H.6.1.4 Bevacizumab vs ranibizumab

| Outcomes | Illustrative comparative risks* (95% CI) | | Relative effect | No of Participants | Quality of the evidence | Comments |
|--|--|---|-----------------------------|--------------------|-------------------------|----------|
| | Corresponding risk | Assumed risk | (95% CI) | (studies) | (GRADE) | |
| | Ranibizumab | Bevacizumab | | | | |
| Gain of 15 letters or more visual acuity at one year | 238 per 1000 (202 to 279) | 258 per 1000 | RR 0.96 (0.85 to 1.08) | 3101 (8 studies) | ⊕⊕⊕⊕ High | |
| Loss of fewer than 15 letters visual acuity at one year | 942 per 1000 (923 to 960) | 942 per 1000 | RR 1.00 (0.98 to 1.02) | 2817 (7 studies) | ⊕⊕⊕⊕ High | |
| Mean change in visual acuity at one year (number of letters) | The mean change in visual acuity in the bevacizumab groups was on average 0.48 fewer letters gained (95% CI 1.47 fewer letters to 0.51 more letters) | The mean change across ranibizumab groups ranged from gains of 3 to 8 letters | MD -0.48 (-1.47 to 0.51) | 3101 (8 studies) | ⊕⊕⊕⊕ High | |
| Serious systemic adverse events at one year | 148 per 1000 (150 to 206) | 175 per 1000 with at least one serious systemic adverse event | RR 1.18 (1.01 to 1.39) | 3038 (5 studies) | ⊕⊕⊕⊝ Moderate¹ | |
| Gastrointestinal disorders | 10 per 1000 | 20 per 1000 | RR 1.85 (1.01, 3.40) | 3038 (5 studies) | ⊕⊕⊕⊝ Moderate¹ | |
| Myocardial infarction | <10 per 1000 | <10 per 1000 | RR 0.51 (0.22 to 1.19) | 3038 (5 studies) | ⊕⊕⊝⊖ Low² | |
| Stroke or cerebral infarction | <10 per 1000 | <10 per 1000 | RR 0.65 (0.25 to 1.67) | 3038 (5 studies) | ⊕⊕⊝⊖ Low² | |
| Venous thrombotic event | <10 per 10000 | <10 per 1000 | RR 2.04 (0.61 to 6.75) | 2721 (4 studies) | ⊕⊕⊖⊖ Low² | |

| Serious ocular adverse events at one year | < 5 per 1000 | <5 per 1000 | Range of RRs 0.51 (0.05 to 5.62) to 7.05 (0.36 to 136.28) | Range 1670 to 2280 (2 to 3 studies) | | Studies reported different ocular adverse events |
|---|---------------|--------------|--|-------------------------------------|-----------|--|
| Retinal detachment | 0 | <10 per 1000 | RR 7.05 (0.36 to 136.28) | 1670 (2 studies) | ⊕⊕⊖⊖ Low² | |
| Severe uveitis | < 10 per 1000 | <10 per 1000 | RR 4.14 (0.46 to 36.97) | 1795 (2 studies) | ⊕⊕⊖⊖ Low² | |
| Endophthalmitis | <10 per 1000 | <10 per 1000 | RR 1.68 (0.40 to 7.00) | 2111 (3 studies) | ⊕⊕⊖⊖ Low² | |
| Retinal pigment epithelial tear | <10 per 1000 | <10 per 1000 | RR 1.37 (0.31 to 6.12) | 2236 (3 studies) | ⊕⊕⊖⊖ Low² | |
| cataract | <10 per 1000 | <10 per 1000 | RR 0.51 (0.05 to 5.62 | 2280 (3 studies) | ⊕⊕⊖⊖ Low² | |

^{*}The basis for the assumed risk is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI)

^{2.} Downgrade two levels for serious imprecision

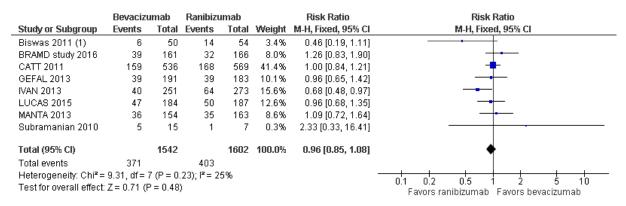
| Number of studies | Risk of bias | Inconsistency | Indirectness | Imprecision | Sample size | Effect (95%CI) | Quality | | |
|---|--------------|---------------|--------------|-------------|-------------|----------------|---------|--|--|
| Bevacizumab vs ranibizumab | | | | | | | | | |
| Number of injections | | | | | | | | | |
| 5 studies (CATT 2011, Biswas 2011, GEFAL 2013, LUCAS 2015, MANTA 2013) Not serious Not serious Not serious 1660 MD=0.60 (0.33, 0.87) | | | | | | Moderate | | | |
| Downgrade for masking of participants and incomplete outcome data. | | | | | | | | | |

