H.6.4 Switching and stopping antiangiogenic treatment for late AMD (wet)

RQ11: What are the indicators for treatment failing and switching?

RQ14: What factors indicate that treatment for neovascular AMD should be stopped?

RQ15: What is the effectiveness of switching therapies for neovascular AMD if the first-line therapy is contraindicated or has failed?

This review was undertaken by the National Clinical Guideline team.

H.6.4.1 The effectiveness of switching therapies

Anti-VEGF switching

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95% CI)	Quality
Ranibizumab to aflibercept vs continuing on ranibizumab								
Visual acuity (ETDRS letters) [change score] (Better indicated by higher values)								
1 (Mantel 2016)	RCT	Very serious[1]	N/A	Not serious	Not serious	21	MD -2.5 (-4.87 to -0.13)	LOW
Ranibizumab to bevacizumab vs bevacizumab to ranibizumab								
Best corrected visual acuity (logMAR) - 12 months (Better indicated by lower values)								
1 (Kucukerdonmez 2015)	Cohort study	Very serious[1]	N/A	Not serious	Not serious	87	MD 0.05 (-2.84 to 2.94)	LOW
Best corrected visual acuity (logMAR) - ≥ 12 months (Better indicated by lower values)								
1 (Kucukerdonmez 2015)	Cohort study	Very serious[1]	N/A	Not serious	Serious[2]	87	MD 0.16 (-0.88 to 1.20)	VERY LOW
Bevacizumab to ranibizumab								
Visual acuity (logMAR) - ≤ 3 months (Better indicated by lower values)								
1 (Moisseiev	Before–after	Very serious[1]	N/A	Not serious	Serious[3]	110	MD- 0.02	VERY LOW

