H.6.3 Adjunctive therapies

RQ13: What is the effectiveness of adjunctive therapies for the treatment of late AMD (wet active)?

H.6.3.1 Anti-VEGF +PDT vs anti-VEGF

Number of RCTs	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Anti-VEGF + PDR vs anti-VEGF								
BCVA (ETDRS letters ≤3 months) - positive values favour combination								
1 (Lazic)*	RCT	Serious[1]	Not serious	Not serious	Serious[2]	106	MD -7.25 (-19.82, 5.31)	LOW
BCVA (ETDRS letters >3 months) - positive values favour combination								
11 (Datseris; Bashshur; Hatz; Kaiser; Krebs; Larsen; Semeraro*; Weingessel; Williams: Gomi; Koh)	RCT	Not serious[3]	Not serious	Not serious	Not serious	1025	MD -0.54 (-1.29, 0.21)	HIGH
BCVA (proportion gain ≥15 letters, >3 months) - values greater than 1 favour combination								
9 (Datseris; Bashshur; Hatz; Kaiser; Larsen; Vallance; Williams: Gomi; Koh)	RCT	Not serious[3]	Not serious	Not serious	Serious[2]	923	RR 0.76 (0.63, 0.92)	MODERATE
Reinjections (>3 months) - positive values favour monotherapy								
5 (Datseris; Bashshur; Larsen; Gomi; Koh)	RCT	Serious[4]	Serious[5]	Not serious	Not serious	488	MD -1.43 (-2.42, -0.45)	LOW
Total number of injections (>3 months) - positive values favour monotherapy								
6 (Lim; Krebs;	RCT	Serious[4]	Serious[5]	Not serious	Not serious	474	MD -0.94	LOW

Number of RCTs	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Larsen; Semeraro; Weignessel, Williams)							(-1.76, -0.12)	
Proportion needing retreatment (>3 months) - values greater than 1 favour combination								
1 (Hatz)	RCT	Serious[6]	N/A	Not serious	Serious[2]	40	RR 0.69 (0.42, 1.13)	LOW
Proportion having ocular adverse events - values greater than 1 favour combination								
5 (Lazic; Bashshur; Hatz; Kaiser; Larsen)	RCT	Not serious[3]	Not serious	Not serious	Not serious	762	RR 1.03 (0.88, 1.21)	HIGH
Proportion having non-ocular adverse events - values greater than 1 favour combination								
1 (Larsen)	RCT	Not serious	N/A	Not serious	Serious[2]	255	RR 1.03 (0.82, 1.29)	MODERATE

