 0.37]
Subtotal (95% CI)		**346**		**309**	**100.0%**	**0.18 [0.09, 0.37]**
Total events	9		44			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.76 (P < 0.00001)						
Test for subgroup differences: Not applicable						

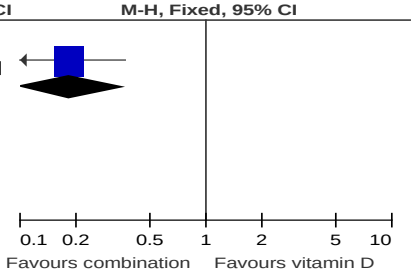


Figure 77: Withdrawal due to treatment failure at 8 weeks

Note: different scale

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Random, 95% CI
9.6.2 Combination (OD) vs calcipotriol OD						
Jemec 2008	2	482	19	234	47.1%	0.05 [0.01, 0.22]
van de Kerkhof 2009	7	527	8	256	52.9%	0.43 [0.16, 1.16]
Subtotal (95% CI)		**1009**		**490**	**100.0%**	**0.16 [0.02, 1.35]**
Total events	9		27			
Heterogeneity: Tau² = 2.02; Chi² = 5.99, df = 1 (P = 0.01); I² = 83%						
Test for overall effect: Z = 1.69 (P = 0.09)						
Test for subgroup differences: Not applicable						

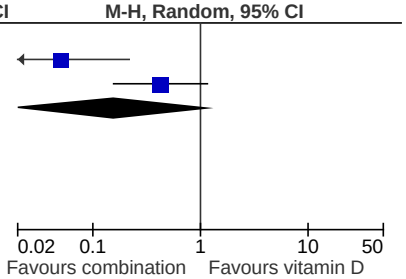
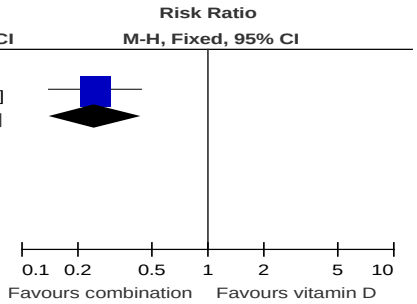


Figure 78: Withdrawal due to treatment failure at 52 weeks

Study or Subgroup	Combination Events	Combination Total	Vitamin D Events	Vitamin D Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.8.2 Combination (OD) vs calcipotriol OD						
Luger 2008	14	351	51	316	100.0%	0.25 [0.14, 0.44]
Subtotal (95% CI)		**351**		**316**	**100.0%**	**0.25 [0.14, 0.44]**
Total events	14		51			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.79 (P < 0.00001)						

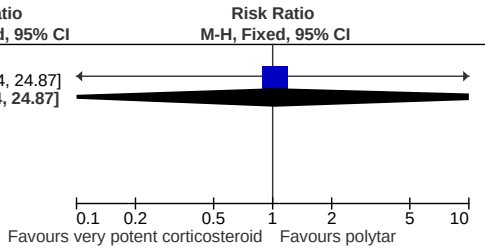


Test for subgroup differences: Not applicable

1.1.2 Scalp: Very potent corticosteroid vs coal tar polytherapy

Figure 79: Withdrawal due to adverse events at 4 weeks

Study or Subgroup	Very potent corticosteroid Events	Very potent corticosteroid Total	Polytar Events	Polytar Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.2.1 Clobetasol propionate vs polytar						
Griffiths 2006A	1	121	0	41	100.0%	1.03 [0.04, 24.87]
Subtotal (95% CI)		**121**		**41**	**100.0%**	**1.03 [0.04, 24.87]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.98)						

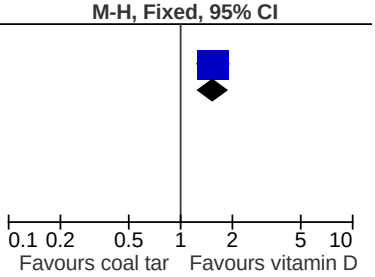


Test for subgroup differences: Not applicable

J.3.10 Scalp: Vitamin D or vitamin D analogue vs coal tar polytherapy

Figure 80: Investigator's assessment (at least moderate improvement) at 8 weeks

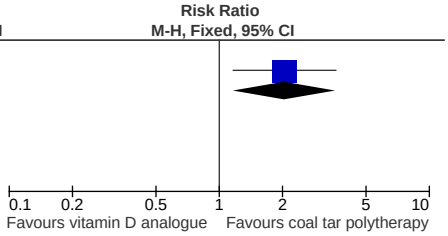
Study or Subgroup	Vitamin D Events	Vitamin D Total	Coal tar Events	Coal tar Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.1.1 Calcipotriol BD vs. coal tar polytherapy OD						
McKinnon 2000	120	210	79	213	100.0%	1.54 [1.25, 1.90]
Subtotal (95% CI)		**210**		**213**	**100.0%**	**1.54 [1.25, 1.90]**
Total events	120		79			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.02 (P < 0.0001)						



Test for subgroup differences: Not applicable

Figure 81: Withdrawals due to adverse events at 8 weeks

Study or Subgroup	Vitamin D analogue Events	Vitamin D analogue Total	Coal tar polytherapy Events	Coal tar polytherapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.2.1 Calcipotriol BD vs. coal tar polytherapy OD						
McKinnon 2000	35	230	16	215	100.0%	2.04 [1.17, 3.59]
Subtotal (95% CI)		**230**		**215**	**100.0%**	**2.04 [1.17, 3.59]**
Total events	35		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.50 (P = 0.01)						



Test for subgroup differences: Not applicable

1.1.3 Face and flexures: Tacrolimus vs placebo

Figure 82: Investigator's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Tacrolimus Events	Tacrolimus Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lebwohl 2004	73	112	17	55	100.0%	2.11 [1.39, 3.20]
Total (95% CI)		**112**		**55**	**100.0%**	**2.11 [1.39, 3.20]**
Total events	73		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.50 (P = 0.0005)

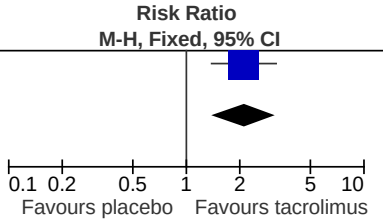


Figure 83: Withdrawal due to adverse events at 8 weeks

Note: different scale

Study or Subgroup	Tacrolimus Events	Tacrolimus Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lebwohl 2004	0	98	1	40	100.0%	0.14 [0.01, 3.32]
Total (95% CI)		**98**		**40**	**100.0%**	**0.14 [0.01, 3.32]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.22 (P = 0.22)

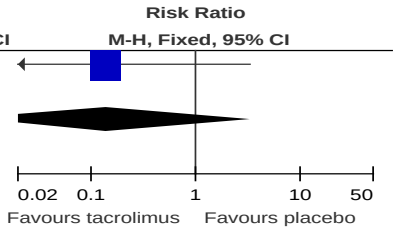
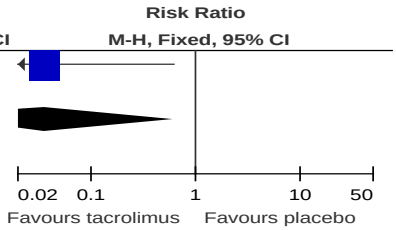


Figure 84: Withdrawal due to lack of efficacy at 8 weeks

Note: different scale

Study or Subgroup	Tacrolimus Events	Tacrolimus Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lebwohl 2004	0	98	6	45	100.0%	0.04 [0.00, 0.62]
Total (95% CI)		**98**		**45**	**100.0%**	**0.04 [0.00, 0.62]**
Total events	0		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.29 (P = 0.02)



J.3.11 Face and flexures: pimecrolimus vs placebo

Figure 85: Investigator's assessment (clear/nearly clear) at 8 weeks

Study or Subgroup	Pimecrolimus Events	Pimecrolimus Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Gribetz 2004	20	28	6	29	100.0%	3.45 [1.63, 7.31]
Total (95% CI)		**28**		**29**	**100.0%**	**3.45 [1.63, 7.31]**
Total events	20		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.24 (P = 0.001)

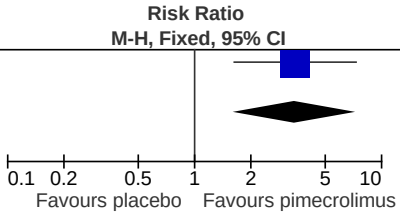
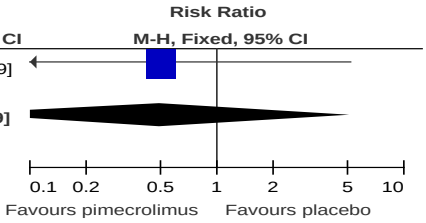


Figure 86: Withdrawal due to lack of efficacy at 8 weeks

Study or Subgroup	Pimecrolimus Events	Pimecrolimus Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Gribetz 2004	1	27	2	27	100.0%	0.50 [0.05, 5.19]
Total (95% CI)		**27**		**27**	**100.0%**	**0.50 [0.05, 5.19]**
Total events	1		2			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.58 (P = 0.56)



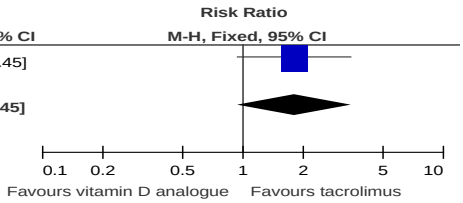
J.3.12 Face and flexures: tacrolimus vs vitamin D or vitamin D analogue

Figure 87: Investigator's assessment (clear/nearly clear) at 6 weeks

Study or Subgroup	Tacrolimus Events	Tacrolimus Total	Vitamin D analogue Events	Vitamin D analogue Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liao 2007	15	25	8	24	100.0%	1.80 [0.94, 3.45]
Total (95% CI)		**25**		**24**	**100.0%**	**1.80 [0.94, 3.45]**
Total events	15		8			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.77 (P = 0.08)



J.4 Phototherapy

J.4.1 Broadband vs narrowband UVB

Figure 88: Clear at the end of treatment

Study or Subgroup	NBUVB Events	NBUVB Total	BBUVB Events	BBUVB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kirke 2007	28	44	20	41	100.0%	1.30 [0.89, 1.92]
Total (95% CI)		**44**		**41**	**100.0%**	**1.30 [0.89, 1.92]**
Total events	28		20			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.35 (P = 0.18)

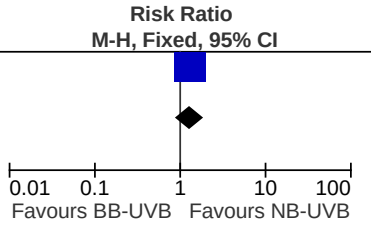


Figure 89: Clear at 3 months post-treatment

Study or Subgroup	NBUVB Events	NBUVB Total	BBUVB Events	BBUVB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kirke 2007	4	25	8	18	100.0%	0.36 [0.13, 1.01]
Total (95% CI)		**25**		**18**	**100.0%**	**0.36 [0.13, 1.01]**
Total events	4		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)

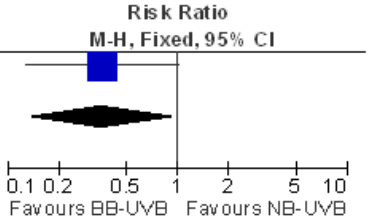


Figure 90: Clear at 6 months post-treatment

Study or Subgroup	NBUVB Events	NBUVB Total	BBUVB Events	BBUVB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kirke 2007	1	19	0	13	100.0%	2.10 [0.09, 47.89]
Total (95% CI)		**19**		**13**	**100.0%**	**2.10 [0.09, 47.89]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.47 (P = 0.64)

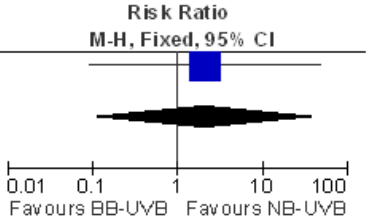
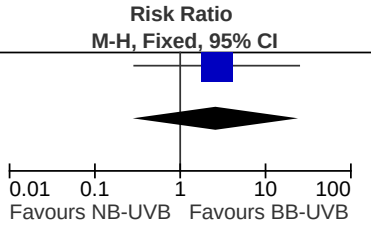


Figure 91: Withdrawal due to toxicity

Study or Subgroup	NBUVB Events	NBUVB Total	BBUVB Events	BBUVB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kirke 2007	3	47	1	42	100.0%	2.68 [0.29, 24.80]
Total (95% CI)		**47**		**42**	**100.0%**	**2.68 [0.29, 24.80]**
Total events	3		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.87 (P = 0.38)



J.4.2 Narrowband vs PUVA

1.1.3.1 Oral PUVA (between patient randomisation)

Figure 92: Clear/nearly clear on PGA at end of treatment (maximum 30-40 exposures)

Study or Subgroup	NBUVB Events	NBUVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Gordon 1999	32	47	41	44	55.5%	0.73 [0.59, 0.90]
Yones 2006	23	38	34	38	44.5%	0.68 [0.51, 0.89]
Total (95% CI)		**85**		**82**	**100.0%**	**0.71 [0.60, 0.84]**
Total events	55		75			

Heterogeneity: Chi² = 0.19, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 4.00 (P < 0.0001)

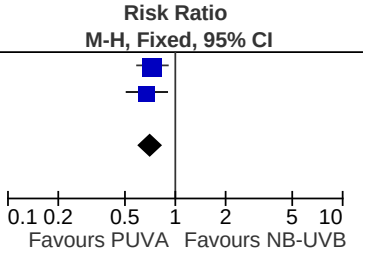


Figure 93: Clear/nearly clear on PGA at end of treatment (maximum 30 exposures; post-hoc skin type subgroup analysis)

Study or Subgroup	NBUVB Events	NBUVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.10.1 Skin type I-IV						
Yones 2006	22	34	31	37	88.4%	0.77 [0.58, 1.03]
Subtotal (95% CI)		**34**		**37**	**88.4%**	**0.77 [0.58, 1.03]**
Total events	22		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.77 (P = 0.08)						
3.10.2 Skin type V-VI						
Yones 2006	1	11	3	6	11.6%	0.18 [0.02, 1.39]
Subtotal (95% CI)		**11**		**6**	**11.6%**	**0.18 [0.02, 1.39]**
Total events	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.64 (P = 0.10)						
Total (95% CI)		**45**		**43**	**100.0%**	**0.70 [0.53, 0.94]**
Total events	23		34			

Heterogeneity: Chi² = 2.11, df = 1 (P = 0.15); I² = 53%
Test for overall effect: Z = 2.37 (P = 0.02)
Test for subgroup differences: Chi² = 1.91, df = 1 (P = 0.17), I² = 47.6%

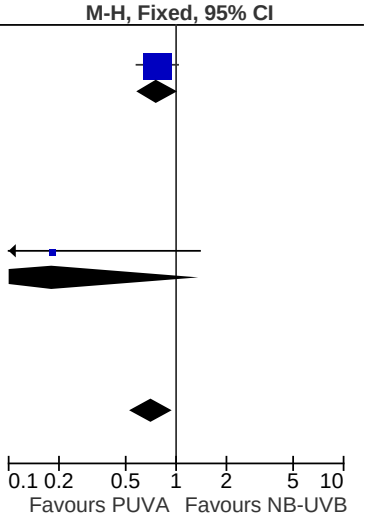


Figure 94: Mean time to PASI75 (weeks) after maximum follow-up of 4 months

Study or Subgroup	NBUVB Mean	NBUVB SD	NBUVB Total	PUVA Mean	PUVA SD	PUVA Total	Weight	Mean Difference IV, Fixed, 95% CI
Chauhan 2011	9.9	3.3	21	9.9	3.5	22	100.0%	0.00 [-2.03, 2.03]
Total (95% CI)			**21**			**22**	**100.0%**	**0.00 [-2.03, 2.03]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

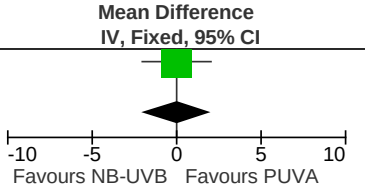


Figure 95: Mean time to clearance (days) after maximum follow-up of 3 months

Study or Subgroup	NBUVB Mean	NBUVB SD	NBUVB Total	PUVA Mean	PUVA SD	PUVA Total	Weight	Mean Difference IV, Fixed, 95% CI
Dayal 2010	65.6	14.59	30	49.2	20.8	30	100.0%	16.40 [7.31, 25.49]
Total (95% CI)			**30**			**30**	**100.0%**	**16.40 [7.31, 25.49]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.54 (P = 0.0004)

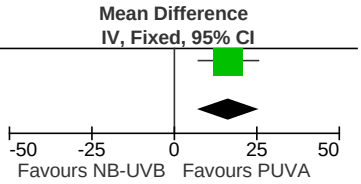


Figure 96: PASI75 at 3-4 months or a maximum of 20 treatments

Study or Subgroup	NBUVB Events	NBUVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 Skin type IV-V (follow-up 3-4 months)						
Chauhan 2011	17	21	18	22	26.2%	0.99 [0.74, 1.32]
Dayal 2010	30	30	30	30	45.5%	1.00 [0.94, 1.07]
Subtotal (95% CI)		**51**		**52**	**71.7%**	**1.00 [0.89, 1.11]**
Total events	47		48			
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.90); I² = 0%						
Test for overall effect: Z = 0.07 (P = 0.95)						
2.5.2 Skin type II-II (follow-up 20 treatments)						
Serwin 2007	21	25	19	25	28.3%	1.11 [0.84, 1.46]
Subtotal (95% CI)		**25**		**25**	**28.3%**	**1.11 [0.84, 1.46]**
Total events	21		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.48)						
Total (95% CI)		**76**		**77**	**100.0%**	**1.03 [0.92, 1.15]**
Total events	68		67			
Heterogeneity: Chi² = 1.00, df = 2 (P = 0.61); I² = 0%						
Test for overall effect: Z = 0.46 (P = 0.65)						
Test for subgroup differences: Chi² = 0.46, df = 1 (P = 0.50), I² = 0%						

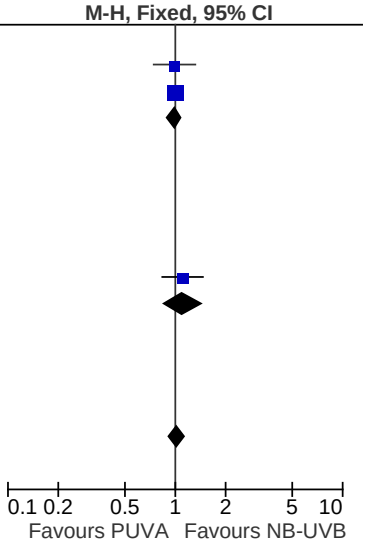


Figure 97: Final PASI after up to 20 treatments

Study or Subgroup	NBUVB Mean	NBUVB SD	NBUVB Total	PUVA Mean	PUVA SD	PUVA Total	Weight	Mean Difference IV, Fixed, 95% CI
2.7.2 Three-times weekly UV								
Serwin 2007	4.42	1.67	25	5.5	2.1	25	19.2%	-1.08 [-2.13, -0.03]
Subtotal (95% CI)			**25**			**25**	**19.2%**	**-1.08 [-2.13, -0.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.01 (P = 0.04)								
2.7.3 Twice weekly UV								
Dayal 2010	1.6	1.2	30	1.39	0.78	30	80.8%	0.21 [-0.30, 0.72]
Subtotal (95% CI)			**30**			**30**	**80.8%**	**0.21 [-0.30, 0.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.80 (P = 0.42)								
Total (95% CI)			**55**			**55**	**100.0%**	**-0.04 [-0.50, 0.42]**
Heterogeneity: Chi² = 4.67, df = 1 (P = 0.03); I² = 79%								
Test for overall effect: Z = 0.16 (P = 0.87)								
Test for subgroup differences: Chi² = 4.67, df = 1 (P = 0.03), I² = 78.6%								

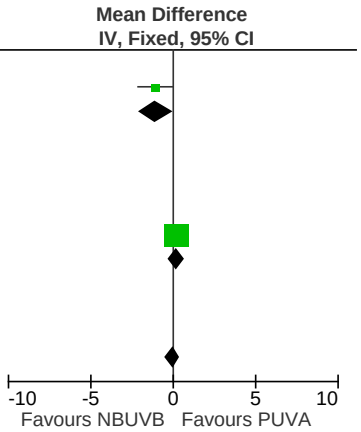


Figure 98: Relapse rate for clearers (6 or 12 months post-treatment)

Study or Subgroup	NBUVB Events	NBUVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.10.1 6 months						
Chauhan 2011	11	15	8	14	18.5%	1.28 [0.74, 2.22]
Gordon 1999	24	31	19	36	39.3%	1.47 [1.02, 2.11]
Yones 2006	15	23	11	34	19.8%	2.02 [1.14, 3.57]
Subtotal (95% CI)		**69**		**84**	**77.6%**	**1.56 [1.19, 2.05]**
Total events	50		38			
Heterogeneity: Chi² = 1.38, df = 2 (P = 0.50); I² = 0%						
Test for overall effect: Z = 3.24 (P = 0.001)						
2.10.2 12 months						
Markham 2003	17	24	9	19	22.4%	1.50 [0.87, 2.56]
Subtotal (95% CI)		**24**		**19**	**22.4%**	**1.50 [0.87, 2.56]**
Total events	17		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.14)						
Total (95% CI)		**93**		**103**	**100.0%**	**1.55 [1.22, 1.97]**
Total events	67		47			
Heterogeneity: Chi² = 1.38, df = 3 (P = 0.71); I² = 0%						
Test for overall effect: Z = 3.54 (P = 0.0004)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.88), I² = 0%						

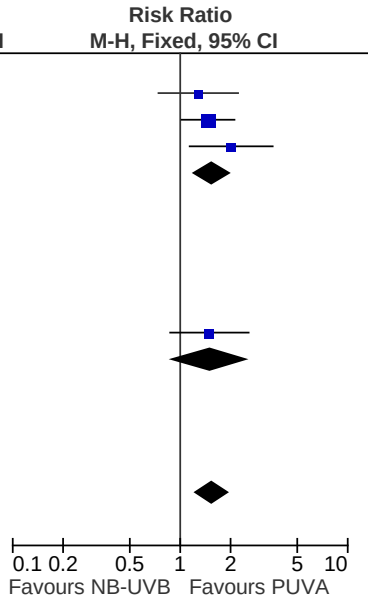
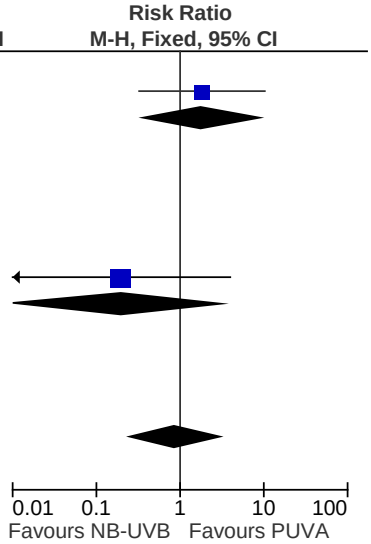


Figure 99: Withdrawal due to toxicity after a maximum of 30-40 treatments

Study or Subgroup	NBUVB Events	NBUVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.9.1 Skin type I-VI						
Yones 2006	3	32	2	39	41.6%	1.83 [0.33, 10.28]
Subtotal (95% CI)		**32**		**39**	**41.6%**	**1.83 [0.33, 10.28]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
3.9.2 Skin type I-IV						
Gordon 1999	0	47	2	46	58.4%	0.20 [0.01, 3.97]
Subtotal (95% CI)		**47**		**46**	**58.4%**	**0.20 [0.01, 3.97]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
Total (95% CI)		**79**		**85**	**100.0%**	**0.88 [0.23, 3.31]**
Total events	3		4			
Heterogeneity: Chi² = 1.65, df = 1 (P = 0.20); I² = 39%						
Test for overall effect: Z = 0.20 (P = 0.84)						
Test for subgroup differences: Chi² = 1.59, df = 1 (P = 0.21), I² = 37.2%						



J.4.3 Bath PUVA (within patient randomisation)

Figure 100: Time-to-remission (clearance or minimal residual activity) after a maximum of 30 treatments

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Dawe 2003	1.2613	0.2924	100.0%	3.53 [1.99, 6.26]
Total (95% CI)			**100.0%**	**3.53 [1.99, 6.26]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 4.31 (P < 0.0001)				

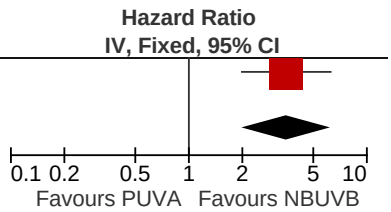


Figure 101: Mean change in PASI at 10 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Snellman 2004	2.714286	0.622372	100.0%	2.71 [1.49, 3.93]
Total (95% CI)			**100.0%**	**2.71 [1.49, 3.93]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.36 (P < 0.0001)

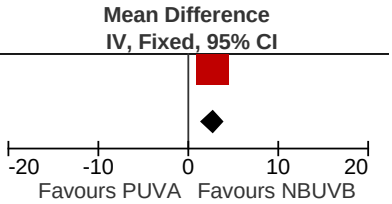


Figure 102: Mean time to relapse (days) after a maximum of 30 exposures

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Dawe 2003	39.27	15.59009	100.0%	39.27 [8.71, 69.83]
Total (95% CI)			**100.0%**	**39.27 [8.71, 69.83]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.52 (P = 0.01)

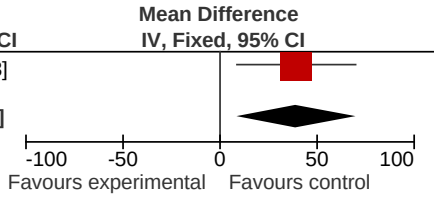


Figure 103: Withdrawal due to toxicity at 10 weeks

Note different scale

Study or Subgroup	NB-UVB Events	NB-UVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Snellman 2004	0	15	1	15	100.0%	0.33 [0.01, 7.58]
Total (95% CI)		**15**		**15**	**100.0%**	**0.33 [0.01, 7.58]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)

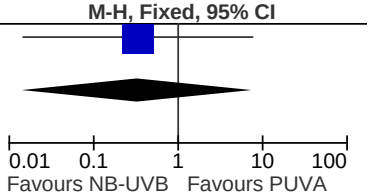
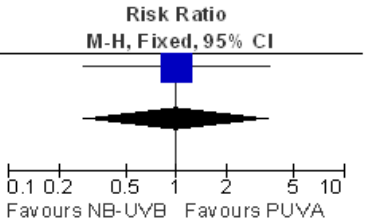


Figure 104: Burn after maximum of 30 treatments

Study or Subgroup	NB-UVB Events	NB-UVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dawe 2003	4	28	4	28	100.0%	1.00 [0.28, 3.61]
Total (95% CI)		**28**		**28**	**100.0%**	**1.00 [0.28, 3.61]**
Total events	4		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

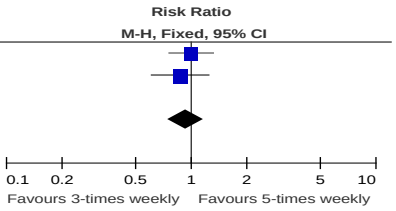


J.4.4 NBUVB five-times vs three-times weekly

Figure 105: Clearance at 4.7-23 weeks or a maximum of 30 treatments

Study or Subgroup	Favours 3-times weekly Events	Total	3-times weekly TL01 Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dawe 1998	16	19	16	19	47.6%	1.00 [0.76, 1.32]
Hallaji 2010	15	22	18	23	52.4%	0.87 [0.61, 1.25]
Total (95% CI)		**41**		**42**	**100.0%**	**0.93 [0.74, 1.17]**
Total events	31		34			

Heterogeneity: Chi² = 0.39, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)



J.4.5 NBUVB two-times vs three-times weekly

Between patient

Figure 106: Clearance

Study or Subgroup	TL01 twice weekly Events	Total	TL01 three-times weekly Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cameron 2002	40	44	44	48	100.0%	0.99 [0.87, 1.13]
Total (95% CI)		**44**		**48**	**100.0%**	**0.99 [0.87, 1.13]**
Total events	40		44			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.13 (P = 0.90)

