

Supplementary Online Content

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eTable 1. Visual Acuity Ranges and Participant Distribution to Visual Acuity Ranges as Reported in EVEREST II

eTable 2. Visual Acuity Ranges and Participant Distributions Used in Model, Stratified by Health State

eTable 3. Parameters and Base-Case Values

eTable 4. Calculation of Utilities for Model Health States Using Best-Seeing Eye and Treated Eye

eTable 5. Transition Probabilities for Base Case and Scenario Analyses

eTable 6. Model Values for Deterministic and Probabilistic Sensitivity Analyses

eTable 7. Incremental Cost-effectiveness Ratio Estimates From 1-Way Deterministic Sensitivity Analysis—Lifetime Horizon

eTable 8. Incremental Cost-effectiveness Ratio Estimates From 1-Way Deterministic Sensitivity Analysis—10-Year Time Horizon

eFigure 1. Incremental Cost-effectiveness Ratio Across 20-Year Decision-Making Time-Horizon

eFigure 2. Two-Way Sensitivity Analysis

eFigure 3. Cost-effectiveness Acceptability Curve Showing Proportion of Cost-effective Iterations Across Willingness-to-Pay Thresholds, Stratified by Treatment

eFigure 4. Incremental Cost-effectiveness Scatter Plot

eReferences.

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Visual Acuity Ranges and Participant Distribution to Visual Acuity Ranges as Reported in EVEREST II

| BCVA range ^a , ETDRS letters (Snellen) | Snellen VA score in feet | ETDRS Letters | Reported Initial Distribution ^a , No. | | Initial Distribution stratified by Snellen VA ^b , No. | |
|---|--------------------------------|------------------|---|--------------------------|---|--------------------------|
| | | | Combination Therapy (N = 168) | Monotherapy (N = 153) | Combination Therapy (N = 168) | Monotherapy (N = 153) |
| ≥ 74 (20/32 or better) | 20/25 | 79 – 83 | 29 | 28 | 14.5 | 14 |
| | 20/32 | 74 – 79 | | | 14.5 | 14 |
| 54 - 73 (20/80 to worse than 20/32) | 20/40 | 69 – 73 | 97 | 87 | 24.25 | 21.75 |
| | 20/50 | 64 – 68 | | | 24.25 | 21.75 |
| | 20/63 | 59 – 63 | | | 24.25 | 21.75 |
| | 20/80 | 54 – 58 | | | 24.25 | 21.75 |
| 39 – 53 (20/160 to Worse than 20/80) | 20/100 | 49 – 53 | 34 | 27 | 11.33 | 9 |
| | 20/125 | 44 – 48 | | | 11.33 | 9 |
| | 20/160 | 39 – 43 | | | 11.33 | 9 |
| < 39 (Worse than 20/160) | 20/200 | 34 – 38 | 8 | 11 | 2.67 | 3.67 |
| | 20/250 | 29 - 33 | | | 2.67 | 3.67 |
| | 20/320 | 24 – 28 | | | 2.67 | 3.67 |

^aKoh et al.¹⁶

^bAuthor calculated by assuming that the initial distribution of participants is equally distributed amongst Snellen acuity ranges. Taking BCVA ≥ 74 (20/32 or better) as an example, Koh et al.¹⁶ reported that 28 participants began in this BCVA range in the monotherapy arm. As patient-level data was not reported we assume that these 28 individuals are equally distributed amongst the Snellen VA ranges with 14 participants entering the model with 20/25 VA and 14 participants entering the model with 20/32 VA.

eTable 2. Visual Acuity Ranges and Participant Distributions Used in Model, Stratified by Health State

| Health State | BCVA range used in cost-effectiveness analysis, ETDRS letters (Snellen) | Snellen VA score in feet | ETDRS Letters | Initial Distribution stratified by Health State, No. | | Initial Distribution stratified by Snellen VA, No. | |
|--------------------|---|--------------------------|---------------|--|------------------------|--|------------------------|
| | | | | Combination Therapy (N = 168) | Mono-therapy (N = 153) | Combination Therapy (N = 168) | Mono-therapy (N = 153) |
| Good Vision | ≥ 69 (20/40 or better) | 20/25 | 79 – 83 | 53 | 50 | 14.5 | 14 |
| | | 20/32 | 74 – 79 | | | 14.5 | 14 |
| | | 20/40 | 69 – 73 | | | 24.25 | 21.75 |
| Moderate Vision | 54 - 68 (20/80 to worse than 20/40) | 20/50 | 64 – 68 | 73 | 65 | 24.25 | 21.75 |
| | | 20/63 | 59 – 63 | | | 24.25 | 21.75 |
| | | 20/80 | 54 – 58 | | | 24.25 | 21.75 |
| Poor Vision | 39 – 53 (20/160 to Worse than 20/80) | 20/100 | 49 – 53 | 34 | 27 | 11.33 | 9 |
| | | 20/125 | 44 – 48 | | | 11.33 | 9 |
| | | 20/160 | 39 – 43 | | | 11.33 | 9 |
| Very poor Vision | < 39 (Worse than 20/160) | 20/200 | 34 – 38 | 8 | 11 | 2.67 | 3.67 |
| | | 20/250 | 29 - 33 | | | 2.67 | 3.67 |
| | | 20/320 | 24 – 28 | | | 2.67 | 3.67 |
| Death ^a | N/A | N/A | N/A | N/A | N/A | N/A | N/A |

^aAll values for the Death health state are not applicable (N/A) as patients can only enter this health state through age-specific all-cause background mortality.

