NICE National Institute for Health and Care Excellence

# Aflibercept for treating visual impairment caused by macular oedema secondary to branch retinal vein occlusion

2nd Committee meeting

13 July 2016

# Preview of key issues for consideration

1. ACD provisionally recommended aflibercept in the same position as ranibizumab and dexamethasone, i.e. as 2nd line treatment. Does this recommendation still hold?
2. ACD provisionally did not recommended aflibercept before laser. Do the ACD consultation comments affect the ACD committee-preferred parameters for:
   - BSE and WSE utilities
   - Delayed benefits of control arm
   - Underestimated delayed benefits of control arm
3. Does the clinical and economic evidence support aflibercept in the 1st line?
4. What are the most plausible ICERs?

# Decision problem

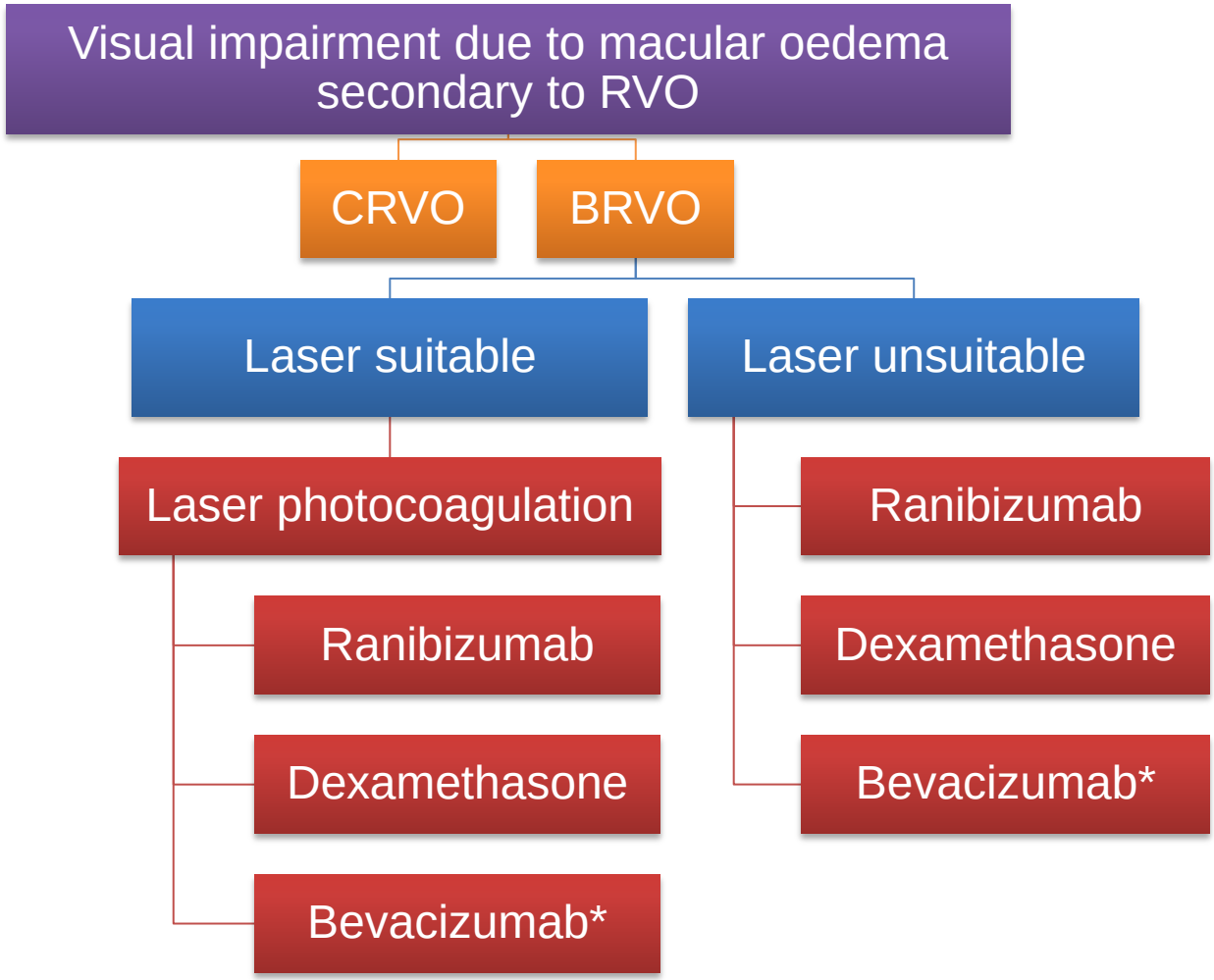
**PICO table from NICE scope (with indication of adherence/deviations in company submission)**

