Characteristics Table for The Clinical Question: In the treatment of GAD, for people who are receiving a pharmacological intervention without adequate response, does augmentation improve outcome?

Comparisons Included in this Clinical Question

Anxiolytic & Risperidone vs Anxiolytic & Placebo
BRAWMAN-MINTZER2005

Fluoxetine & Olanzapine vs Fluoxetine & Placebo
POLLACK2006

Paroxetine & Quetiapine vs Paroxetne & Placebo
SIMON2008

Risperidone augmentation vs Placebo augmentation
Pandina2007

Ziprasidone augmentation vs Placebo augmentation
LOHOFF2010

Characteristics of Included Studies

Methods	Participants	Outcomes	Interventions	Notes
BRAWMAN-MINTZER2005 Study Type: RCT Study Description: Ppts who continued to experience GAD despite anxiolytic treatment of at least 4 weeks given placebo or risperidone at doses of 0.5 to 1.5mg/day. Type of Analysis: ITT (LOCF method) Blindness: Double blind Duration (days): Mean 35 Setting: Outpatients: US. Notes: RANDOMISATION: no details given. Info on Screening Process: No details provided.	n= 40 Age: Mean 50 Sex: 7 males 33 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Diagnosis of MDD within 1 month of study entry and subjects with substance use disorders wtihin 6 months of study entry. Subjects with current or past history of bipolar or any psychotic disorder. Notes: Ppts had HAM-A score >=18, score >=2 on items 1 and 2, moderate score on CGI-S and Covi Anxiety Scale total higher than Raskin Severity of Depression Scale score. Flexible dosage. Baseline: HAM-A at baseline: 22.1 (3.8) in the risperidone group and 20.4 (1.7) in the placebo group.	**Data Used** CGI-I HAMA Adverse events Hospital Anxiety and Depression Scale (anxiety) Leaving the study due to adverse events Leaving the study early for any reason	**Group 1 N= 20** Placebo - No details provided. **Group 2 N= 19** Other active treatments - Risperidone. Increased weekly from 0.5mg/day to 1.5mg/day according to tolerability and clinical response.	Funding: Janssen Pharmaceutica, Inc. Quality assessed +.
LOHOFF2010 Study Type: RCT Study Description: Assesses the efficacy, safety and tolerability of ziprasidone in adults with treatment resistant GAD Type of Analysis: LOCF Blindness: Double blind Duration (days): Mean 56 Setting: Subjects recruited from the University of Pennsylvania Mood and Anxiety Disorders Section. Info on Screening Process: 73 subjects with GAD were recruited. 62 randomized. Inclusion criteria: subjects had to be 18yrs+ and meet DSM-IV criteria for GAD, treatment failure of 1 trial of an SSRI, SNRI, BZ or combination.	n= 62 Age: Sex: Diagnosis: Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: <16 on HAM-A, <4 on CGI-S. History of mania, bipolar disorder, schizophrenia or other psychotic disorder or diagnosis that may affect clinical assessment. Clinically significant abnormailies on physical examination or unstable medical conditions. Females whoa are pregnant, breast feeding. Baseline: Not reported	**Data Used** Discontinuation adverse events (DAEs) HAD CGI-S CGI-I HAMA	**Group 1 N= 41** Ziprasidone. Mean dose 20mg - Flexible dose strategy. Daily dose increased in weekly increments by 20mg/d up to 80mg/d. **Group 2 N= 21** Placebo - Identical placebo capsules	
Pandina2007				