eTable 3. Model Parameters and Base Case Values^a

| Model Parameter | Parameter Value | | | |
|--|--|------------------|-----------------------------------|------------------|
| | Base on Better-Seeing Eye ^b | | Based on Treated Eye ^c | |
| Vision | | | | |
| Good | 0.75 | | 0.84 | |
| Moderate | 0.63 | | 0.80 | |
| Poor | 0.57 | | 0.77 | |
| Very poor | 0.54 | | 0.66 | |
| Costs, \$ | Singapore Dollars | | US Dollars ^d | |
| Disaggregated ^e | | | | |
| 0.5-mg ranibizumab injection | 850 | | 621 | |
| Ranibizumab injection preparation | 393 | | 287 | |
| Standard fluence photodynamic therapy with verteporfin | 3825 | | 2792 | |
| First consultation | 102 | | 74 | |
| Subsequent consultations | 75 | | 55 | |
| Optical coherence tomography | 70 | | 51 | |
| Indocyanine green angiography | 156 | | 114 | |
| Aggregated ^f | | | | |
| Combination therapy first year | 13 582 | | 9915 | |
| Combination therapy subsequent years | 7486 | | 5465 | |
| Monotherapy first year | 10 605 | | 7742 | |
| Monotherapy subsequent years | 7818 | | 5707 | |
| | Combination Therapy | | Monotherapy | |
| | 1st Year | Subsequent Years | 1st Year | Subsequent Years |
| Resource utilization | | | | |
| First consultation | 1 ^g | None | 1 ^g | None |
| Subsequent consultations | 5 ^g | 4 ^h | 7 ^g | 6 ^h |
| 0.5-mg Ranibizumab injection | 5.2 ^g | 2.9 ⁱ | 7.3 ^g | 5.2 ⁱ |
| Ranibizumab injection preparation ⁱ | 5.2 | 2.9 | 7.3 | 5.2 |
| Standard fluence photodynamic therapy | 1.5 ^g | 0.7 ⁱ | None | None |

| | | | | | | |
|--|---------------------|---------------------|-------------------------|--------------------|---------------------|-------------------------|
| Optical coherence tomography ^k | 4 | 4 | 4 | 4 | 4 | 4 |
| Indocyanine green angiography ^k | 4 | 4 | 4 | 4 | 4 | 4 |
| | Combination Therapy | | | Monotherapy | | |
| | Year | | | | | |
| | First ^l | Second ^m | Subsequent ⁿ | First ^l | Second ^m | Subsequent ⁿ |
| Transition probabilities | | | | | | |
| Good to moderate | 0.006 | 0.010 | 0 | 0.020 | 0 | 0 |
| Moderate to good | 0.082 | 0.021 | 0 | 0.047 | 0.034 | 0 |
| Moderate to poor | 0.006 | 0.010 | 0 | 0.020 | 0 | 0 |
| Poor to moderate | 0.082 | 0.021 | 0 | 0.047 | 0.034 | 0 |
| Poor to very poor | 0.006 | 0.010 | 0 | 0.020 | 0 | 0 |
| Very poor to poor | 0.082 | 0.021 | 0 | 0.047 | 0.034 | 0 |

^aCombination therapy consists of intravitreal ranibizumab with verteporfin photodynamic therapy; monotherapy, ranibizumab. Good vision indicates Snellen visual acuity of 20/40 or better; moderate vision, 20/80 to worse than 20/40; poor vision, 20/160 to worse than 20/80; and very poor vision, worse than 20/160 to 20/320.

^bCalculated using utilities equation from Sharma et al³ and best-corrected visual acuities as reported in Koh et al.¹ Refer to eTable 4 for details on how best-seeing eye utilities were calculated.

^cCalculated by aligning utilities from the RESTORE trial⁴ reported for best-corrected visual acuity (BCVA) categories to BCVA ranges used in our study to define the 4 vision health states. Refer to eTable 2 for the BCVA ranges used in our study to define the 4 vision health states and eTable 4 for details on how the treated eye utilities from the RESTORE trial were aligned to these BCVA ranges.

^dIn Singapore dollars, 1 equals US \$0.73 as of September 5, 2018, based on XE Currency Converter.

^eData are from the Singapore National Eye Centre.

^fCalculated using resource utilization values multiplied by disaggregated unit cost values.

^gData are from Koh et al.¹

^hSubsequent consultations after year one are assumed to occur once every three months or rounded up from the average number of ranibizumab injections.

ⁱEstimated from Singh and Chhablani.²

^jRanibizumab injection preparations are assumed to be equal to the number of ranibizumab injections.

^kAssumed to occur once every three months.

^lCalculated from net efficacy as reported in Koh et al¹ by assuming the proportion of participants who gained or lost 15 or more letters were equally distributed across the relevant health states. For example, in year 1, 24.5% of participants receiving combination therapy gained 15 or more letters. Assuming these participants were equally distributed across the health states of very poor, poor, and moderate vision (note that participants who started in the good vision health state could not gain 15 or more letters), we calculated the transition probability for each health state as 24.5% multiplied by one-third (eg, $0.245 \times 0.333 = 0.082$). The same approach was also used to calculate the remaining transition probabilities in both year 1 and year 2.

^mYear 2 transition probabilities were calculated by subtracting the year 1 proportions reported by Koh et al¹ from the cumulative 2-year proportions reported in Singh and Chhablani.² For example, in year 1, 24.5% of participants receiving combination therapy gained 15 or more letters and at year 2 this had increased to 30.8% of participants. The difference between these 2 proportions (6.3%) was then used to calculate the year 2 transition probabilities, again assuming the participants were equally distributed across the relevant health states (eg, $0.063 \times 0.333 = 0.021$). It should be noted that for participants receiving monotherapy, there was a small decrease in the proportion of participants losing 15 or more letters at year 2 when compared with the year 1 proportion. We therefore assumed that no participants receiving monotherapy lost 15 or more letters in year 2.