| | | ✓ / ✕ |
|---|---|---|
| **Intervention(s)** | Aflibercept solution for injection | ✓ |
| **Population(s)** | Adults with visual impairment caused by macular oedema secondary to branch retinal vein occlusion | ✓ |
| **Comparators** | • Laser photocoagulation<br>• Bevacizumab (not licensed in the UK for this indication)<br>For people for whom laser photocoagulation has not been beneficial or is not suitable:<br>• Ranibizumab<br>• Dexamethasone intravitreal implant<br>• Bevacizumab (not licensed in the UK for this indication) | ✓<br>✕<br><br>✓<br>✓<br>✕ |
| **Outcomes** | • visual acuity (the affected eye)<br>• visual acuity (the whole person)<br>• adverse effects of treatment<br>• health-related quality of life<br>• mortality | ✓<br>✓<br>✓<br>✓<br>✓ |

# Aflibercept

- Aflibercept has a marketing authorisation in adults for the treatment of visual impairment due to macular oedema secondary to BRVO or CRVO (February 2015)
- Aflibercept is a soluble vascular endothelial growth factor (VEGF) receptor fusion protein which binds to all forms of VEGF-A, VEGF-B, and the placental growth factor, to inhibit VEGF
- Administered by intravitreal injection – the usual dose is 2mg
- The company have agreed an aflibercept patient access scheme (PAS) with Department of Health. The size of the discount is commercial in confidence

# Treatment pathway




* Not licensed for this indication

# NICE Existing Guidance

- Existing NICE guidance:
  - TA229 (Jul 2011)

    **Recommends dexamethasone in BRVO only where laser treatment has failed or cannot be used**

    Recommends dexamethasone intravitreal implant for the treatment of macular oedema secondary to CRVO.
  - TA283 (May 2013)

    **Recommends ranibizumab in BRVO only where laser treatment has failed or cannot be used**

    Recommends ranibizumab for treating visual impairment caused by macular oedema secondary to CRVO.
  - TA305 (Feb 2014)

    Recommends aflibercept for treating visual impairment caused by macular oedema secondary to CVRO

# Preliminary ACD recommendations

- Aflibercept is recommended as an option for treating visual impairment in adults caused by macular oedema after branch retinal vein occlusion, only if:
  - laser photocoagulation has not been beneficial or laser photocoagulation is not suitable because of the extent of macular haemorrhage and
  - the company provides aflibercept with the discount agreed in the patient access scheme.

# Company clinical evidence

**RCT evidence**

- The company presented evidence from 1 clinical trial VIBRANT assessing aflibercept compared with grid laser photocoagulation
- Phase III multicentre randomised double-masked, sham-controlled study (n=183)

**Network meta-analysis (NMA)**

- No direct trial evidence for the comparison of dexamethasone and ranibizumab, NMA was conducted to assess the relative efficacy
- Assessed the gaining ≥15 letters at 6 months for aflibercept compared with dexamethasone and ranibizumab for 1st line treatment

# Company VIBRANT trial results

| | Week 24 | | Week 52 | |
|---|---|---|---|---|
| | Aflib (n=91) | Laser (n=90) | Aflib (n=91) | Laser (n=90) |
| **Gaining ≥15 letters in BVCA** | | | | |
| **Event, n (%)** | 48 (52.7) | 24 (26.7) | 52 (57.1) | 37 (41.1) |
| **Difference** | 26.1% | | 16.0 | |
| **Adjusted difference (95% CI)** | 26.6 (13.0, 40.1) | | 16.2 (2.0, 30.5) | |
| **p-value** | 0.0003 | | 0.0296 (nominal) | |
| **Change in BCVA (ETDRS letter score)** | | | | |
| **Mean change from baseline (± SD)** | 17.0 (± 11.88) | 6.9 (± 12.91) | 17.1 (±13.07) | 12.2 (±11.94) |
| **LS mean change in BCVA** | 13.7 | 3.2 | 12.4 | 7.1 |
| **Difference in LS mean vs. Laser [+aflibercept] (95% CI) c** | 10.5 (7.1, 14.0) | | 5.2 (1.7 to 8.7) | |
| **p-value c** | <0.0001 | | <0.005 | |
| **Received rescue treatment** | | | | |
| **N(%) 24 weeks and 36 weeks** | | | 9 (10) | 67 (74) |

