Slides for committee, projector and public part 1 – no confidential information

Committee presentation

Aflibercept for treating myopic choroidal neovascularisation

1st Appraisal Committee meeting

Committee C

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ERG: Aberdeen HTA Group

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The technologies

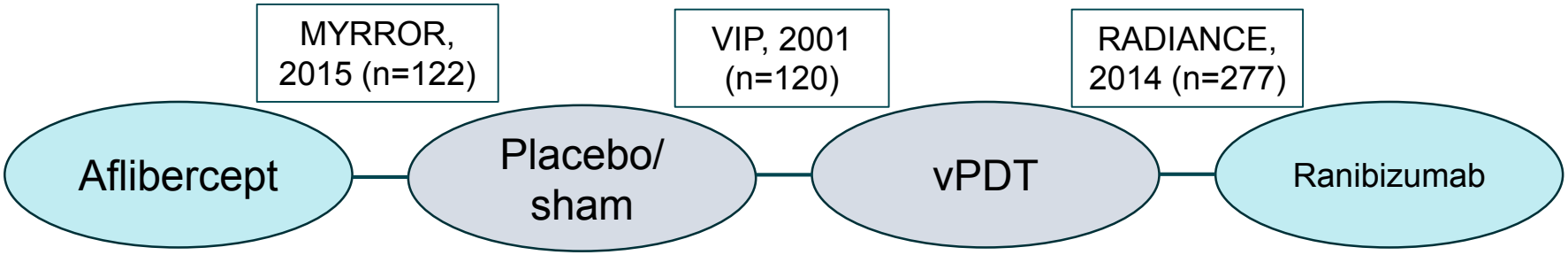
	Aflibercept (intervention)	Ranibizumab (comparator)
Mechanism of action	Vascular endothelial growth factor inhibitor	Vascular endothelial growth factor inhibitor
Marketing authorisation	Visual impairment due to myopic choroidal neovascularisation	Visual impairment due to choroidal neovascularisation
Administration and dose	• Single, 2 mg intravitreal injection • Additional injections if monitoring reveals disease activity or reduced visual acuity	• Single, 0.5 mg intravitreal injection • Additional injections if monitoring reveals disease activity or reduced visual acuity
Monitoring	• The schedule for monitoring should be determined by the treating physician	• The schedule for monitoring should be determined by the treating physician

Key drivers of the cost-effectiveness of the comparator – ranibizumab (TA298)

Clinical outcomes	• Mean change best-corrected visual acuity (BCVA) and proportions gaining or losing 5, 10 and 15 ETDRS letters • Adverse effects of treatment • Health related quality of life
Key clinical drivers	• Treatment effectiveness: BCVA and ETDRS letter outcomes
Clinical uncertainties	• Uncertainty about long-term effectiveness of ranibizumab, as outcomes measured at 3 months • Treatment benefit assumed to continue indefinitely
Resource use assumptions	• Number of injections: 3.5 in year 1 and 1 in year 2
Resource use uncertainties	• 1 injection in year 2 may be too low – ERG scenario 1.7 • Cost of blindness may have been too high • Administration costs may have been too low
Cost-effectiveness estimate	• Ranibizumab dominated vPDT • Not sensitive to alternative clinical or resource use scenarios

Clinical effectiveness evidence
Indirect treatment comparison

- Indirect treatment comparison for mean change in BCVA at 3 months - this is the only common measurement time point



- RADIANCE (ranibizumab) and VIP (vPDT) used in TA298
- Retreatment criteria differ
  - MYRROR (aflibercept): loss of visual acuity or disease progression
  - RADIANCE ranibizumab arm A: loss of visual acuity, ranibizumab arm B: disease activity
- Difference in baseline characteristics:
  - VIP: 91% Caucasian, RADIANCE: 57% Caucasian, MYRROR: 100% east Asian

Similarity of health benefits and safety
Company conclusion

Indirect treatment comparison results	Mean 3-month gain in BCVA
Aflibercept vs. ranibizumab (arm A: vision) (95% CI)	1.34 (-5.35 to 8.00)
Aflibercept vs. ranibizumab (arm B: disease) (95% CI)	0.94 (-5.67 to 7.56)

- Point estimates favour aflibercept, but confidence intervals overlap
- Not possible to include adverse events in indirect treatment comparison
  - EPAR: no new safety concerns identified in MYRROR compared with the existing indications for aflibercept
  - rate of adverse events in head-to-head trial of aflibercept vs. ranibizumab for wet age-related macular degeneration are similar
  - rate of adverse events in MYRROR and RADIANCE seem similar
- Aflibercept and ranibizumab are from same therapeutic class, therefore similarity in health benefits biologically plausible