ⁿAfter 2 years we assume that participants continue treatment but treatment will only help maintain and not improve visual acuity.

eTable 4. Calculation of Utilities for Model Health States Using Best-Seeing Eye and Treated Eye

| Health State | BCVA range used in cost-effectiveness analysis, ETDRS letters (Snellen) | ETDRS Letters within each range | Snellen VA score in feet within each range | Snellen VA score as a decimal within each range | Utilities for each Snellen VA score as a decimal ^a | Mean utilities based on best-seeing eye | Aligned BCVA categories from RESTORE | Utilities for BCVA categories from RESTORE | Mean utilities based on treated eye |
|------------------|---|---------------------------------|--|---|---|---|--------------------------------------|--|-------------------------------------|
| Good Vision | ≥ 69 (20/40 or better) | 79-83 | 20/25 | 0.800 | 0.813 | 0.75 | 86-100 | 0.860 | 0.84 |
| | | 74-79 | 20/32 | 0.630 | 0.750 | | 76-85 | 0.860 | |
| | | 69-73 | 20/40 | 0.500 | 0.701 | | 66-75 | 0.813 | |
| Moderate Vision | 54 - 68 (20/80 to worse than 20/40) | 64-68 | 20/50 | 0.400 | 0.664 | 0.63 | 64-68 | 0.813 | 0.80 |
| | | 59-63 | 20/63 | 0.320 | 0.634 | | 59-63 | 0.802 | |
| | | 54-58 | 20/80 | 0.250 | 0.608 | | 54-58 | 0.770 | |
| Poor Vision | 39 – 53 (20/160 to Worse than 20/80) | 49-53 | 20/100 | 0.200 | 0.589 | 0.574 | 46-55 | 0.770 | 0.77 |
| | | 44-48 | 20/125 | 0.160 | 0.574 | | 36-45 | 0.760 | |
| | | 39-43 | 20/160 | 0.125 | 0.561 | | | | |
| Very poor Vision | < 39 (Worse than 20/160) | 34-38 | 20/200 | 0.100 | 0.551 | 0.54 | 36-45 | 0.760 | 0.66 |
| | | 29-33 | 20/250 | 0.080 | 0.544 | | 26-35 | 0.681 | |
| | | 24-28 | 20/320 | 0.060 | 0.536 | | 0-25 | 0.547 | |

Abbreviations: BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; VA = visual acuity

^a Calculated using utilities equation from Sharma et al.

eTable 5. Transition Probabilities for Base Case and Scenario Analyses

| A. Base Case | Combination Therapy Transition Probabilities, mean | | | Monotherapy Transition Probabilities, mean | | |
|--|---|--------------------------------------|---|---|--------------------------------------|---|
| | First Year ^a | Second Year ^b | Subsequent Years ^c | First Year ^a | Second Year ^b | Subsequent Years ^c |
| Good to Moderate | 0.006 | 0.010 | 0 | 0.020 | 0 | 0 |
| Moderate to Good | 0.082 | 0.021 | 0 | 0.047 | 0.034 | 0 |
| Moderate to Poor | 0.006 | 0.010 | 0 | 0.020 | 0 | 0 |
| Poor to Moderate | 0.082 | 0.021 | 0 | 0.047 | 0.034 | 0 |
| Poor to Very poor | 0.006 | 0.010 | 0 | 0.020 | 0 | 0 |
| Very poor to poor | 0.082 | 0.021 | 0 | 0.047 | 0.034 | 0 |
| B. Participants with better vision have a greater probability of improving and participants with worse vision have a greater probability of deteriorating | First Year^{d,e} | Second Year^{d,e} | Subsequent Years^c | First Year^{d,e} | Second Year^{d,e} | Subsequent Years^c |
| Good to Moderate | 0 | 0 | 0 | 0 | 0 | 0 |
| Moderate to Good | 0.562 | 0.344 | 0 | 0.323 | 0.364 | 0 |
| Moderate to Poor | 0 | 0 | 0 | 0 | 0 | 0 |
| Poor to Moderate | 0 | 0 | 0 | 0 | 0 | 0 |
| Poor to Very poor | 0.088 | 0.161 | 0 | 0.333 | 0 | 0 |
| Very poor to poor | 0 | 0 | 0 | 0 | 0 | 0 |
| C. Participants with better vision have a greater probability of deteriorating and participants with worse vision have a greater probability of improving | First Year^{f,g} | Second Year^{f,g} | Subsequent Years^c | First Year^{f,g} | Second Year^{f,g} | Subsequent Years^c |
| Good to Moderate | 0.058 | 0.100 | 0 | 0.018 | 0 | 0 |
| Moderate to Good | 0 | 0.137 | 0 | 0 | 0 | 0 |
| Moderate to Poor | 0 | 0 | 0 | 0 | 0 | 0 |
| Poor to Moderate | 0.971 | 1.000 | 0 | 0.370 | 0.941 | 0 |
| Poor to Very poor | 0 | 0 | 0 | 0 | 0 | 0 |
| Very poor to poor | 1.000 | 0 | 0 | 1.000 | 0 | 0 |

Abbreviations: Combination therapy = Ranibizumab with verteporfin photodynamic therapy; Good vision = Snellen 20/40 or better; Moderate vision = Snellen 20/80 to worse than 20/40; Monotherapy = Ranibizumab only; Poor vision = Snellen 20/160 to worse than 20/80; Very poor vision = Snellen worse than 20/160 to 20/320.

^a Calculated from net efficacy – Koh et al.¹⁶

^b Two year transition probability as reported in Singh and Chhablani²⁰ and then converted from a 2-year probability to an annual probability

^c After 2 years we assume that participants remain on treatment but treatment will only help maintain and not improve visual acuity.

^d Author calculated assuming the proportion of participants gaining 15 letters or more can only come from the participants that started in the Moderate Vision health state. For example, of the 168 participants receiving combination therapy, 24.5% (41 participants) gained 15 or more letters in year one. Assuming these all came from the Moderate Vision health state means that the transition probability for moving from Moderate Vision to Good Vision would be 41/73=0.562. In year two, 6.3% (11 participants) of participants receiving combination therapy gained 15 or more letters. Again assuming these all came from the Moderate Vision health state means that the transition probability of moving from Moderate Vision to Good Vision would be 11/(73-41)=0.344.

^e Author calculated assuming the proportion of participants losing 15 letters or more can only come from the participants that started in the Poor Vision health state. For example, of the 153 participants receiving monotherapy, 5.9% (9 participants) lost 15 or more letters in year one. Assuming these all came from the Poor Vision health state means that the transition

probability for moving from Poor Vision to Very Poor Vision would be $9/27=0.333$. In year two, none of participants receiving monotherapy lost 15 or more letters. Therefore the transition probability of moving from Poor Vision to Very Poor Vision would be 0.