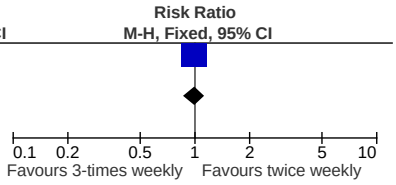


Figure 107: Withdrawal due to toxicity

Note different scale

Study or Subgroup	TL01 twice weekly Events	Total	TL01 three-times weekly Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cameron 2002	2	42	1	45	100.0%	2.14 [0.20, 22.77]
Total (95% CI)		**42**		**45**	**100.0%**	**2.14 [0.20, 22.77]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

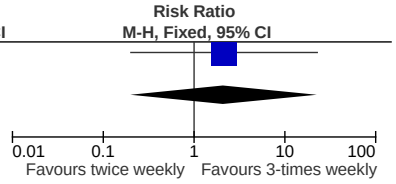
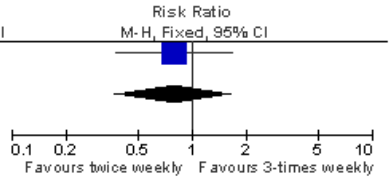


Figure 108: Burn

Study or Subgroup	TL01 twice weekly Events	Total	TL01 three-times weekly Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cameron 2002	10	58	12	55	100.0%	0.79 [0.37, 1.68]
Total (95% CI)		58		55	100.0%	0.79 [0.37, 1.68]
Total events	10		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.61 (P = 0.54)



J.4.6 Oral PUVA three-times vs two-times weekly

Within and between patient

Figure 109: Clear/nearly clear on IAGI at 12 weeks

Study or Subgroup	PUVA three-times weekly Events	Total	PUVA twice weekly Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
El-Mofty 2008	4	9	9	10	100.0%	0.49 [0.23, 1.05]
Total (95% CI)		9		10	100.0%	0.49 [0.23, 1.05]
Total events	4		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.82 (P = 0.07)

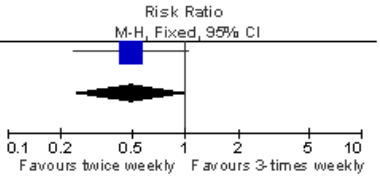


Figure 110: Percentage change in PASI at 12 weeks

Study or Subgroup	PUVA three-times weekly Mean	SD	Total	PUVA twice weekly Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
El-Mofty 2008	66.88	29.31	9	82.31	18.22	10	100.0%	-15.43 [-37.66, 6.80]
Total (95% CI)			9			10	100.0%	-15.43 [-37.66, 6.80]

Heterogeneity: Not applicable
Test for overall effect: Z = 1.36 (P = 0.17)

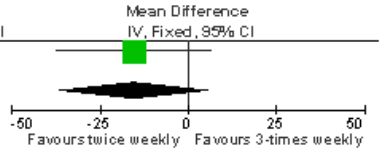
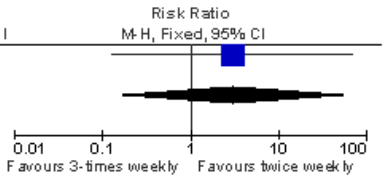


Figure 111: Burn after a maximum of 25 treatments

Note different scale

Study or Subgroup	Three-times weekly PUVA Events	Total	Twice weekly PUVA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Valbuena 2007	1	23	0	23	100.0%	3.00 [0.13, 70.02]
Total (95% CI)		23		23	100.0%	3.00 [0.13, 70.02]
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.49)



J.4.7 Oral hand and foot PUVA vs no treatment for palmoplantar pustulosis

Figure 112: Clearance at 7.5-12 weeks

Note different scale

Study or Subgroup	Oral PUVA Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Murray 1980	12	22	0	22	50.0%	25.00 [1.57, 397.76]
Rosen 1987	3	12	0	12	50.0%	7.00 [0.40, 122.44]
Total (95% CI)		**34**		**34**	**100.0%**	**16.00 [2.23, 114.89]**
Total events	15		0			

Heterogeneity: Chi² = 0.42, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 2.76 (P = 0.006)

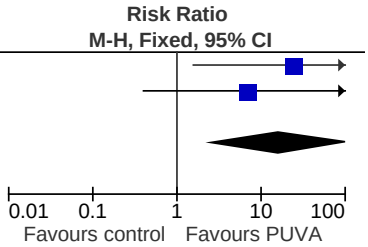


Figure 113: Improved at 7.5-12 weeks

Study or Subgroup	Oral PUVA Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Murray 1980	22	22	13	22	77.1%	1.67 [1.18, 2.36]
Rosen 1987	10	12	4	12	22.9%	2.50 [1.08, 5.79]
Total (95% CI)		**34**		**34**	**100.0%**	**1.86 [1.32, 2.60]**
Total events	32		17			

Heterogeneity: Chi² = 0.85, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 3.59 (P = 0.0003)

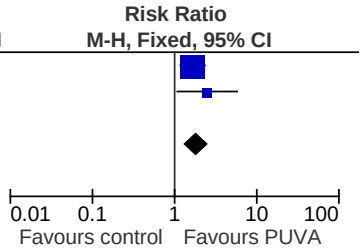


Figure 114: Withdrawal due to toxicity at 7.5-12 weeks

Note different scale

Study or Subgroup	Oral PUVA Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Murray 1980	0	22	0	22		Not estimable
Rosen 1987	1	13	0	12	100.0%	2.79 [0.12, 62.48]
Total (95% CI)		**35**		**34**	**100.0%**	**2.79 [0.12, 62.48]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.52)

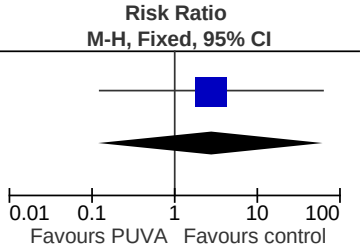


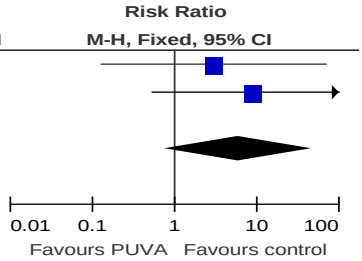
Figure 115: Burn at 7.5-12 weeks

Note different scale

Study or Subgroup	Oral PUVA Events	Oral PUVA Total	No treatment Events	No treatment Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Murray 1980	1	22	0	22	50.0%	3.00 [0.13, 69.87]
Rosen 1987	4	12	0	12	50.0%	9.00 [0.54, 150.81]
Total (95% CI)		**34**		**34**	**100.0%**	**6.00 [0.77, 46.79]**
Total events	5		0			

Heterogeneity: Chi² = 0.27, df = 1 (P = 0.61); I² = 0%

Test for overall effect: Z = 1.71 (P = 0.09)



J.4.8 Cream hand and foot PUVA vs NBUVB for palmoplantar pustulosis

Figure 116: Clear/nearly clear on IAGI at 9 weeks

Study or Subgroup	NB-UVB Events	NB-UVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sezer 2007	9	21	20	21	100.0%	0.45 [0.27, 0.74]
Total (95% CI)		**21**		**21**	**100.0%**	**0.45 [0.27, 0.74]**
Total events	9		20			

Heterogeneity: Not applicable

Test for overall effect: Z = 3.11 (P = 0.002)

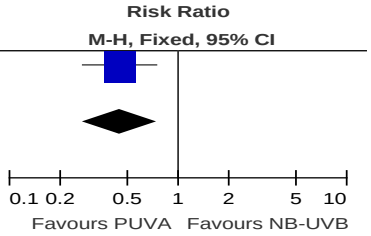


Figure 117: Withdrawal due to toxicity at 9 weeks

Note different scale

Study or Subgroup	NB-UVB Events	NB-UVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sezer 2007	0	21	1	22	100.0%	0.35 [0.01, 8.11]
Total (95% CI)		**21**		**22**	**100.0%**	**0.35 [0.01, 8.11]**
Total events	0		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.66 (P = 0.51)

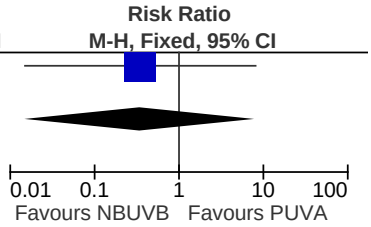
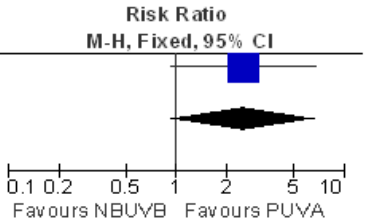


Figure 118: Relapse 10 weeks post-treatment

Study or Subgroup	NB-UVB Events	NB-UVB Total	PUVA Events	PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sezer 2007	10	21	4	21	100.0%	2.50 [0.93, 6.72]
Total (95% CI)		**21**		**21**	**100.0%**	**2.50 [0.93, 6.72]**
Total events	10		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.82 (P = 0.07)



J.4.9 Home vs hospital UVB for psoriasis

Figure 119: Clear/nearly clear (PASI90) at a maximum of 46 treatments

Study or Subgroup	Home Events	Home Total	Hospital Events	Hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Koek 2009	18	94	16	91	100.0%	1.09 [0.59, 2.00]
Total (95% CI)		**94**		**91**	**100.0%**	**1.09 [0.59, 2.00]**
Total events	18		16			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.27 (P = 0.78)

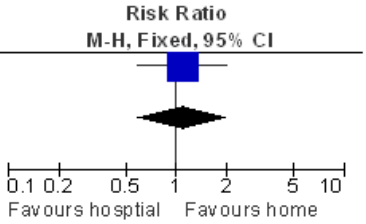


Figure 120: PASI75 at a maximum of 46 treatments

Study or Subgroup	Home Events	Home Total	Hospital Events	Hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Koek 2009	37	94	35	91	100.0%	1.02 [0.71, 1.47]
Total (95% CI)		**94**		**91**	**100.0%**	**1.02 [0.71, 1.47]**
Total events	37		35			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.13 (P = 0.90)

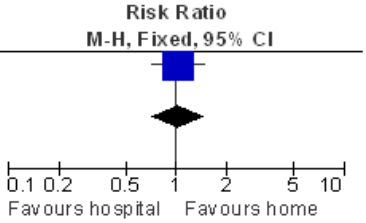
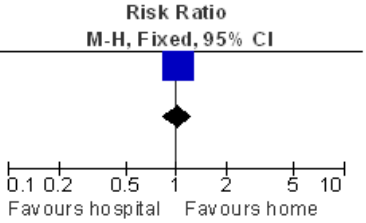


Figure 121: PASI50 at a maximum of 46 treatments

Study or Subgroup	Home Events	Home Total	Hospital Events	Hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Koek 2009	64	94	61	91	100.0%	1.02 [0.83, 1.24]
Total (95% CI)		**94**		**91**	**100.0%**	**1.02 [0.83, 1.24]**
Total events	64		61			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.15 (P = 0.88)



J.5 Phototherapy combined with acitretin

J.5.1 Acitretin vs acitretin plus BBUVB

Figure 122: Clear/nearly clear on IAGI at a maximum of 30 treatments

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
IEST1989	2.5649	0.4082489	100.0%	13.00 [5.84, 28.94]
Total (95% CI)			**100.0%**	**13.00 [5.84, 28.94]**

Heterogeneity: Not applicable
Test for overall effect: Z = 6.28 (P < 0.00001)

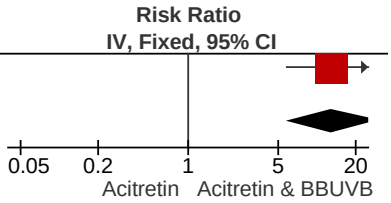
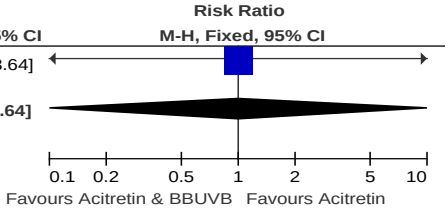


Figure 123: Withdrawal due to drug toxicity at a maximum of 30 treatments

Study or Subgroup	Acitretin Events	Acitretin Total	Acitretin & BBUVB Events	Acitretin & BBUVB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IEST1989	1	9	1	9	100.0%	1.00 [0.07, 13.64]
Total (95% CI)		**9**		**9**	**100.0%**	**1.00 [0.07, 13.64]**
Total events	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



J.5.2 Acitretin plus BBUVB vs Placebo plus BBUVB

Figure 124: Clear/nearly clear on IAGI at 8 weeks

Study or Subgroup	Acitretin & BBUVB Events	Acitretin & BBUVB Total	Placebo & BBUVB Events	Placebo & BBUVB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RUZICKA1990	16	40	6	38	100.0%	2.53 [1.11, 5.79]
Total (95% CI)		**40**		**38**	**100.0%**	**2.53 [1.11, 5.79]**
Total events	16		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.20 (P = 0.03)

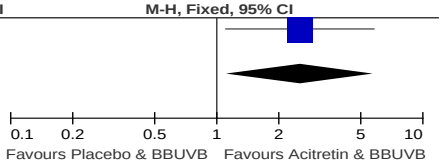
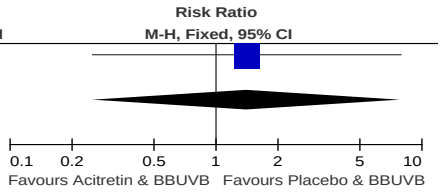


Figure 125: Withdrawal due to drug toxicity at 8 weeks

Study or Subgroup	Acitretin & BBUVB Events	Acitretin & BBUVB Total	Placebo & BBUVB Events	Placebo & BBUVB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RUZICKA1990	3	34	2	32	100.0%	1.41 [0.25, 7.91]
Total (95% CI)		**34**		**32**	**100.0%**	**1.41 [0.25, 7.91]**
Total events	3		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.69)



J.5.3 Acritretin plus NBUVB versus Acitretin plus PUVA

Figure 126: PASI75 at 8 weeks

Study or Subgroup	Acitretin & TL-01 Events	Acitretin & TL-01 Total	Acitretin & PUVA Events	Acitretin & PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OZDEMIR2008	17	30	19	30	100.0%	0.89 [0.59, 1.35]
Total (95% CI)		**30**		**30**	**100.0%**	**0.89 [0.59, 1.35]**
Total events	17		19			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.53 (P = 0.60)

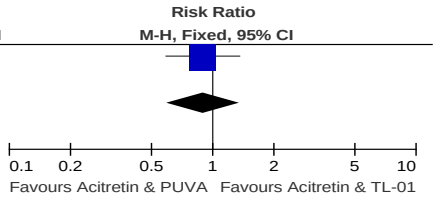


Figure 127: PASI50 at 8 weeks

Study or Subgroup	Acitretin & TL-01 Events	Acitretin & TL-01 Total	Acitretin & PUVA Events	Acitretin & PUVA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OZDEMIR2008	21	30	23	30	100.0%	0.91 [0.67, 1.24]
Total (95% CI)		**30**		**30**	**100.0%**	**0.91 [0.67, 1.24]**
Total events	21		23			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)

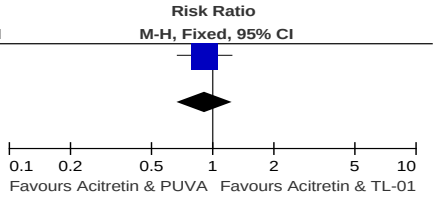


Figure 128: Number of UV treatments at 8 weeks

Study or Subgroup	Acitretin & TL-01 Mean	SD	Total	Acitretin & PUVA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
OZDEMIR2008	20.7	5.1	30	20.4	6.5	30	100.0%	0.30 [-2.66, 3.26]
Total (95% CI)			30			30	100.0%	0.30 [-2.66, 3.26]

Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)

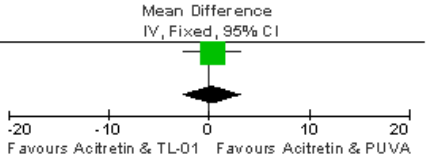


Figure 129: Maintenance of remission (at 3 months)

Study or Subgroup	Acitretin & TL-01 Events	Total	Acitretin & PUVA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OZDEMIR2008	17	17	19	19	100.0%	1.00 [0.90, 1.11]
Total (95% CI)		**17**		**19**	**100.0%**	**1.00 [0.90, 1.11]**
Total events	17		19			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

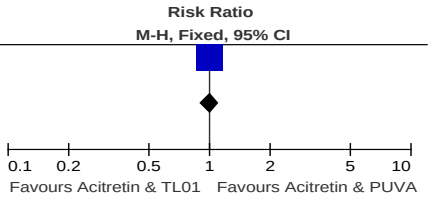


Figure 130: Burn at 8 weeks

Study or Subgroup	Acitretin & TL-01 Events	Total	Acitretin & PUVA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OZDEMIR2008	1	30	0	30	100.0%	3.00 [0.13, 70.83]
Total (95% CI)		30		30	100.0%	3.00 [0.13, 70.83]
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)

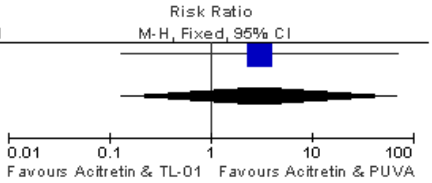
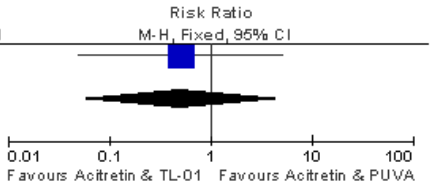


Figure 131: Withdrawal due to drug toxicity at 8 weeks

Study or Subgroup	Acitretin & TL-01 Events	Total	Acitretin & PUVA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OZDEMIR2008	1	30	2	30	100.0%	0.50 [0.05, 5.22]
Total (95% CI)		30		30	100.0%	0.50 [0.05, 5.22]
Total events	1		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



J.5.4 Acitretin plus PUVA vs Placebo plus PUVA

Figure 132: Clear or nearly clear on IAGI at 8-12 weeks

Study or Subgroup	Acitretin & PUVA Events	Total	Placebo & PUVA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SAURAT1988	17	18	16	20	28.8%	1.18 [0.92, 1.51]
SOMMERBERG1993	28	40	19	43	34.8%	1.58 [1.07, 2.35]
TANEW1991	22	23	20	25	36.4%	1.20 [0.96, 1.48]
Total (95% CI)		**81**		**88**	**100.0%**	**1.33 [1.11, 1.59]**
Total events	67		55			

Heterogeneity: Chi² = 2.55, df = 2 (P = 0.28); I² = 22%
Test for overall effect: Z = 3.08 (P = 0.002)

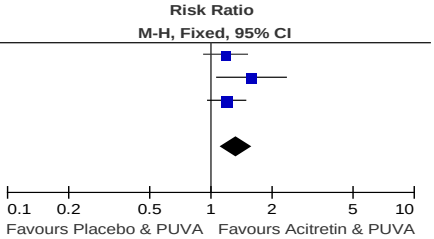


Figure 133: Time to remission after a maximum of 12 weeks

Study or Subgroup	Acitretin & PUVA Mean	SD	Total	Placebo & PUVA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
SAURAT1988	47.8	9.5	18	65.4	16.4	20	100.0%	-17.60 [-26.02, -9.18]
Total (95% CI)			18			20	100.0%	-17.60 [-26.02, -9.18]

Heterogeneity: Not applicable
Test for overall effect: Z = 4.10 (P < 0.0001)

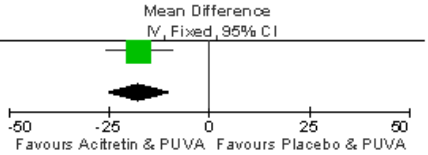


Figure 134: Mean number of UVA treatments after a maximum of 8 weeks

Study or Subgroup	Acitretin & PUVA Mean	SD	Total	Placebo & PUVA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.9.1 Number of UVA treatments (ITT analysis)								
SOMMERBERG1993	19.6	5.7	40	19.4	7.2	43	54.2%	0.20 [-2.58, 2.98]
Subtotal (95% CI)			**40**			**43**	**54.2%**	**0.20 [-2.58, 2.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.14 (P = 0.89)								
2.9.2 Number of UVA treatments (available case analysis)								
SAURAT1988	13.7	3.8	18	19.9	7.2	20	32.2%	-6.20 [-9.81, -2.59]
TANEW1991	15.3	9.1	23	21.4	10.5	25	13.6%	-6.10 [-11.65, -0.55]
Subtotal (95% CI)			**41**			**45**	**45.8%**	**-6.17 [-9.20, -3.14]**
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%								
Test for overall effect: Z = 4.00 (P < 0.0001)								
Total (95% CI)			**81**			**88**	**100.0%**	**-2.72 [-4.77, -0.67]**
Heterogeneity: Chi² = 9.22, df = 2 (P = 0.010); I² = 78%								
Test for overall effect: Z = 2.60 (P = 0.009)								
Test for subgroup differences: Chi² = 9.22, df = 1 (P = 0.002), I² = 89.2%								

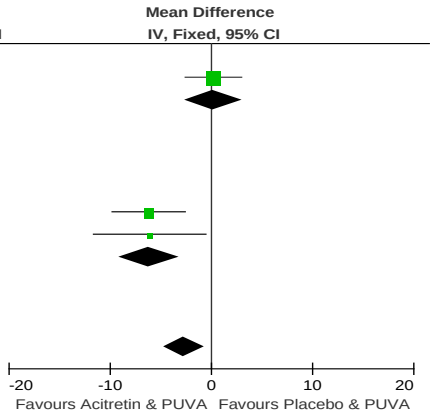


Figure 135: Withdrawal due to drug toxicity at 8-12 weeks

Study or Subgroup	Acitretin & PUVA Events	Total	Placebo & PUVA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SAURAT1988	1	19	1	21	20.5%	1.11 [0.07, 16.47]
SOMMERBERG1993	3	36	3	32	68.5%	0.89 [0.19, 4.10]
TANEW1991	3	26	0	25	11.0%	6.74 [0.37, 124.21]
Total (95% CI)		**81**		**78**	**100.0%**	**1.58 [0.51, 4.87]**
Total events	7		4			
Heterogeneity: Chi² = 1.56, df = 2 (P = 0.46); I² = 0%						
Test for overall effect: Z = 0.79 (P = 0.43)						

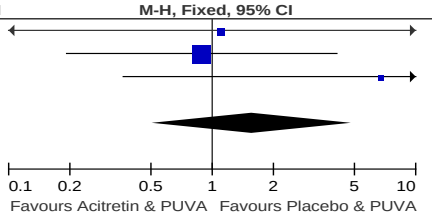
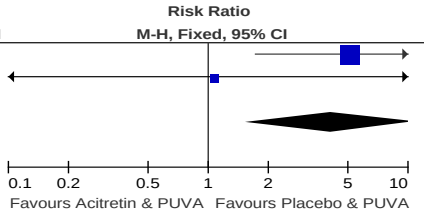


Figure 136: Severe adverse events at 12 weeks

Study or Subgroup	Acitretin & PUVA Events	Total	Placebo & PUVA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SAURAT1988	14	20	3	22	74.8%	5.13 [1.73, 15.27]
SOMMERBERG1993	1	40	1	43	25.2%	1.07 [0.07, 16.62]
Total (95% CI)		**60**		**65**	**100.0%**	**4.11 [1.55, 10.92]**
Total events	15		4			
Heterogeneity: Chi² = 1.08, df = 1 (P = 0.30); I² = 8%						
Test for overall effect: Z = 2.84 (P = 0.005)						



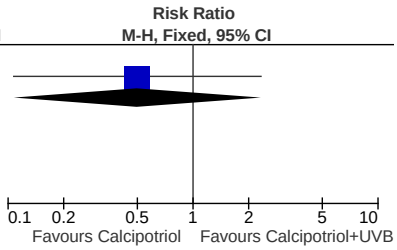
J.6 Dithranol, coal tar and vitamin D or vitamin D analogues combined with UVB

J.6.1 Vitamin D or vitamin D analogue plus NBUVB vs vitamin D or vitamin D analogue alone

Figure 137: Clearance at 3 months

Study or Subgroup	Calcipotriol + NB-UVB Events	Total	Calcipotriol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Calcipotriol						
Roussaki-Schulze, 2005	2	15	4	15	100.0%	0.50 [0.11, 2.33]
Subtotal (95% CI)		**15**		**15**	**100.0%**	**0.50 [0.11, 2.33]**
Total events	2		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)

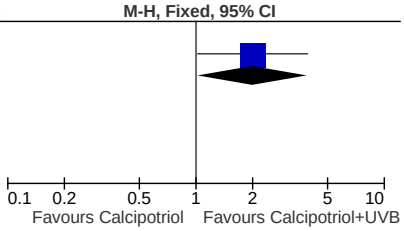


Test for subgroup differences: Not applicable

Figure 138: PASI50 at 3 months

Study or Subgroup	Calcipotriol + NB-UVB Events	Total	Calcipotriol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Calcipotriol						
Roussaki-Schulze, 2005	12	15	6	15	100.0%	2.00 [1.02, 3.91]
Subtotal (95% CI)		**15**		**15**	**100.0%**	**2.00 [1.02, 3.91]**
Total events	12		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.03 (P = 0.04)

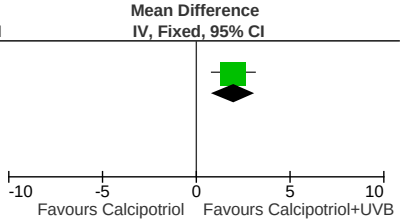


Test for subgroup differences: Not applicable

Figure 139: Mean reduction in PASI at 3 months

Study or Subgroup	Calcipotriol + NB-UVB Mean	SD	Total	Calcipotriol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 Calcipotriol								
Roussaki-Schulze, 2005	3.22	1.7	15	1.24	1.54	15	100.0%	1.98 [0.82, 3.14]
Subtotal (95% CI)			**15**			**15**	**100.0%**	**1.98 [0.82, 3.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.34 (P = 0.0008)

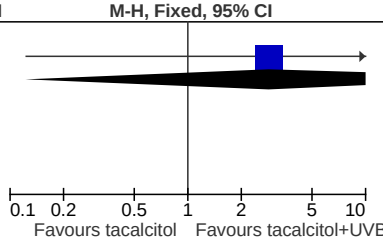


Test for subgroup differences: Not applicable

Figure 140: Withdrawal due to adverse events at 3 weeks

Study or Subgroup	Tacalcitol + NB-UVB Events	Total	Tacalcitol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Tacalcitol						
Rocken, 1998	1	23	0	22	100.0%	2.88 [0.12, 67.03]
Subtotal (95% CI)		**23**		**22**	**100.0%**	**2.88 [0.12, 67.03]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)



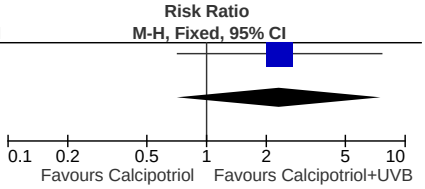
Test for subgroup differences: Not applicable

J.6.2 Calcipotriol plus BBUVB versus Calcipotriol

Figure 141: Clearance at 8 weeks

Study or Subgroup	Calcipotriol + BB-UVB Events	Total	Calcipotriol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kragballe, 1990	7	18	3	18	100.0%	2.33 [0.71, 7.63]
Total (95% CI)		**18**		**18**	**100.0%**	**2.33 [0.71, 7.63]**
Total events	7		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.40 (P = 0.16)



J.6.3 Calcipotriol plus NBUVB vs Plcaebo plus NBUVB

Figure 142: Clearance at 6 weeks

Study or Subgroup	Calcipotriol + NB-UVB Events	Total	Placebo + NB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rim, 2002	9	10	11	18	100.0%	1.47 [0.97, 2.25]
Total (95% CI)		**10**		**18**	**100.0%**	**1.47 [0.97, 2.25]**
Total events	9		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.80 (P = 0.07)

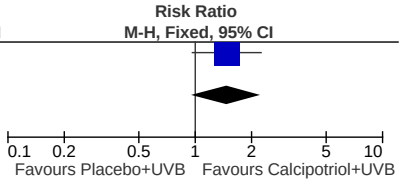


Figure 143: Percentage change in PASI

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Brands, 1999	3.8	12.99701	100.0%	3.80 [-21.67, 29.27]
Total (95% CI)			**100.0%**	**3.80 [-21.67, 29.27]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.29 (P = 0.77)