^{1.} Adverse vent outcome downgrade to moderate quality as not all eligible trials reported these outcomes and numbers of some adverse events were small (<1 %), and 95%CI of estimated effect under the possibility of significant and non-significant values

Bevacizumab vs ranibizumab

One year

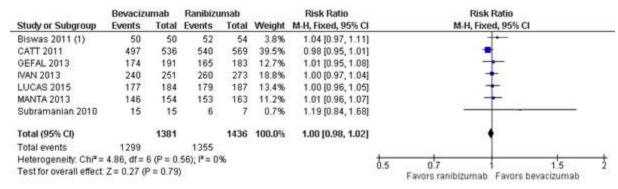
Visual acuity (gain of 15 letters or more at one year)



Footnotes

(1) follow-up was 18 months

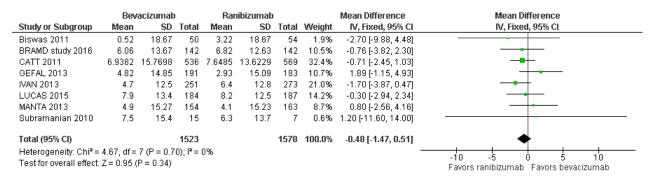
Visual acuity (loss of fewer than 15 letters at one year)



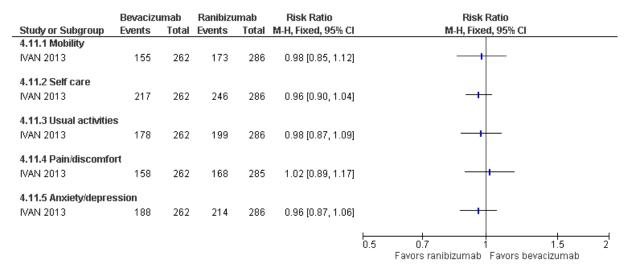
Footnotes

(1) follow-up was 18 months

Visual acuity (mean change in number of letters)



Quality of life (no problem in quality of life)

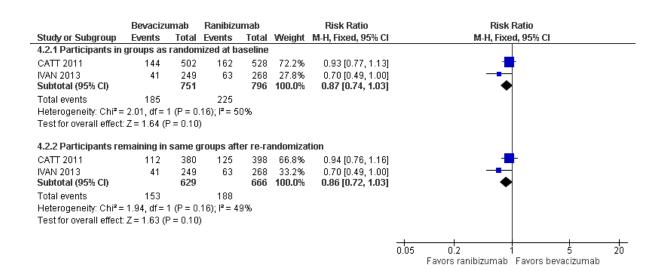


Number of injections

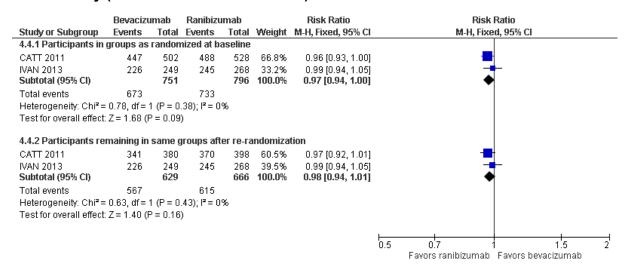
| | Beva | cizum | ab | Ranibizumab | | Mean Difference | | Mean Difference | |
|---|------|-------|-------|-------------|-----|-----------------|--------|---|-------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Biswas 2011 | 4.3 | 0 | 50 | 5.6 | 0 | 54 | | Not estimable | |
| CATT 2011 | 7.7 | 3.5 | 300 | 6.9 | 3 | 298 | 25.9% | 0.80 [0.28, 1.32] | — |
| GEFAL 2013 | 6.8 | 2.7 | 191 | 6.5 | 2.4 | 183 | 26.5% | 0.30 [-0.22, 0.82] | +- |
| LUCAS 2015 | 8.9 | 2.6 | 184 | 8 | 2.3 | 187 | 28.3% | 0.90 [0.40, 1.40] | |
| MANTA 2013 | 6.1 | 2.8 | 154 | 5.8 | 2.7 | 163 | 19.3% | 0.30 [-0.31, 0.91] | - |
| Total (95% CI) | | | 829 | | | 831 | 100.0% | 0.60 [0.33, 0.87] | • |
| Heterogeneity: Chi² = 4.18, df = 3 (P = 0.24); ² = 28% | | | | | | | | | |
| Test for overall effect: Z = 4.42 (P < 0.00001) | | | | | | | | Favours ranibizumab Favours bevacicumab | |

Two years

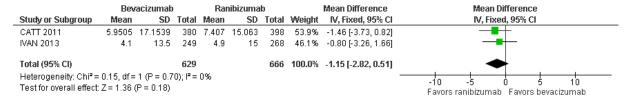
Visual acuity (gain of 15 letters or more)



Visual acuity (loss of fewer than 15 letters)



Visual acuity (mean change in number of letters)



Quality of life (no problem in quality of life)