^f Author calculated assuming the proportion of participants gaining 15 letters or more first come from the participants that started in the Very Poor Vision health state, then from the Poor Vision health state and then the Moderate Vision health state. For example, of the 168 participants receiving combination therapy, 24.5% (41 participants) gained 15 or more letters in year one. Assuming these first came from the Very Poor Vision health state means that the transition probability for moving from Very Poor Vision to Poor Vision would be $8/8=1.00$. As there are still participants ($41-8=33$) who gained 15 or more letters it was assumed that they then came from the next worst health state (Poor Vision; transition probability for moving from Poor Vision to Moderate Vision would be $33/34=0.971$). In year two, 6.3% of participants (11 participants) receiving combination therapy gained 15 or more letters. Again assuming these first came from the next worst health state (Poor Vision as there are no more participants left in the Very Poor Vision health state) means that the transition probability of moving from Poor Vision to Moderate Vision would be $1/(34-33)=1.00$. As there are still participants ($11-1=10$) who gained 15 or more letters it was assumed that they then came from the next worst health state (Moderate Vision; transition probability for moving from Moderate Vision to Good Vision would be $10/73=0.137$). Note that because two of the transition probabilities were equal to 1.00 (Very Poor to Poor in year 1 and Poor to Moderate in year 2) it was necessary to make the background mortality in cycles 1 and 2 equal to zero so that the transition probabilities for each health state would sum to 1.00.

^g Author calculated assuming the proportion of participants losing 15 letters or more first come from the participants that started in the Good Vision health state. For example, of the 153 participants receiving monotherapy, 5.9% (9 participants) lost 15 or more letters in year one. Assuming these all came from the Good Vision health state means that the transition probability for moving from Good Vision to Moderate Vision would be $9/50=0.180$. In year two, none of the participants receiving monotherapy therapy lost 15 or more letters. Therefore the transition probability of moving from Good Vision to Moderate Vision would be 0.

eTable 6. Model Values for Deterministic and Probabilistic Sensitivity Analyses

| Variable | Deterministic Sensitivity Analysis Range (95% CI or range) | Probabilistic Sensitivity Analysis Distribution |
|---|--|---|
| Costs | | |
| First Visit | 89 - 115 | Gamma ($\alpha = 61.56; \gamma = 0.60$) |
| Subsequent Visit | 63 - 90 | Gamma ($\alpha = 31.55; \gamma = 0.42$) |
| Ranibizumab Injection Preparation | 379 - 400 | Gamma ($\alpha = 1335.56; \gamma = 3.42$) |
| Photodynamic therapy with verteporfin | 3750 - 3860 | Gamma ($\alpha = 4600.00; \gamma = 1.21$) |
| Utilities | | |
| Good Vision | 0.66 – 0.84 | Beta ($\alpha = 15.51; \beta = 5.17$) |
| Moderate Vision | 0.54 – 0.72 | Beta ($\alpha = 16.35; \beta = 9.60$) |
| Poor Vision | 0.48 – 0.66 | Beta ($\alpha = 15.58; \beta = 11.76$) |
| Very Poor Vision | 0.45 – 0.63 | Beta ($\alpha = 14.97; \beta = 12.75$) |
| Transition Probabilities | | |
| Combination Therapy Year 1 | | |
| Good to Moderate | 0.000 – 0.018 | Beta ($\alpha = 1.00; \beta = 167$) |
| Moderate to Good | 0.040 – 0.123 | Beta ($\alpha = 13.70; \beta = 154.30$) |
| Moderate to Poor | 0.000 – 0.018 | Beta ($\alpha = 1.00; \beta = 167$) |
| Poor to Moderate | 0.040 – 0.123 | Beta ($\alpha = 13.70; \beta = 154.30$) |
| Poor to Very poor | 0.000 – 0.018 | Beta ($\alpha = 1; \beta = 167$) |
| Very poor to Poor | 0.040 – 0.123 | Beta ($\alpha = 13.70; \beta = 154.30$) |
| Combination Therapy Year 2 | | |
| Good to Moderate | 0.000 – 0.025 | Beta ($\alpha = 1.67; \beta = 166.33$) |
| Moderate to Good | 0.000 – 0.042 | Beta ($\alpha = 3.33; \beta = 164.67$) |
| Moderate to Poor | 0.000 – 0.025 | Beta ($\alpha = 1.67; \beta = 166.33$) |
| Poor to Moderate | 0.000 – 0.042 | Beta ($\alpha = 3.33; \beta = 164.67$) |
| Poor to Very poor | 0.000 – 0.025 | Beta ($\alpha = 1.67; \beta = 166.33$) |
| Very poor to Poor | 0.000 – 0.042 | Beta ($\alpha = 3.33; \beta = 164.67$) |
| Monotherapy Year 1 | | |
| Good to Moderate | 0.000 – 0.042 | Beta ($\alpha = 3; \beta = 150$) |
| Moderate to Good | 0.014 – 0.080 | Beta ($\alpha = 7; \beta = 146$) |
| Moderate to Poor | 0.000 – 0.042 | Beta ($\alpha = 3; \beta = 150$) |
| Poor to Moderate | 0.014 – 0.080 | Beta ($\alpha = 7; \beta = 146$) |
| Poor to Very poor | 0.000 – 0.042 | Beta ($\alpha = 3; \beta = 150$) |
| Very poor to Poor | 0.014 – 0.080 | Beta ($\alpha = 7; \beta = 146$) |
| Monotherapy Year 2 | | |
| Good to Moderate | 0.000 – 0.004 | Beta ($\alpha = 0.10; \beta = 152.90$) |
| Moderate to Good | 0.005 – 0.063 | Beta ($\alpha = 5.3; \beta = 147.7$) |
| Moderate to Poor | 0.000 – 0.004 | Beta ($\alpha = 0.10; \beta = 152.90$) |
| Poor to Moderate | 0.005 – 0.063 | Beta ($\alpha = 5.3; \beta = 147.70$) |
| Poor to Very poor | 0.000 – 0.004 | Beta ($\alpha = 0.10; \beta = 152.90$) |
| Very poor to Poor | 0.005 – 0.063 | Beta ($\alpha = 5.3; \beta = 147.7$) |
| Abbreviations: Combination therapy = Ranibizumab with verteporfin photodynamic therapy; Good vision = Snellen 20/40 or better; Moderate vision = Snellen 20/80 to worse than 20/40; Monotherapy = Ranibizumab only; Poor vision = Snellen 20/160 to worse than 20/80; Very poor vision = Snellen worse than 20/160 to 20/320. | | |