Study Type: RCT Study Description: Adjunctive risperidone in the treatment of GAD Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 28 Notes: Randomization: An independent statistician provided randomization codes administered by telephone interactive voice response system. Info on Screening Process: 453 screened. 417 randomized, 390 in ITT population	n= 390 Age: Mean 44 Range 18-65 Sex: 114 males 276 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Females with known or suspected pregnancy, serious suicide risk or serious medical/neurological illness, active substance use disorders, history of clozapine treatment or currently taking over-the-counter and/or dietary psychotropic treatments to manage anxiety. Any Axis I diagnosis other than GAD, or no access to a touch-tone telephone. Notes: Subjects continued their standard anxiolytic/antidepressent regimen and dosage and were assigned to adjunctive risperidone or placebo augmentation using tablets of matching appearance, taste and smell. Baseline: HAMA: Risperidone 24.1 (6.8) Placebo 23.9 (6.4) Q-LES-Q Total Score: Risperidone 56.2 (12.4) Placebo 55.6 (11.9)	**Data Used** Q-LES-Q Remission (less than 7 on HAMA) Response (50% reduction in HAMA score) HAMA	**Group 1 N= 196** Risperidone. Mean dose 1mg - 0.25mg day 1-3. 0.5mg day 4-15. 1.0 mg day 16-28. On day 29 of the 6 week study, dose could increase to 2mg per day for patients considered to have insufficient response, (reduced to 1mg per day if intolerant). **Group 2 N= 194** Placebo - Placebo augmentation used tablets of matching appearance, taste and smell.	Funding: Not reported
POLLACK2006 Study Type: RCT Study Description: Ppts remaining symptomatic after 6 weeks treatment with fluoxetine (20mg/day) were randomised to 6 weeks of olanzapine or placebo augmentation. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 84 Setting: Outpatients. USA. Notes: RANDOMISATION: no details provided. Info on Screening Process: 46 ppts were in open-label fluoxetine treatment.	n= 24 Age: Mean 44 Sex: 11 males 13 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Bipolar disorder, psychotic disorders, alcohol or substance abuse in last 6 months, those receiving concurrent psychotherapies directed at GAD. Notes: Co-morbid depression or dysthymia and other anxiety disorders were permitted if clinician considered GAD to be primary. Baseline: HAM-A at baseline. Olanzapine: 17.4 (6.5) and Placebo: 22.6 (5.2).	**Data Used** CGI-I HAMA Adverse events Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score)	**Group 1 N= 12** Placebo **Group 2 N= 12** Other active treatments - Olanzapine. Week 1: 2.5mg/day, week 2: 5mg/day and then flexible titration in 5mg/day increments per week according to clinical response and tolerability up to a maximum of 20mg/day.	Funding: Eli Lilly. Quality assessed: +.
SIMON2008 Study Type: RCT Study Description: 2 phase 18 week prospective treatment trial. Phase 1 was open label 10 week parox trial. Phase 2 was trial open to those who did not remit in phase 1. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 56 Setting: Outpatients recruited from academic centers via advertisement and clinical referral. Notes: RANDOMISATION: 1:1 ratio. Info on Screening Process: 101 recruited: 54 entered phase 1 of the trial and 22 entered phase 2. Most exclusions were due to not meeting entry criteria.	n= 22 Age: Mean 42 Sex: Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Pregnant or lactating women, women of childbearing potential not using acceptable means of birth control, a primary diagnosis of major depression, dysthymia, panic disorder, or social phobia, a lifetime history of bipolar disorder, schizophrenia, or other psychotic conditions, posttraumatic stress disorder, obsessive-compulsive disorder, alcohol or substance abuse or dependence within the last 6 months, significant unstable medical illness, cataracts, severe personality disorders, ongoing psychotherapy directed towards GAD, prior hypersensitivity to paroxetine CR, paroxetine or quietiapine, and concurrent use of psychotropic medications within 2 weeks of study entry, including herbs and dietary supplements with known	**Data Used** CGI-I HAMA Adverse events Q-LES-Q-SF Leaving the study due to adverse events Leaving the study early for any reason	**Group 1 N= 11** Placebo - No details provided. **Group 2 N= 11** Other active treatments. Mean dose 120.5mg/day - Quetiapine augmentation.	Funding: GlaxoSmithKline. Quality assessed: +.

	psychotropic properties. Notes: Ppts had a HAM-A score >=18, MADRS score <=20 and MADRS item 10 score <3. Baseline: HAM-A at baseline. Quetiapine 16.27 (5.04) and Placebo 15.82 (4.77).			

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
FAVA2009	primary outcome insomnia not anxiety

References of Included Studies

BRAWMAN-MINTZER2005 (Published Data Only)

Brawman-Mintzer, O., Knapp, R.G., & Nietert, P.J. (2005) Adjunctive risperidone in generalized anxiety disorder: a double-blind, placebo-controlled study. Journal of Clinical Psychiatry, 66, 1321-1325.

LOHOFF2010 (Published Data Only)

Lohoff, F.W., Etemad, B., Mandos, L.A. et al. (2010) Ziprasidone treatment of refractory generalized anxiety disorder. Journal of Clinical Psychopharmacology, 30, 185-189.

Pandina2007 (Unpublished Data Only)

Pandina, G. J., Canuso, C., Turkoz, et al. (2007) Adjunctive rispiridone in the treatment of generalized anxiety disorder: a double-blind, prospective, placebo-controlled, randomized trial. Psychopharmacology Bulletin, 40, 41-57.

POLLACK2006 (Published Data Only)

Pollack, M.H., Simon, N.M., Zalta, A.K., Worthington, J.J., Hoge, E.A., Mick, E., Kinrys, G., & Oppenheimer, J. (2006) Olanzapine augmentation of fluoxetine for refractory generalized anxiety disorder: A placebo-controlled study. Biological Psychiatry, 59, 211-215.

SIMON2008 (Published Data Only)

Simon, N.M., Connor, K.M., LeBeau, R.T., Hoge, E.A., Worthington III., J.J., Zhang, W., Davidson, J.R.T., & Pollack, M.H. (2008) Quetiapine augmentation of paroxetine CR for the treatment of refractory generalized anxiety disorder: preliminary findings. Psychopharmacology, 197, 675-681.

References of Excluded Studies

FAVA2009 (Published Data Only)

Fava, M., Asnis, G.M., Shrivastava, R., et al. (2009) Zolpidem extended-release improves sleep and next-day symptoms in comorbid insomnia and generalized anxiety disorder. Journal of clinical psychopharmacology, 29, 222-230.