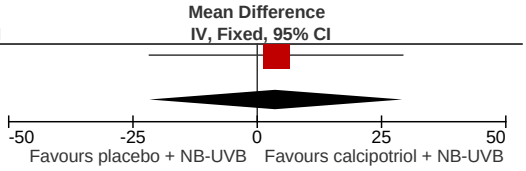


Figure 144: Change in PASI at 6.7 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Woo, 2003	2	1.94	100.0%	2.00 [-1.80, 5.80]
Total (95% CI)			**100.0%**	**2.00 [-1.80, 5.80]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.03 (P = 0.30)

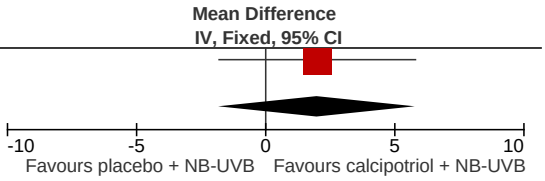


Figure 145: Mean number of UVB treatments (trunk) at 6 weeks

Study or Subgroup	Calcipotriol + NB-UVB Mean	SD	Total	Placebo + NB-UVB Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Rim, 2002	14.3	5.8	10	15.7	4.1	18	100.0%	-1.40 [-5.46, 2.66]
Total (95% CI)			**10**			**18**	**100.0%**	**-1.40 [-5.46, 2.66]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)

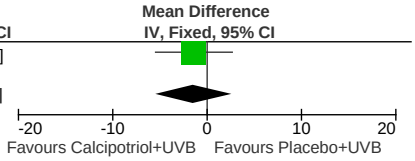


Figure 146: Mean number of UVB treatments (extremities) at 6 weeks

Study or Subgroup	Calcipotriol + NB-UVB Mean	SD	Total	Placebo + NB-UVB Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Rim, 2002	16	4.3	10	18.5	4.8	18	100.0%	-2.50 [-5.97, 0.97]
Total (95% CI)			**10**			**18**	**100.0%**	**-2.50 [-5.97, 0.97]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.41 (P = 0.16)

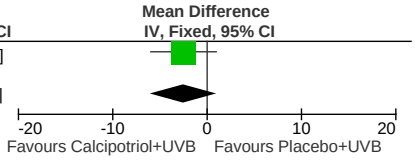


Figure 147: Mean number of UVB treatments at 6 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Brands, 1999	-0.7	2.9115	10.6%	-0.70 [-6.41, 5.01]
Woo, 2003	-1.7	1.002715	89.4%	-1.70 [-3.67, 0.27]
Total (95% CI)			**100.0%**	**-1.59 [-3.45, 0.26]**

Heterogeneity: Chi² = 0.11, df = 1 (P = 0.75); I² = 0%
Test for overall effect: Z = 1.68 (P = 0.09)

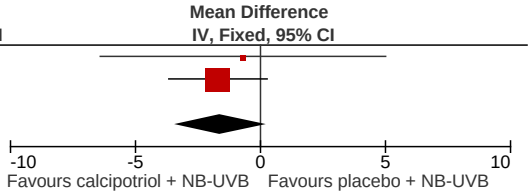


Figure 148: Mild to moderate burn at 6 weeks

Study or Subgroup	Calcipotriol + NB-UVB Events	Total	Placebo + NB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rim, 2002	2	10	2	18	100.0%	1.80 [0.30, 10.90]
Total (95% CI)		**10**		**18**	**100.0%**	**1.80 [0.30, 10.90]**
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)

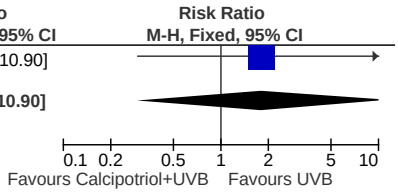
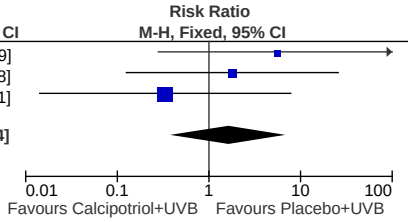


Figure 149: Withdrawal due to adverse events at 6-6.7 weeks

Study or Subgroup	Calcipotriol + NB-UVB Events	Total	Placebo + NB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brands, 1999	2	25	0	28	17.6%	5.58 [0.28, 110.89]
Rim, 2002	1	10	1	18	26.6%	1.80 [0.13, 25.78]
Woo, 2003	0	25	1	25	55.8%	0.33 [0.01, 7.81]
Total (95% CI)		**60**		**71**	**100.0%**	**1.65 [0.38, 7.04]**
Total events	3		2			

Heterogeneity: Chi² = 1.63, df = 2 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.67 (P = 0.50)

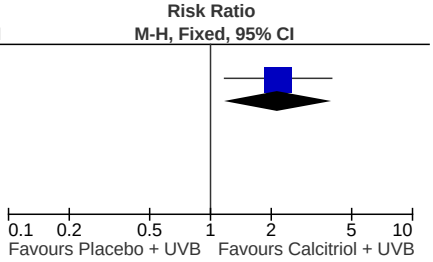


J.6.4 Vitamin D or vitamin D analogues plus BBUVB vs Placebo plus BBUVB

Figure 150: Clear or nearly clear on IAGI at 8 weeks

Study or Subgroup	Calcitriol + UVB Events	Total	Placebo + UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.1 Calcitriol						
Ring, 2001	22	49	11	53	100.0%	2.16 [1.17, 3.98]
Subtotal (95% CI)		**49**		**53**	**100.0%**	**2.16 [1.17, 3.98]**
Total events	22		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.48 (P = 0.01)

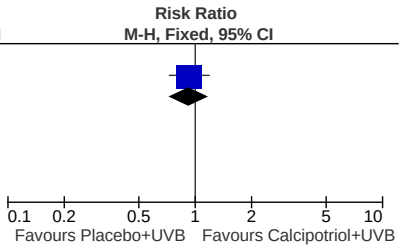


Test for subgroup differences: Not applicable

Figure 151: Clearance at 3 months

Study or Subgroup	Calcipotriol + BB-UVB Events	Total	Plaecbo + BB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.1 Calcipotriol						
Ramsay, 2000	48	80	51	79	100.0%	0.93 [0.73, 1.18]
Subtotal (95% CI)		**80**		**79**	**100.0%**	**0.93 [0.73, 1.18]**
Total events	48		51			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.55)

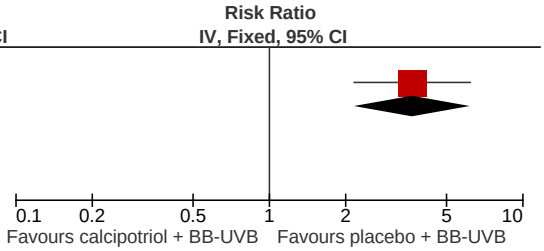


Test for subgroup differences: Not applicable

Figure 152: Number of UV treatments for clearance at 3 months

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
4.3.1 Calcipotriol				
Ramsay, 2000	1.2975	0.2691	100.0%	3.66 [2.16, 6.20]
Subtotal (95% CI)			**100.0%**	**3.66 [2.16, 6.20]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.82 (P < 0.00001)

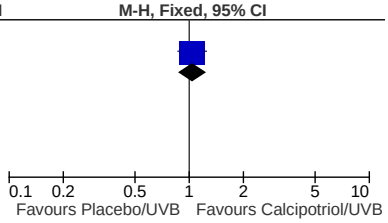


Test for subgroup differences: Not applicable

Figure 153: Modified PASI80 at 3 months

Study or Subgroup	Calcipotriol + BB-UVB Events	Total	Plaecbo + BB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.4.1 Calcipotriol						
Ramsay, 2000	61	80	58	79	100.0%	1.04 [0.87, 1.24]
Subtotal (95% CI)		**80**		**79**	**100.0%**	**1.04 [0.87, 1.24]**
Total events	61		58			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.41 (P = 0.68)

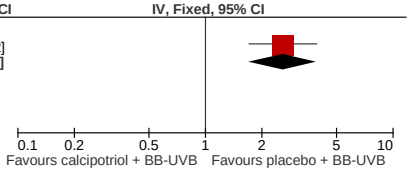


Test for subgroup differences: Not applicable

Figure 154: Number of UV treatments for modified PASI80 at 3 months

Study or Subgroup	log[Risk Ratio]	SE	Calcipotriol + BB-UVB Total	Placebo + BB-UVB Total	Weight	Risk Ratio IV, Fixed, 95% CI
4.5.1 Calcipotriol						
Ramsay, 2000	0.9517	0.2118	80	79	100.0%	2.59 [1.71, 3.92]
Subtotal (95% CI)			**80**	**79**	**100.0%**	**2.59 [1.71, 3.92]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.49 (P < 0.00001)

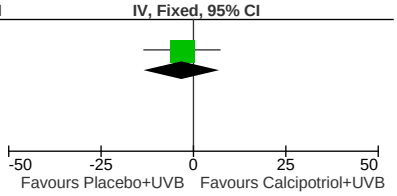


Test for subgroup differences: Not applicable

Figure 155: Percentage change in modified PASI at 3 months

Study or Subgroup	Calcipotriol + BB-UVB Mean	SD	Total	Placebo + BB-UVB Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.6.1 Calcipotriol								
Ramsay, 2000	77	39.4	80	80.1	25.2	79	100.0%	-3.10 [-13.37, 7.17]
Subtotal (95% CI)			**80**			**79**	**100.0%**	**-3.10 [-13.37, 7.17]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.55)

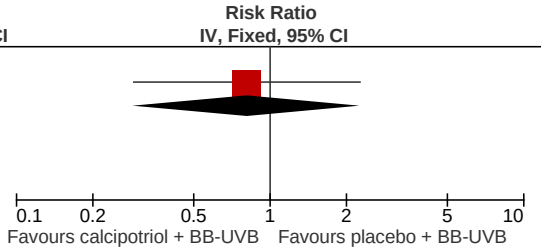


Test for subgroup differences: Not applicable

Figure 156: Relapse rate post-treatment among clearers at 12 weeks post treatment

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
4.7.1 Calcipotriol				
Ramsay, 2000	-0.2107	0.5241	100.0%	0.81 [0.29, 2.26]
Subtotal (95% CI)			**100.0%**	**0.81 [0.29, 2.26]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)



Test for subgroup differences: Not applicable

Figure 157: Burn/erythema/pruritis

Study or Subgroup	Calcipotriol + BB-UVB Events	Total	Plaecbo + BB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.8.1 Calcipotriol						
Ramsay, 2000	22	80	33	79	100.0%	0.66 [0.42, 1.02]
Subtotal (95% CI)		**80**		**79**	**100.0%**	**0.66 [0.42, 1.02]**
Total events	22		33			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.86 (P = 0.06)

Test for subgroup differences: Not applicable

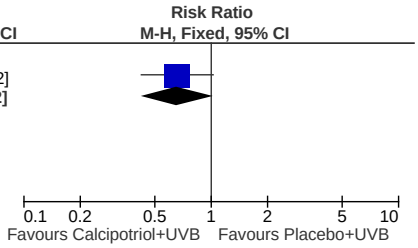
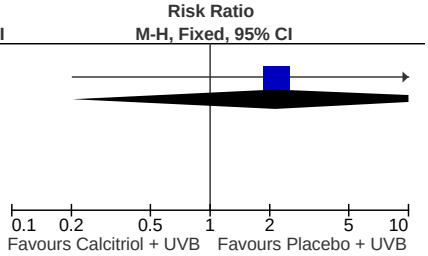


Figure 158: Withdrawal due to adverse events at 8 weeks

Study or Subgroup	Calcitriol + UVB Events	Total	Placebo + UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.9.1 Calcitriol						
Ring, 2001	2	49	1	53	100.0%	2.16 [0.20, 23.11]
Subtotal (95% CI)		**49**		**53**	**100.0%**	**2.16 [0.20, 23.11]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)

Test for subgroup differences: Not applicable



J.6.5 LCD plus NBUVB vs NBUVB

Figure 159: Clearance at 12 weeks

Study or Subgroup	LCD + NB-UVB Events	Total	NB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bagel, 2009	7	12	6	12	100.0%	1.17 [0.56, 2.45]
Total (95% CI)		**12**		**12**	**100.0%**	**1.17 [0.56, 2.45]**
Total events	7		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.41 (P = 0.68)

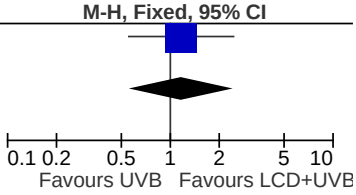
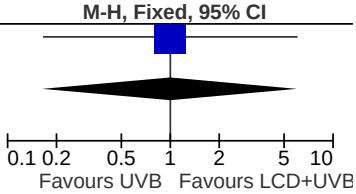


Figure 160: Moderate burn at 12 weeks

Study or Subgroup	LCD + NB-UVB Events	Total	NB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bagel, 2009	2	12	2	12	100.0%	1.00 [0.17, 5.98]
Total (95% CI)		**12**		**12**	**100.0%**	**1.00 [0.17, 5.98]**
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

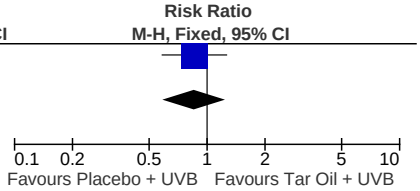


J.6.6 Tar oil plus sub-erythemogenic BBUVB vs Placebo plus maximally erythemogenic BBUVB

Figure 161: Clearance at 12 weeks

Study or Subgroup	Tar Oil+lowUVB Events	Total	Placebo+highUVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Menkes, 1985	19	30	14	19	100.0%	0.86 [0.59, 1.26]
Total (95% CI)		**30**		**19**	**100.0%**	**0.86 [0.59, 1.26]**
Total events	19		14			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.78 (P = 0.44)



J.6.7 Dithranol plus BBUVB vs Dithranol alone

Figure 162: Clear or nearly clear (≤1% BSA, ≤1 on all severity scores) at 8 weeks

Study or Subgroup	Dithranol + BB-UVB Events	Total	Dithranol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Gerritsen, 1998	15	24	7	24	100.0%	2.14 [1.07, 4.30]
Total (95% CI)		**24**		**24**	**100.0%**	**2.14 [1.07, 4.30]**
Total events	15		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.15 (P = 0.03)

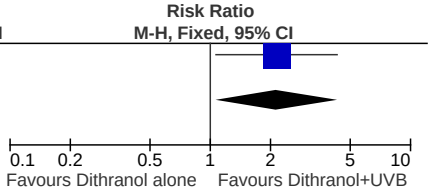
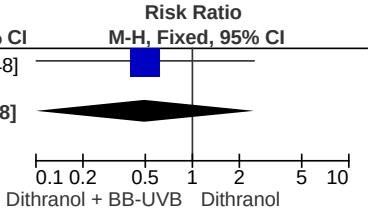


Figure 163: Irritation (requiring adjustment of dithranol) at 8 weeks

Study or Subgroup	Dithranol + BB-UVB Events	Total	Dithranol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Gerritsen, 1998	2	24	4	24	100.0%	0.50 [0.10, 2.48]
Total (95% CI)		**24**		**24**	**100.0%**	**0.50 [0.10, 2.48]**
Total events	2		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.85 (P = 0.40)

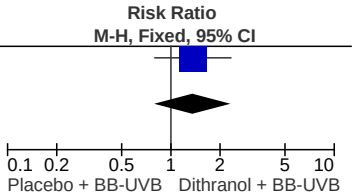


J.6.8 Dithranol plus BBUVB vs Placebo plus BBUVB

Figure 164: Clear or nearly clear (≤1% BSA, ≤1 on all severity scores) at 8 weeks

Study or Subgroup	Dithranol + BB-UVB Events	Total	Placebo + BB-UVB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Gerritsen, 1998	15	24	11	24	100.0%	1.36 [0.80, 2.33]
Total (95% CI)		**24**		**24**	**100.0%**	**1.36 [0.80, 2.33]**
Total events	15		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.14 (P = 0.25)



J.6.9 Dithranol plus coal tar plus BBUVB vs dithranol

Figure 165: Clearance at 3 weeks

Study or Subgroup	Dithranol + Coal Tar + UV Events	Total	Dithranol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Paramsothy, 1988	20	27	16	26	100.0%	1.20 [0.83, 1.75]
Total (95% CI)		**27**		**26**	**100.0%**	**1.20 [0.83, 1.75]**
Total events	20		16			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)

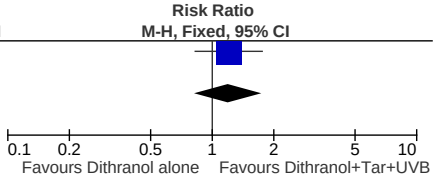


Figure 166: Mean number of days to clearance at 3 weeks

Study or Subgroup	Dithranol + Coal Tar + UV Mean	SD	Total	Dithranol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Paramsothy, 1988	20.3	1.6	27	19.5	2.6	26	100.0%	0.80 [-0.37, 1.97]
Total (95% CI)			**27**			**26**	**100.0%**	**0.80 [-0.37, 1.97]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.34 (P = 0.18)

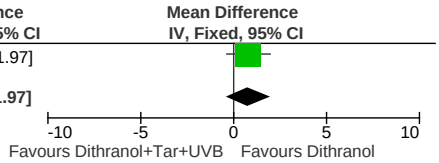
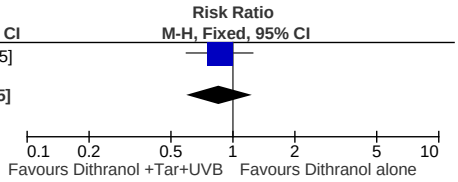


Figure 167: Relapse rate post-treatment

Study or Subgroup	Dithranol + Coal Tar + UV Events	Total	Dithranol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Paramsothy, 1988	14	20	13	16	100.0%	0.86 [0.59, 1.25]
Total (95% CI)		**20**		**16**	**100.0%**	**0.86 [0.59, 1.25]**
Total events	14		13			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)



J.7 Systemic therapy

J.7.1 Methotrexate vs placebo for maintenance of remission

Figure 168: PASI90 at 16 weeks

Study or Subgroup	MTX Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Saurat 2008	15	104	6	52	100.0%	1.25 [0.52, 3.03]
Total (95% CI)		**104**		**52**	**100.0%**	**1.25 [0.52, 3.03]**
Total events	15		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.49 (P = 0.62)

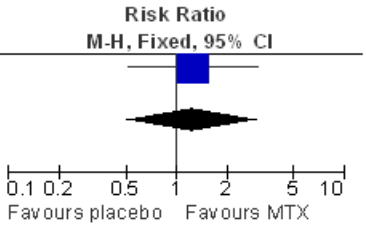


Figure 169: Clear/nearly clear on PGA at 16 weeks

Study or Subgroup	MTX Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Saurat 2008	33	104	6	52	100.0%	2.75 [1.23, 6.14]
Total (95% CI)		**104**		**52**	**100.0%**	**2.75 [1.23, 6.14]**
Total events	33		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.47 (P = 0.01)

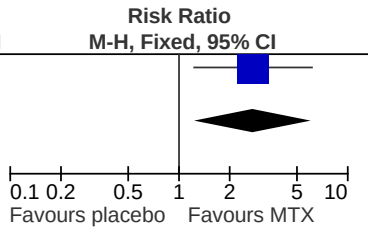


Figure 170: PASI75 at 4-6 months

Study or Subgroup	MTX Events	MTX Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ho2010	12	19	3	17	19.2%	3.58 [1.21, 10.57]
Saurat 2008	39	104	10	52	80.8%	1.95 [1.06, 3.59]
Total (95% CI)		**123**		**69**	**100.0%**	**2.26 [1.34, 3.83]**
Total events	51		13			

Heterogeneity: Chi² = 0.92, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 3.04 (P = 0.002)

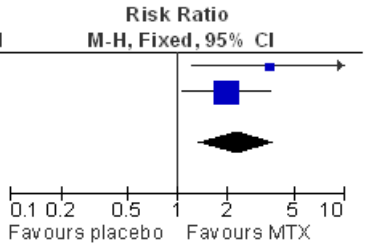


Figure 171: PASI50 at 4-6 months

Study or Subgroup	MTX Events	MTX Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ho2010	15	19	4	17	16.5%	3.36 [1.38, 8.15]
Saurat 2008	68	104	16	52	83.5%	2.13 [1.38, 3.27]
Total (95% CI)		**123**		**69**	**100.0%**	**2.33 [1.58, 3.43]**
Total events	83		20			

Heterogeneity: Chi² = 0.82, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 4.29 (P < 0.0001)

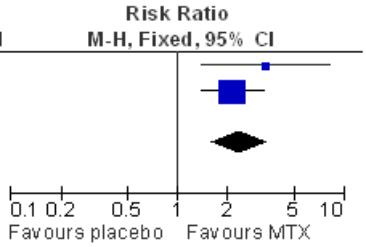


Figure 172: PASI change/final score at 4-6 months

Study or Subgroup	MTX Mean	MTX SD	MTX Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
Ho2010	5.7	8.5	19	13.9	10.1	17	20.6%	-8.20 [-14.34, -2.06]
Saurat 2008	-10.9	8.3	104	-4.6	9.9	52	79.4%	-6.30 [-9.43, -3.17]
Total (95% CI)			**123**			**69**	**100.0%**	**-6.69 [-9.48, -3.90]**

Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² = 0%
Test for overall effect: Z = 4.71 (P < 0.00001)

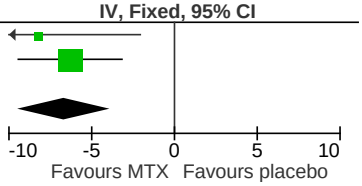


Figure 173: Severe adverse events at 26 weeks

Study or Subgroup	MTX Events	MTX Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Saurat 2008	1	110	1	53	100.0%	0.48 [0.03, 7.55]
Total (95% CI)		**110**		**53**	**100.0%**	**0.48 [0.03, 7.55]**
Total events	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.52 (P = 0.60)

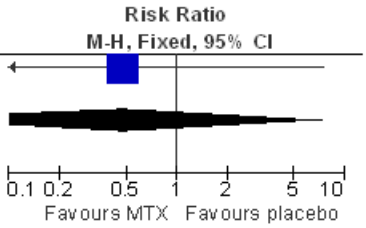


Figure 174: Withdrawal due to toxicity at 26 weeks

Study or Subgroup	MTX Events	MTX Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Saurat 2008	6	110	1	49	100.0%	2.67 [0.33, 21.61]
Total (95% CI)		**110**		**49**	**100.0%**	**2.67 [0.33, 21.61]**
Total events	6		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.92 (P = 0.36)

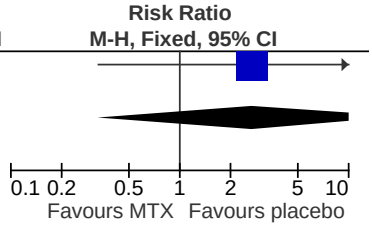
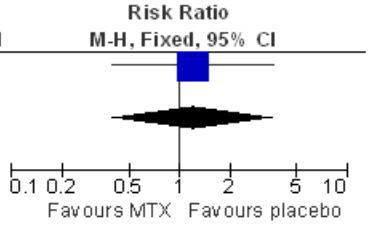


Figure 175: Raised liver enzymes at 26 weeks

Study or Subgroup	MTX Events	MTX Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Saurat 2008	10	110	4	53	100.0%	1.20 [0.40, 3.66]
Total (95% CI)		**110**		**53**	**100.0%**	**1.20 [0.40, 3.66]**
Total events	10		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)



J.7.2 Methotrexate vs ciclosporin for induction of remission

Figure 176: Clear/nearly clear (PASI90) at 12-16 weeks

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Incremental dose MTX (7.5 up to 15 mg/wk)						
Flytstrom 2008 (+ folic)	9	31	4	37	100.0%	2.69 [0.91, 7.88]
Subtotal (95% CI)		**31**		**37**	**100.0%**	**2.69 [0.91, 7.88]**
Total events	9		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.80 (P = 0.07)						
2.1.2 Incremental dose MTX (15 up to 22.5 mg/wk)						
Heydendael 2003	14	42	17	43	100.0%	0.84 [0.48, 1.48]
Subtotal (95% CI)		**42**		**43**	**100.0%**	**0.84 [0.48, 1.48]**
Total events	14		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.55)						

Test for subgroup differences: Chi² = 3.49, df = 1 (P = 0.06), I² = 71.3%

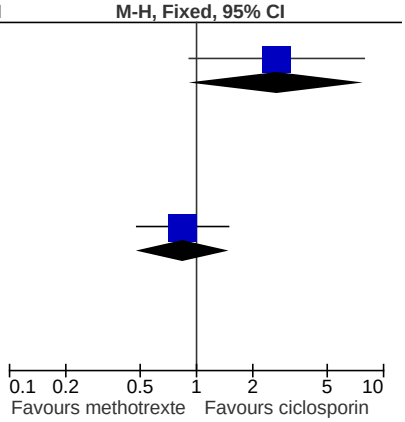


Figure 177: Clearanceat 10 weeks

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.3 High dose MTX (0.5 mg/kg/wk)						
Sandhu 2003 (+ folic)	6	15	13	15	100.0%	0.46 [0.24, 0.88]
Subtotal (95% CI)		**15**		**15**	**100.0%**	**0.46 [0.24, 0.88]**
Total events	6		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.33 (P = 0.02)						

Test for subgroup differences: Not applicable

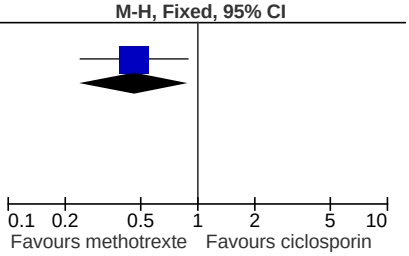
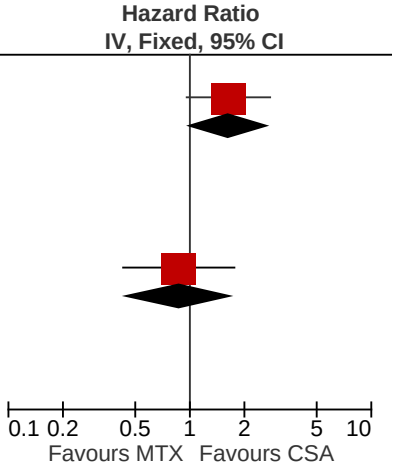


Figure 178: Time to remission (follow-up for a maximum of 16 weeks)

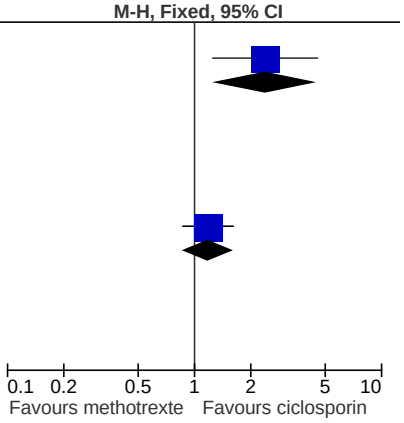
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
2.13.1 PASI75				
Heydendael 2003	0.49	0.27	100.0%	1.63 [0.96, 2.77]
Subtotal (95% CI)			**100.0%**	**1.63 [0.96, 2.77]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.81 (P = 0.07)				
2.13.2 PASI90				
Heydendael 2003	-0.14	0.36	100.0%	0.87 [0.43, 1.76]
Subtotal (95% CI)			**100.0%**	**0.87 [0.43, 1.76]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.39 (P = 0.70)				



Test for subgroup differences: Chi² = 1.96, df = 1 (P = 0.16), I² = 49.0%

Figure 179: PASI75 at 12-16 weeks

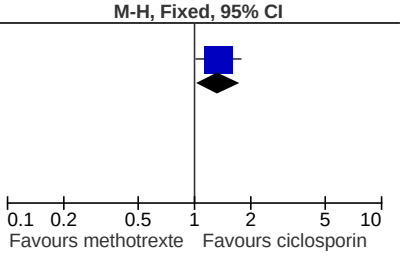
Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.1 Incremental dose MTX (7.5 up to 15 mg/wk)						
Flytstrom 2008 (+ folic)	18	31	9	37	100.0%	2.39 [1.26, 4.54]
Subtotal (95% CI)		**31**		**37**	**100.0%**	**2.39 [1.26, 4.54]**
Total events	18		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.66 (P = 0.008)						
2.3.2 Incremental dose MTX (15 up to 22.5 mg/wk)						
Heydendael 2003	30	42	26	43	100.0%	1.18 [0.87, 1.61]
Subtotal (95% CI)		**42**		**43**	**100.0%**	**1.18 [0.87, 1.61]**
Total events	30		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						