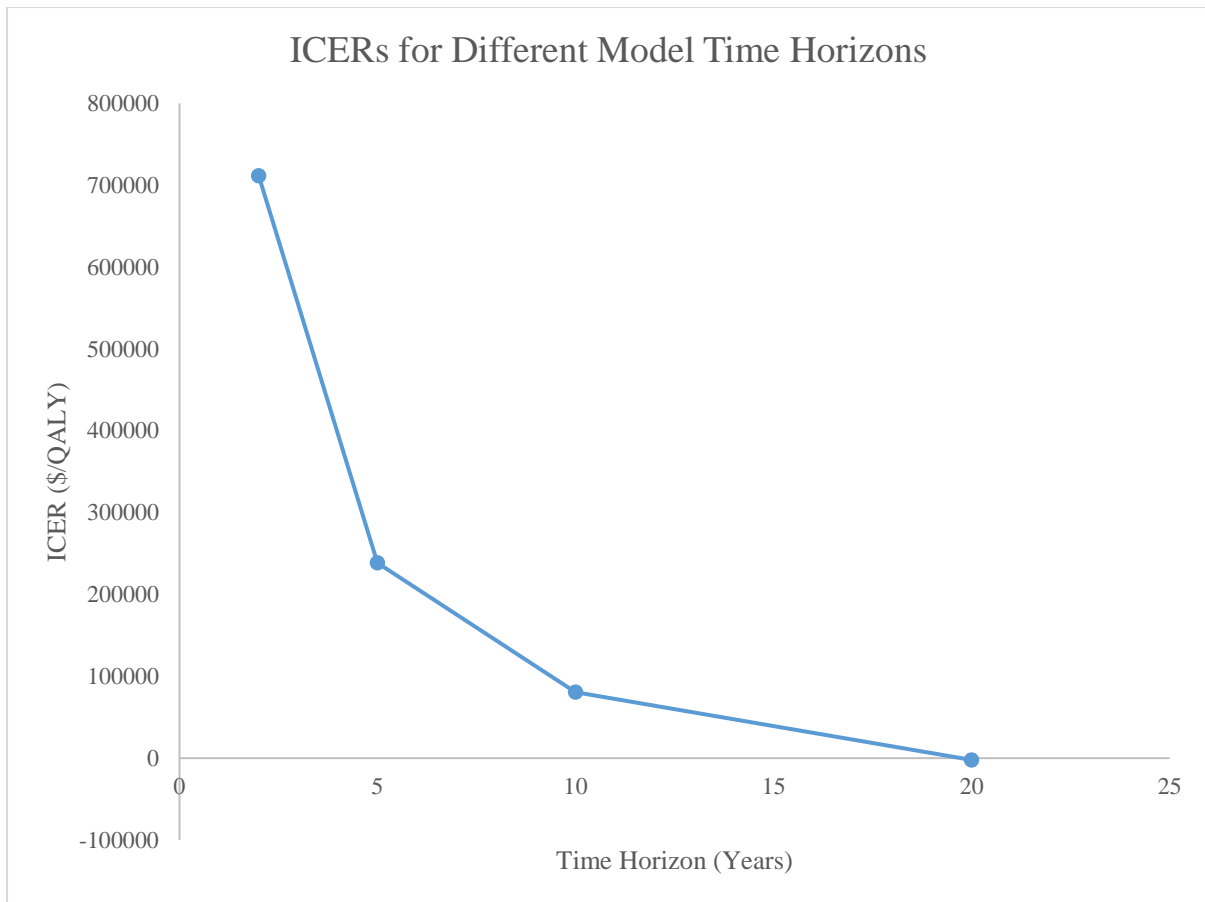
eTable 7. Incremental Cost-effectiveness Ratio Estimates from One-Way Deterministic Sensitivity Analysis–Lifetime Horizon

| Variable | ICER Range (low parameter value – high parameter value) |
|--|---|
| Costs | |
| First Visit | Monotherapy dominated – Monotherapy dominated |
| Subsequent Visit | Monotherapy dominated – Monotherapy dominated |
| Ranibizumab Injection Preparation | Monotherapy dominated – Monotherapy dominated |
| Photodynamic therapy with verteporfin | Monotherapy dominated – Monotherapy dominated |
| Utilities | |
| Good Vision | Monotherapy dominated – Monotherapy dominated |
| Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision | Monotherapy dominated – Monotherapy dominated |
| Very poor Vision ^a | Monotherapy dominated – 6757 |
| Transition Probabilities | |
| Monotherapy Year 1 | |
| Good Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Moderate Vision to Good Vision ^a | Monotherapy dominated – 7347 |
| Moderate Vision to Poor Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Very Poor Vision ^b | Monotherapy dominated – 11450 |
| Very Poor Vision to Poor Vision ^b | 6381 – Monotherapy dominated |
| Monotherapy Year 2 | |
| Good Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Moderate Vision to Good Vision ^a | Monotherapy dominated – 73675 |
| Moderate Vision to Poor Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Very Poor Vision ^b | Monotherapy dominated – 605 |
| Very Poor Vision to Poor Vision ^b | 5702 – Monotherapy dominated |
| Combination Therapy Year 1 | |
| Good Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Moderate Vision to Good Vision ^a | 3148 – Monotherapy dominated |
| Moderate Vision to Poor Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Very Poor Vision ^b | 2133 – Monotherapy dominated |
| Very Poor Vision to Poor Vision ^b | Monotherapy dominated – 4649 |
| Combination Therapy Year 2 | |
| Good Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Moderate Vision to Good Vision | Monotherapy dominated – Monotherapy dominated |
| Moderate Vision to Poor Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Moderate Vision | Monotherapy dominated – Monotherapy dominated |
| Poor Vision to Very Poor Vision ^b | 4774 – Monotherapy dominated |
| Very Poor Vision to Poor Vision ^b | Monotherapy dominated – 1305 |
| Abbreviations: Combination Therapy = ranibizumab with verteporfin photodynamic therapy; ICER = incremental cost-effectiveness ratio; Monotherapy = intravitreal ranibizumab only; Poor vision = Snellen 20/160 to worse than 20/80; QALY = quality-adjusted life-year; Very poor vision = Snellen worse than 20/160 to 20/320. | |
| ^a ICER represents combination therapy being both less expensive and less effective compared to monotherapy | |
| ^b ICER represents combination therapy being both more expensive and more effective compared to monotherapy | |