ERG review
Clinical effectiveness evidence

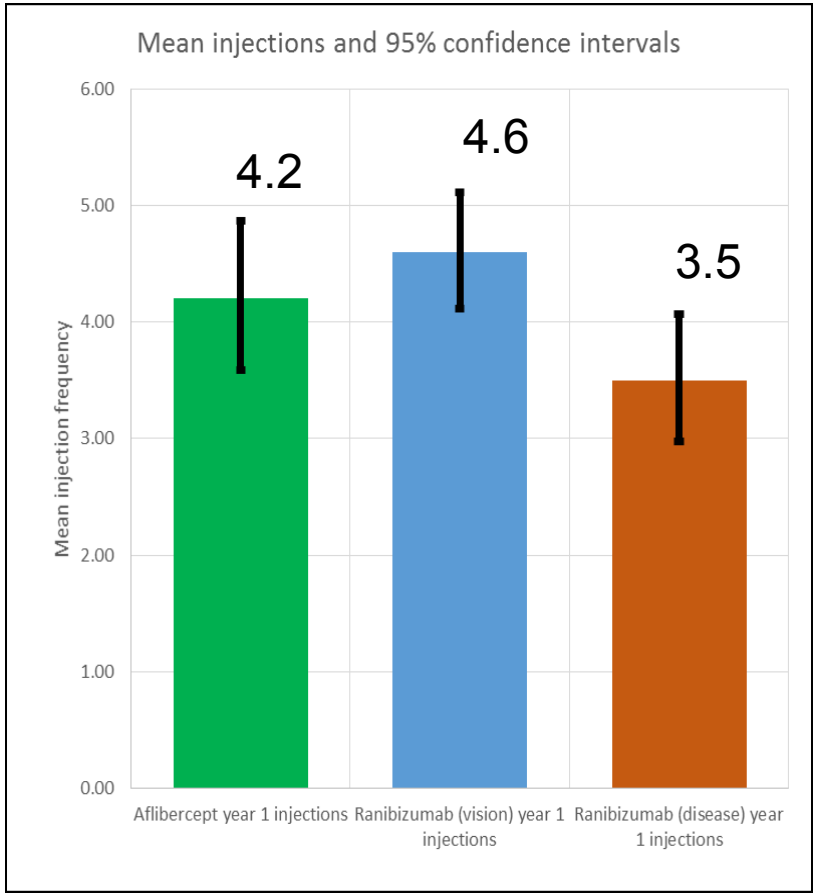
- ERG clinical adviser has no concerns about generalisability of the results of aflibercept trials to the NHS
  - no evidence that the effect of aflibercept differs by ethnicity
- Proportion of people gaining or losing 5,10 or 15 ETDRS letters could not be included in the indirect comparison (limited data in VIP), but important model driver in TA298
  - provided by company at clarification, ERG concluded proportions similar

ETDRS letter gain and loss at 3 months		Aflibercept	Ranibizumab - visual acuity	Ranibizumab - disease activity
Proportion (%)	≥15 letters gain	38.9	38.1	43.1
	≥10 letters gain	63.3	61.9	65.5
	≥10 letters loss	0	1.9	0.9
	≥15 letters loss	0	1.9	0

Similarity of health benefits and safety
ERG conclusion

- ERG conclude aflibercept and ranibizumab are similarly effective in treating myopic choroidal neovascularisation, based on:
  - difference in mean gain in best corrected visual acuity from indirect comparison
  - comparison of proportion of people gaining and losing 5, 10 and 15 EDTRS letters
- ERG conclude that safety profile of aflibercept and ranibizumab are similar, based on:
  - adverse events reported in MYRROR similar to adverse events seen with aflibercept in other eye indications
  - adverse events of aflibercept similar to those with ranibizumab in head to head trials for wet AMD

Resource use assumptions
Company submission (1)



- Injection frequencies assumed to be the same, as confidence intervals for year 1 injections overlap:
  - 4.2 in year 1, based on aflibercept trial
  - 1 in year 2, based on TA298
- Rationale: market research study of ophthalmologists shows that the MYRROR retreatment protocol reflects clinical practice in England
- Market research also suggests that clinicians expect to administer less than half the number of aflibercept injections than ranibizumab injections
  - equal injection frequency assumption may overestimate number of aflibercept injections used in clinical practice

Resource use assumptions
Company submission (2)

- No costs differences assumed for:
  - administration; no additional resources required as injection frequency equal
  - monitoring; number of visits assumed equal as injection frequency equal
  - blindness – visual outcomes assumed to be the same
  - adverse events – assumed to be equal

Resource use assumptions
ERG review

- Equal injection frequency assumption drives cost comparison
- ERG believes that the re-treatment criteria in aflibercept trial more closely reflect ranibizumab retreatment criteria based on disease activity
- ERG scenario analysis uses year 1 injection frequency from RADIANCE arm with retreatment based on disease activity for ranibizumab (3.5) and 4.2 for aflibercept from MYRROR
- Using these assumptions, total costs of aflibercept are higher than for ranibizumab - although confidence intervals around injection frequency overlap
- However, ERG's clinical adviser agrees with company assumption that injection frequency is unlikely to differ

Patient, professional organisation and expert submissions

RNIB

- The disease develops at a younger age than other eye conditions and can be a serious threat to vision for people of working age
- Clinicians consider aflibercept to be more potent than ranibizumab, meaning that people may need fewer injections to stabilise the condition