**Abbreviations: BCVA, best corrected visual acuity; N, number; CI, confidence intervals; SD, standard deviation; ETDRS, Early Treatment Diabetic Retinopathy Study ; LS, least squared**

# Company network meta-analysis results

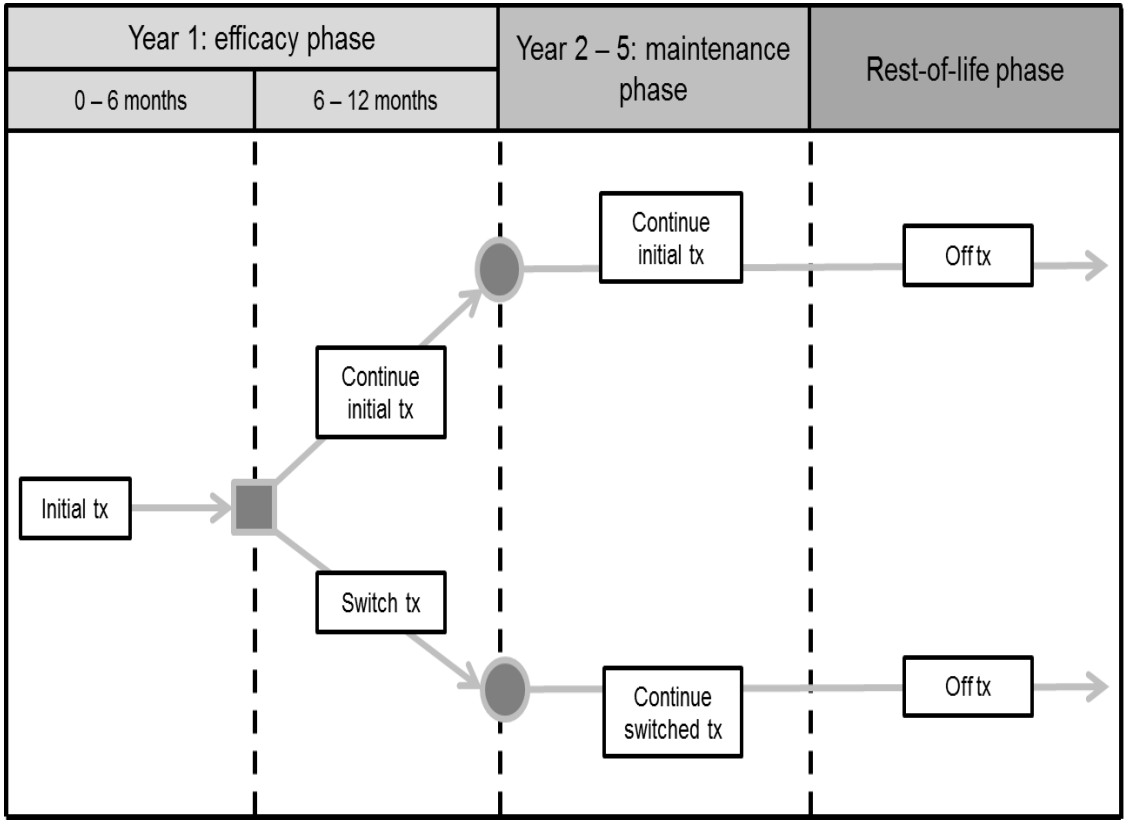
**Network meta-analysis results from a fixed effect model**

| | Mean OR (CrI) | Median OR (CrI) |
|---|---|---|
| **Gaining ≥15 letters in BVCA** | | |
| **Ranibizumab vs. Aflibercept** | 1.04 (0.38, 2.31) | 0.93 (0.38, 2.31) |
| **Dexamethasone vs. Aflibercept** | 0.39 (0.12, 0.96) | 0.34 (0.12, 0.96) |
| **Change in BCVA (ETDRS letter score)** | Mean PAIRDIFF | Median PAIRDIFF |
| **Ranibizumab vs. Aflibercept** | -2.68 (-7.43, 2.05) | -2.68 (-7.43, 2.05) |
| **Dexamethasone vs. Aflibercept** | -10.59 (-16.08, -5.10) | -10.59 (-16.08, -5.10) |