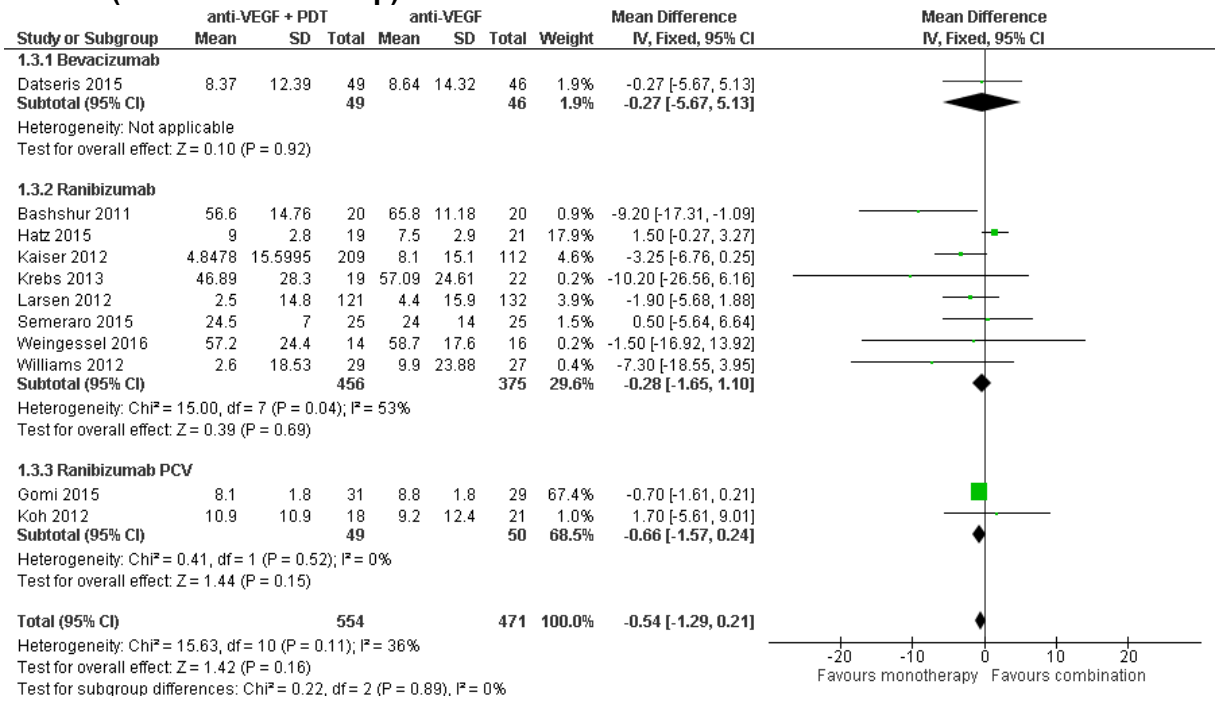
1. Downgraded one level for study design (open label, single blinded)
2. Downgraded one level for confidence interval crossing 1 line of a defined minimal important difference.
3. Some individual studies at high-risk of bias, but overall risk of bias rated low due to consistency of effect size estimates between high and low quality studies.
4. Downgraded one level for includes open label studies; lack of appropriate assessor masking.
5. Downgraded one level for heterogeneity (i^2>50%).
6. Downgraded one level for selection bias (differences in baseline characteristics between treatment groups)

*visual acuity outcome reported in the study used logMAR, and was converted to number of letters (logMAR=no. of letters × -0.02).

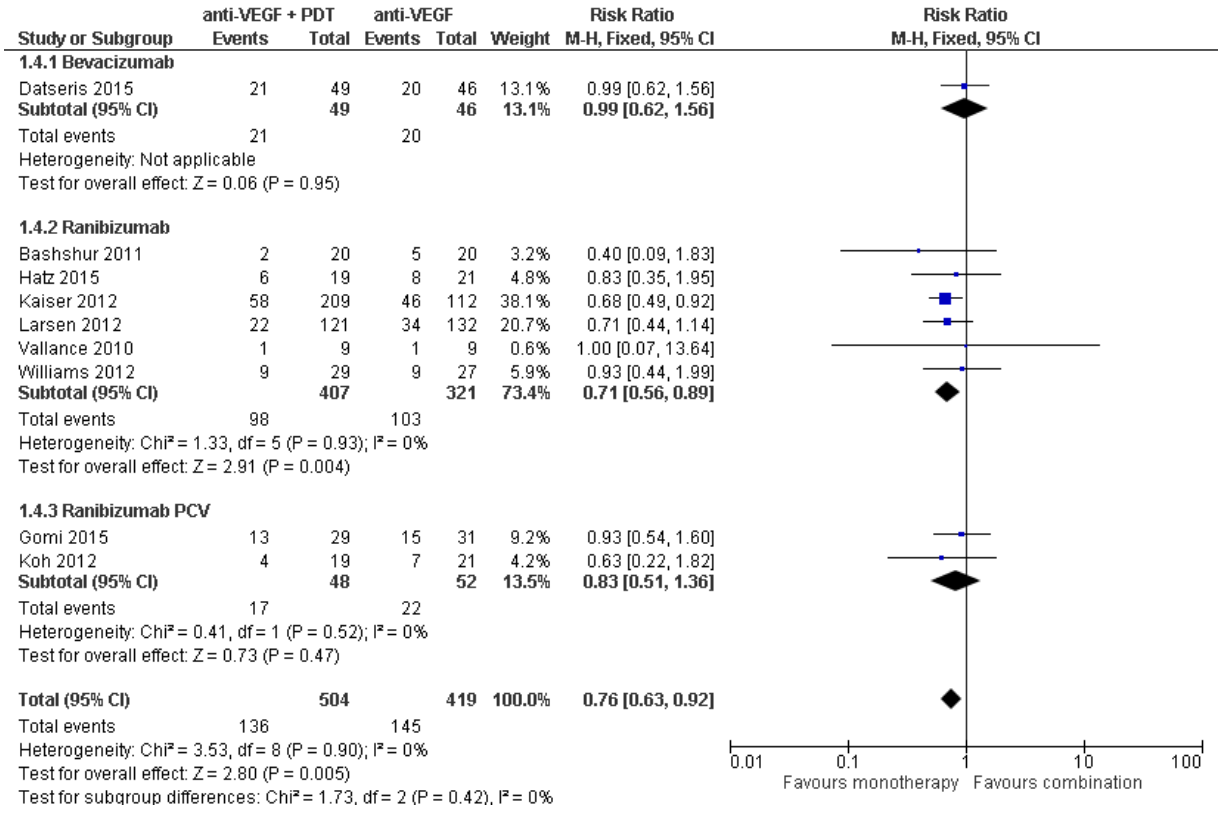
Meta-analysis: Anti-VEGF + PDT vs anti-VEGF