Royal College of Ophthalmologists

- Increasingly aflibercept replacing ranibizumab for other eye conditions as biological studies and clinical trials have found it is more potent
- As aflibercept may be more effective than ranibizumab it would be beneficial to have as a possible first-line option
- No additional resources required - fewer injections may be needed

Clinical experts

- Expect a similar number of injections to ranibizumab, but could be fewer in small subset of patients needing more injections to stabilise disease

Company's cost comparison results

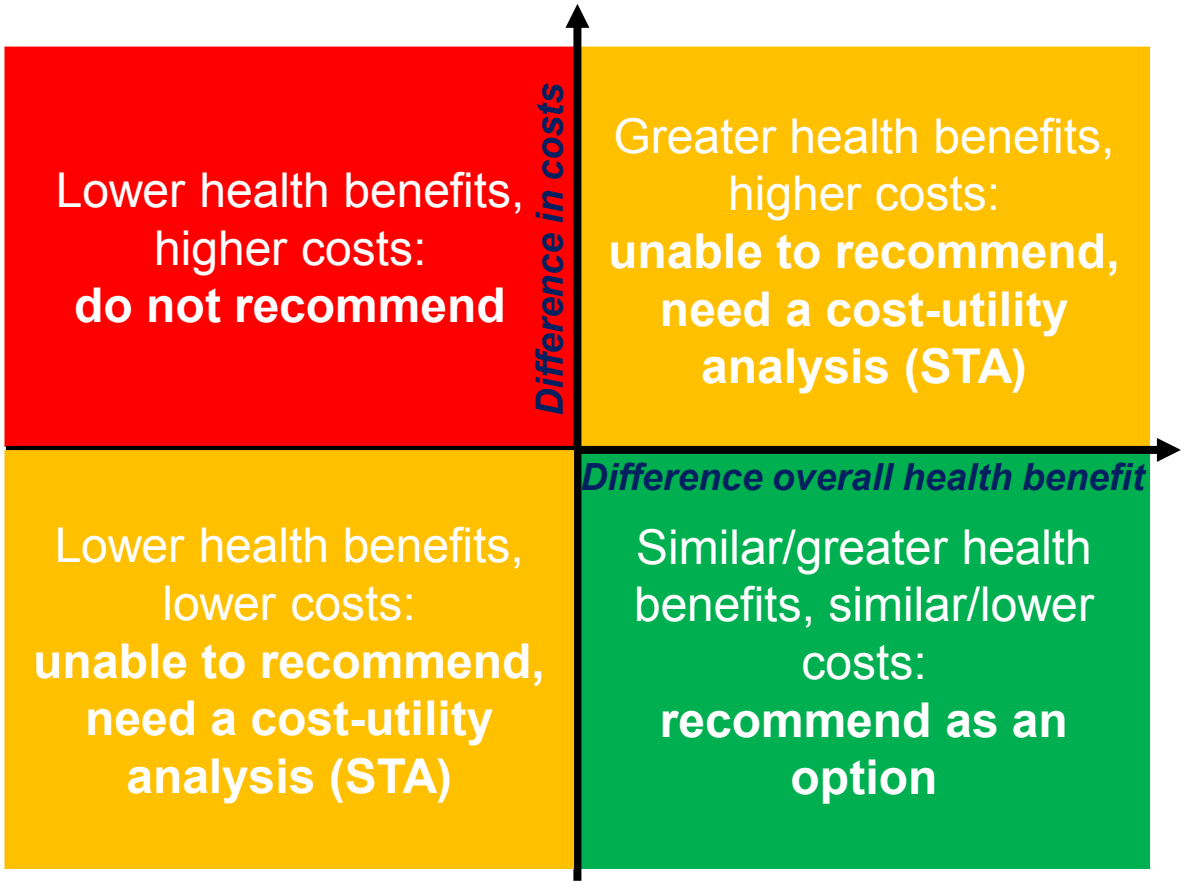
- The total costs of aflibercept are similar or lower than the total costs of ranibizumab, taking all discounts into account
- These discounts are confidential so the results of the cost comparison will be discussed in private in part 2 of the meeting

Technical team recommendation and rationale

Criteria for cost comparison case are met

- Company's indirect treatment comparison shows no statistically significant difference in mean gain in best corrected visual acuity
- ERG agrees that data for other clinical outcomes and adverse events are similar
- Main driver of cost comparison is injection frequency - company assumes that this would be the same for aflibercept and ranibizumab as confidence intervals from trials overlap
- Clinical experts, patient and professional organisations and the ERG's clinical adviser agree that injection frequency likely to be similar or lower compared with ranibizumab
- Total costs including all discounts are similar or lower than total costs of ranibizumab
- Risk associated with decision low: even if aflibercept injection frequency is higher, indirect comparison suggests aflibercept slightly more effective

Potential recommendations: cost comparison



Key issues

- Is it appropriate to assume the same number of aflibercept and ranibizumab injections?