**Abbreviations: BCVA, best corrected visual acuity; ETDRS, Early treatment diabetic retinopathy study; CrI, credible interval; OR, odds ratio**

# Company economic model structure

- Health states (HS) defined by the visual acuity (VA) in both the SE and the FE
- **Efficacy phase**: HS can improve, remain stable, or worsen (by 15 letter BCVA change) for those on treatment  This is the only phase where VA improves
- **Maintenance phase**: patients remain on treatment throughout the phase
- **Rest-of-life phase**: All patients continue off treatment and VA declines steadily throughout the remainder to their life



# Company's model assumptions

**Utilities**

- Utilities were drawn from the Czoski-Murray study, and it was assumed that any change in the BCVA of the worst seeing eye (WSE) has 30% of the quality of life impact of the same change in the best seeing eye (BSE)

**Dosing**

- Dosing is based on the mean number of treatments in the VIBRANT study in the efficacy phase, and on clinical expert opinion during the maintenance phase. No treatment was assumed after year 5

**Last observation carried forward (LOCF)**

- LOCF was used to impute missing data except baseline values and many patients will not have resolved when they drop out
- Rebound may be bigger in aflibercept arm, particularly among patients discontinuing before 6 months

# Company's model assumptions (2)

**Transition probabilities (TPs)**

- TPs for afilbercept-laser and laser-aflibercept from pooled 4-weekly data in VIBRANT. TPs for laser-dexamethasone, laser-ranibizumab derived by applying the NMA odds ratios of gaining 15 letters.
- ERG estimated TPs directly from the trial data in the form of shift tables

# Company's deterministic base case results

**Incremental cost-effectiveness results from the base case (inc PAS for aflibercept only)**

| | Cost | QALYs | Inc. cost | Inc. QALYs | ICER |
|---|---|---|---|---|---|
| Laser-dexamethasone | [redacted] | [redacted] | | | |
| Laser-aflibercept | [redacted] | [redacted] | [redacted] | [redacted] | £11,792 |
| Laser-ranibizumab* | [redacted] | [redacted] | [redacted] | [redacted] | Dominated |
| Aflibercept-laser | [redacted] | [redacted] | [redacted] | [redacted] | £15,365 |



**Please note that the list price of ranibizumab has change from £742.00 to £551.00 per vial since the 1st committee meeting**

* This does not include the most recent list price for ranibizumab

# ERG's corrected base case

Based upon clinical expert opinion, the ERG has revised the company's economic model to:

- Assume quarterly monitoring for 1st year laser based upon expert opinion
- Assume 80% of administration visits can double as monitoring visits
- Assume 100% of fellow eye involvement will be treated

The ERG has also revised the model to:

- Applied shift-tables to estimate TMP
- Correct indexing for fellow eye costing
- Correct 1st year indexing of rescue costs
- Correct referencing for laser costs in aflibercept-laser
- Assume the same administration costs for laser as for anti-VEGF
- Correct the mortality averaging during the first 7 cycles of the model
- Apply ongoing mortality for cycles 396+, as previously outlined
- Revise dosing inputs to take into account discontinuations and cross-over, as previously outlined. Note that the ERG has not revised the dosing for dexamethasone due to time constraints.
- Anti-VEGF dosing for years 6+ of 3.2 annual administrations for 30% of patients for 5 years, implemented as previously outlined
- Not apply the cataract QALY decrement to IOP, by simply setting this to zero in the summary of results.
- Include fellow eye SAE disutilities