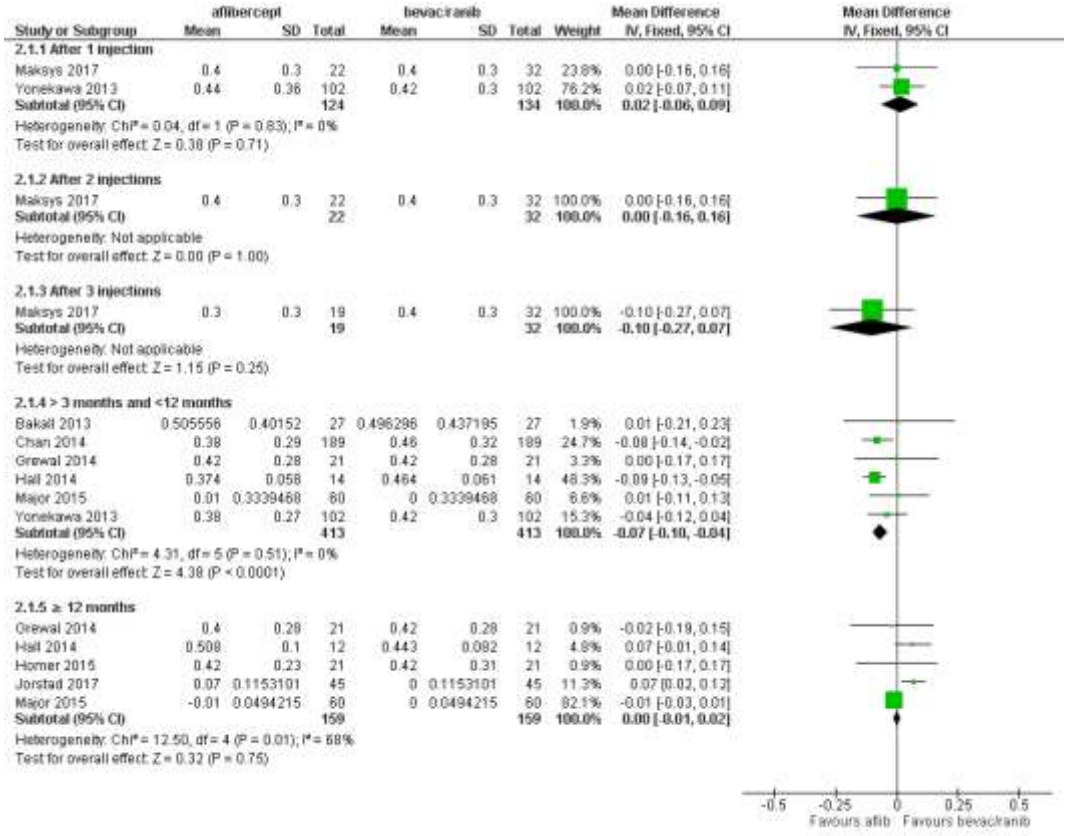
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95% CI)	Quality
2015)	study						(-0.11 to 0.07)	
Visual acuity (logMAR) – at least 4 months (Better indicated by lower values)								
1 (Moisseiev 2015)	Before–after study	Very serious[1]	N/A	Not serious	Serious[3]	110	MD -0.04 (-0.06 to 0.14)	VERY LOW
Bevacizumab to aflibercept								
Best corrected visual acuity (ETDRS) - > 3 months and <12 months (Better indicated by higher values)								
1 (Tiosano 2017)	Before–after study	Very serious[1]	N/A	Not serious	Serious[3]	47	MD 2.8 (-2.35, 7.95)	VERY LOW
Best corrected visual acuity (ETDRS) - ≥ 12 months (Better indicated by higher values)								
1 (Pinheiro-Costa 2015)	Observational study	Very serious[1]	N/A	Not serious	Serious[3]	39	MD -2.4 (-10.15 to 5.35)	VERY LOW
Bevacizumab and/or ranibizumab to aflibercept								
Best corrected visual acuity (logMAR) - After 1 injection (Better indicated by lower values)								
2 (Maksys 2017, Yonekawa 2013)	Observational study	Very serious[1]	Not serious	Not serious	Serious[3]	134	MD 0.02 (-0.06 to 0.09)	VERY LOW
Best corrected visual acuity (logMAR) - After 2 injections (Better indicated by lower values)								
1 (Maksys 2017)	Observational study	Very serious[1]	N/A	Not serious	Serious[3]	32	MD 0.00 (-0.16 to 0.16)	VERY LOW
Best corrected visual acuity (logMAR) - After 3 injections (Better indicated by lower values)								
1 (Maksys 2017)	Observational study	Very serious[1]	N/A	Not serious	Serious[3]	32	MD -0.10 (-0.27 to 0.07)	VERY LOW
Best corrected visual acuity (logMAR) - > 3 months and <12 months (Better indicated by lower values)								
6 (Bakall 2013, Chan 2014, Grewal 2014, Hall 2014, Major	Observational study	Very serious[1]	N/A	Not serious	Serious[3]	413	MD -0.07 (-0.10 to -0.04)	VERY LOW

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95% CI)	Quality
2015, Yonekawa 2013)								
Best corrected visual acuity (logMAR) - ≥ 12 months (Better indicated by lower values)								
5 (Grewal 2014, Hall 2014, Homer 2015, Jorstad 2017, Major 2015)	Observational study	Very serious[1]	N/A	Not serious	Not serious	159	MD 0.00 (-0.01 to 0.02)	LOW
Best corrected visual acuity (ETDRS) - After 1 injections (Better indicated by higher values)								
1 (Hariri 2015)	Observational study	Very serious[1]	N/A	Not serious	Serious[3]	31	MD 3.1 (-4.06 to 10.26)	VERY LOW
Best corrected visual acuity (ETDRS) - After 3 injections (Better indicated by higher values)								
1 (Gharbiya 2014)	Observational study	Very serious[1]	N/A	Not serious	Serious[3]	31	MD -0.2 (-5.95 to 5.55)	VERY LOW
Best corrected visual acuity (ETDRS) - > 3 months and <12 months (Better indicated by higher values)								
2 (Gharbiya 2014, Thorell 2014)	Observational studies	Very serious[1]	N/A	Not serious	Not serious	104	MD 0.44 (-2.59 l to 3.48)	LOW