Visual acuity

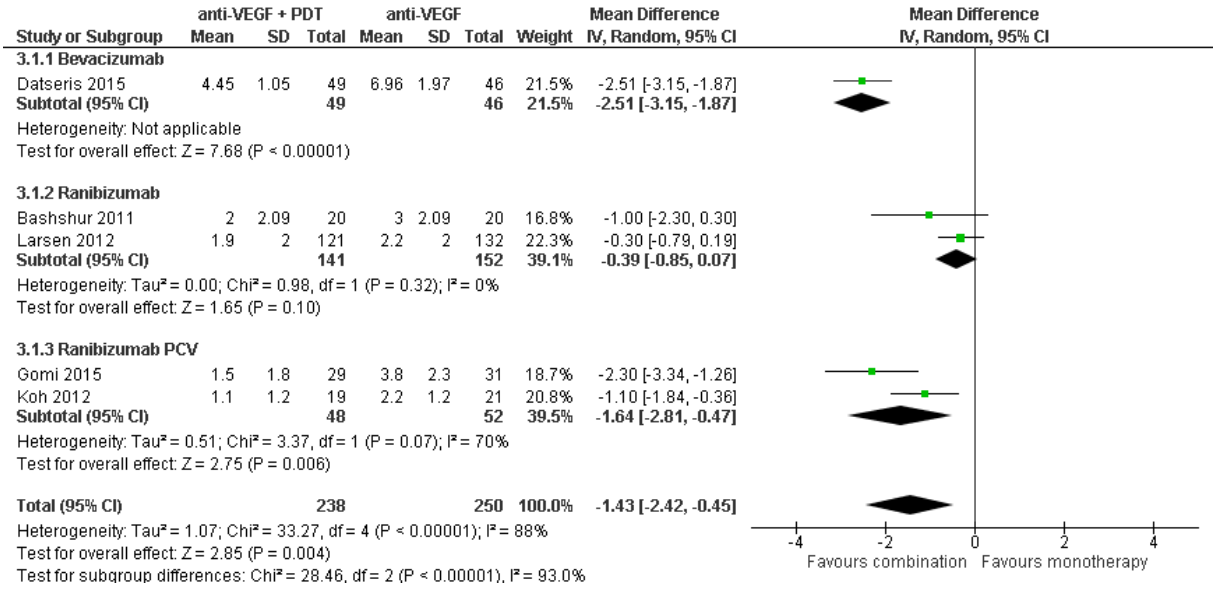
Letters (>3 month follow-up)