Test for subgroup differences: Chi² = 3.75, df = 1 (P = 0.05), I² = 73.3%

Figure 180: PASI50 at 12 weeks

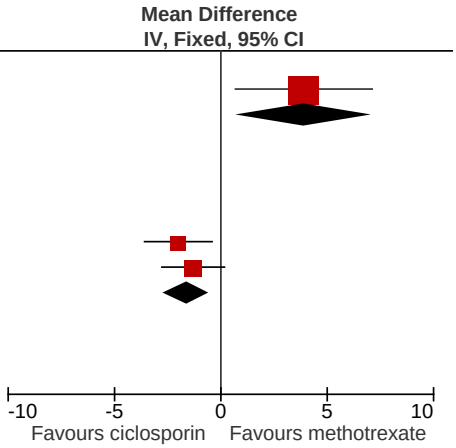
Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 Incremental dose MTX (7.5 up to 15 mg/wk)						
Flytstrom 2008 (+ folic)	27	31	24	37	100.0%	1.34 [1.02, 1.76]
Subtotal (95% CI)		**31**		**37**	**100.0%**	**1.34 [1.02, 1.76]**
Total events	27		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.11 (P = 0.03)						



Test for subgroup differences: Not applicable

Figure 181: Final PASI at 12-16 weeks

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
2.17.2 High dose MTX (0.5 mg/kg/wk)				
Sandhu 2003 (+ folic)	3.9	1.64	100.0%	3.90 [0.69, 7.11]
Subtotal (95% CI)			**100.0%**	**3.90 [0.69, 7.11]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.38 (P = 0.02)				
2.17.3 Incremental dosing (within licenced range; maximum 22.5 mg/wk)				
Flytstrom 2008 (+ folic)	-2	0.81	46.2%	-2.00 [-3.59, -0.41]
Heydendael 2003	-1.3	0.75	53.8%	-1.30 [-2.77, 0.17]
Subtotal (95% CI)			**100.0%**	**-1.62 [-2.70, -0.54]**
Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² = 0%				
Test for overall effect: Z = 2.95 (P = 0.003)				



Test for subgroup differences: Chi² = 10.19, df = 1 (P = 0.001), I² = 90.2%

Figure 182: Change in NAPSI at 6 months

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Gumusel 2011 (+ folic)	4.8	4.35152	100.0%	4.80 [-3.73, 13.33]
Total (95% CI)			**100.0%**	**4.80 [-3.73, 13.33]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.10 (P = 0.27)				

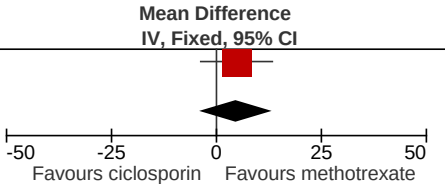


Figure 183: Remaining clear at 12 weeks (after tapering)

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sandhu 2003 (+ folic)	2	6	13	13	100.0%	0.37 [0.14, 1.01]
Total (95% CI)		**6**		**13**	**100.0%**	**0.37 [0.14, 1.01]**
Total events	2		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.95 (P = 0.05)						

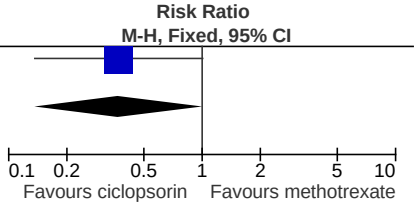


Figure 184: Elevated liver enzymes at 12-24 weeks

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Flytstrom 2008 (+ folic)	0	31	7	37	33.0%	0.08 [0.00, 1.33]
Gumusel 2011 (+ folic)	0	19	1	18	7.4%	0.32 [0.01, 7.30]
Heydendael 2003	0	42	12	43	59.5%	0.04 [0.00, 0.67]
Total (95% CI)		**92**		**98**	**100.0%**	**0.07 [0.01, 0.38]**
Total events	0		20			
Heterogeneity: Chi² = 1.00, df = 2 (P = 0.61); I² = 0%						
Test for overall effect: Z = 3.11 (P = 0.002)						

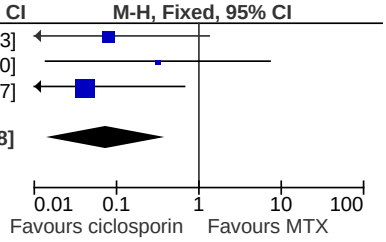


Figure 185: Elevated creatinine at 12-24 weeks

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Flytstrom 2008 (+ folic)	6	31	0	37	47.1%	15.44 [0.90, 263.63]
Gumusel 2011 (+ folic)	2	19	0	18	52.9%	4.75 [0.24, 92.65]
Total (95% CI)		**50**		**55**	**100.0%**	**9.79 [1.32, 72.65]**
Total events	8		0			

Heterogeneity: Chi² = 0.33, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 2.23 (P = 0.03)

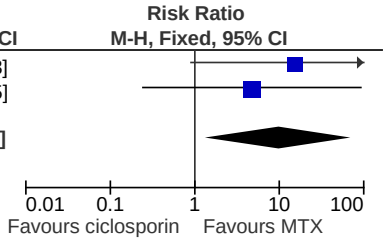


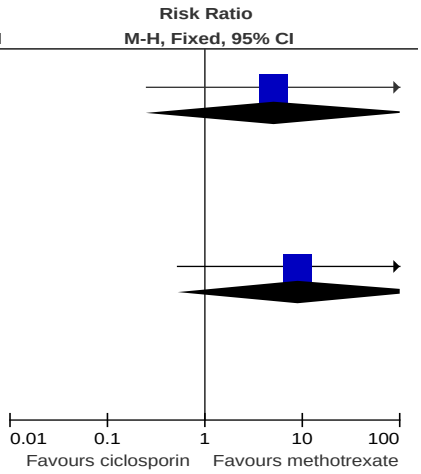
Figure 186: Hypertension at 12-16 weeks

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.10.1 Incremental dose MTX (15 up to 22.5 mg/wk)						
Heydendael 2003	2	42	0	43	100.0%	5.12 [0.25, 103.50]
Subtotal (95% CI)		**42**		**43**	**100.0%**	**5.12 [0.25, 103.50]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.10.2 Diastolic hypertension - High dose MTX (0.5 mg/kg/wk)						
Sandhu 2003 (+ folic)	4	15	0	15	100.0%	9.00 [0.53, 153.79]
Subtotal (95% CI)		**15**		**15**	**100.0%**	**9.00 [0.53, 153.79]**
Total events	4		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)



Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.79), I² = 0%

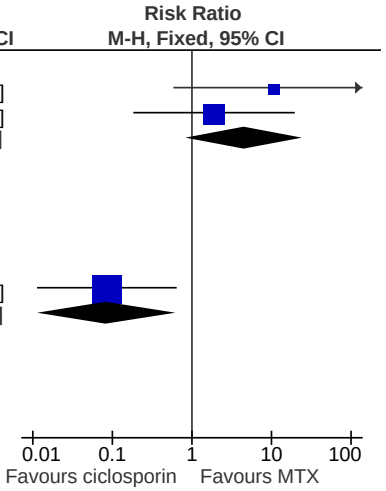
Figure 187: Withdrawal due to toxicity at 12-16 weeks

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.9.1 Standard MTX dose range (maximum 15 mg/wk)						
Flytstrom 2008 (+ folic)	4	31	0	37	30.8%	10.69 [0.60, 191.09]
Gumusel 2011 (+ folic)	2	19	1	18	69.2%	1.89 [0.19, 19.13]
Subtotal (95% CI)		**50**		**55**	**100.0%**	**4.60 [0.84, 25.16]**
Total events	6		1			

Heterogeneity: Chi² = 0.89, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 1.76 (P = 0.08)

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Methotrexate Events	Methotrexate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.9.2 Incremental dose MTX (15 up to 22.5 mg/wk)						
Heydendael 2003	1	42	12	43	100.0%	0.09 [0.01, 0.63]
Subtotal (95% CI)		**42**		**43**	**100.0%**	**0.09 [0.01, 0.63]**
Total events	1		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.42 (P = 0.02)

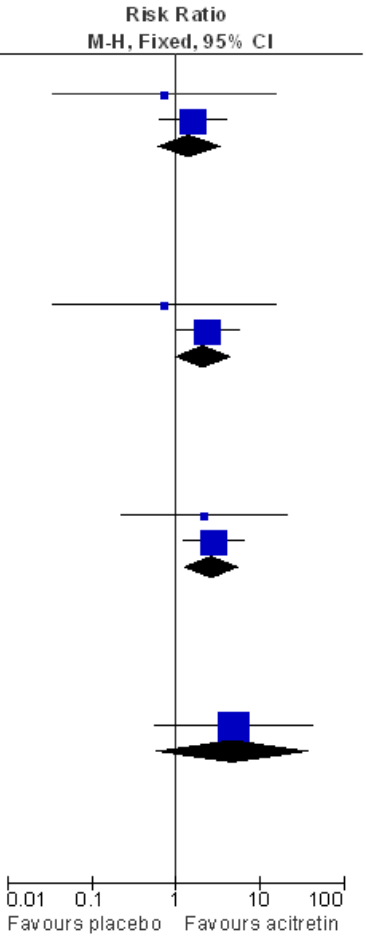


Test for subgroup differences: Chi² = 8.90, df = 1 (P = 0.003), I² = 88.8%

J.7.3 Acitretin vs placebo for induction of remission

Figure 188: PASI75 at 8 weeks

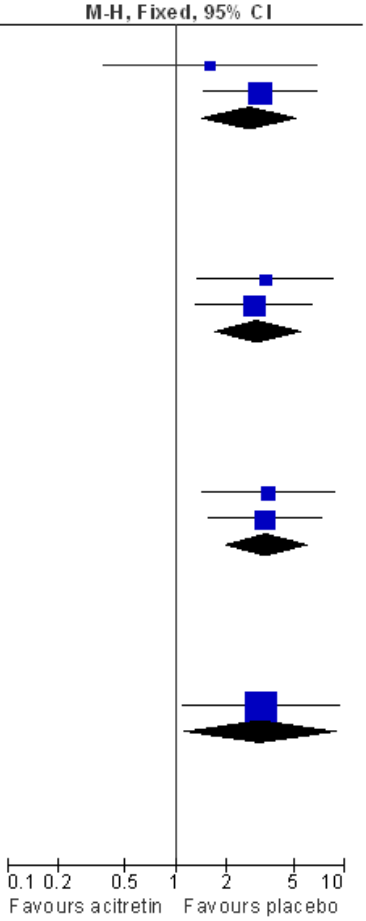
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 10 mg acitretin						
Goldfarb 1988	0	5	1	12	15.9%	0.72 [0.03, 15.26]
Lassus 1987	8	20	5	20	84.1%	1.60 [0.63, 4.05]
Subtotal (95% CI)		**25**		**32**	**100.0%**	**1.46 [0.60, 3.54]**
Total events	8		6			
Heterogeneity: Chi² = 0.24, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 0.84 (P = 0.40)						
3.1.2 25 mg acitretin						
Goldfarb 1988	0	5	1	12	15.9%	0.72 [0.03, 15.26]
Lassus 1987	12	20	5	20	84.1%	2.40 [1.04, 5.55]
Subtotal (95% CI)		**25**		**32**	**100.0%**	**2.13 [0.96, 4.75]**
Total events	12		6			
Heterogeneity: Chi² = 0.56, df = 1 (P = 0.45); I² = 0%						
Test for overall effect: Z = 1.86 (P = 0.06)						
3.1.3 50 mg acitretin						
Goldfarb 1988	2	11	1	12	16.1%	2.18 [0.23, 20.84]
Lassus 1987	14	20	5	20	83.9%	2.80 [1.24, 6.30]
Subtotal (95% CI)		**31**		**32**	**100.0%**	**2.70 [1.26, 5.81]**
Total events	16		6			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%						
Test for overall effect: Z = 2.54 (P = 0.01)						
3.1.4 75 mg acitretin						
Goldfarb 1988	2	5	1	12	100.0%	4.80 [0.55, 41.70]
Subtotal (95% CI)		**5**		**12**	**100.0%**	**4.80 [0.55, 41.70]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.42 (P = 0.15)						



Test for subgroup differences: Chi² = 1.60, df = 3 (P = 0.66), I² = 0%

Figure 189: Cheilitis at 8 weeks

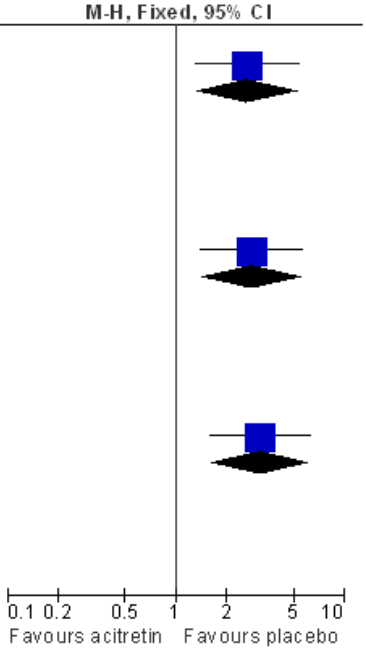
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 10 mg acitretin						
Goldfarb 1988	2	5	3	12	26.6%	1.60 [0.37, 6.85]
Lassus 1987	15	18	5	19	73.4%	3.17 [1.45, 6.91]
Subtotal (95% CI)		**23**		**31**	**100.0%**	**2.75 [1.39, 5.44]**
Total events	17		8			
Heterogeneity: Chi² = 0.66, df = 1 (P = 0.42); I² = 0%						
Test for overall effect: Z = 2.91 (P = 0.004)						
3.3.2 25 mg acitretin						
Goldfarb 1988	5	5	3	12	31.9%	3.40 [1.35, 8.61]
Lassus 1987	13	17	5	19	68.1%	2.91 [1.31, 6.45]
Subtotal (95% CI)		**22**		**31**	**100.0%**	**3.06 [1.66, 5.66]**
Total events	18		8			
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.80); I² = 0%						
Test for overall effect: Z = 3.58 (P = 0.0003)						
3.3.3 50 mg acitretin						
Goldfarb 1988	11	11	3	12	40.9%	3.56 [1.44, 8.78]
Lassus 1987	16	18	5	19	59.1%	3.38 [1.56, 7.29]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**3.45 [1.92, 6.20]**
Total events	27		8			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%						
Test for overall effect: Z = 4.14 (P < 0.0001)						
3.3.4 75 mg acitretin						
Goldfarb 1988	4	5	3	12	100.0%	3.20 [1.09, 9.36]
Subtotal (95% CI)		**5**		**12**	**100.0%**	**3.20 [1.09, 9.36]**
Total events	4		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.12 (P = 0.03)						



Test for subgroup differences: Chi² = 0.25, df = 3 (P = 0.97), I² = 0%

Figure 190: Cheilitis at 6 months

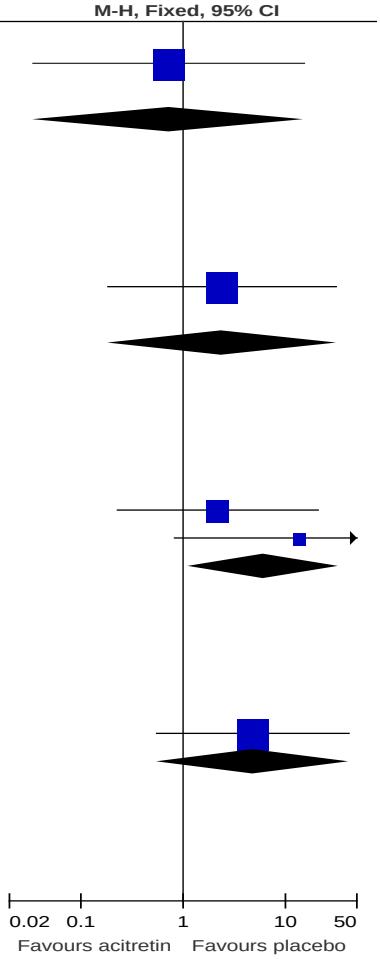
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.4.1 10 mg acitretin						
Lassus 1987	16	20	6	20	100.0%	2.67 [1.32, 5.39]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**2.67 [1.32, 5.39]**
Total events	16		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.73 (P = 0.006)						
3.4.2 25 mg acitretin						
Lassus 1987	17	20	6	20	100.0%	2.83 [1.42, 5.67]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**2.83 [1.42, 5.67]**
Total events	17		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.94 (P = 0.003)						
3.4.3 50 mg acitretin						
Lassus 1987	19	20	6	20	100.0%	3.17 [1.61, 6.23]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**3.17 [1.61, 6.23]**
Total events	19		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.34 (P = 0.0008)						



Test for subgroup differences: Chi² = 0.12, df = 2 (P = 0.94), I² = 0%

Figure 191: Hair loss at 8 weeks

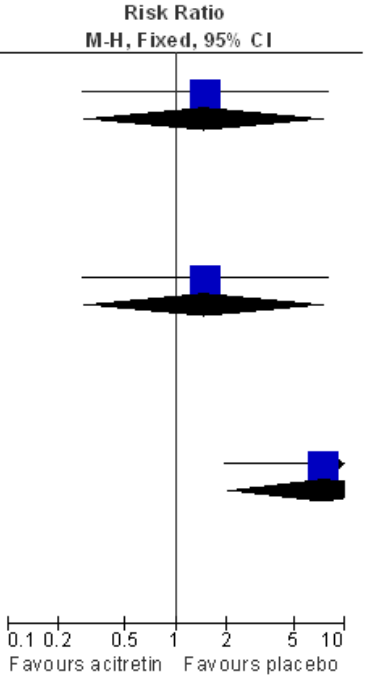
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.5.1 10 mg acitretin						
Goldfarb 1988	0	5	1	12	100.0%	0.72 [0.03, 15.26]
Lassus 1987	0	18	0	19		Not estimable
Subtotal (95% CI)		**23**		**31**	**100.0%**	**0.72 [0.03, 15.26]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.83)						
3.5.2 25 mg acitretin						
Goldfarb 1988	1	5	1	12	100.0%	2.40 [0.18, 31.29]
Lassus 1987	0	17	0	19		Not estimable
Subtotal (95% CI)		**22**		**31**	**100.0%**	**2.40 [0.18, 31.29]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.50)						
3.5.3 50 mg acitretin						
Goldfarb 1988	2	11	1	12	66.3%	2.18 [0.23, 20.84]
Lassus 1987	6	18	0	19	33.7%	13.68 [0.83, 226.63]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**6.06 [1.13, 32.60]**
Total events	8		1			
Heterogeneity: Chi² = 1.11, df = 1 (P = 0.29); I² = 10%						
Test for overall effect: Z = 2.10 (P = 0.04)						
3.5.4 75 mg acitretin						
Goldfarb 1988	2	5	1	12	100.0%	4.80 [0.55, 41.70]
Subtotal (95% CI)		**5**		**12**	**100.0%**	**4.80 [0.55, 41.70]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.42 (P = 0.15)						



Test for subgroup differences: Chi² = 1.60, df = 3 (P = 0.66), I² = 0%

Figure 192: Hair loss at 6 months

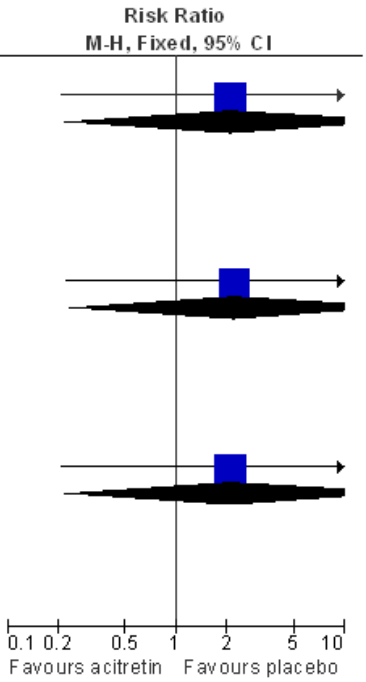
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.6.1 10 mg acitretin						
Lassus 1987	3	20	2	20	100.0%	1.50 [0.28, 8.04]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**1.50 [0.28, 8.04]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
3.6.2 25 mg acitretin						
Lassus 1987	3	20	2	20	100.0%	1.50 [0.28, 8.04]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**1.50 [0.28, 8.04]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
3.6.3 50 mg acitretin						
Lassus 1987	15	20	2	20	100.0%	7.50 [1.97, 28.61]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**7.50 [1.97, 28.61]**
Total events	15		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.95 (P = 0.003)						



Test for subgroup differences: Chi² = 3.11, df = 2 (P = 0.21), I² = 35.7%

Figure 193: Increased triglycerides at 8 weeks

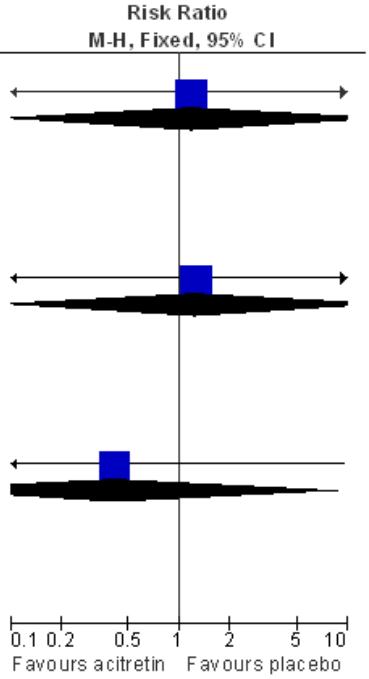
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.7.1 10 mg acitretin						
Lassus 1987	2	18	1	19	100.0%	2.11 [0.21, 21.32]
Subtotal (95% CI)		**18**		**19**	**100.0%**	**2.11 [0.21, 21.32]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						
3.7.2 25 mg acitretin						
Lassus 1987	2	17	1	19	100.0%	2.24 [0.22, 22.51]
Subtotal (95% CI)		**17**		**19**	**100.0%**	**2.24 [0.22, 22.51]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
3.7.3 50 mg acitretin						
Lassus 1987	2	18	1	19	100.0%	2.11 [0.21, 21.32]
Subtotal (95% CI)		**18**		**19**	**100.0%**	**2.11 [0.21, 21.32]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						



Test for subgroup differences: Chi² = 0.00, df = 2 (P = 1.00), I² = 0%

Figure 194: Increased triglycerides at 6 months

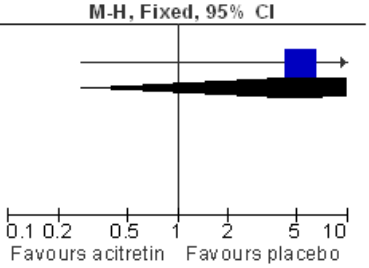
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.8.1 10 mg acitretin						
Lassus 1987	1	16	1	19	100.0%	1.19 [0.08, 17.51]
Subtotal (95% CI)		**16**		**19**	**100.0%**	**1.19 [0.08, 17.51]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						
3.8.2 25 mg acitretin						
Lassus 1987	1	15	1	19	100.0%	1.27 [0.09, 18.62]
Subtotal (95% CI)		**15**		**19**	**100.0%**	**1.27 [0.09, 18.62]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.17 (P = 0.86)						
3.8.3 50 mg acitretin						
Lassus 1987	0	15	1	19	100.0%	0.42 [0.02, 9.55]
Subtotal (95% CI)		**15**		**19**	**100.0%**	**0.42 [0.02, 9.55]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.55 (P = 0.58)						



Test for subgroup differences: $Chi^2 = 0.33$, df = 2 (P = 0.85), $I^2 = 0\%$

Figure 195: Increased liver enzymes at 8 weeks

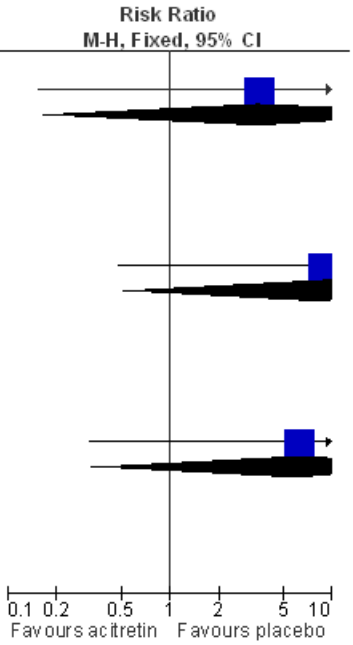
Study or Subgroup	Acitretin Events	Acitretin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.9.1 10 mg acitretin						
Lassus 1987	2	18	0	19	100.0%	5.26 [0.27, 102.66]
Subtotal (95% CI)		**18**		**19**	**100.0%**	**5.26 [0.27, 102.66]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						



Test for subgroup differences: Not applicable

Figure 196: Increased liver enzymes at 6 months

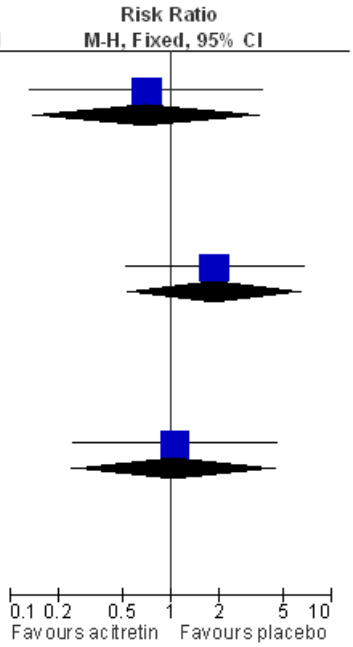
Study or Subgroup	Favours acitretin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.10.1 10 mg acitretin						
Lassus 1987	1	16	0	19	100.0%	3.53 [0.15, 81.11]
Subtotal (95% CI)		**16**		**19**	**100.0%**	**3.53 [0.15, 81.11]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
3.10.2 25 mg acitretin						
Lassus 1987	3	15	0	19	100.0%	8.75 [0.49, 157.34]
Subtotal (95% CI)		**15**		**19**	**100.0%**	**8.75 [0.49, 157.34]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						
3.10.3 50 mg acitretin						
Lassus 1987	2	15	0	19	100.0%	6.25 [0.32, 121.14]
Subtotal (95% CI)		**15**		**19**	**100.0%**	**6.25 [0.32, 121.14]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.21 (P = 0.23)						



Test for subgroup differences: Chi² = 0.18, df = 2 (P = 0.92), I² = 0%

Figure 197: Increased cholesterol at 8 weeks

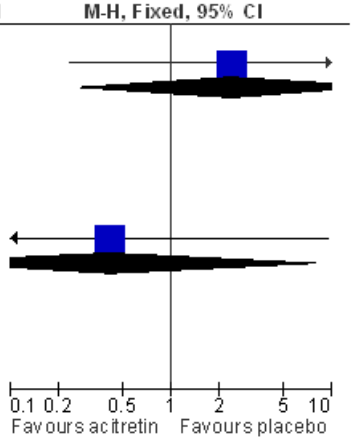
Study or Subgroup	Favours acitretin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.11.1 10 mg acitretin						
Lassus 1987	2	18	3	19	100.0%	0.70 [0.13, 3.73]
Subtotal (95% CI)		**18**		**19**	**100.0%**	**0.70 [0.13, 3.73]**
Total events	2		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						
3.11.2 25 mg acitretin						
Lassus 1987	5	17	3	19	100.0%	1.86 [0.52, 6.65]
Subtotal (95% CI)		**17**		**19**	**100.0%**	**1.86 [0.52, 6.65]**
Total events	5		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.96 (P = 0.34)						
3.11.3 50 mg acitretin						
Lassus 1987	3	18	3	19	100.0%	1.06 [0.24, 4.57]
Subtotal (95% CI)		**18**		**19**	**100.0%**	**1.06 [0.24, 4.57]**
Total events	3		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.07 (P = 0.94)						