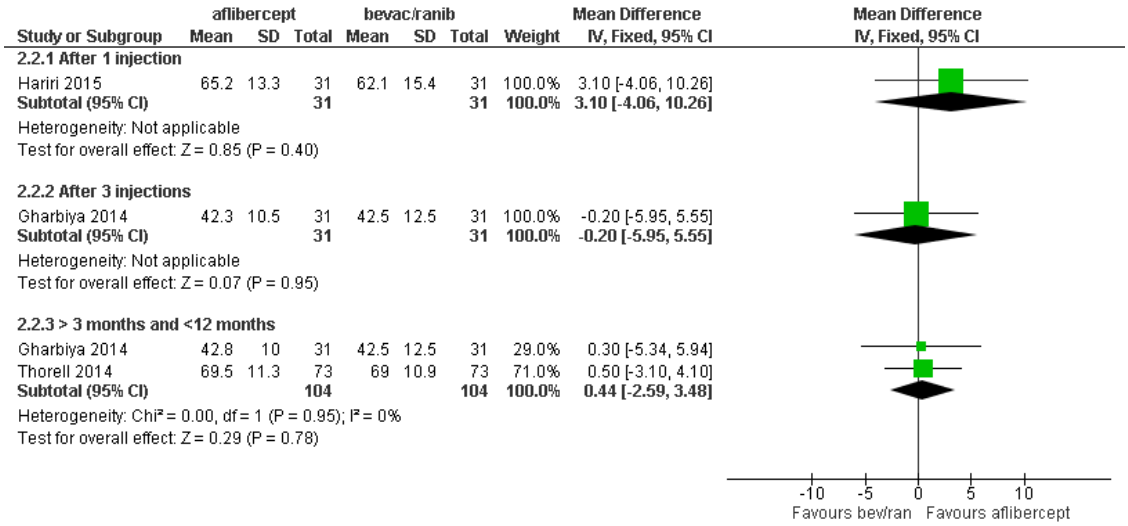
1. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
2. Downgraded one level for non-significant effect.
3. Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Meta-analysis (forest plots) for bevacizumab and/or ranibizumab to aflibercept

Best corrected visual acuity (logMAR)



Best corrected visual acuity (ETDRS)