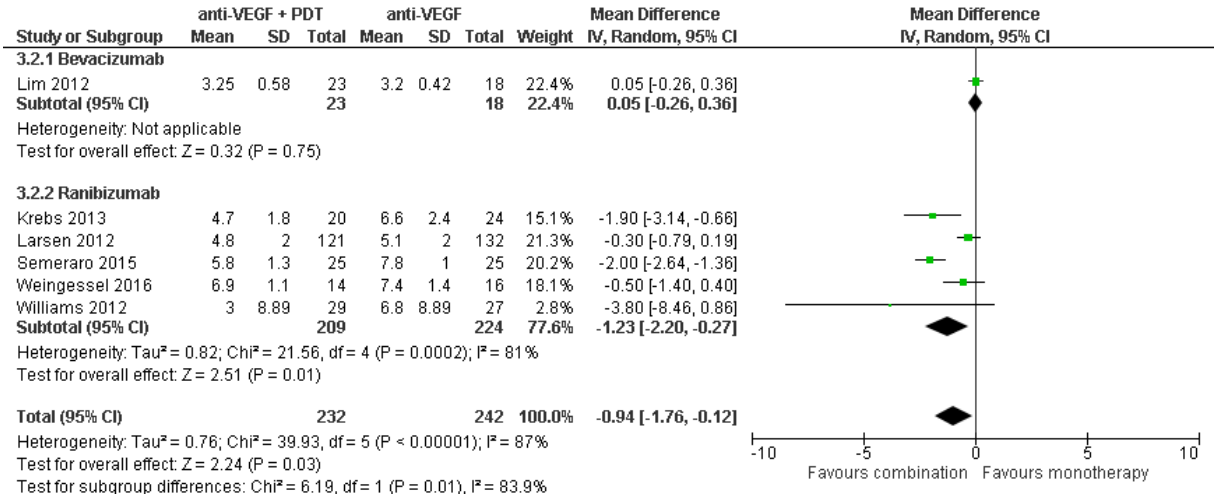
Letters gained (proportion 15 or more letters)