Test for subgroup differences: Chi² = 0.88, df = 2 (P = 0.64), I² = 0%

Figure 198: Increased cholesterol at 6 months

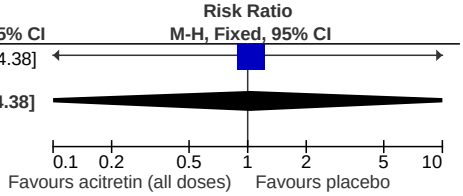
Study or Subgroup	Favours acitretin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.12.1 10 mg acitretin						
Lassus 1987	2	16	1	19	100.0%	2.38 [0.24, 23.84]
Subtotal (95% CI)		**16**		**19**	**100.0%**	**2.38 [0.24, 23.84]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.74 (P = 0.46)						
3.12.2 25 mg acitretin						
Lassus 1987	0	15	1	19	100.0%	0.42 [0.02, 9.55]
Subtotal (95% CI)		**15**		**19**	**100.0%**	**0.42 [0.02, 9.55]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.55 (P = 0.58)						



Test for subgroup differences: Chi² = 0.77, df = 1 (P = 0.38), I² = 0%

Figure 199: Withdrawal due to toxicity at 6 months

Study or Subgroup	Acitretin (all doses) Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lassus 1987	1	57	0	19	100.0%	1.03 [0.04, 24.38]
Total (95% CI)		**57**		**19**	**100.0%**	**1.03 [0.04, 24.38]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.98)						



J.7.4 Increasing vs decreasing acitretin dosing schedule for induction of remission

Figure 200: Cheilitis at 6 weeks

Study or Subgroup	Decreasing dose Events	Total	Increasing dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Berbis 1989	21	21	21	21	100.0%	1.00 [0.91, 1.09]
Total (95% CI)		**21**		**21**	**100.0%**	**1.00 [0.91, 1.09]**
Total events	21		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						

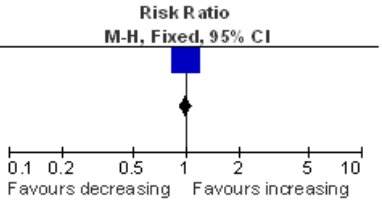


Figure 201: Hair loss at 6 weeks

Study or Subgroup	Decreasing dose Events	Total	Increasing dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Berbis 1989	6	21	1	21	100.0%	6.00 [0.79, 45.63]
Total (95% CI)		**21**		**21**	**100.0%**	**6.00 [0.79, 45.63]**
Total events	6		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.73 (P = 0.08)						

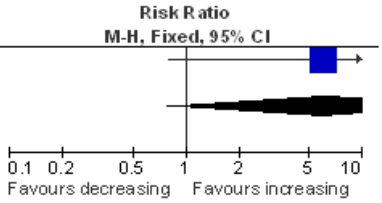
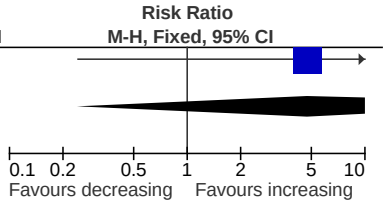


Figure 202: Withdrawal due to toxicity at 6 weeks

Study or Subgroup	Decreasing dose Events	Total	Increasing dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Berbis 1989	2	21	0	20	100.0%	4.77 [0.24, 93.67]
Total (95% CI)		**21**		**20**	**100.0%**	**4.77 [0.24, 93.67]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.03 (P = 0.30)



J.7.5 Increasing vs constant acitretin dosing schedule of induction of remission

Figure 203: Cheilitis at 6 weeks

Study or Subgroup	Constant Events	Total	Increasing Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Berbis 1989	23	23	21	21	100.0%	1.00 [0.92, 1.09]
Total (95% CI)		**23**		**21**	**100.0%**	**1.00 [0.92, 1.09]**
Total events	23		21			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

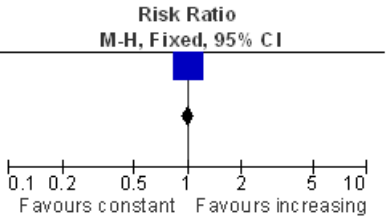


Figure 204: Hair loss at 6 weeks

Study or Subgroup	Constant Events	Total	Increasing Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Berbis 1989	2	23	1	21	100.0%	1.83 [0.18, 18.70]
Total (95% CI)		**23**		**21**	**100.0%**	**1.83 [0.18, 18.70]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.51 (P = 0.61)

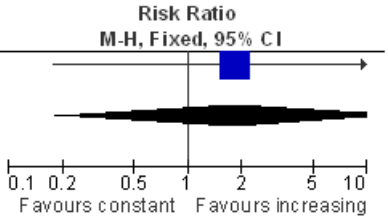
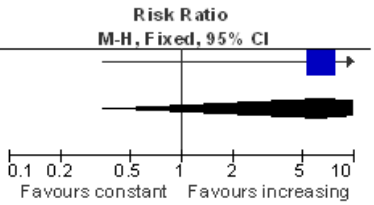


Figure 205: Withdrawal due to toxicity at 6 weeks

Study or Subgroup	Constant dose Events	Total	Increasing dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Berbis 1989	3	22	0	20	100.0%	6.39 [0.35, 116.57]
Total (95% CI)		**22**		**20**	**100.0%**	**6.39 [0.35, 116.57]**
Total events	3		0			

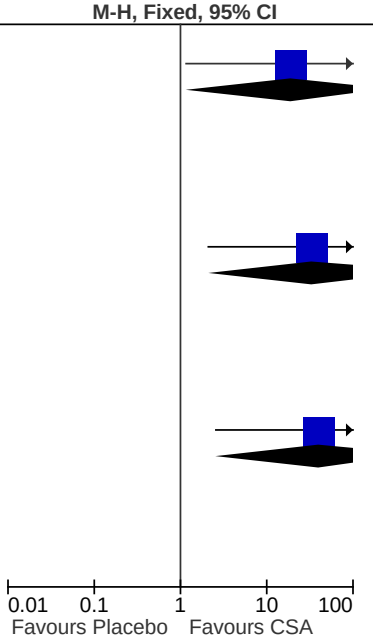
Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)



J.7.6 Ciclosporin vs placebo for induction of remission

Figure 206: Clear/nearly clear on PGA at 8 weeks

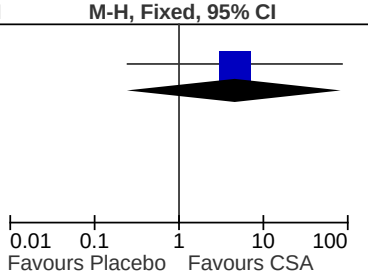
Study or Subgroup	CSA Events	CSA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.1.1 CSA 3 mg/kg						
Ellis 1991	9	25	0	25	100.0%	19.00 [1.17, 309.77]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**19.00 [1.17, 309.77]**
Total events	9		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.07 (P = 0.04)						
7.1.2 CSA 5 mg/kg						
Ellis 1991	13	20	0	25	100.0%	33.43 [2.11, 530.00]
Subtotal (95% CI)		**20**		**25**	**100.0%**	**33.43 [2.11, 530.00]**
Total events	13		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.49 (P = 0.01)						
7.1.3 CSA 7.5 mg/kg						
Ellis 1991	12	15	0	25	100.0%	40.63 [2.58, 640.10]
Subtotal (95% CI)		**15**		**25**	**100.0%**	**40.63 [2.58, 640.10]**
Total events	12		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.63 (P = 0.008)						



Test for subgroup differences: Chi² = 0.15, df = 2 (P = 0.93), I² = 0%

Figure 207: Clearance at 4 weeks

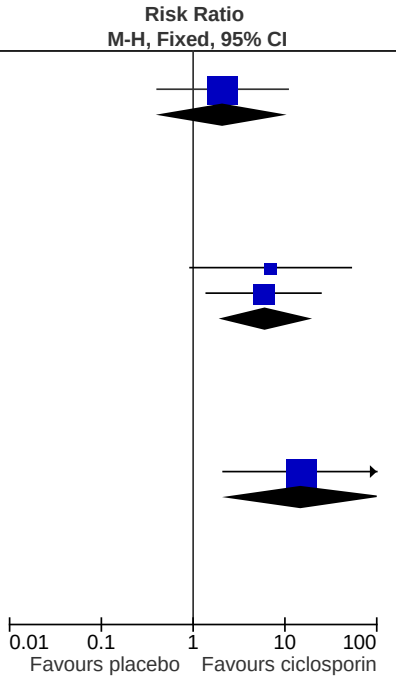
Study or Subgroup	CSA Events	CSA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.2.1 CSA 14 mg/kg						
Ellis 1986	2	11	0	10	100.0%	4.58 [0.25, 85.33]
Subtotal (95% CI)		**11**		**10**	**100.0%**	**4.58 [0.25, 85.33]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						



Test for subgroup differences: Not applicable

Figure 208: PASI75 at 8-10 weeks

Study or Subgroup	CSA Events	CSA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.5.1 CSA 1.25 mg/kg						
Meffert 1997	4	41	2	43	100.0%	2.10 [0.41, 10.84]
Subtotal (95% CI)		**41**		**43**	**100.0%**	**2.10 [0.41, 10.84]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.88 (P = 0.38)						
7.5.2 CSA 2.5-3.0 mg/kg						
Ellis 1991	7	25	1	25	33.1%	7.00 [0.93, 52.80]
Meffert 1997	12	44	2	43	66.9%	5.86 [1.39, 24.67]
Subtotal (95% CI)		**69**		**68**	**100.0%**	**6.24 [1.94, 20.11]**
Total events	19		3			
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%						
Test for overall effect: Z = 3.07 (P = 0.002)						
7.5.4 CSA 5 mg/kg						
Ellis 1991	12	20	1	25	100.0%	15.00 [2.13, 105.79]
Subtotal (95% CI)		**20**		**25**	**100.0%**	**15.00 [2.13, 105.79]**
Total events	12		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.72 (P = 0.007)						



Test for subgroup differences: Chi² = 2.38, df = 2 (P = 0.30), I² = 16.0%

Figure 209: PASI50 at 4-10 weeks

Study or Subgroup	CSA Events	CSA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Guenther 1991	11	12	1	11	67.6%	10.08 [1.54, 65.85]
van Joost 1988	9	10	0	10	32.4%	19.00 [1.25, 287.92]
Total (95% CI)		**22**		**21**	**100.0%**	**12.97 [2.77, 60.81]**
Total events	20		1			
Heterogeneity: Chi² = 0.14, df = 1 (P = 0.70); I² = 0%						
Test for overall effect: Z = 3.25 (P = 0.001)						

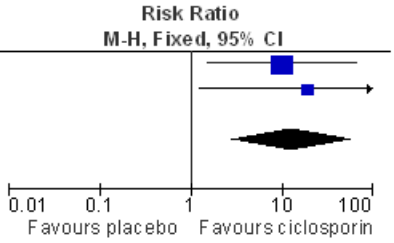
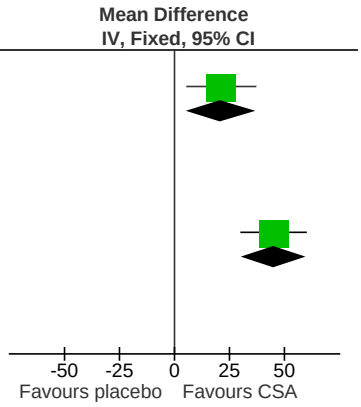


Figure 210: Percentage change in PASI at 10 weeks

Study or Subgroup	CSA Mean	CSA SD	CSA Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
7.3.1 CSA 1.25 mg/kg/day								
Meffert 1997	27.2	34.6	40	5.9	36.1	39	100.0%	21.30 [5.70, 36.90]
Subtotal (95% CI)			**40**			**39**	**100.0%**	**21.30 [5.70, 36.90]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.68 (P = 0.007)								
7.3.2 CSA 2.5 mg/kg/day								
Meffert 1997	51	30.9	41	5.9	36.1	39	100.0%	45.10 [30.34, 59.86]
Subtotal (95% CI)			**41**			**39**	**100.0%**	**45.10 [30.34, 59.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.99 (P < 0.00001)								



Test for subgroup differences: Chi² = 4.72, df = 1 (P = 0.03), I² = 78.8%

Figure 211: Hypertension at 8-10 weeks

Study or Subgroup	CSA Events	CSA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ellis 1986	7	11	7	10	93.4%	0.91 [0.50, 1.66]
Guenther 1991	2	12	0	11	6.6%	4.62 [0.25, 86.72]
Total (95% CI)		**23**		**21**	**100.0%**	**1.15 [0.61, 2.17]**
Total events	9		7			

Heterogeneity: Chi² = 1.46, df = 1 (P = 0.23); I² = 31%
Test for overall effect: Z = 0.44 (P = 0.66)

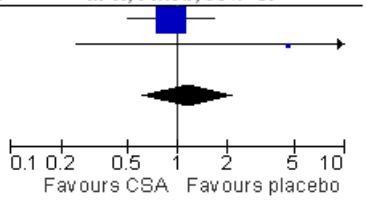
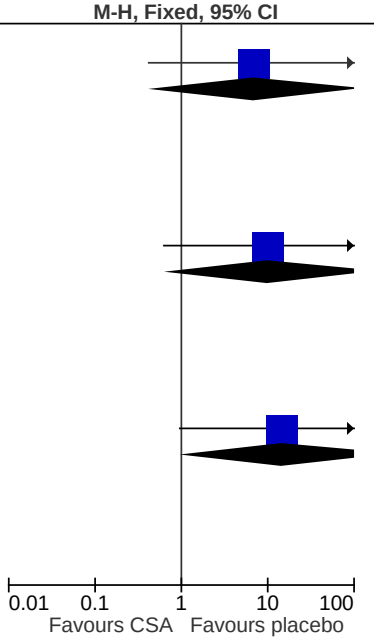


Figure 212: Decrease in glomerular filtration rate at 8 weeks

Study or Subgroup	CSA Events	CSA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.8.2 CSA 3 mg/kg						
Ellis 1991	4	12	0	9	100.0%	6.92 [0.42, 114.19]
Subtotal (95% CI)		**12**		**9**	**100.0%**	**6.92 [0.42, 114.19]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.35 (P = 0.18)						
7.8.3 CSA 5 mg/kg						
Ellis 1991	5	10	0	9	100.0%	10.00 [0.63, 158.87]
Subtotal (95% CI)		**10**		**9**	**100.0%**	**10.00 [0.63, 158.87]**
Total events	5		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.63 (P = 0.10)						
7.8.4 CSA 7.5 mg/kg						
Ellis 1991	9	12	0	9	100.0%	14.62 [0.96, 222.24]
Subtotal (95% CI)		**12**		**9**	**100.0%**	**14.62 [0.96, 222.24]**
Total events	9		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.93 (P = 0.05)						

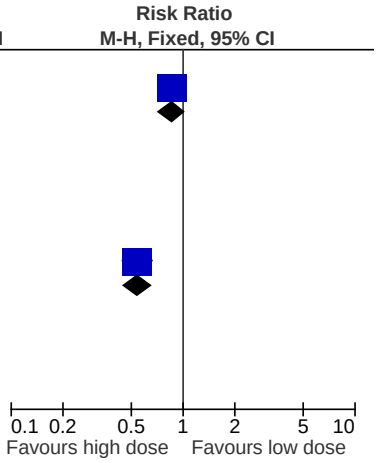


Test for subgroup differences: Chi² = 0.14, df = 2 (P = 0.93), I² = 0%

J.7.7 Ciclosporin dosage comparisons for induction of remission

Figure 213: PASI75 at 12-36 weeks

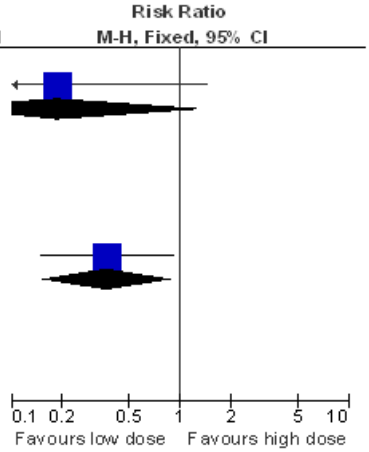
Study or Subgroup	CSA low dose Events	CSA low dose Total	CSA high dose Events	CSA high dose Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.1.1 CSA 1.25 starting dose vs 2.5 mg/kg starting dose						
Christophers 1992	68	109	78	108	100.0%	0.86 [0.72, 1.04]
Subtotal (95% CI)		**109**		**108**	**100.0%**	**0.86 [0.72, 1.04]**
Total events	68		78			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						
8.1.2 CSA 2.5 vs 5.0 mg/kg						
Laburte 1994	57	119	117	132	100.0%	0.54 [0.44, 0.66]
Subtotal (95% CI)		**119**		**132**	**100.0%**	**0.54 [0.44, 0.66]**
Total events	57		117			
Heterogeneity: Not applicable						
Test for overall effect: Z = 6.12 (P < 0.00001)						



Test for subgroup differences: Chi² = 11.45, df = 1 (P = 0.0007), I² = 91.3%

Figure 214: Elevated creatinine at 12-36 weeks

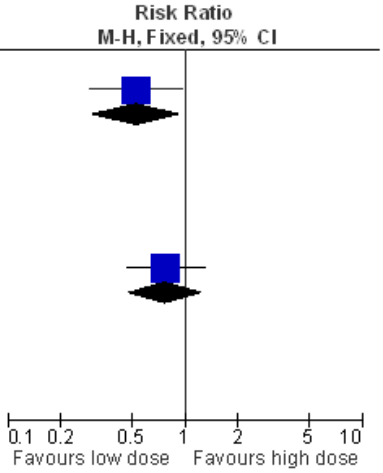
Study or Subgroup	CSA 1.25 mg/kg Events	Total	CSA 2.5 mg/kg Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.2.1 CSA 1.25 mg/kg vs CSA 2.5 mg/kg						
Christophers 1992	1	109	9	183	100.0%	0.19 [0.02, 1.45]
Subtotal (95% CI)		**109**		**183**	**100.0%**	**0.19 [0.02, 1.45]**
Total events	1		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.60 (P = 0.11)						
8.2.2 CSA 2.5 mg/kg vs CSA 5 mg/kg						
Christophers 1992	9	183	8	60	100.0%	0.37 [0.15, 0.91]
Subtotal (95% CI)		**183**		**60**	**100.0%**	**0.37 [0.15, 0.91]**
Total events	9		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.16 (P = 0.03)						



Test for subgroup differences: Chi² = 0.35, df = 1 (P = 0.55), I² = 0%

Figure 215: Hypertension at 12-36 weeks

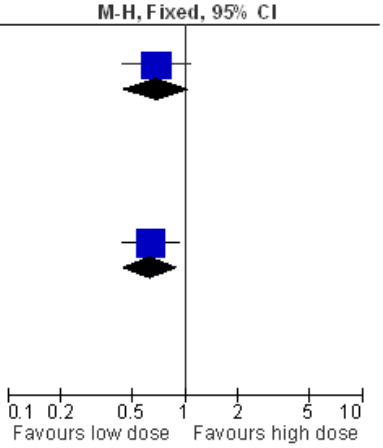
Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.3.1 CSA 1.25 mg/kg vs CSA 2.5 mg/kg						
Christophers 1992	12	109	38	183	100.0%	0.53 [0.29, 0.97]
Subtotal (95% CI)		**109**		**183**	**100.0%**	**0.53 [0.29, 0.97]**
Total events	12		38			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.06 (P = 0.04)						
8.3.2 CSA 2.5 mg/kg vs CSA 5 mg/kg						
Christophers 1992	38	183	16	60	100.0%	0.78 [0.47, 1.29]
Subtotal (95% CI)		**183**		**60**	**100.0%**	**0.78 [0.47, 1.29]**
Total events	38		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						



Test for subgroup differences: Chi² = 0.91, df = 1 (P = 0.34), I² = 0%

Figure 216: Elevated uric acid at 12-36 weeks

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.4.1 CSA 1.25 mg/kg vs CSA 2.5 mg/kg						
Christophers 1992	21	109	51	183	100.0%	0.69 [0.44, 1.08]
Subtotal (95% CI)		**109**		**183**	**100.0%**	**0.69 [0.44, 1.08]**
Total events	21		51			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.61 (P = 0.11)						
8.4.2 CSA 2.5 mg/kg vs CSA 5 mg/kg						
Christophers 1992	51	183	26	60	100.0%	0.64 [0.44, 0.93]
Subtotal (95% CI)		**183**		**60**	**100.0%**	**0.64 [0.44, 0.93]**
Total events	51		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.33 (P = 0.02)						



Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%

J.7.8 Ciclosporin vs placebo for maintenance of remission

Figure 217: PASI75 at 24 weeks

Study or Subgroup	CSA 5 mg/kg/day Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Colombo 2010	85	127	33	62	100.0%	1.26 [0.97, 1.64]
Total (95% CI)		**127**		**62**	**100.0%**	**1.26 [0.97, 1.64]**
Total events	85		33			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.70 (P = 0.09)

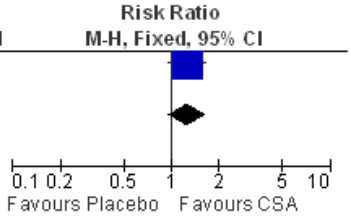


Figure 218: Final PASI at 24 weeks

Study or Subgroup	CSA 5 mg/kg/day Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Colombo 2010	7.3	8.5	127	8.8	8.8	62	100.0%	-1.50 [-4.14, 1.14]
Total (95% CI)			**127**			**62**	**100.0%**	**-1.50 [-4.14, 1.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.11 (P = 0.27)

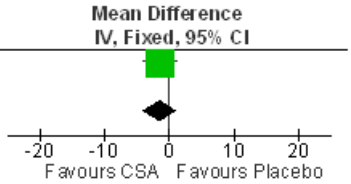


Figure 219: Maintaining at least mild psoriasis after indiction of PASI75 at 12 weeks

Study or Subgroup	CSA Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Thaci 2002	14	31	5	22	100.0%	1.99 [0.84, 4.71]
Total (95% CI)		**31**		**22**	**100.0%**	**1.99 [0.84, 4.71]**
Total events	14		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.56 (P = 0.12)

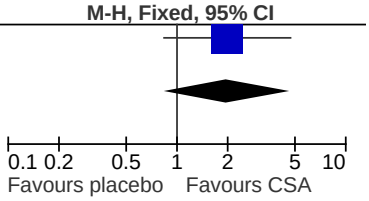
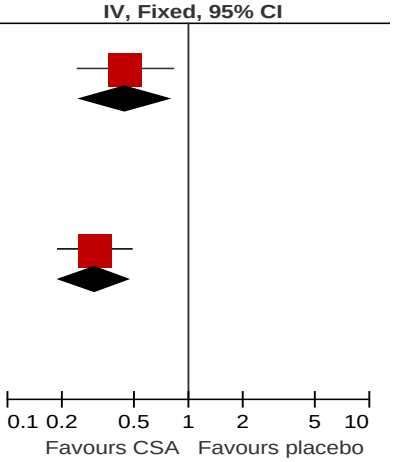


Figure 220: Time to relapse at 12-24 weeks

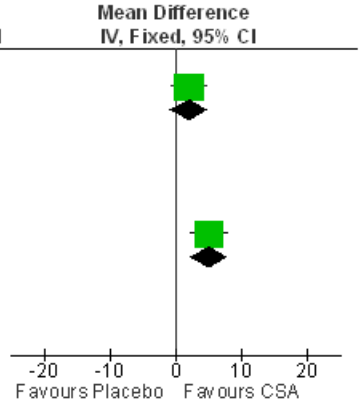
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
9.9.1 – CSA three-times weekly				
Thaci 2002	-0.8	0.31	100.0%	0.45 [0.24, 0.82]
Subtotal (95% CI)			**100.0%**	**0.45 [0.24, 0.82]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.58 (P = 0.010)				
9.9.2 – CSA 3mg/kg/day				
Shupack 1997	-1.19	0.24	100.0%	0.30 [0.19, 0.49]
Subtotal (95% CI)			**100.0%**	**0.30 [0.19, 0.49]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 4.96 (P < 0.00001)				



Test for subgroup differences: Chi² = 0.99, df = 1 (P = 0.32), I² = 0%

Figure 221: Mean time to relapse at 4 months

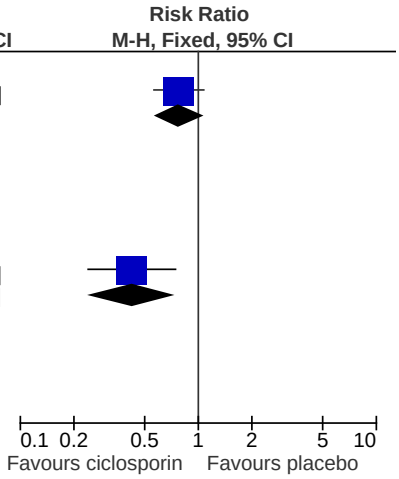
Study or Subgroup	CSA Mean	CSA SD	CSA Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
11.5.2 CSA 1.5 mg/kg/day								
Ellis 1995	9	4.47	20	7	4.47	20	100.0%	2.00 [-0.77, 4.77]
Subtotal (95% CI)			**20**			**20**	**100.0%**	**2.00 [-0.77, 4.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.41 (P = 0.16)								
11.5.3 CSA 3 mg/kg/day								
Ellis 1995	12	4.58	21	7	4.47	20	100.0%	5.00 [2.23, 7.77]
Subtotal (95% CI)			**21**			**20**	**100.0%**	**5.00 [2.23, 7.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.54 (P = 0.0004)								



Test for subgroup differences: Chi² = 2.25, df = 1 (P = 0.13), I² = 55.6%

Figure 222: Relapse rate at 4 months

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.10.1 CSA 1.5 mg/kg/day						
Ellis 1995	14	20	18	20	100.0%	0.78 [0.56, 1.07]
Subtotal (95% CI)		**20**		**20**	**100.0%**	**0.78 [0.56, 1.07]**
Total events	14		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.53 (P = 0.13)						
9.10.2 CSA 3 mg/kg/day						
Ellis 1995	8	21	18	20	100.0%	0.42 [0.24, 0.74]
Subtotal (95% CI)		**21**		**20**	**100.0%**	**0.42 [0.24, 0.74]**
Total events	8		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.99 (P = 0.003)						



Test for subgroup differences: Chi² = 3.37, df = 1 (P = 0.07), I² = 70.3%

Figure 223: Relapse rate at 24 weeks - weekend only dosing

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Colombo 2010	42	127	29	62	100.0%	0.71 [0.49, 1.02]
Total (95% CI)		**127**		**62**	**100.0%**	**0.71 [0.49, 1.02]**
Total events	42		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.87 (P = 0.06)						

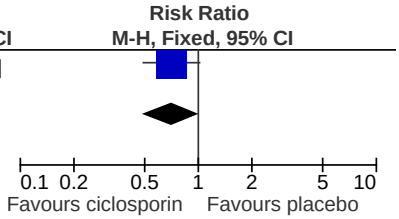


Figure 224: Withdrawal due to toxicity at 24 weeks

Study or Subgroup	CSA 5 mg/kg/day Events	CSA 5 mg/kg/day Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Colombo 2010	8	160	2	79	100.0%	1.98 [0.43, 9.08]
Total (95% CI)		**160**		**79**	**100.0%**	**1.97 [0.43, 9.08]**
Total events	8		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.87 (P = 0.38)						

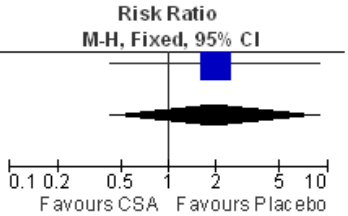


Figure 225: Severe adverse events at 24 weeks

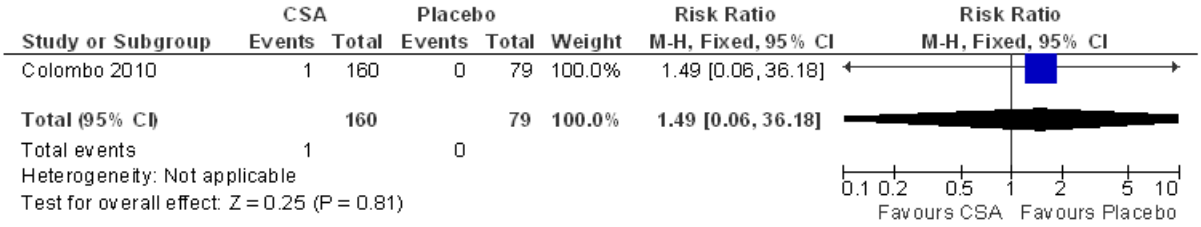
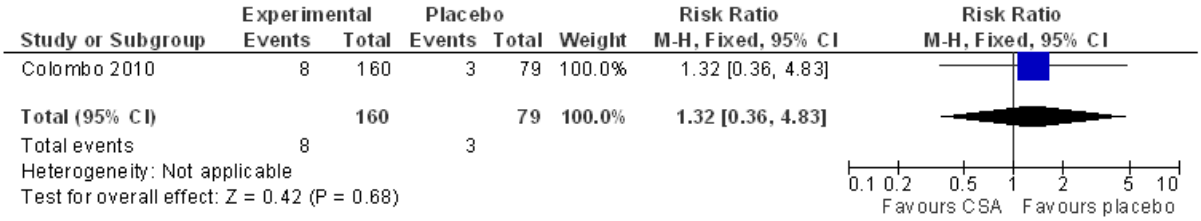