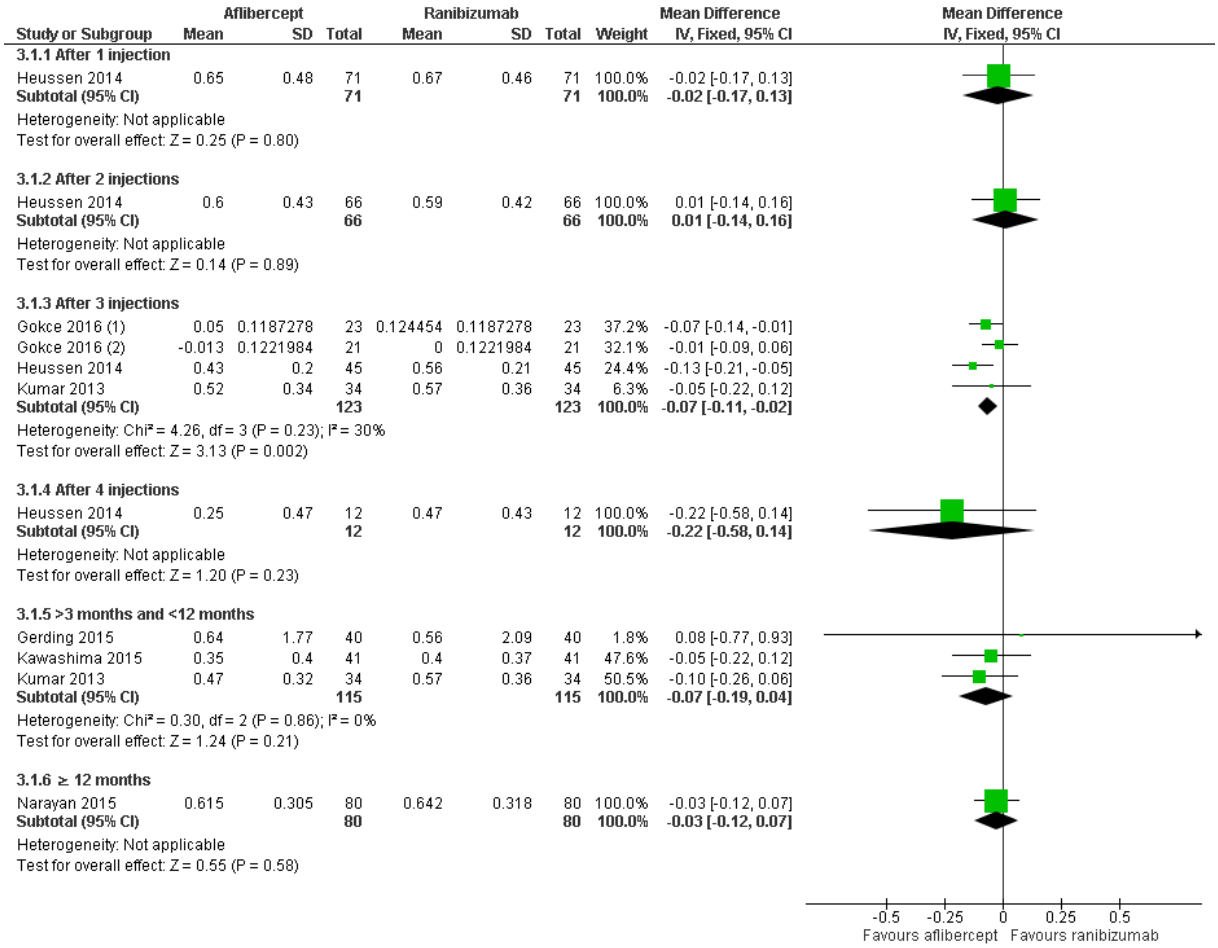
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Ranibizumab to aflibercept								
Best corrected visual acuity (logMAR) - After 1 injection (Better indicated by lower values)								
1 (Heussen 2014)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	71	MD -0.02 (-0.17 l to 0.13)	VERY LOW
Best corrected visual acuity (logMAR) - After 2 injections (Better indicated by lower values)								
1 (Heussen 2014)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	66	MD 0.01 (-0.14 to 0.16)	VERY LOW
Best corrected visual acuity (logMAR) - After 3 injections (Better indicated by lower values)								
3 (Gokce 2016, Kumar 2013, Heussen 2014)	Observational studies	Very serious[1]	N/A	Not serious	Serious[2]	123	MD -0.07 (-0.11 to -0.02)	VERY LOW
Best corrected visual acuity (logMAR) - After 4 injections (Better indicated by lower values)								
1 (Heussen 2014)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	12	MD -0.22 (-0.58 to 0.14)	VERY LOW
Best corrected visual acuity (logMAR) - > 3 months and <12 months (Better indicated by lower values)								
3 (Gerding 2015, Kawshima 2015, Kumar 2013)	Observational studies	Very serious[1]	N/A	Not serious	Serious[2]	115	MD -0.07 (-0.19 to 0.04)	VERY LOW
Best corrected visual acuity (logMAR) - ≥ 12 months (Better indicated by lower values)								
1 (Narayan 2015)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	80	MD -0.03 (-0.12 to 0.07)	VERY LOW
Best corrected visual acuity (ETDRS) - > 3 months and <12 months (Better indicated by higher values)								
4 (Chang 2015, Hatz	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	216	MD 0.57 (-0.43 to 1.56)	VERY LOW