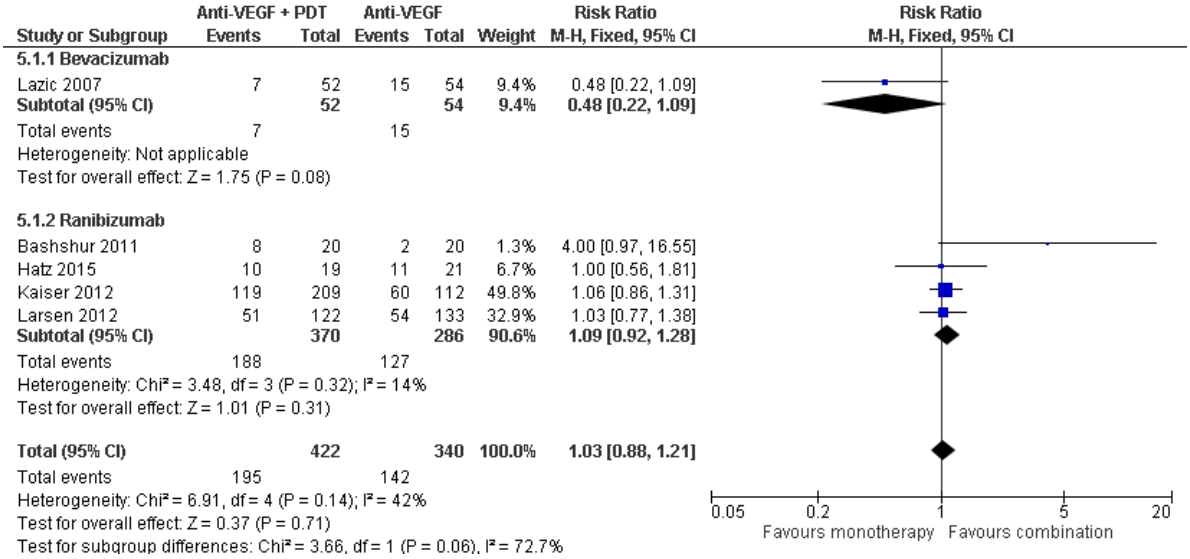
Number of injections: reinjections



Number of injections: total number of injections



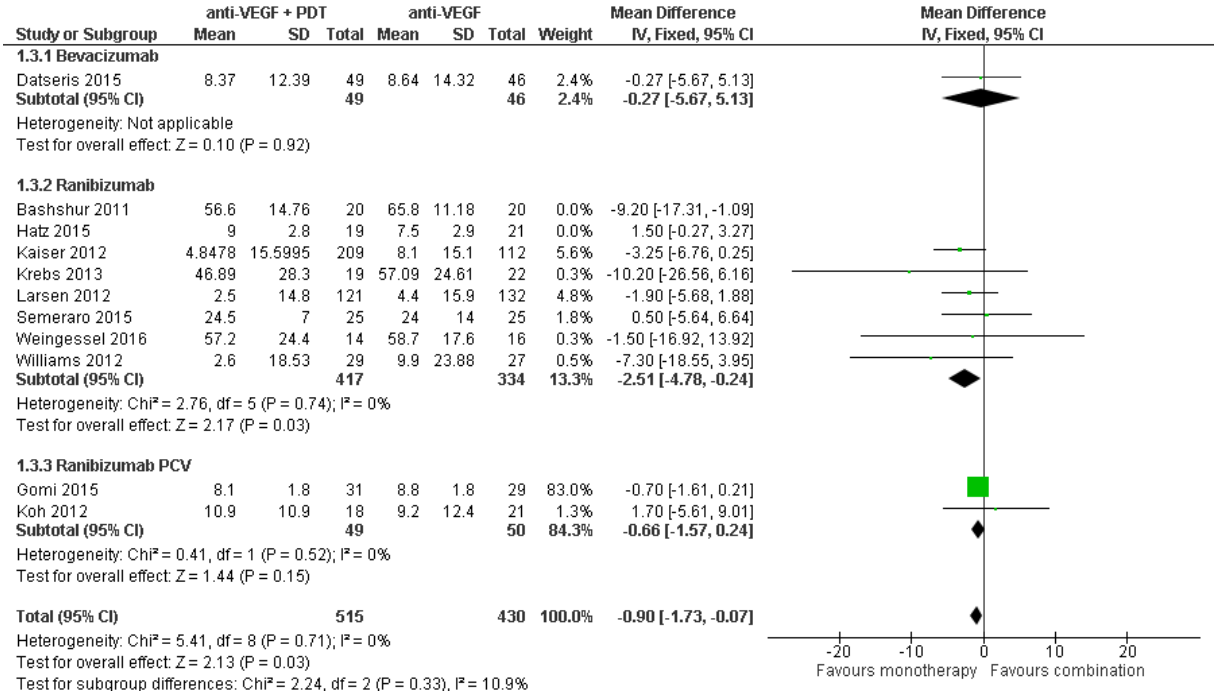
Ocular adverse events



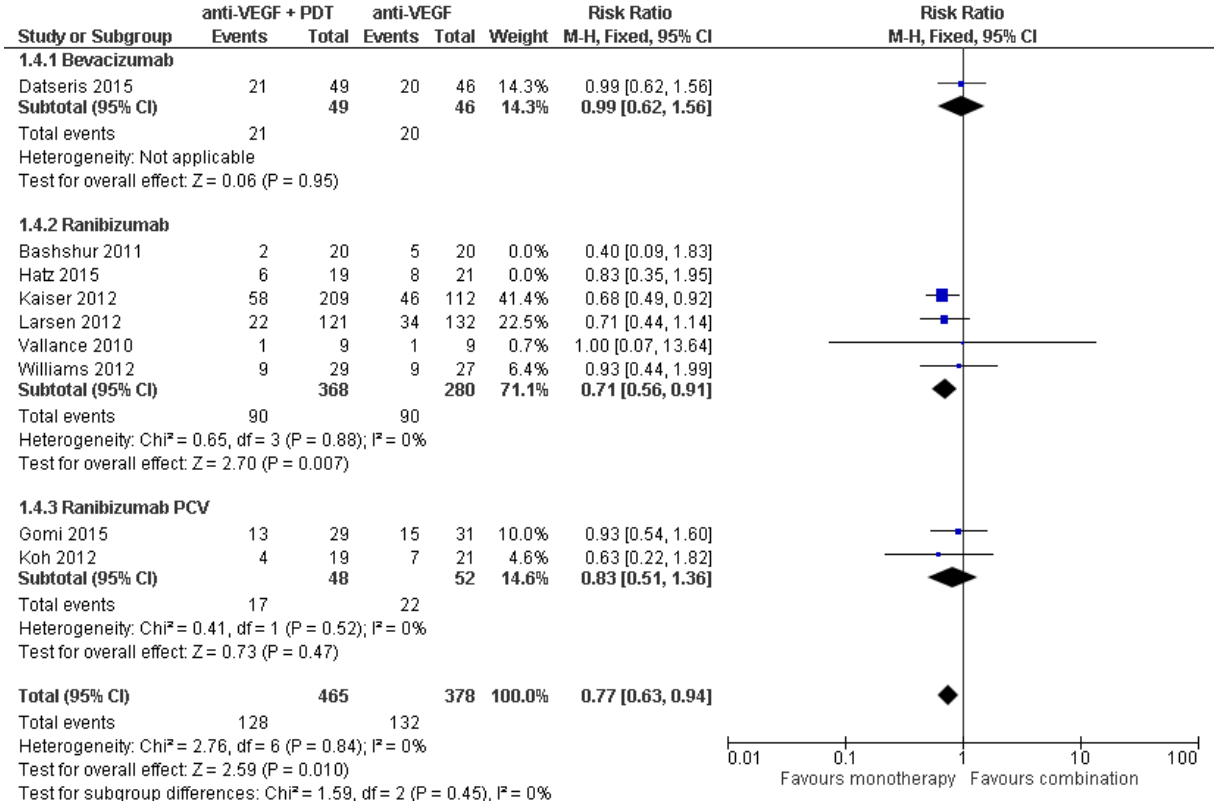