Figure 226: Elevated serum creatinine at 12 weeks



J.7.8.1 Intermittent (abrupt cessation) vs continuous ciclosporin for maintenance of remission

Figure 227: Clear/nearly clear (PASI90) at 9 months

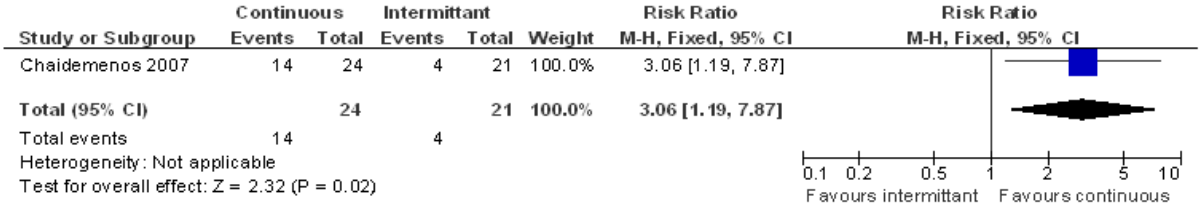


Figure 228: PASI75 at 9 months

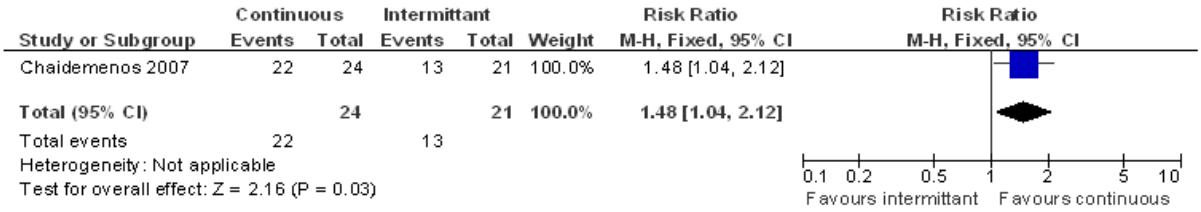


Figure 229: PASI50 at 9 months

Study or Subgroup	Continuous Events	Continuous Total	Intermittant Events	Intermittant Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chaidemenos 2007	23	24	20	21	100.0%	1.01 [0.89, 1.14]
Total (95% CI)		**24**		**21**	**100.0%**	**1.01 [0.89, 1.14]**
Total events	23		20			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.10 (P = 0.92)

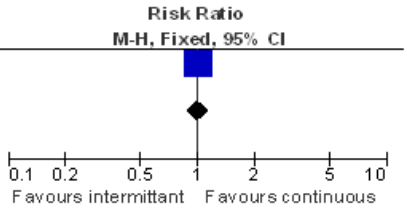


Figure 230: Time to relapse after a maximum follow-up of 1 year

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Ho1999	-0.26	0.12	100.0%	0.77 [0.61, 0.98]
Total (95% CI)			**100.0%**	**0.77 [0.61, 0.98]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.17 (P = 0.03)

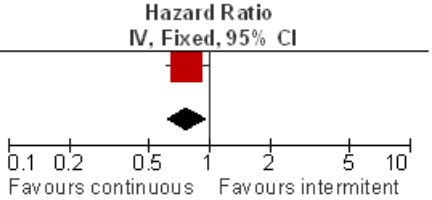


Figure 231: Increased serum creatinine at 9 months

Study or Subgroup	Continuous Events	Continuous Total	Intermittant Events	Intermittant Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chaidemenos 2007	2	24	2	21	100.0%	0.88 [0.13, 5.68]
Total (95% CI)		**24**		**21**	**100.0%**	**0.88 [0.13, 5.68]**
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.14 (P = 0.89)

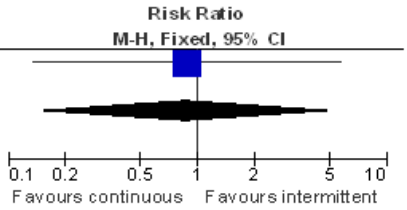
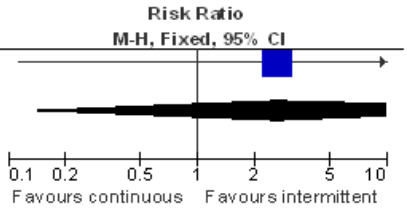


Figure 232: Hypertension at 9 months

Study or Subgroup	Continuous Events	Continuous Total	Intermittant Events	Intermittant Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chaidemenos 2007	1	24	0	21	100.0%	2.64 [0.11, 61.54]
Total (95% CI)		**24**		**21**	**100.0%**	**2.64 [0.11, 61.54]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)



1.1.5 Intermittent (taper to cessation) vs continuous ciclosporin for maintenance of remission

Figure 233: % change in PASI at 48 months

Study or Subgroup	Intermittent Mean	Intermittent SD	Intermittent Total	Continuous Mean	Continuous SD	Continuous Total	Weight	Mean Difference IV, Fixed, 95% CI
Ozawa 1999	71.26	5.27	20	61.96	4.8	17	100.0%	9.30 [6.05, 12.55]
Total (95% CI)			**20**			**17**	**100.0%**	**9.30 [6.05, 12.55]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.61 (P < 0.00001)

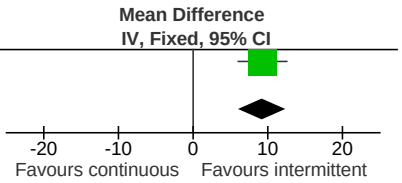


Figure 234: Final PASI at 48 months

Study or Subgroup	Intermittent Mean	Intermittent SD	Intermittent Total	Continuous Mean	Continuous SD	Continuous Total	Weight	Mean Difference IV, Fixed, 95% CI
Ohtsuki 2003	9.59	2.22	16	6.03	0.95	15	100.0%	3.56 [2.37, 4.75]
Total (95% CI)			**16**			**15**	**100.0%**	**3.56 [2.37, 4.75]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.87 (P < 0.00001)

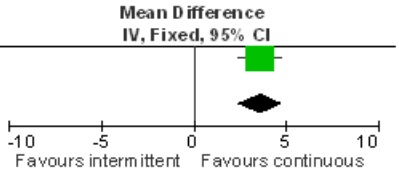


Figure 235: Withdrawal due to toxicity at 48 months

Study or Subgroup	Intermittent Events	Intermittent Total	Continuous Events	Continuous Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ozawa 1999	2	33	1	35	100.0%	2.12 [0.20, 22.31]
Total (95% CI)		**33**		**35**	**100.0%**	**2.12 [0.20, 22.31]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

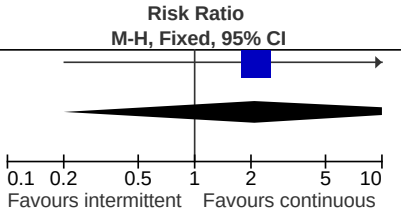


Figure 236: Hypertension at 1 year

Study or Subgroup	Intermittent Events	Intermittent Total	Continuous Events	Continuous Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ohtsuki 2003	10	61	6	61	100.0%	1.67 [0.65, 4.30]
Total (95% CI)		**61**		**61**	**100.0%**	**1.67 [0.65, 4.30]**
Total events	10		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)

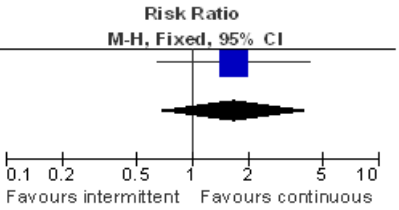


Figure 237: Increased creatinine at 1 year

Study or Subgroup	Intermittent Events	Intermittent Total	Continuous Events	Continuous Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ohtsuki 2003	3	61	2	61	100.0%	1.50 [0.26, 8.66]
Total (95% CI)		**61**		**61**	**100.0%**	**1.50 [0.26, 8.66]**
Total events	3		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.45 (P = 0.65)

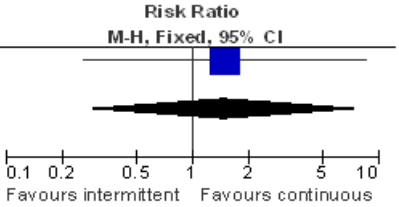


Figure 238: Hyperuricaemia at 1 year

Study or Subgroup	Intermittent Events	Intermittent Total	Continuous Events	Continuous Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ohtsuki 2003	6	61	3	61	100.0%	2.00 [0.52, 7.64]
Total (95% CI)		**61**		**61**	**100.0%**	**2.00 [0.52, 7.64]**
Total events	6		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.01 (P = 0.31)

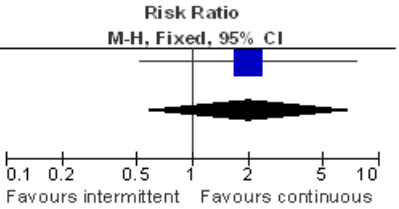
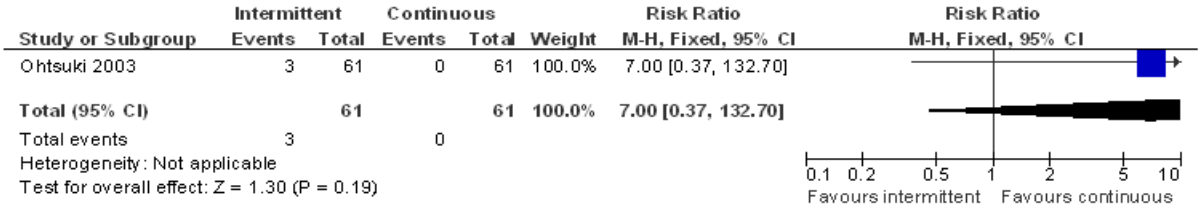


Figure 239: Increased liver enzymes at 1 year



J.7.9 Ciclosporin dosage comparisons for maintenance of remission

Figure 240: Severe adverse events at 18 months

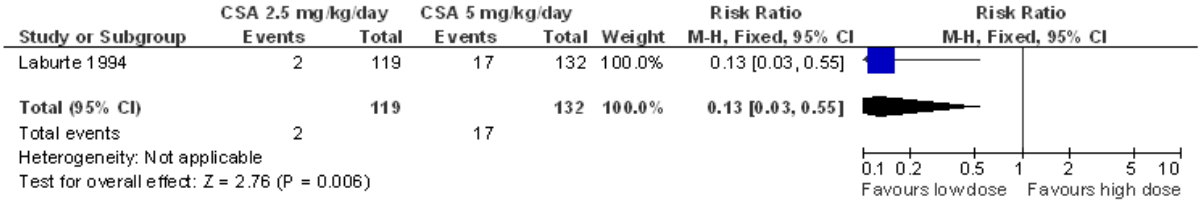


Figure 241: Hypertension at 18 months

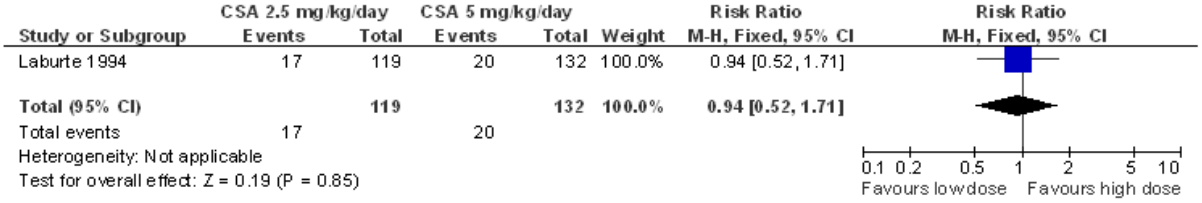


Figure 242: Elevated uric acid at 18 months

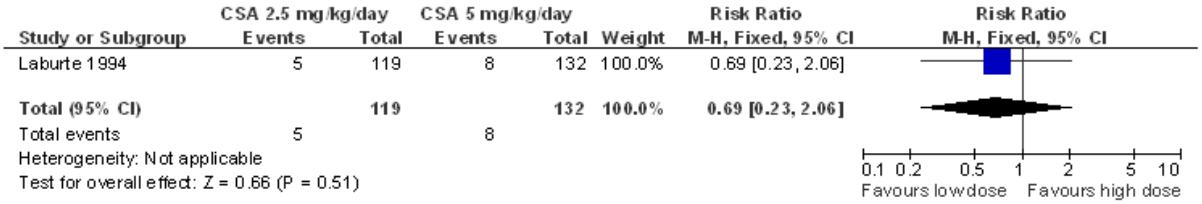
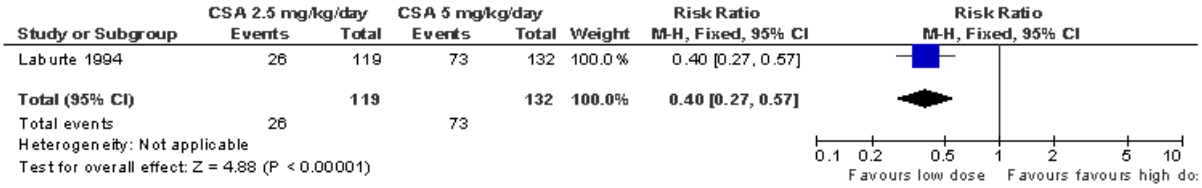


Figure 243: Elevated creatinine at 18 months



J.7.9.1 Ciclosporin vs placebo for induction of remission in palmoplantar pustulosis

Figure 244: Improvement at 4 weeks

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Erkko 1998	13	27	6	31	58.3%	2.49 [1.10, 5.64]
Reitamo 1993	17	19	4	19	41.7%	4.25 [1.76, 10.29]
Total (95% CI)		**46**		**50**	**100.0%**	**3.22 [1.78, 5.85]**
Total events	30		10			

Heterogeneity: Chi² = 0.76, df = 1 (P = 0.38); I² = 0%
Test for overall effect: Z = 3.85 (P = 0.0001)

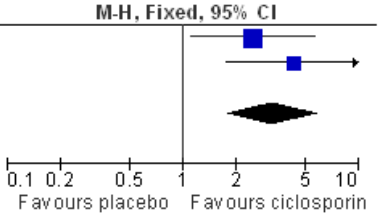


Figure 245: Hypertension at 1 month

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Erkko 1998	1	27	0	31	100.0%	3.43 [0.15, 80.83]
Total (95% CI)		**27**		**31**	**100.0%**	**3.43 [0.15, 80.83]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.76 (P = 0.44)

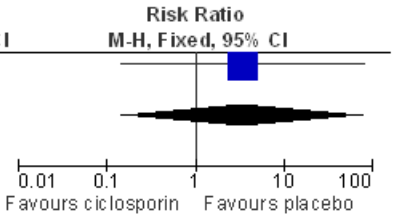


Figure 246: Hypertension at 12 months

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Erkko 1998	7	27	0	31	100.0%	17.14 [1.02, 286.86]
Total (95% CI)		**27**		**31**	**100.0%**	**17.14 [1.02, 286.86]**
Total events	7		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.98 (P = 0.05)

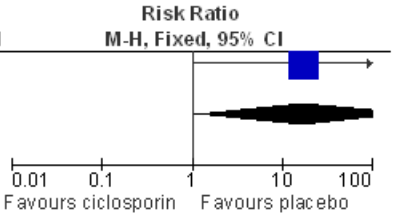


Figure 247: Increased serum creatinine at 12 months

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Erkko 1998	2	27	0	31	100.0%	5.71 [0.29, 114.05]
Total (95% CI)		**27**		**31**	**100.0%**	**5.71 [0.29, 114.05]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.14 (P = 0.25)

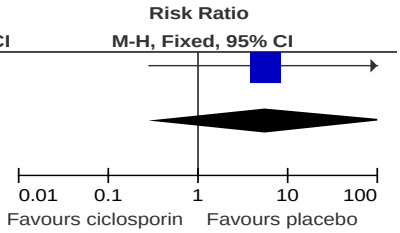


Figure 248: Improvement (open phase)

Study or Subgroup	Ciclosporin Events	Ciclosporin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Reitamo 1993	10	14	10	14	100.0%	1.00 [0.63, 1.60]
Total (95% CI)		**14**		**14**	**100.0%**	**1.00 [0.63, 1.60]**
Total events	10		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

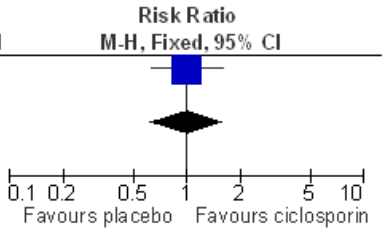


Figure 249: Relapse rate (open phase)

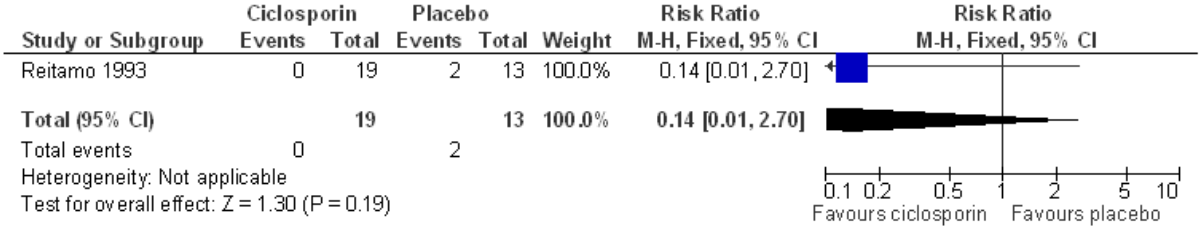
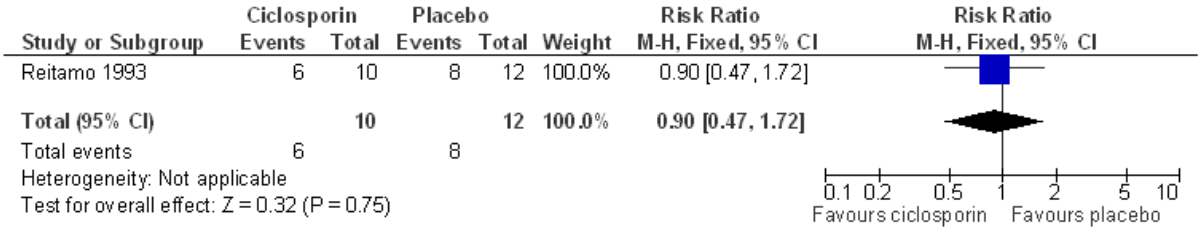


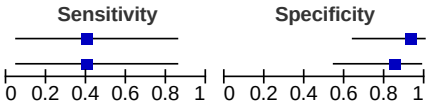
Figure 250: Relapse rate (withdrawal phase)



J.8 Methotrexate and monitoring for hepatotoxicity

Figure 251: ALT vs biopsy

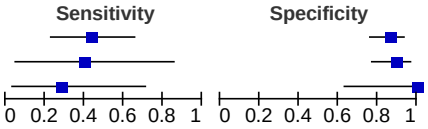
Study	TP	FP	FN	TN	Sensitivity	Specificity
Ho 1986 (TH >40 U/L)	2	1	3	12	0.40 [0.05, 0.85]	0.92 [0.64, 1.00]
Ho 1986 (TH>32 U/L)	2	2	3	11	0.40 [0.05, 0.85]	0.85 [0.55, 0.98]



Note: all of the data are from the same population

Figure 252: AST vs biopsy

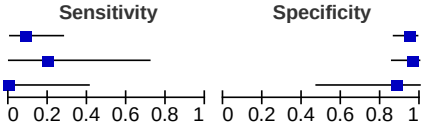
Study	TP	FP	FN	TN	Sensitivity	Specificity
O'Connor 1989 (post-MTX)	10	10	13	62	0.43 [0.23, 0.66]	0.86 [0.76, 0.93]
O'Connor 1989 (pre-MTX)	2	5	3	42	0.40 [0.05, 0.85]	0.89 [0.77, 0.96]
Paramsothy 1988	2	0	5	8	0.29 [0.04, 0.71]	1.00 [0.63, 1.00]



Note: all of the O'Connor data are from the same population

Figure 253: Bilirubin vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
O'Connor 1989 (post-MTX)	2	4	21	68	0.09 [0.01, 0.28]	0.94 [0.86, 0.98]
O'Connor 1989 (pre-MTX)	1	2	4	45	0.20 [0.01, 0.72]	0.96 [0.85, 0.99]
Paramsothy 1988	0	1	7	7	0.00 [0.00, 0.41]	0.88 [0.47, 1.00]



Note: all of the O'Connor data are from the same population

Figure 254: Galactose vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Lenler-Petersen 1982	15	3	90	43	0.14 [0.08, 0.22]	0.93 [0.82, 0.99]

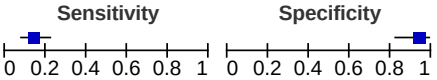


Figure 255: Albumin vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Paramsothy 1988	2	0	5	8	0.29 [0.04, 0.71]	1.00 [0.63, 1.00]

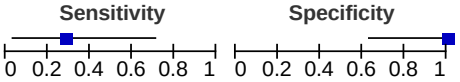
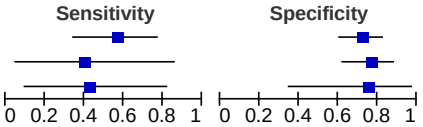


Figure 256: Alkaline phosphatase vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
O'Connor 1989 (post-MTX)	13	20	10	52	0.57 [0.34, 0.77]	0.72 [0.60, 0.82]
O'Connor 1989 (pre-MTX)	2	11	3	36	0.40 [0.05, 0.85]	0.77 [0.62, 0.88]
Paramsothy 1988	3	2	4	6	0.43 [0.10, 0.82]	0.75 [0.35, 0.97]



Note: all of the O'Connor data are from the same population

Figure 257: Gamma-glutamyl transferase vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Paramsothy 1988	2	3	4	5	0.33 [0.04, 0.78]	0.63 [0.24, 0.91]

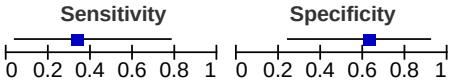


Figure 258: Liver scintigraphy vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Geronemus 1982	4	6	3	11	0.57 [0.18, 0.90]	0.65 [0.38, 0.86]
McHenry 1992	5	15	1	66	0.83 [0.36, 1.00]	0.81 [0.71, 0.89]
Mitchell 1987	6	10	6	27	0.50 [0.21, 0.79]	0.73 [0.56, 0.86]

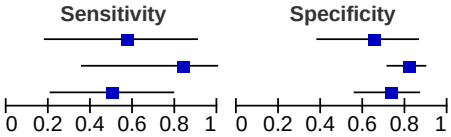
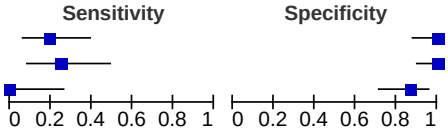


Figure 259: Ultrasound vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Coulson 1987	5	0	21	28	0.19 [0.07, 0.39]	1.00 [0.88, 1.00]
Coulson 1987 - portal	5	0	15	34	0.25 [0.09, 0.49]	1.00 [0.90, 1.00]
Mitchell 1987	0	5	12	32	0.00 [0.00, 0.26]	0.86 [0.71, 0.95]



Note: all of the Coulson data are from the same population

Figure 260: PIIINP vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Boffa 1996	17	24	4	42	0.81 [0.58, 0.95]	0.64 [0.51, 0.75]
Maurice 2005	15	49	9	102	0.63 [0.41, 0.81]	0.68 [0.59, 0.75]
Risteli 1988/Zachariae 89	19	1	6	46	0.76 [0.55, 0.91]	0.98 [0.89, 1.00]
Zachariae 2001	4	2	0	63	1.00 [0.40, 1.00]	0.97 [0.89, 1.00]

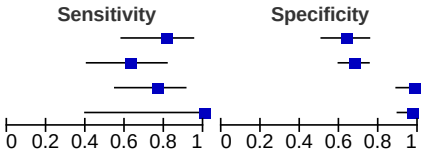


Figure 261: Fibrotest vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Berends 2007	5	7	1	11	0.83 [0.36, 1.00]	0.61 [0.36, 0.83]

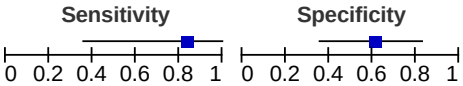
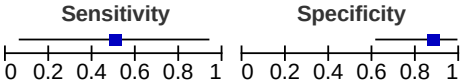


Figure 262: Fibroscan vs biopsy

Study	TP	FP	FN	TN	Sensitivity	Specificity
Berends 2007	2	2	2	14	0.50 [0.07, 0.93]	0.88 [0.62, 0.98]



Note: there is uncertainty about the accuracy of the values for TP, FP, FN and TN for this test

J.9 Seqeuncing of biologic therapy

The majority of the data presented in the forest plots below are derived from observational studies and must be interpreted with caution. Note also that all observational study data have been considered individually and the forest plots do not represent combined data from multiple studies.