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
2016, Sarao 2016, Wykoff 2014)								
Best corrected visual acuity (ETDRS) - ≥ 12 months (Better indicated by lower values)								
2 (Chang 2015, Sarao 2016)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	141	MD 3.06 (-0.86 to 6.92)	VERY LOW
Ranibizumab to pegaptanib								
Best corrected visual acuity (logMAR) - ≥ 12 months (Better indicated by lower values)								
1 (Shiragami 2014)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	50	MD -0.07 (-0.23 to 0.09)	VERY LOW

1. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
2. Downgraded by 1 increment if the confidence interval crossing 1 MID or by 2 increments if the confidence interval crossing both MIDs

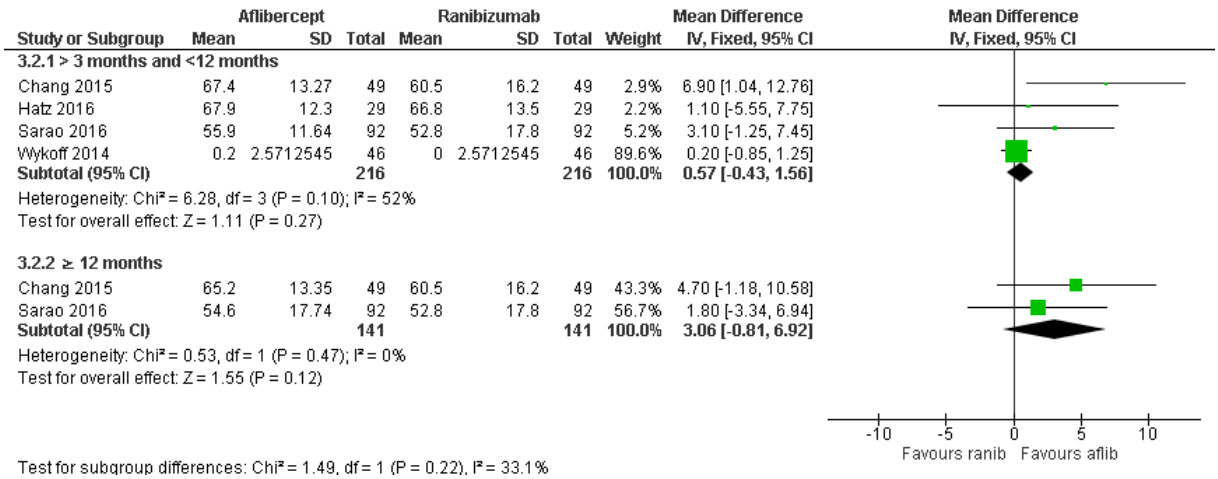
Meta-analysis (forest plots) for ranibizumab to aflibercept

Best corrected visual acuity (logMAR)



Footnotes
(1) Coplete ranibizumab resistance
(2) Tachyphylaxis

Best corrected visual acuity (letter)



Test for subgroup differences: Chi² = 1.49, df = 1 (P = 0.22), I² = 33.1%

Bevacizumab to bevacizumab + triamcinolone acetonide

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95% CI)	Quality
Bevacizumab to bevacizumab + triamcinolone acetonide								
Best corrected visual acuity (logMAR) - ≤ 3 months (Better indicated by lower values)								
1 (Tao 2010)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	31	MD -0.11 (-0.3 to 0.08)	VERY LOW
Best corrected visual acuity (logMAR) - > 3 months and <12 months (Better indicated by lower values)								
1 (Tao 2010)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	31	MD -0.07 (-0.26 to 0.12)	VERY LOW
1 (Tao 2010)	Observational study	Very serious[1]	N/A	Not serious	Serious[2]	31	MD -0.02 (-0.21 to 0.17)	VERY LOW

1. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
2. Downgraded by 1 increment if the confidence interval crossing 1 MID or by 2 increments if the confidence interval crossing both MIDs