# ERG's base case results

**ERG's corrected base case cost effectiveness estimates laser-aflibercept compared with laser-ranibizumab and laser-dexamethasone (inc PAS for aflibercept only)**

| | Incremental costs | Incremental QALYs | ICER |
|---|---|---|---|
| Laser-aflibercept | | | |
| Laser-ranibizumab* | [redacted] | [redacted] | DOM |
| Laser-dexamethasone | [redacted] | [redacted] | £18,542 |
| | | | |
| Laser-aflibercept | | | |
| Aflibercept-laser | [redacted] | [redacted] | £28,813 |



* Please note that this does not include the most recent list price for ranibizumab

# ERG's sensitivity analysis

SA01: Applying the R MSM derived TPMs for the comparison of aflibercept-laser with laser-aflibercept

SA02: Applying the 8 studies median ORs of gaining at least 15 letters of 1.08 for ranibizumab and 0.40 for dexamethasone

SA03: Revising the QoL of life percentage for the WSE to be 15%

SA04: Revising the QoL percentage for the WSE to be 43%

SA05: Revising the QoL function to have a coefficient of -0.292 (Brown)

SA06: Revising the quality of life to be the VIBRANT EQ-5D OLS linear model

SA07: Revising the quality of life to be the VIBRANT EQ-5D REs linear model

SA08: Altering anti-VEGF dosing for years 6+ lasting 0, 5 and 10 years

SA09: Altering anti-VEGF dosing for years 6+ of an annual 2.0 doses

SA10: Altering ranibizumab to have one less administration than aflibercept during year 1

# Committee preferred assumptions

**Utilities**

- Committee expressed a preference for utilities from Brown study
- Committee concluded that the proportional impact of BSE on the WSE was likely to be less than 30%

**Dosing**

- Committee concluded that it was likely that ongoing treatment would be required for a proportion of the population

**Transition probabilities**

- The committee concluded that using shift tables to estimate transition probabilities is a preferable approach

# ERG's sensitivity analysis

| | |
|---|---|
| SA01: | Applying the R MSM derived TPMs for the comparison of aflibercept-laser with laser-aflibercept |
| SA02: | Applying the 8 studies median ORs of gaining at least 15 letters of 1.08 for ranibizumab and 0.40 for dexamethasone |
| SA03: | Revising the QoL of life percentage for the WSE to be 15% |
| SA04: | Revising the QoL percentage for the WSE to be 43% |
| SA05: | Revising the QoL function to have a coefficient of -0.292 (Brown) |
| SA06: | Revising the quality of life to be the VIBRANT EQ-5D OLS linear model |
| SA07: | Revising the quality of life to be the VIBRANT EQ-5D REs linear model |
| SA08: | Altering anti-VEGF dosing for years 6+ lasting 0, 5 and 10 years |
| SA09: | Altering anti-VEGF dosing for years 6+ of an annual 2.0 doses |
| SA10: | Altering ranibizumab to have one less administration than aflibercept during year 1 |

# ERG's sensitivity analysis

**Comparison of ICERs for aflibercept for untreated patients and after treatment with laser**

| | afilbercept-laser vs laser-aflibercept | laser-aflibercept vs laser-ranibizumab | laser-aflibercept vs laser-dexamethasone |
|---|---|---|---|
| **Base case** | £28,813 | DOM | £18,542 |
| **SA01** | £25,549 | n.a. | n.a. |
| **SA02** | n.a. | £204k | £20,969 |
| **SA03 (15% WSE)** | £33,380 | DOM | £21,468 |
| **SA04** | £26,309 | DOM | £17,162 |
| **SA05 (Brown)** | £36,631 | DOM | £23,518 |
| **SA06** | £50,578 | DOM | £32,846 |
| **SA07** | £74,405 | DOM | £48,815 |
| **SA08a** | £18,355 | n.a. | n.a. |
| **SA08b** | n.a. | DOM | n.a. |
| **SA08c (+10 years dosing)** | £33,178 | DOM | n.a. |
| **SA09** | £24,709 | DOM | n.a. |
| **SA10** | n.a. | DOM | n.a. |

# ERG's sensitivity analysis

**Comparison of ICERs for aflibercept for untreated patients and after treatment with laser**

| | afilbercept-laser vs laser-aflibercept | laser-aflibercept vs laser-ranibizumab | laser-aflibercept vs laser-dexamethasone |
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| **SA09** | £24,709 | DOM | n.a. |
| **SA10** | n.a. | DOM | n.a. |