eTable 8. Incremental Cost-effectiveness Ratio Estimates from 1-Way Deterministic Sensitivity Analysis–10-Year Time Horizon

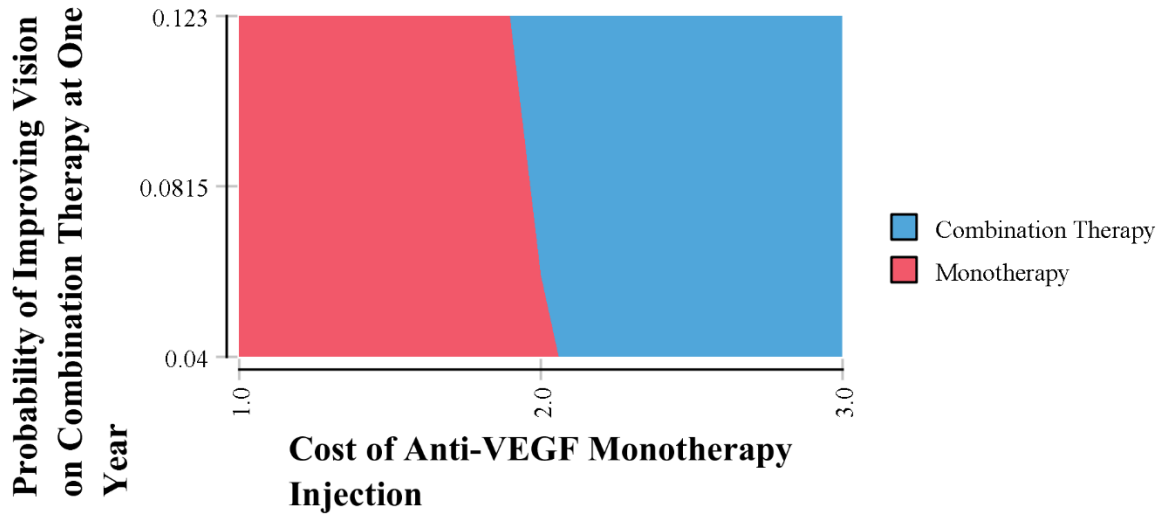
| Variable | ICER Range (low parameter value – high parameter value) |
|--|---|
| Costs | |
| First Visit | 80655 – 80655 |
| Subsequent Visit | 78841 – 82107 |
| Ranibizumab Injection Preparation | 79766 – 82433 |
| Photodynamic therapy with verteporfin | 73851 – 83830 |
| Utilities | |
| Good Vision | 66186 – 103222 |
| Moderate Vision | 67818 – 99488 |
| Poor Vision | 42411 – 821049 |
| Very poor Vision ^a | 34920 – Combination therapy dominated |
| Transition Probabilities | |
| Monotherapy Year 1 | |
| Good Vision to Moderate Vision | 63606 – 106641 |
| Moderate Vision to Good Vision ^a | 35859 – Combination therapy dominated |
| Moderate Vision to Poor Vision | 55924 – 134880 |
| Poor Vision to Moderate Vision | 66886 – 101563 |
| Poor Vision to Very Poor Vision | 74488 – 86607 |
| Very Poor Vision to Poor Vision | 76598 – 84386 |
| Monotherapy Year 2 | |
| Good Vision to Moderate Vision | 76851 – 80655 |
| Moderate Vision to Good Vision | 41511 – 1414828 |
| Moderate Vision to Poor Vision | 75730 – 80655 |
| Poor Vision to Moderate Vision | 69769 – 95568 |
| Poor Vision to Very Poor Vision | 80688 – 82053 |
| Very Poor Vision to Poor Vision | 76408 – 84644 |
| Combination Therapy Year 1 | |
| Good Vision to Moderate Vision | 75417 – 93666 |
| Moderate Vision to Good Vision ^a | Combination therapy dominated – 31171 |
| Moderate Vision to Poor Vision | 72072 – 106004 |
| Poor Vision to Moderate Vision | 62780 – 114169 |
| Poor Vision to Very Poor Vision | 76736 – 82494 |
| Very Poor Vision to Poor Vision | 77453 – 83574 |
| Combination Therapy Year 2 | |
| Good Vision to Moderate Vision | 71274 – 100497 |
| Moderate Vision to Good Vision | 47869 – 255982 |
| Moderate Vision to Poor Vision | 69346 – 106773 |
| Poor Vision to Moderate Vision | 71963 – 91736 |
| Poor Vision to Very Poor Vision | 75140 – 84075 |
| Very Poor Vision to Poor Vision | 78901 - 82360 |
| Abbreviations: Combination Therapy = ranibizumab with verteporfin photodynamic therapy; ICER = incremental cost-effectiveness ratio; Monotherapy = intravitreal ranibizumab only; Poor vision = Snellen 20/160 to worse than 20/80; QALY = quality-adjusted life-year; Very poor vision = Snellen worse than 20/160 to 20/320. | |
| ^a ICER represents combination therapy being both more expensive and more effective compared to monotherapy | |

eFigure 1. Incremental Cost-effectiveness Ratio Across 20 Year Decision-Making Time-Horizon