Meta-analysis (excluded study population with previous treatment history)

Visual acuity

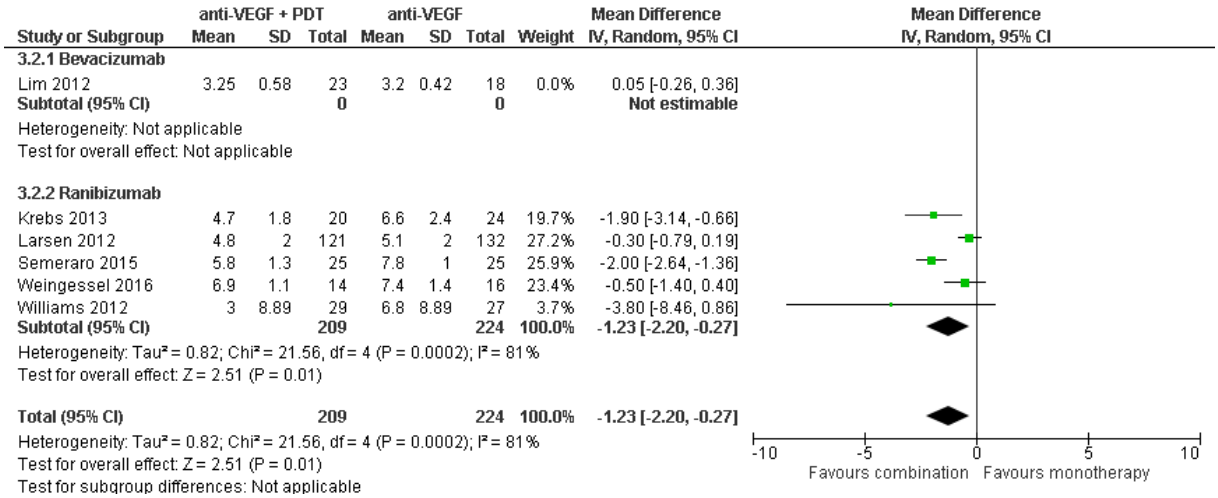
Letters (>3 month follow-up)



Letters gained (proportion 15 or more letters)



Total number of injections



Proportion of people had ocular adverse events