# ACD consultation comments

- Received comments from 6 consultees and commentators:
  - Bayer, aflibercept
  - Royal College of Nursing
  - Royal College of Ophthalmologists
  - Royal National Institute for the Blind
  - Patient expert
  - Novartis, comparator ranibizumab

# ACD comments: The recommendation

Positive guidance has been welcomed for aflibercept as a treatment option after laser photocoagulation or where laser photocoagulation is unsuitable (RNIB, RCOphth)

However, a number of consultees and commentators were disappointed that it was not recommended in untreated patients

- NICE's ranibizumab recommendation not as a 1st line treatment should not influence this decision. More mature evidence is now available and recent RCOphth guidelines recommend anti-VEGF in the 1st line (Bayer aflibercept)
- As per to RCOphth guidelines anti-VEGF should be used in the 1st line (RCOphth)
  - Laser is inferior to aflibercept
  - Laser treatment will delay aflibercept and deprive patients of full benefit
  - Similar evidence for the efficacy of ranibizumab
  - Preference to apply a stopping rule to restrict aflibercept rather than not recommending as a 1st line treatment

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# ACD comments: The recommendation (2)

- There is evidence to show aflibercept effectiveness in untreated patients. Patients don't receive full benefit of aflibercept if they are delayed in receiving it (RNIB)

- High binding affinity of aflibercept justifies it to be a 1st line treatment (Patient expert)

# ACD comments: Other comments

- Dominating: the wording around aflibercept dominating ranibizumab in the various sections of the ACD could be misleading and needs to be contextualised . For example, whether it includes the list or PAS price. (Novartis, comparator ranibizumab)

- We agree with the committee about being mindful of the conclusions regarding the clinical effectiveness of aflibercept compared with ranibizumab and ask that this view be made clear across the entire document (Novartis, comparator ranibizumab)

# ACD comments: Modelling errors

The company highlighted 2 errors in the ERGs revised modelling:

1. 100% of people were given on-going anti-VEGF treatment years 6+ instead of 30%
2. An adjustment factor has been applied that reintroduced patients who have previously been discontinued

The ERG responded to each point:

1. This is a modelling error
2. This adjustment factor has been applied appropriately

ERG corrected the model and have provided further analysis

In light of the corrected model the Company believe that aflibercept is cost effective as a first line treatment

# ACD comments: Modelling assumptions

**Utilities (Bayer, aflibercept)**

- In TA283 Czoski-Murray values were considered "acceptable". Using utilities different utilities in the same disease area is "difficult to justify"
- EQ5D is insensitive to severity of visual impairment, therefore ICERs including EQ5D utilities are not relevant

**Proportional impact between WSE and BSE (Novartis, comparator ranibizumab)**

- In TA283, the committee concluded that a utility gain of 0.1 associated with treated the WSE was appropriate. Using anything else is inconsistent.

# ACD comments: Modelling assumptions (2)

**Equal administration (Novartis, comparator ranibizumab)**

- The number of 2nd line rescue ranibizumab treatments during the first year is assumed to be equal to that of 2nd line rescue aflibercept.
- Inconsistent with other appraisals:
  - TA283, the injection frequency was derived from trial data
  - TA305, the company derived the number of injections from the trial
  - TA346, the injections were derived from a weighted average based on reported data on the number of injections from the studies in the NMA
  - In a recent study by Adedokun and Burke (2016), dosing frequency in year 1 was 9 injections for aflibercept and 7.9 injections for ranibizumab

# ACD comments: Modelling assumptions (3)

**Last observation carried forward (Bayer, aflibercept)**

- The company has run 'extreme scenario analysis' to address the uncertainty around the use of last observation carried forward to handle drop out data
- The scenario modelled patients who discontinue aflibercept during the first six months have their visual acuity return immediately to baseline.

| Δ Costs | Δ QALYs | ICER |
|---|---|---|
| **ERG base case** | | |
| [redacted] | [redacted] | 28,813 |
| **Scenario analysis – patients who discontinue aflibercept have VA return to baseline value (ERG base case costs)** | | |
| [redacted] | [redacted] | 29,560 |