eFigure 2. Two-Way Sensitivity Analysis
A. Lifetime Horizon

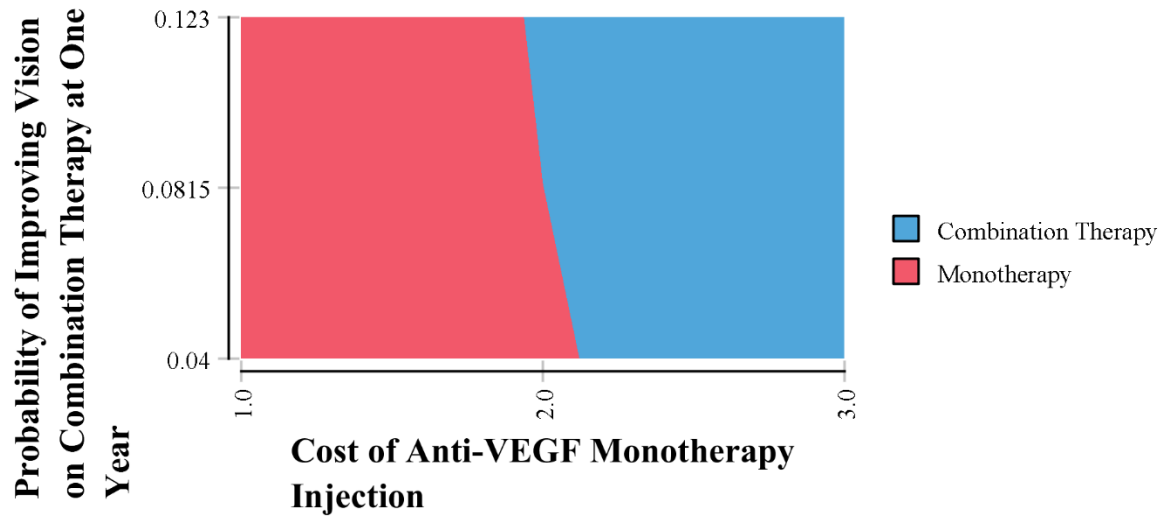
Two-Way Sensitivity Analysis - Lifetime Horizon
(Net Benefit, WTP=SGD 79,357)



Note that the values on the x-axis (1.0, 2.0 and 3.0) represent using different costs of a single anti-VEGF monotherapy injection (SGD118, SGD850 and SGD1250 respectively) in the model. Whereas, the values on the y-axis represent different probabilities for transitioning to a better vision health state (from moderate to good vision, from poor to moderate vision and from very poor to poor vision) when receiving combination therapy in year one of the model.

B. Ten-Year Time Horizon

Two-Way Sensitivity Analysis - Ten-Year Time-Horizon (Net Benefit, WTP=SGD79,357)

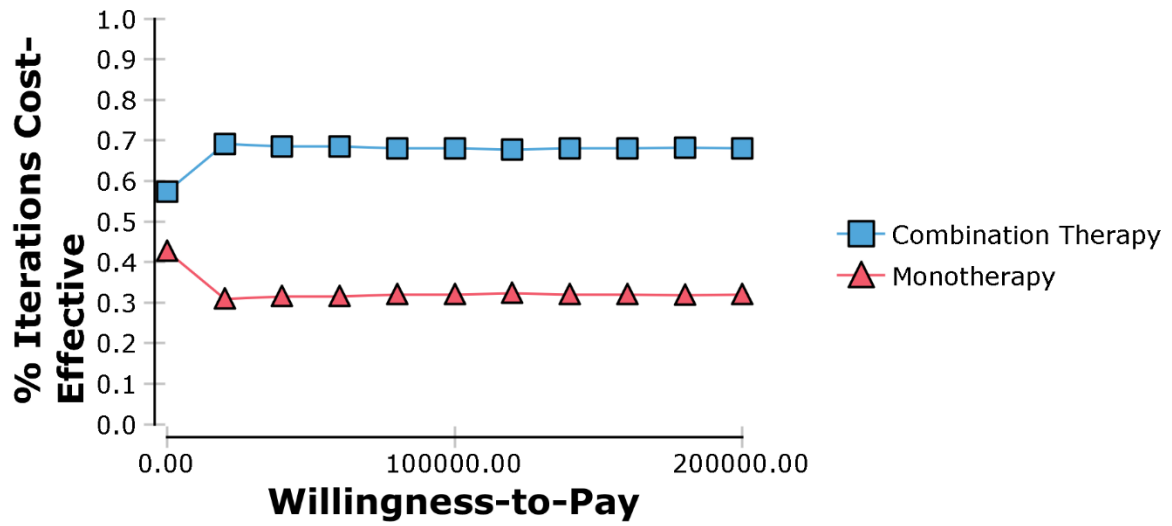


Note that the values on the x-axis (1.0, 2.0 and 3.0) represent using different costs of a single anti-VEGF monotherapy injection (SGD118, SGD850 and SGD1250 respectively) in the model. Whereas, the values on the y-axis represent different probabilities for transitioning to a better vision health state (from moderate to good vision, from poor to moderate vision and from very poor to poor vision) when receiving combination therapy in year one of the model.

eFigure 3. Cost-effectiveness Acceptability Curve Showing Proportion of Cost-effective Iterations Across Willingness-to-Pay Thresholds, Stratified by Treatment