J.9.1 Previous biologic vs no previous biologic

J.9.1.1 Etanercept

Figure 263: Clear/nearly clear (PASI 90) at week 12

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	4	27	76	319	100.0%	0.62 [0.25, 1.57]
Total (95% CI)		**27**		**319**	**100.0%**	**0.62 [0.25, 1.57]**
Total events	4		76			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.01 (P = 0.31)

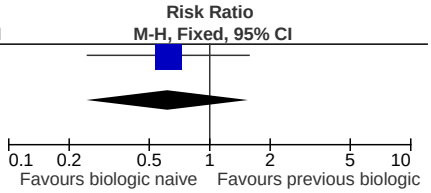


Figure 264: Clear/nearly clear (PGA) at week 12

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	10	27	159	319	100.0%	0.74 [0.45, 1.23]
Total (95% CI)		**27**		**319**	**100.0%**	**0.74 [0.45, 1.23]**
Total events	10		159			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.15 (P = 0.25)

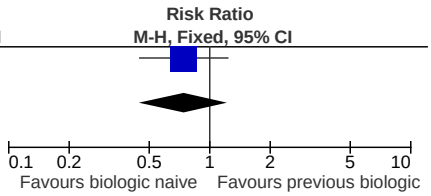


Figure 265: PASI75 (week 12)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Psoriasis						
Mazzotta 2009	8	26	43	98	47.9%	0.70 [0.38, 1.30]
Subtotal (95% CI)		**26**		**98**	**47.9%**	**0.70 [0.38, 1.30]**
Total events	8		43			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.12 (P = 0.26)

1.2.2 Psoriatic arthritis						
Mazzotta 2009	11	30	36	80	52.1%	0.81 [0.48, 1.38]
Subtotal (95% CI)		**30**		**80**	**52.1%**	**0.81 [0.48, 1.38]**
Total events	11		36			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.76 (P = 0.45)

Total (95% CI)		**56**		**178**	**100.0%**	**0.76 [0.51, 1.14]**
Total events	19		79			

Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 1.33 (P = 0.18)
Test for subgroup differences: Chi² = 0.13, df = 1 (P = 0.72), I² = 0%

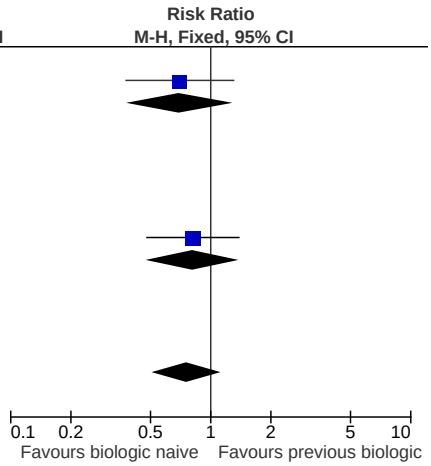


Figure 266: PASI75 (week 12)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	10	27	186	319	100.0%	0.64 [0.39, 1.05]
Total (95% CI)		**27**		**319**	**100.0%**	**0.64 [0.39, 1.05]**
Total events	10		186			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.78 (P = 0.08)

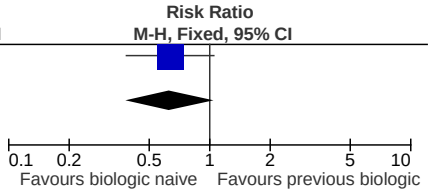


Figure 267: PASI75 at week 24

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.10.1 Psoriasis						
Mazzotta 2009	17	26	74	98	49.1%	0.87 [0.64, 1.17]
Subtotal (95% CI)		**26**		**98**	**49.1%**	**0.87 [0.64, 1.17]**
Total events	17		74			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						
1.10.2 Psoriatic arthritis						
Mazzotta 2009	9	30	59	80	50.9%	0.41 [0.23, 0.71]
Subtotal (95% CI)		**30**		**80**	**50.9%**	**0.41 [0.23, 0.71]**
Total events	9		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.14 (P = 0.002)						
Total (95% CI)		**56**		**178**	**100.0%**	**0.63 [0.47, 0.84]**
Total events	26		133			
Heterogeneity: Chi² = 6.55, df = 1 (P = 0.01); I² = 85%						
Test for overall effect: Z = 3.13 (P = 0.002)						
Test for subgroup differences: Chi² = 5.39, df = 1 (P = 0.02), I² = 81.4%						

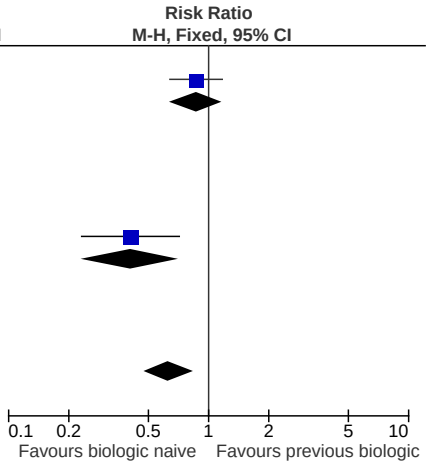


Figure 268: PASI50 (week 12)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 Psoriasis						
Mazzotta 2009	18	26	79	98	53.4%	0.86 [0.65, 1.13]
Subtotal (95% CI)		**26**		**98**	**53.4%**	**0.86 [0.65, 1.13]**
Total events	18		79			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.28)						
1.5.2 Psoriatic arthritis						
Mazzotta 2009	18	30	53	80	46.6%	0.91 [0.65, 1.26]
Subtotal (95% CI)		**30**		**80**	**46.6%**	**0.91 [0.65, 1.26]**
Total events	18		53			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
Total (95% CI)		**56**		**178**	**100.0%**	**0.88 [0.71, 1.09]**
Total events	36		132			
Heterogeneity: Chi² = 0.06, df = 1 (P = 0.81); I² = 0%						
Test for overall effect: Z = 1.17 (P = 0.24)						
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%						

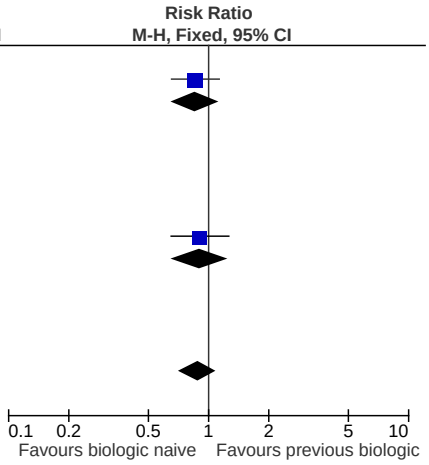


Figure 269: PASI50 (week 12)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	20	27	265	319	100.0%	0.89 [0.71, 1.12]
Total (95% CI)		**27**		**319**	**100.0%**	**0.89 [0.71, 1.12]**
Total events	20		265			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						

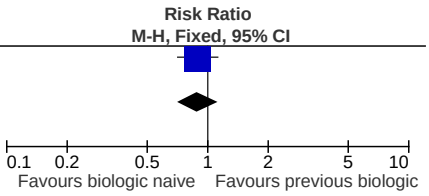


Figure 270: PASI 50 (week 24)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 Psoriasis						
Mazzotta 2009	18	26	88	98	47.8%	0.77 [0.59, 1.00]
Subtotal (95% CI)		**26**		**98**	**47.8%**	**0.77 [0.59, 1.00]**
Total events	18		88			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.93 (P = 0.05)						
1.6.2 Psoriatic arthritis						
Mazzotta 2009	14	30	74	80	52.2%	0.50 [0.34, 0.74]
Subtotal (95% CI)		**30**		**80**	**52.2%**	**0.50 [0.34, 0.74]**
Total events	14		74			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.46 (P = 0.0005)						
Total (95% CI)		**56**		**178**	**100.0%**	**0.63 [0.50, 0.79]**
Total events	32		162			
Heterogeneity: Chi² = 3.47, df = 1 (P = 0.06); I² = 71%						
Test for overall effect: Z = 3.94 (P < 0.0001)						
Test for subgroup differences: Chi² = 3.14, df = 1 (P = 0.08), I² = 68.1%						

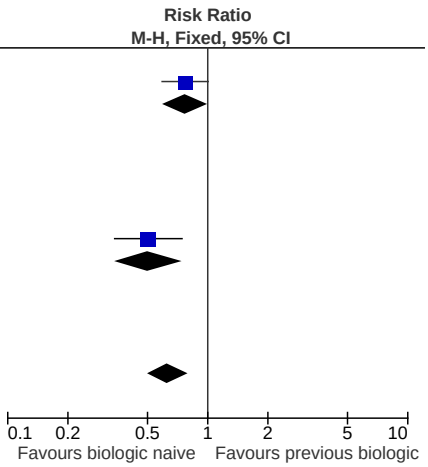


Figure 271: % improvement in PASI (week 12)

Study or Subgroup	Previous biologic Mean	Previous biologic SD	Previous biologic Total	Biologic naive Mean	Biologic naive SD	Biologic naive Total	Weight	Mean Difference IV, Fixed, 95% CI
ACCEPT - CFE	65.55	25.87	27	72.59	25.953	311	100.0%	-7.04 [-17.22, 3.14]
Total (95% CI)			**27**			**311**	**100.0%**	**-7.04 [-17.22, 3.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.36 (P = 0.18)								

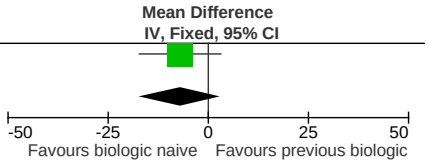


Figure 272: Final PASI (week 12)

Study or Subgroup	Previous biologic Mean	Previous biologic SD	Previous biologic Total	Biologic naive Mean	Biologic naive SD	Biologic naive Total	Weight	Mean Difference IV, Fixed, 95% CI
1.15.1 Psoriasis								
Mazzotta 2009	5.4	3.8	26	4.9	4	98	35.6%	0.50 [-1.16, 2.16]
Subtotal (95% CI)			**26**			**98**	**35.6%**	**0.50 [-1.16, 2.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.59 (P = 0.56)								
1.15.2 Psoriatic arthritis								
Mazzotta 2009	2.9	2.6	30	2.9	3.7	80	64.4%	0.00 [-1.23, 1.23]
Subtotal (95% CI)			**30**			**80**	**64.4%**	**0.00 [-1.23, 1.23]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**56**			**178**	**100.0%**	**0.18 [-0.81, 1.17]**
Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%								
Test for overall effect: Z = 0.35 (P = 0.73)								
Test for subgroup differences: Chi² = 0.22, df = 1 (P = 0.64), I² = 0%								

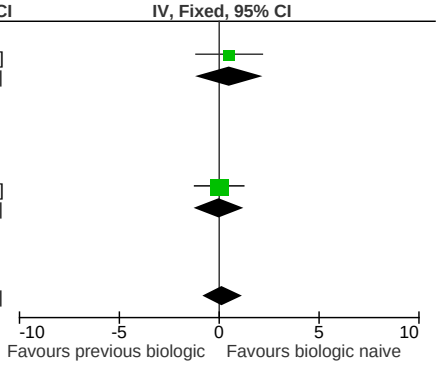
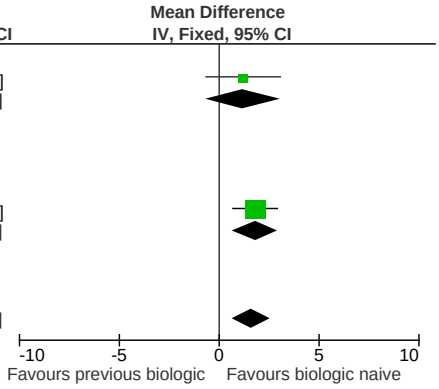


Figure 273: Final PASI (week 24)

Study or Subgroup	Previous biologic Mean	SD	Total	Biologic naive Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.16.1 Psoriasis								
Mazzotta 2009	4	4.5	26	2.8	3.4	98	26.3%	1.20 [-0.66, 3.06]
Subtotal (95% CI)			**26**			**98**	**26.3%**	**1.20 [-0.66, 3.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.27 (P = 0.21)								
1.16.2 Psoriatic arthritis								
Mazzotta 2009	3	2.9	30	1.2	1.8	80	73.7%	1.80 [0.69, 2.91]
Subtotal (95% CI)			**30**			**80**	**73.7%**	**1.80 [0.69, 2.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.18 (P = 0.001)								
Total (95% CI)			**56**			**178**	**100.0%**	**1.64 [0.69, 2.59]**
Heterogeneity: Chi² = 0.30, df = 1 (P = 0.59); I² = 0%								
Test for overall effect: Z = 3.38 (P = 0.0007)								
Test for subgroup differences: Chi² = 0.30, df = 1 (P = 0.59), I² = 0%								



J.9.1.2 Adalimumab

Figure 274: Clear/nearly clear at 12 months

Study or Subgroup	Previous biologic Events	Total	Biologic naive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Any previous biologic						
Van 2008	31	39	7	10	100.0%	1.14 [0.73, 1.76]
Subtotal (95% CI)		**39**		**10**	**100.0%**	**1.14 [0.73, 1.76]**
Total events	31		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.57 (P = 0.57)						
1.1.2 Previous TNF antagonist						
Van 2008	29	37	7	10	100.0%	1.12 [0.72, 1.74]
Subtotal (95% CI)		**37**		**10**	**100.0%**	**1.12 [0.72, 1.74]**
Total events	29		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.61)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%						

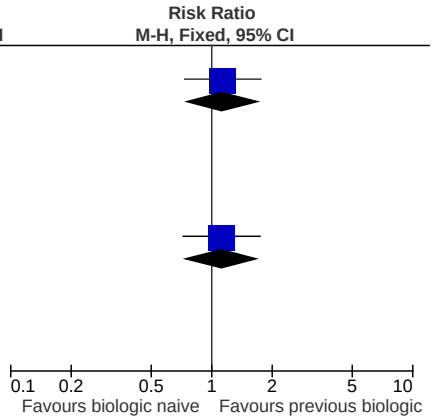
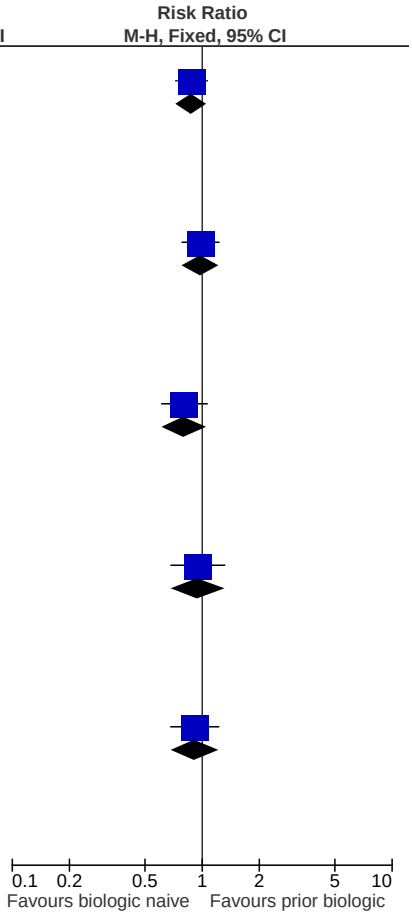


Figure 275: PASI75 (week 16)

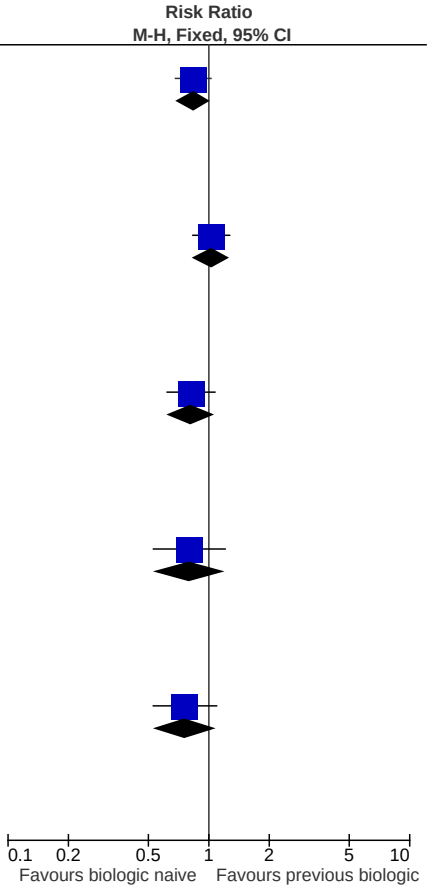
Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Any biologic exposure vs none						
Papp 2012 - CFE	51	78	93	125	100.0%	0.88 [0.73, 1.06]
Subtotal (95% CI)		**78**		**125**	**100.0%**	**0.88 [0.73, 1.06]**
Total events	51		93			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.32 (P = 0.19)						
2.2.3 Any anti-TNF exposure vs no biologic exposure						
Papp 2012 - CFE	27	37	93	125	100.0%	0.98 [0.79, 1.22]
Subtotal (95% CI)		**37**		**125**	**100.0%**	**0.98 [0.79, 1.22]**
Total events	27		93			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.17 (P = 0.86)						
2.2.4 Failed prior biologic vs no biologic exposure						
Papp 2012 - CFE	24	40	93	125	100.0%	0.81 [0.61, 1.06]
Subtotal (95% CI)		**40**		**125**	**100.0%**	**0.81 [0.61, 1.06]**
Total events	24		93			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						
2.2.5 Failed prior anti-TNF vs no biologic exposure						
Papp 2012 - CFE	12	17	93	125	100.0%	0.95 [0.69, 1.31]
Subtotal (95% CI)		**17**		**125**	**100.0%**	**0.95 [0.69, 1.31]**
Total events	12		93			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						
2.2.6 Failed at least 2 prior biologics vs no biologic exposure						
Papp 2012 - CFE	17	25	93	125	100.0%	0.91 [0.69, 1.22]
Subtotal (95% CI)		**25**		**125**	**100.0%**	**0.91 [0.69, 1.22]**
Total events	17		93			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						



Test for subgroup differences: Chi² = 1.37, df = 4 (P = 0.85), I² = 0%

Figure 276: PASI75 (week 24)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.6.1 Any biologic exposure vs none						
Papp 2012 - CFE	48	78	92	125	100.0%	0.84 [0.68, 1.03]
Subtotal (95% CI)		**78**		**125**	**100.0%**	**0.84 [0.68, 1.03]**
Total events	48		92			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.72 (P = 0.09)						
2.6.2 Any anti-TNF exposure vs no biologic exposure						
Papp 2012 - CFE	28	37	92	125	100.0%	1.03 [0.83, 1.27]
Subtotal (95% CI)		**37**		**125**	**100.0%**	**1.03 [0.83, 1.27]**
Total events	28		92			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.80)						
2.6.3 Failed prior biologic vs no biologic exposure						
Papp 2012 - CFE	24	40	92	125	100.0%	0.82 [0.62, 1.07]
Subtotal (95% CI)		**40**		**125**	**100.0%**	**0.82 [0.62, 1.07]**
Total events	24		92			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.14)						
2.6.4 Failed prior anti-TNF vs no biologic exposure						
Papp 2012 - CFE	10	17	92	125	100.0%	0.80 [0.53, 1.21]
Subtotal (95% CI)		**17**		**125**	**100.0%**	**0.80 [0.53, 1.21]**
Total events	10		92			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.29)						
2.6.5 Failed at least 2 prior biologics vs no biologic exposure						
Papp 2012 - CFE	14	25	92	125	100.0%	0.76 [0.53, 1.09]
Subtotal (95% CI)		**25**		**125**	**100.0%**	**0.76 [0.53, 1.09]**
Total events	14		92			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.48 (P = 0.14)						

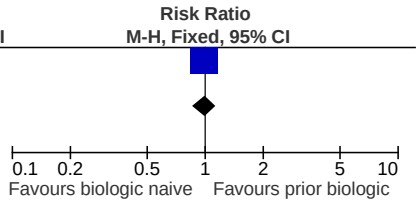


Test for subgroup differences: Chi² = 3.45, df = 4 (P = 0.48), I² = 0%

J.9.1.3 Infliximab

Figure 277: PASI75 (week 10)

Study or Subgroup	Prior biologic Events	Prior biologic Total	No prior biologic Events	No prior biologic Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Menter 2007	68	94	389	533	100.0%	0.99 [0.87, 1.13]
Total (95% CI)		**94**		**533**	**100.0%**	**0.99 [0.87, 1.13]**
Total events	68		389			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						



J.9.1.4 Ustekinumab

Figure 278: Clear/nearly clear (PASI90) at weeks 12, 24 and 52

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Week 12 (ITT)					
ACCEPT - CFE	10	36	221	519	0.65 [0.38, 1.12]
PHOENIX1 - CFE	75	212	125	299	0.85 [0.68, 1.06]
PHOENIX2 - CFE	94	250	288	570	0.74 [0.62, 0.89]
3.1.2 Week 24 (ACA)					
PHOENIX1 - CFE	114	207	182	290	0.88 [0.75, 1.02]
PHOENIX2 - CFE	113	242	329	558	0.79 [0.68, 0.92]
3.1.3 Week 52 (ACA)					
PHOENIX1 - CFE	39	59	66	103	1.03 [0.82, 1.30]
PHOENIX2 - CFE	86	148	276	389	0.82 [0.70, 0.95]

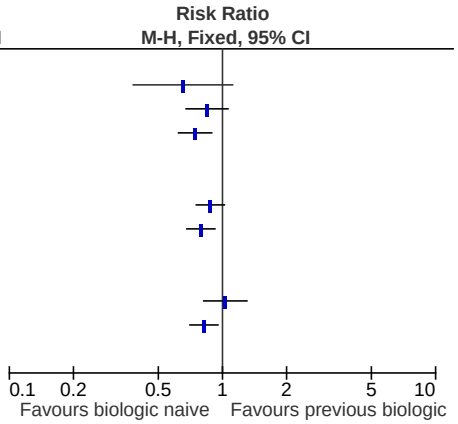


Figure 279: Clear/nearly clear (PGA) at weeks 12, 24 and 52

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Risk Ratio M-H, Fixed, 95% CI
3.2.1 Week 12 (ITT)					
ACCEPT - CFE	19	36	362	519	0.76 [0.55, 1.04]
PHOENIX1 - CFE	122	212	190	299	0.91 [0.78, 1.05]
PHOENIX2 - CFE	162	250	418	570	0.88 [0.80, 0.98]
3.2.2 Week 24 (ACA)					
PHOENIX1 - CFE	137	207	213	290	0.90 [0.80, 1.02]
PHOENIX2 - CFE	159	242	419	558	0.87 [0.79, 0.97]
3.2.3 Week 52 (ACA)					
PHOENIX1 - CFE	43	59	72	103	1.04 [0.85, 1.27]
PHOENIX2 - CFE	98	148	291	389	0.89 [0.78, 1.01]

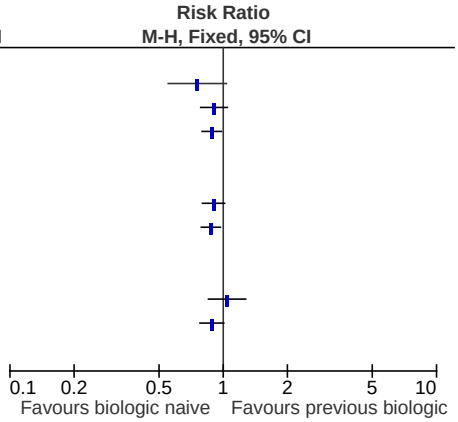


Figure 280: PASI75 at weeks 12, 24 and 52

Study or Subgroup	Favours biologic naive Events	Favours biologic naive Total	Biologic naive Events	Biologic naive Total	Risk Ratio M-H, Fixed, 95% CI
3.3.1 Week 12 (ITT)					
ACCEPT - CFE	20	36	377	519	0.76 [0.57, 1.03]
PHOENIX1 - CFE	128	212	213	299	0.85 [0.74, 0.97]
PHOENIX2 - CFE	158	250	426	570	0.85 [0.76, 0.94]
3.3.2 Week 24 (ACA)					
PHOENIX1 - CFE	155	207	245	290	0.89 [0.81, 0.97]
PHOENIX2 - CFE	181	242	446	558	0.94 [0.86, 1.02]
3.3.3 Week 28 (ACA)					
Papp 2008	209	307	380	513	0.92 [0.84, 1.01]
3.3.4 Week 52 (ACA)					
PHOENIX1 - CFE	51	59	93	103	0.96 [0.85, 1.08]
PHOENIX2 - CFE	127	148	360	389	0.93 [0.86, 1.00]

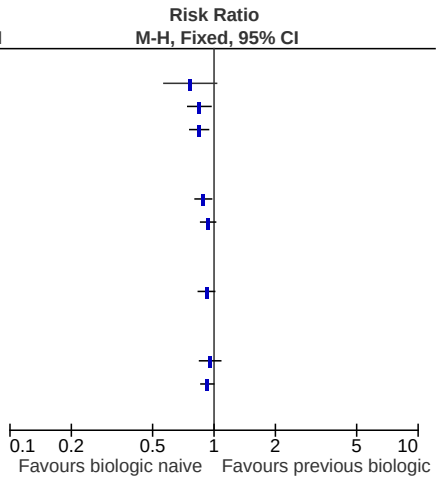


Figure 281: PASI75 (week 16)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Risk Ratio M-H, Fixed, 95% CI
3.26.2 Any biologic exposure vs none					
Laws 2011 - CFE	64	106	16	21	0.79 [0.60, 1.05]
3.26.7 None or one prior biologic vs 2-4 prior biologics					
Laws 2011 - CFE	45	79	35	48	0.78 [0.60, 1.01]

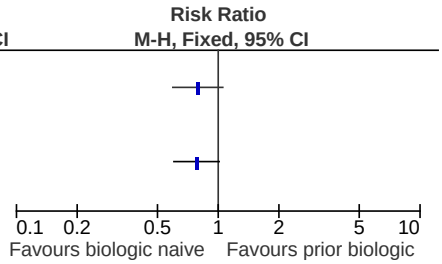


Figure 282: PASI50 (weeks 12, 24 and 52)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Risk Ratio M-H, Fixed, 95% CI
3.6.1 Week 12 (ITT)					
ACCEPT - CFE	28	36	473	519	0.85 [0.72, 1.02]
PHOENIX1 - CFE	171	212	262	299	0.92 [0.85, 1.00]
PHOENIX2 - CFE	213	250	496	570	0.98 [0.92, 1.04]
3.6.2 Week 24 (ACA)					
PHOENIX1 - CFE	186	207	275	290	0.95 [0.90, 1.00]
PHOENIX2 - CFE	225	242	517	558	1.00 [0.96, 1.05]
3.6.3 Week 52 (ACA)					
PHOENIX1 - CFE	57	59	101	103	0.99 [0.93, 1.04]
PHOENIX2 - CFE	146	148	386	389	0.99 [0.97, 1.02]

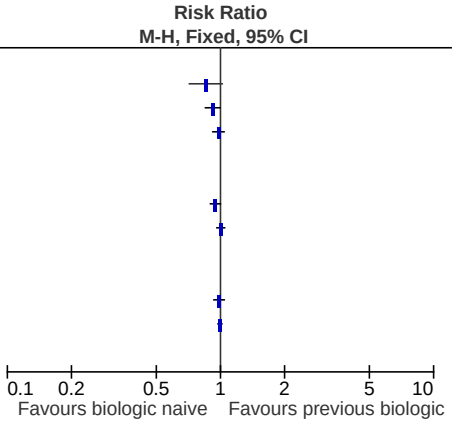


Figure 283: % improvement in PASI (weeks 12, 24 and 52)

Study or Subgroup	Previous biologic Mean	Previous biologic SD	Previous biologic Total	Biologic naive Mean	Biologic naive SD	Biologic naive Total	Mean Difference IV, Fixed, 95% CI
3.7.1 Week 12 (ITT)							
ACCEPT - CFE	68.3	31.676	35	82.05	20.799	508	-13.75 [-24.40, -3.10]
PHOENIX1 - CFE	73.14	27.856	208	78.69	23.338	298	-5.55 [-10.17, -0.93]
PHOENIX2 - CFE	76.61	23.638	248	80.8	24.558	564	-4.19 [-7.76, -0.62]
3.7.2 Week 24 (ACA)							
PHOENIX1 - CFE	82.59	23.52	207	86.96	19.36	290	-4.37 [-8.27, -0.47]
PHOENIX2 - CFE	82.38	21.478	123	85.07	21.64	283	-2.69 [-7.25, 1.87]
3.7.3 Week 52 (ACA)							
PHOENIX1 - CFE	89.45	14.73	59	90.15	14.62	103	-0.70 [-5.40, 4.00]
PHOENIX2 - CFE	88.12	14.464	148	91.86	12.67	389	-3.74 [-6.39, -1.09]

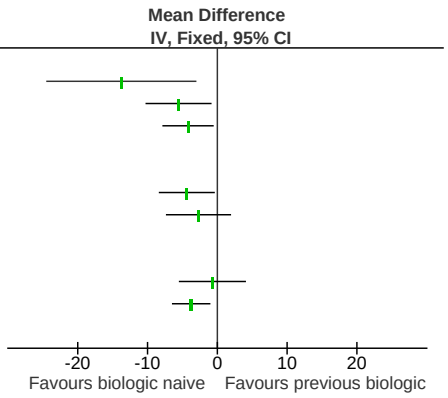
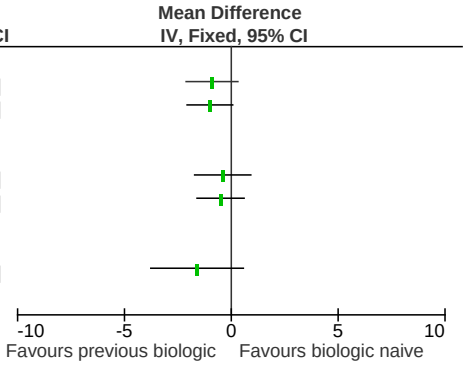


Figure 284: Change in DLQI (weeks 12, 24 and 52)

Study or Subgroup	Previous biologic Mean	SD	Total	Biologic naive Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
3.26.1 Week 12 (ITT)							
PHOENIX1 - CFE	-8.9	7.15	207	-8	6.31	296	-0.90 [-2.11, 0.31]
PHOENIX2 - CFE	-10.3	7.24	243	-9.3	6.74	560	-1.00 [-2.07, 0.07]
3.26.2 Week 28 (ACA)							
PHOENIX1 - CFE	-9.1	7.52	204	-8.7	7.03	286	-0.40 [-1.71, 0.91]
PHOENIX2 - CFE	-10.2	7.36	238	-9.7	7.01	555	-0.50 [-1.60, 0.60]
3.26.3 Week 52 (ACA)							
PHOENIX1 - CFE	-10.6	6.73	59	-9	6.84	103	-1.60 [-3.77, 0.57]



J.9.2 Adalimumab as a first TNF antagonist vs adalimumab following discontinuation of a previous TNF antagonist

Figure 285: Clear/nearly clear (PASI90; 16 weeks)