# ERG response to LOCF

1. Company's 'extreme scenario' only affects QALYs and not costs
   - If costs are included it lowers the ICER
2. ERG noted an error in the patient count of the transition probabilities
   - Those lost to follow up are not conditioned by mortality in the same way as those on treatment, thus fewer people die in the 1st year of aflib-laser arm compared to laser-aflib.
   - This provides an ongoing benefit in the aflib-laser arm



**ERG 'extreme scenario' accounting for LOCF, including on-going benefit correction**

| AFL-LSR *vs* LSR-AFL | Δ Costs | Δ QALYs | ICER |
|---|---|---|---|
| ERG base case | [redacted] | [redacted] | £28,812 |
| LOCF revised costs and QALYs | [redacted] | [redacted] | £28,292 |
| LOCF revised QALYs | [redacted] | [redacted] | £31,003 |

# Utilities: Committee's conclusions from TA283 (ranibizumab for RVO)

- Considered TA274 (ranibizumab for diabetic MO) where the range of utility values was accepted to lie somewhere in **between** those estimated by Czoski-Murray and those from the Brown study
- For the **best seeing eye**, although uncertain, the use of utilities as applied using the **Czoski-Murray** (CzM) equation was acceptable – only 10% of population
- For the **worst seeing eye** (90% of population), the ERG's exploratory analysis assumed a maximum utility benefit of 0.1 from treating the 'worse-seeing eye', instead of the manufacturer's value of 0.3 - both 0.1 and 0.3 were based on **Brown**

# Previous use utilities values in RVO

- TA229 (dexamethasone for RVO) - utility values were derived from a preference-based scoring algorithm produced through direct valuation from the general population
- TA283 – (ranibizumab for RVO)
  - CzM for best seeing eye (10% of the population)
  - Brown for worse seeing eye (90%)
- TA305 – (aflibercept for CRVO)  The use of CzM or Brown did not affect the cost-effectiveness

# Comparison of utility values

| STA | | TA283 | TA229 | Current | Current | Current | Current |
|---|---|---|---|---|---|---|---|
| **Source** | | **Brown** | **..** | **Czoski** | **Brown** | **Czoski** | **Brown** |
| **WSE %** | | **..** | **..** | **30%** | **30%** | **15%** | **15%** |
| **Health state** | **ETDRS** | **QoL** | **QoL** | **QoL** | **QoL** | **QoL** | **QoL** |
| HS1 | 86–100 | 0.920 | [redacted] | 0.854 | 0.842 | 0.854 | 0.842 |
| HS2 | 76–85 | 0.916 | [redacted] | 0.833 | 0.825 | 0.842 | 0.832 |
| HS3 | 66–75 | 0.909 | [redacted] | 0.816 | 0.811 | 0.832 | 0.825 |
| HS4 | 56–65 | 0.898 | [redacted] | 0.799 | 0.798 | 0.823 | 0.817 |
| HS5 | 46–55 | 0.885 | [redacted] | 0.782 | 0.784 | 0.813 | 0.809 |
| HS6 | 36–45 | 0.868 | [redacted] | 0.765 | 0.771 | 0.803 | 0.802 |
| HS7 | 26–35 | 0.848 | [redacted] | 0.748 | 0.757 | 0.794 | 0.794 |
| HS8 | <25 | 0.822 | [redacted] | 0.717 | 0.733 | 0.777 | 0.780 |
| **Utility benefit** | | **0.098** | [redacted] | **0.137** | **0.109** | **0.077** | **0.062** |

# New ERG analyses

1. The ERG corrected the model so that only 30% of the population received aflibercept for years 6+

2. The ERG also ran additional sensitivity analyses to include the committee assumptions of:
   - SA03: Revising the quality of life percentage for the WSE to be 15%
   - SA05: Revising the quality of life function to have a coefficient of -0.292 (Brown)
   - SA08c: Altering anti-VEGF dosing for years 6+ lasting 10 yrs

3. Revised dosing schedule of dexamethasone
   - Revised aflibercept dosing beyond year 6 and no revised dosing of dexamethasone
   - No revised dosing of dexamethasone or aflibercept