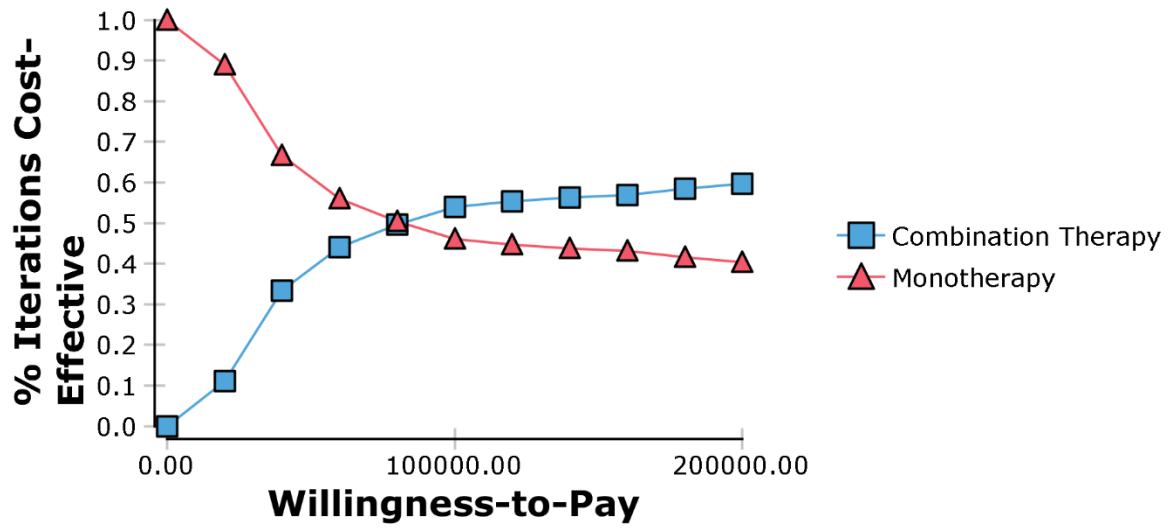
A. Lifetime Horizon

**Cost-Effectiveness Acceptability Curve -
Lifetime Horizon**



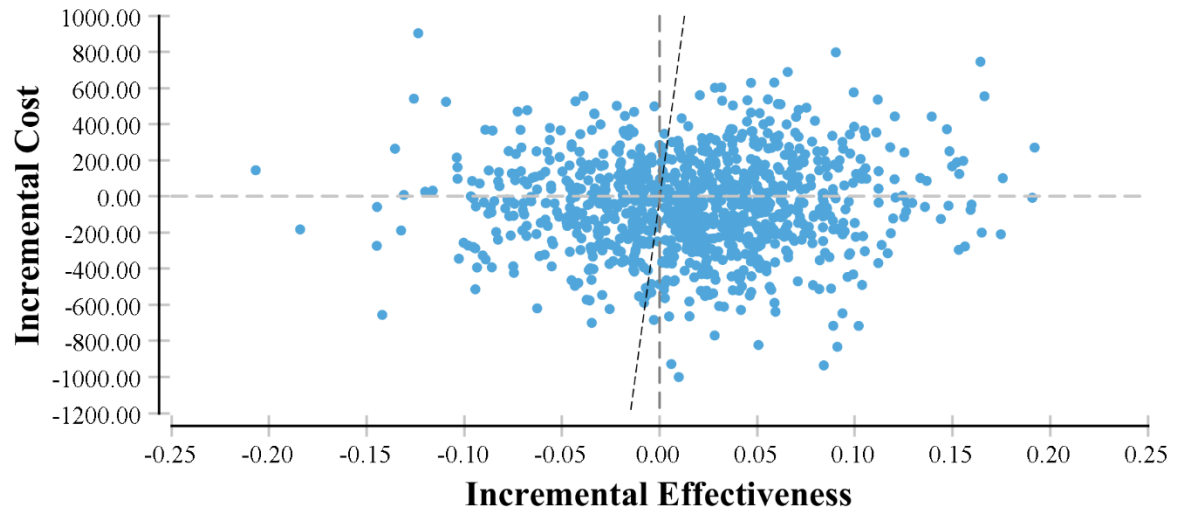
B. Ten-Year Time Horizon

Cost-Effectiveness Acceptability Curve - Ten-Year Time-Horizon



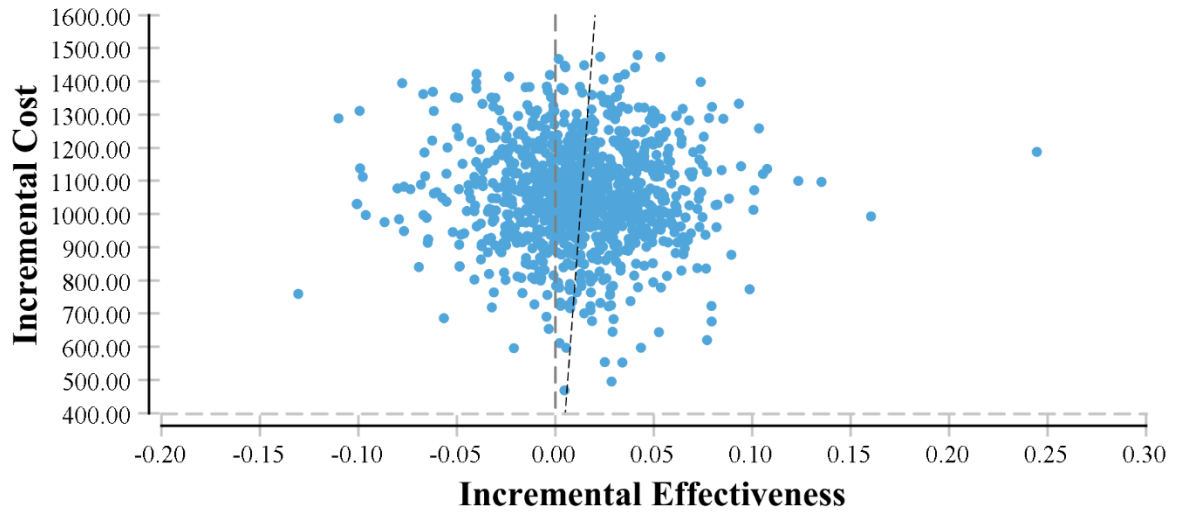
**eFigure 4. Incremental Cost-effectiveness Scatter Plot
A. Lifetime Horizon**

**Incremental Cost-Effectiveness, Combination Therapy
v. Monotherapy - Lifetime Horizon**



B. Ten-Year Time Horizon

**Incremental Cost-Effectiveness, Combination Therapy
v. Monotherapy - Ten-Year Time-Horizon**



eReferences.

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