Study or Subgroup	Previous TNF antagonist Events	Total	TNF antagonist naive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.1.1 Psoriasis						
Ortonne 2011	70	187	167	338	70.0%	0.76 [0.61, 0.94]
Subtotal (95% CI)		**187**		**338**	**70.0%**	**0.76 [0.61, 0.94]**
Total events	70		167			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.54 (P = 0.01)						
5.1.2 Psoriatic arthritis						
Ortonne 2011	33	95	55	110	30.0%	0.69 [0.50, 0.97]
Subtotal (95% CI)		**95**		**110**	**30.0%**	**0.69 [0.50, 0.97]**
Total events	33		55			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.14 (P = 0.03)						
Total (95% CI)		**282**		**448**	**100.0%**	**0.74 [0.62, 0.88]**
Total events	103		222			
Heterogeneity: Chi² = 0.18, df = 1 (P = 0.67); I² = 0%						
Test for overall effect: Z = 3.29 (P = 0.0010)						
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%						

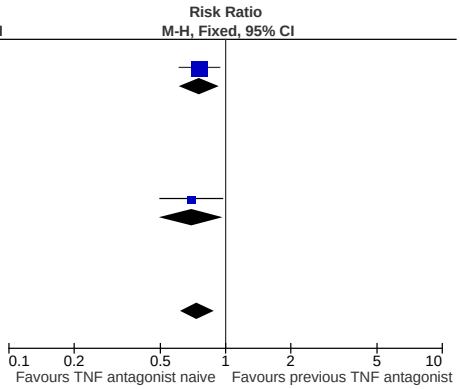


Figure 286: Clear/nearly clear (PGA; 16 weeks)

Study or Subgroup	Previous TNF antagonist Events	Total	TNF antagonist naive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.2.1 Psoriasis						
Ortonne 2011	100	187	221	338	70.2%	0.82 [0.70, 0.95]
Subtotal (95% CI)		**187**		**338**	**70.2%**	**0.82 [0.70, 0.95]**
Total events	100		221			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.55 (P = 0.01)						
5.2.2 Psoriatic arthritis						
Ortonne 2011	49	95	72	110	29.8%	0.79 [0.62, 1.00]
Subtotal (95% CI)		**95**		**110**	**29.8%**	**0.79 [0.62, 1.00]**
Total events	49		72			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.97 (P = 0.05)						
Total (95% CI)		**282**		**448**	**100.0%**	**0.81 [0.71, 0.92]**
Total events	149		293			
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.80); I² = 0%						
Test for overall effect: Z = 3.21 (P = 0.001)						
Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.80), I² = 0%						

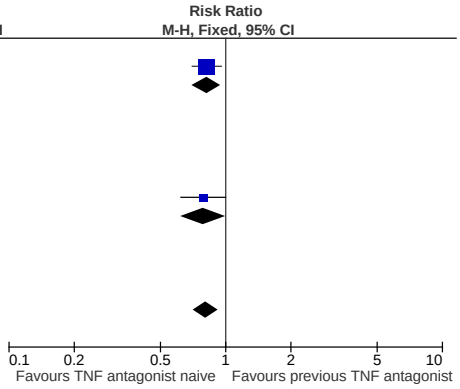


Figure 287: Clear/nearly clear (PGA; week 16)

Study or Subgroup	Failed etanercept Events	Total	Failed conventional Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Strober 2011	40	77	39	66	100.0%	0.88 [0.66, 1.18]
Total (95% CI)		**77**		**66**	**100.0%**	**0.88 [0.66, 1.18]**
Total events	40		39			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)

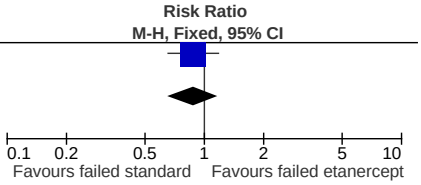


Figure 288: Clear/nearly clear (PGA; week 16)

Study or Subgroup	Failed etanercept Events	Total	Failed conventional Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.2.1 Primary non-responder						
Strober 2011-CFE	15	26	28	45	61.4%	0.93 [0.62, 1.38]
Subtotal (95% CI)		**26**		**45**	**61.4%**	**0.93 [0.62, 1.38]**
Total events	15		28			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
6.2.2 Secondary non-responder						
Strober 2011-CFE	27	58	9	23	38.6%	1.19 [0.67, 2.12]
Subtotal (95% CI)		**58**		**23**	**38.6%**	**1.19 [0.67, 2.12]**
Total events	27		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
Total (95% CI)		**84**		**68**	**100.0%**	**1.03 [0.74, 1.44]**
Total events	42		37			

Heterogeneity: Chi² = 0.50, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.16 (P = 0.87)
Test for subgroup differences: Chi² = 0.48, df = 1 (P = 0.49), I² = 0%

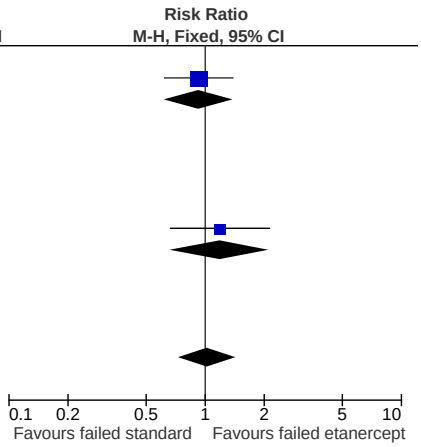


Figure 289: PASI75 (week 16)

Study or Subgroup	Previous TNF antagonist Events	Total	TNF antagonist naive Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Psoriasis						
Ortonne 2011	123	187	244	338	70.9%	0.91 [0.81, 1.03]
Subtotal (95% CI)		**187**		**338**	**70.9%**	**0.91 [0.81, 1.03]**
Total events	123		244			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.49 (P = 0.14)						
2.2.2 Psoriatic arthritis						
Ortonne 2011	51	95	77	110	29.1%	0.77 [0.61, 0.96]
Subtotal (95% CI)		**95**		**110**	**29.1%**	**0.77 [0.61, 0.96]**
Total events	51		77			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.33 (P = 0.02)						
Total (95% CI)		**282**		**448**	**100.0%**	**0.87 [0.78, 0.97]**
Total events	174		321			

Heterogeneity: Chi² = 1.77, df = 1 (P = 0.18); I² = 44%
Test for overall effect: Z = 2.54 (P = 0.01)
Test for subgroup differences: Chi² = 1.76, df = 1 (P = 0.18), I² = 43.1%

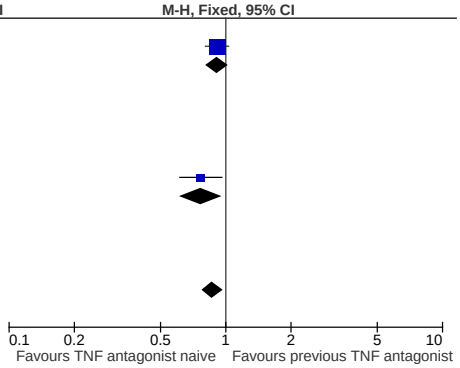


Figure 290: Withdrawal due to lack of efficacy at week 16

Study or Subgroup	Previous TNF antagonist Events	Total	TNF antagonist naive Events	Total	Risk Ratio M-H, Fixed, 95% CI
Ortonne 2011	3	270	5	414	0.92 [0.22, 3.82]
Strober 2011	4	77	3	66	1.14 [0.27, 4.92]

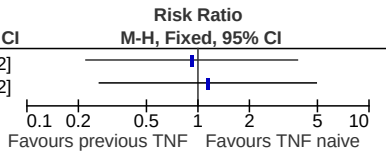


Figure 291: Withdrawal due to toxicity at week 16

Study or Subgroup	Previous TNF antagonist Events	Previous TNF antagonist Total	TNF antagonist naive Events	TNF antagonist naive Total	Risk Ratio M-H, Fixed, 95% CI
Ortonne 2011	5	272	22	431	0.36 [0.14, 0.94]
Strober 2011	0	73	1	64	0.29 [0.01, 7.06]

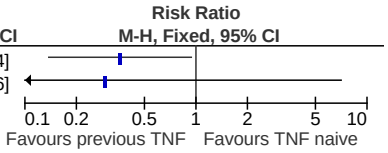
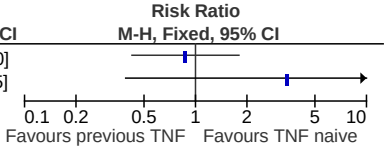


Figure 292: Serious adverse events after 16 weeks (plus 70 days post-treatment)

Study or Subgroup	Previous TNF antagonist Events	Previous TNF antagonist Total	TNF antagonist naive Events	TNF antagonist naive Total	Risk Ratio M-H, Fixed, 95% CI
Ortonne 2011	11	282	20	448	0.87 [0.43, 1.80]
Strober 2011	4	82	1	70	3.41 [0.39, 29.85]

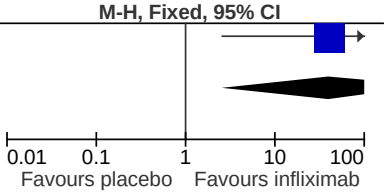


J.9.3 Infliximab vs placebo

Figure 293: PASI75 (week 10)

Study or Subgroup	Infliximab Events	Infliximab Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Menter 2007	68	94	0	27	100.0%	40.38 [2.58, 631.50]
Total (95% CI)		**94**		**27**	**100.0%**	**40.38 [2.58, 631.50]**
Total events	68		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.64 (P = 0.008)



J.9.4 Ustekinumab vs placebo

Figure 294: Clear/nearly clear (PASI90; week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
PHOENIX1 - CFE	75	212	0	105	33.3%	75.15 [4.70, 1200.65]
PHOENIX2 - CFE	94	250	1	124	66.7%	46.62 [6.58, 330.52]
Total (95% CI)		**462**		**229**	**100.0%**	**56.12 [11.34, 277.82]**
Total events	169		1			

Heterogeneity: Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 4.94 (P < 0.00001)

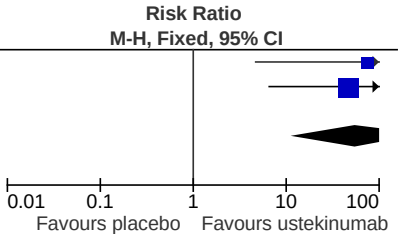


Figure 295: Clear/nearly clear (PGA; week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
PHOENIX1 - CFE	122	212	2	105	40.0%	30.21 [7.62, 119.79]
PHOENIX2 - CFE	162	250	3	124	60.0%	26.78 [8.73, 82.22]
Total (95% CI)		**462**		**229**	**100.0%**	**28.16 [11.80, 67.19]**
Total events	284		5			

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 7.52 (P < 0.00001)

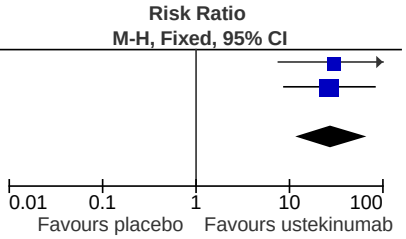


Figure 296: PASI75 (week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
PHOENIX1 - CFE	128	212	0	105	11.1%	127.90 [8.04, 2035.77]
PHOENIX2 - CFE	158	250	4	124	88.9%	19.59 [7.44, 51.61]
Total (95% CI)		**462**		**229**	**100.0%**	**31.61 [12.63, 79.11]**
Total events	286		4			

Heterogeneity: Chi² = 1.92, df = 1 (P = 0.17); I² = 48%
Test for overall effect: Z = 7.38 (P < 0.00001)

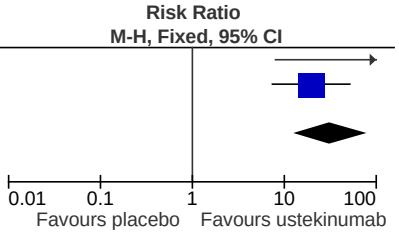


Figure 297: PASI50 (week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
PHOENIX1 - CFE	171	212	2	105	37.4%	42.35 [10.72, 167.35]
PHOENIX2 - CFE	213	250	8	124	62.6%	13.21 [6.74, 25.86]
Total (95% CI)		**462**		**229**	**100.0%**	**20.42 [6.43, 64.86]**
Total events	384		10			

Heterogeneity: Tau² = 0.44; Chi² = 2.44, df = 1 (P = 0.12); I² = 59%
Test for overall effect: Z = 5.12 (P < 0.00001)

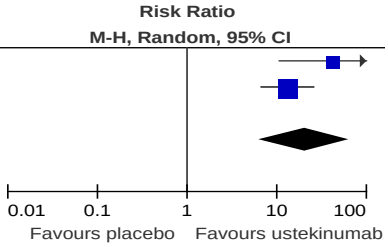


Figure 298: % improvement in PASI (week 12)

Study or Subgroup	Ustekinumab Mean	Ustekinumab SD	Ustekinumab Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
PHOENIX1 - CFE	73.14	27.856	208	-1.07	26.701	105	51.7%	74.21 [67.85, 80.57]
PHOENIX2 - CFE	76.61	23.638	248	-1.1	33.256	123	48.3%	77.71 [71.14, 84.28]
Total (95% CI)			**456**			**228**	**100.0%**	**75.90 [71.33, 80.47]**

Heterogeneity: Chi² = 0.56, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 32.56 (P < 0.00001)

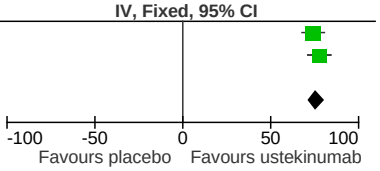
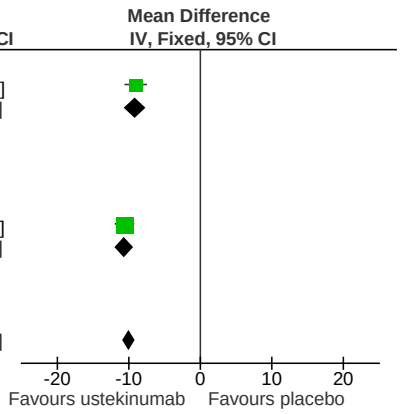


Figure 299: Change in DLQI (week 12)

Study or Subgroup	Ustekinumab Mean	Ustekinumab SD	Ustekinumab Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
9.6.1 Lower baseline DLQI								
PHOENIX1 - CFE	-8.9	7.15	207	0.14	5.78	105	42.0%	-9.04 [-10.51, -7.57]
Subtotal (95% CI)			**207**			**105**	**42.0%**	**-9.04 [-10.51, -7.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 12.03 (P < 0.00001)								
9.6.2 Higher baseline DLQI								
PHOENIX2 - CFE	-10.3	7.24	243	0.3	4.88	123	58.0%	-10.60 [-11.85, -9.35]
Subtotal (95% CI)			**243**			**123**	**58.0%**	**-10.60 [-11.85, -9.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 16.57 (P < 0.00001)								
Total (95% CI)			**450**			**228**	**100.0%**	**-9.94 [-10.90, -8.99]**

Heterogeneity: Chi² = 2.50, df = 1 (P = 0.11); I² = 60%
Test for overall effect: Z = 20.41 (P < 0.00001)
Test for subgroup differences: Chi² = 2.50, df = 1 (P = 0.11), I² = 60.0%



J.9.5 Ustekinumab vs etanercept

Figure 300: Clear/nearly clear (PASI90; week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Etanercept Events	Etanercept Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	10	36	4	27	100.0%	1.88 [0.66, 5.34]
Total (95% CI)		**36**		**27**	**100.0%**	**1.88 [0.66, 5.34]**
Total events	10		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.18 (P = 0.24)

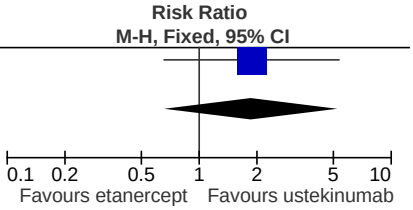


Figure 301: Clear/nearly clear (PGA; week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Etanercept Events	Etanercept Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	19	36	10	27	100.0%	1.43 [0.80, 2.55]
Total (95% CI)		**36**		**27**	**100.0%**	**1.43 [0.80, 2.55]**
Total events	19		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.20 (P = 0.23)

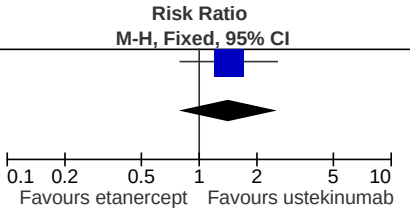


Figure 302: PASI75 (week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Etanercept Events	Etanercept Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	20	36	10	27	100.0%	1.50 [0.85, 2.66]
Total (95% CI)		**36**		**27**	**100.0%**	**1.50 [0.85, 2.66]**
Total events	20		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.16)

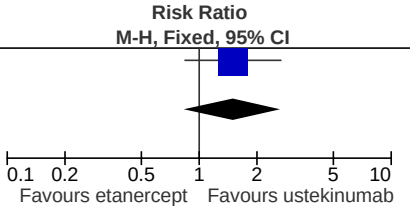


Figure 303: PASI50 (week 12)

Study or Subgroup	Ustekinumab Events	Ustekinumab Total	Etanercept Events	Etanercept Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACCEPT - CFE	28	36	20	27	100.0%	1.05 [0.79, 1.39]
Total (95% CI)		**36**		**27**	**100.0%**	**1.05 [0.79, 1.39]**
Total events	28		20			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.74)

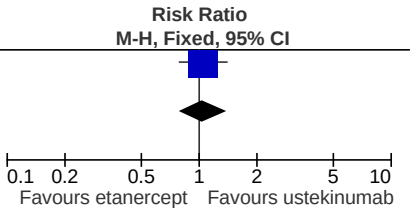
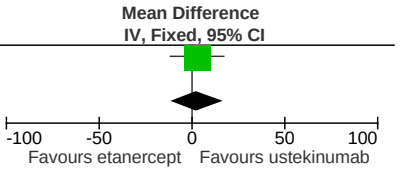


Figure 304: % improvement in PASI (week 12)

Study or Subgroup	Ustekinumab Mean	Ustekinumab SD	Ustekinumab Total	Etanercept Mean	Etanercept SD	Etanercept Total	Weight	Mean Difference IV, Fixed, 95% CI
ACCEPT - CFE	68.3	31.676	35	65.55	25.87	27	100.0%	2.75 [-11.58, 17.08]
Total (95% CI)			**35**			**27**	**100.0%**	**2.75 [-11.58, 17.08]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.38 (P = 0.71)



J.10 Cognitive behavioural therapy

Figure 305: PASI75 at 6 months

Study or Subgroup	CBT Events	CBT Total	Standard care Events	Standard care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fortune 2002b	18	28	7	30	100.0%	2.76 [1.36, 5.58]
Total (95% CI)		**28**		**30**	**100.0%**	**2.76 [1.36, 5.58]**
Total events	18		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.82 (P = 0.005)

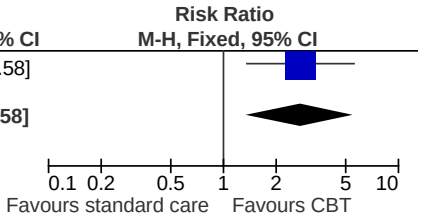
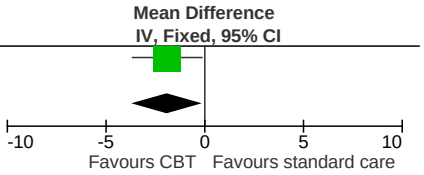


Figure 306: Final PASI at 6 weeks

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Standard care Mean	Standard care SD	Standard care Total	Weight	Mean Difference IV, Fixed, 95% CI
Fortune 2002b	6.5	4.1	40	8.4	4.5	53	100.0%	-1.90 [-3.66, -0.14]
Total (95% CI)			**40**			**53**	**100.0%**	**-1.90 [-3.66, -0.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.12 (P = 0.03)



J.11 Self-management

J.11.1 Additional self-management support (provided by nurse-specialist/trained practice nurse) vs standard care

Figure 307: Change in DLQI at 6 weeks-4 months

Study or Subgroup	Mean Difference	SE	Standard care + nurse Total	Standard care Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Mild to moderate disease						
Ersser 2011	-0.2	0.699	26	33	100.0%	-0.20 [-1.57, 1.17]
Subtotal (95% CI)			**26**	**33**	**100.0%**	**-0.20 [-1.57, 1.17]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.29 (P = 0.77)						
1.1.2 Moderate disease						
Ersser 2011	-1.21	1.372	9	13	100.0%	-1.21 [-3.90, 1.48]
Subtotal (95% CI)			**9**	**13**	**100.0%**	**-1.21 [-3.90, 1.48]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.88 (P = 0.38)						
1.1.3 Mild to severe disease						
Gradwell 2002	-0.27	1.27	28	28	100.0%	-0.27 [-2.76, 2.22]
Subtotal (95% CI)			**28**	**28**	**100.0%**	**-0.27 [-2.76, 2.22]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.83)						

Test for subgroup differences: Chi² = 0.44, df = 2 (P = 0.80), I² = 0%

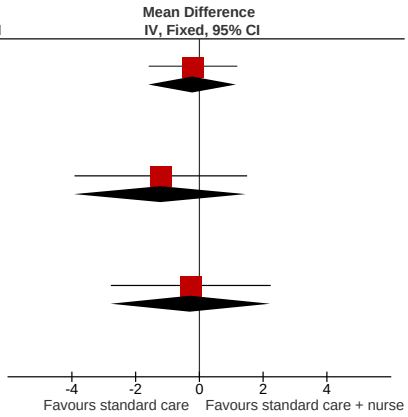
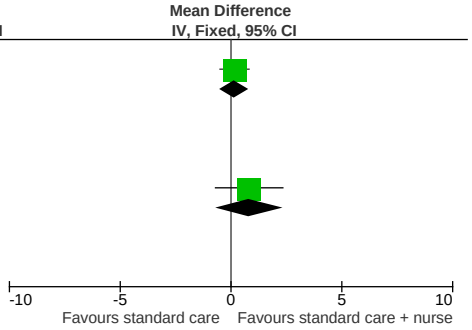


Figure 308: Change in PASI at 6 weeks

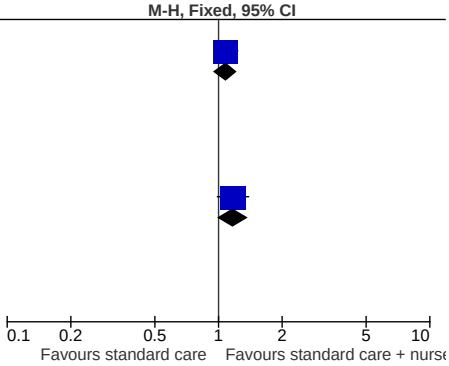
Study or Subgroup	Standard care + nurse Mean	SD	Total	Standard care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 Mild to moderate disease								
Ersser 2011	0.56	1.42	26	0.4	1.06	33	100.0%	0.16 [-0.49, 0.81]
Subtotal (95% CI)			**26**			**33**	**100.0%**	**0.16 [-0.49, 0.81]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.48 (P = 0.63)								
1.2.2 Moderate disease subgroup								
Ersser 2011	1.44	2.06	9	0.62	1.3	13	100.0%	0.82 [-0.70, 2.34]
Subtotal (95% CI)			**9**			**13**	**100.0%**	**0.82 [-0.70, 2.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.06 (P = 0.29)								



Test for subgroup differences: Chi² = 0.61, df = 1 (P = 0.43), I² = 0%

Figure 309: Treatment concordance/knowledge at 6 weeks

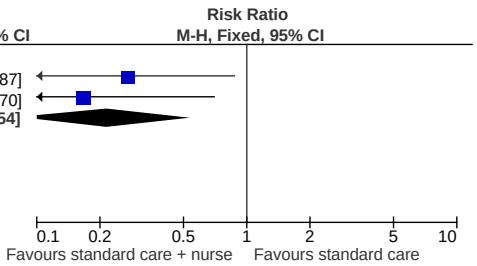
Study or Subgroup	Standard care + nurse Events	Total	Standard care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 How much treatment to apply						
Gradwell 2002	28	28	24	26	100.0%	1.08 [0.95, 1.23]
Subtotal (95% CI)		**28**		**26**	**100.0%**	**1.08 [0.95, 1.23]**
Total events	28		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.20 (P = 0.23)						
1.2.2 How long to apply for						
Gradwell 2002	28	28	23	27	100.0%	1.17 [0.99, 1.39]
Subtotal (95% CI)		**28**		**27**	**100.0%**	**1.17 [0.99, 1.39]**
Total events	28		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.83 (P = 0.07)						



Test for subgroup differences: Chi² = 0.51, df = 1 (P = 0.47), I² = 0%

Figure 310: Additional service use required at 6-24 weeks

Study or Subgroup	Standard care + nurse Events	Total	Standard care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Number needing GP visit during follow-up						
Gradwell 2002	3	28	11	28	46.1%	0.27 [0.09, 0.87]
Kernick 2000	2	46	14	54	53.9%	0.17 [0.04, 0.70]
Subtotal (95% CI)		**74**		**82**	**100.0%**	**0.22 [0.09, 0.54]**
Total events	5		25			
Heterogeneity: Chi² = 0.27, df = 1 (P = 0.60); I² = 0%						
Test for overall effect: Z = 3.31 (P = 0.0009)						

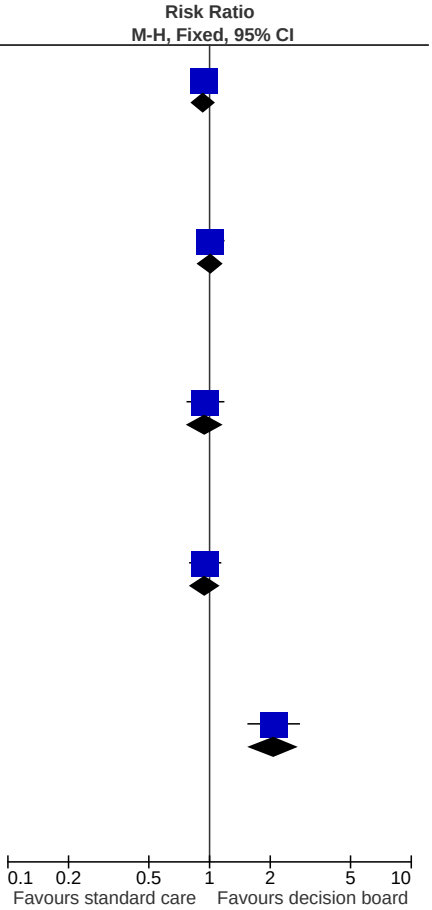


Test for subgroup differences: Not applicable

J.11.2 Decision board aid vs standard consultation

Figure 311: Patient satisfaction

Study or Subgroup	Decision board Events	Decision board Total	Standard care Events	Standard care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Overall satisfaction with care						
Renzi 2006	144	231	114	171	100.0%	0.94 [0.81, 1.08]
Subtotal (95% CI)		**231**		**171**	**100.0%**	**0.94 [0.81, 1.08]**
Total events	144		114			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.90 (P = 0.37)						
2.1.2 Satisfaction with decision making						
Renzi 2006	146	231	107	171	100.0%	1.01 [0.87, 1.18]
Subtotal (95% CI)		**231**		**171**	**100.0%**	**1.01 [0.87, 1.18]**
Total events	146		107			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						
2.1.3 Opportuity to express opinions						
Renzi 2006	107	231	83	171	100.0%	0.95 [0.78, 1.17]
Subtotal (95% CI)		**231**		**171**	**100.0%**	**0.95 [0.78, 1.17]**
Total events	107		83			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.44 (P = 0.66)						
2.1.4 Information on treatment options						
Renzi 2006	126	231	98	171	100.0%	0.95 [0.80, 1.13]
Subtotal (95% CI)		**231**		**171**	**100.0%**	**0.95 [0.80, 1.13]**
Total events	126		98			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.55 (P = 0.58)						
2.1.5 Information on treatment side effects						
Renzi 2006	118	231	42	171	100.0%	2.08 [1.55, 2.78]
Subtotal (95% CI)		**231**		**171**	**100.0%**	**2.08 [1.55, 2.78]**
Total events	118		42			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.92 (P < 0.00001)						



Test for subgroup differences: Chi² = 25.34, df = 4 (P < 0.0001), I² = 84.2%