# Corrected ERG results: aflibercept before laser

| | Original model | Corrected model |
|---|---|---|
| | AFL-LSR vs LSR-AFL | AFL-LSR vs LSR-AFL |
| **ERG's corrected base case** | £28,813 | £21,492 |
| **SA03 (CzM - 15% WSE)** | £33,380 | £24,899 |
| **SA05 (Brown - 30% WSE)** | £36,631 | £27,324 |
| **SA08c (+10 years dosing)** | £33,178 | £22,801 |
| **SA03, and SA05 combined** | £43,597 | £32,520 |
| **SA03, SA05 and SA08c combined** | £50,202 | £34,502 |
| **Possible factors impacting the ICER:**<br>• **LOCF**<br>• **Control arm delayed benefits** | | |

- Model corrected so that only 30% receive on-going anti-VEGF years 6+
- SA03,05 ( and 08c) were committee's preferred assumptions in the ACD

# Corrected ERG results: ranibizumab

| | Original model | Corrected model |
|---|---|---|
| | LSR-AFL vs LSR-RAN | LSR-AFL vs LSR-RAN |
| **ERG's corrected base case** | DOM | DOM |
| **SA03 (CzM - 15% WSE)** | DOM | DOM |
| **SA05 (Brown - 30% WSE)** | DOM | DOM |
| **SA08c (+10 years dosing)** | DOM | DOM |
| **SA03, and SA05 combined** | n.a. | n.a. |
| **SA03, SA05 and SA08c combined** | n.a. | n.a. |

- Model corrected so that only 30% receive on-going anti-VEGF years 6+
- SA03,05 ( and 08c) were committee's preferred assumptions in the ACD
- Please note that this does not include the most recent list price for ranibizumab or the PAS discount
- Dosing has not corrected for ranibizumab following Novartis comments

# Corrected ERG results: dexamethasone

| | Original model | Corrected model |
|---|---|---|
| | LSR-AFL vs LSR-DEX | LSR-AFL vs LSR-DEX |
| **ERG's corrected base case** | £18,542 | £29,152 |
| **SA03 (CzM - 15% WSE)** | £21,468 | £33,752 |
| **SA05 (Brown - 30% WSE)** | £23,518 | £36,976 |
| **SA08c (+10 years dosing)** | n.a. | n.a. |
| **SA03, and SA05 combined** | £27,706 | £43,558 |
| **SA03, SA05 and SA08c combined** | n.a. | n.a. |

- Model corrected so that only 30% receive on-going anti-VEGF years 6+
- SA03,05 ( and 08c) were committee's preferred assumptions in the ACD

# Frequency of dosing

| Company model | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Years 6+ |
|---|---|---|---|---|---|---|
| Aflibercept 1st line | 9 | 4.15 | 2.61 | 1.12 | 0.58 | 0 |
| Aflibercept 2nd line | 4.4 | 4.15 | 2.61 | 1.12 | 0.58 | 0 |
| Ranibizumab 2nd line | 4.4 | 4.15 | 2.61 | 1.12 | 0.58 | 0 |
| Dexamethasone 2nd line | 1 | 1.69 | 0.93 | 0.21 | 0.1 | 0 |

| ERG model | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Years 6+ |
|---|---|---|---|---|---|---|
| Aflibercept 1st line | 9 | 4.15 | 3.2 | 3.2 | 3.2 | 3.2 |
| Aflibercept 2nd line | 4.4 | 4.15 | 3.2 | 3.2 | 3.2 | 3.2 |
| Ranibizumab 2nd line | 4.4 | 4.15 | 3.2 | 3.2 | 3.2 | 3.2 |
| Dexamethasone 2nd line | 1 | 1.69 | 0.93 | 0.21 | 0.1 | 0 |

# Equality issues

- No equality concerns were identified during the consultation period

# Key issues for consideration

1. ACD provisionally recommended aflibercept in the same position as ranibizumab and dexamethasone, i.e. as 2nd line treatment. Does this recommendation still hold?
2. ACD provisionally did not recommended aflibercept before laser. Do the ACD consultation comments affect the ACD committee-preferred parameters for:
   - BSE and WSE utilities
   - Delayed benefits of control arm
   - Underestimated delayed benefits of control arm
3. Does the clinical and economic evidence support aflibercept in the 1st line?
4. What are the most plausible ICERs?