H.6.1.5 Aflibercept 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)		
	Alfibercept	Ranibizumab					
Mean change in BCVA in ETDRS letters at 1 year	Mean change in visual acuity in aflibercept groups was on average 0.15 fewer letters gained (95% CI 1.47 fewer letters to 1.17 more letters)	Mean change in visual acuity across ranibizumab groups ranged from gains of 8.57 letters to 8.71 letters	MD -0.15 (-1.47 to 1.17)	2412 (2 studies)	⊕⊕⊕⊕ High		
Gain of 15 of BCVA at one year	314 per 1000 (275 to 360)	324 per 1000	RR 0.97 (0.85 to 1.11)	2412 (2 studies)	⊕⊕⊕ High		
Quality of life measures at 1 year (national eye institute-visual function questionnaire)	Mean improvement in composite NEI-VQF score in intervention groups was on average 0.39 points lower (95% CI 1.71 points lower to 0.93 points higher)	Mean improvement in composite NEI-VQF score ranged across control groups from 4.9 to 6.3 points	MD -0.39 (-1.71 to 0.93)	2412 (2 studies)	⊕⊕⊕High		
Adverse events (serious systemic events at 1 year)	138 per 1000 (110 to 174)	139 per 1000	RR 0.99 (0.79 to 1.25)	2419 (2 studies)	⊕⊕⊕⊖ Moderate¹		
Adverse events (serious ocular events at 1 year)	20 per 1000 (12 to 34)	32 per 1000	RR 0.62 (0.36 to 1.07)	2419 (2 studies)	⊕⊕⊕⊖ Moderate¹		

^{*}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)

^{1.} Adverse vent outcome downgrade to moderate quality as the numbers of events were small (wide confidence intervals), and 95%Cl of estimated effect under the possibility of significant and non-significant values

The data presented in the GRADE table below were identified by update searches undertaken after the search date of the Cochrane systematic reviews used above.

Aflibercept vs ranibizumab: NEI-VFQ 25

<u>-</u>			1	i		1	i
Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Proportion of people gainin follow –up						<u> </u>	
2 (VIEW 1, VIEW2)	Not serious	Serious ¹	Not serious	Not serious	1193	RR 0.97 (0.86, 1.10)	MODERATE
NEI-VFQ-25 subscale score	changes from baseli	ne to week 52 (hig	her scores indi	cate better Qol	_)		
General vision	Not serious	Not serious	Not serious	Not serious	1193	MD 0.06 (-2.00, 2.13)	HIGH
Near activities	Not serious	Not serious	Not serious	Not serious	1193	MD -0.62 (-3.09, 1.86)	HIGH
Distance activities	Not serious	Not serious	Not serious	Serious ²	1193	MD 0.08 (-2.43, 2.58)	MODERATE
Mental health	Not serious	Not serious	Not serious	Serious ²	1193	MD 0.14 (-2.41, 2.70)	MODERATE
Role difficulities	Not serious	Not serious	Not serious	Serious ²	1193	MD 1.09 (-2.04, 4.23)	MODERATE
Dependency	Not serious	Not serious	Not serious	Serious ²	1193	MD -1.29 (-4.00, 1.43)	MODERATE
Social funictioning	Not serious	Not serious	Not serious	Serious ²	1193	MD 0.18 (-2.35, 2.70)	MODERATE
Driving	Not serious	Not serious	Not serious	Serious ²	1193	MD 1.51 (-1.15, 4.17)	MODERATE
Colour vision	Not serious	Not serious	Not serious	Not serious	1193	MD -2.04 (-4.33, 0.26)	HIGH

Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Ocular pain	Not serious	Not serious	Not serious	Not serious	1193	MD -0.94 (-3.21, 1.32)	HIGH
Peripheral vision	Not serious	Not serious	Not serious	Not serious	1193	MD 0.86 (-3.73, 2.00)	HIGH
General health	Not serious	Not serious	Not serious	Not serious	1193	MD -0.23 (-2.56, 2.10)	HIGH

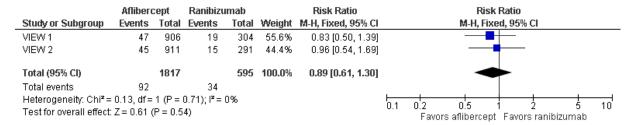
- 1. Downgraded one level for inconsistency due to heterogenioty (i2>50%)
- 2. Downgraded one level for imprecision due to 95%CI of estimated effect crossing 1 line of a defined minimal important difference (2.3 point)

Aflibercept vs ranibizumab (one year)

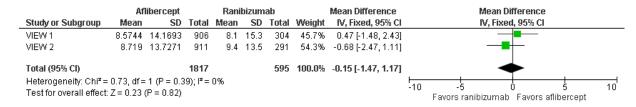
Gain of ≥ 15 letters of BCVA

	Aflibero	cept	Ranibizu	ımab		Risk Ratio			Risk	Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI			M-H, Fixe	d, 95% (CI		
VIEW 1	281	906	94	304	48.4%	1.00 [0.83, 1.22]			-	-			
VIEW 2	290	911	99	291	51.6%	0.94 [0.78, 1.13]			-	-			
Total (95% CI)		1817		595	100.0%	0.97 [0.85, 1.11]			•				
Total events	571		193										
Heterogeneity: Chi²=	0.26, df=	1 (P=	0.61); I*=	0%			<u> </u>	- 1-	0/5	! 	! 	ļ 	10
Test for overall effect:	Z = 0.47	P = 0.6	4)				0.1	0.2 Favors	0.5 ranibizumab	ر Favors	∠ afliberce;	o t	10

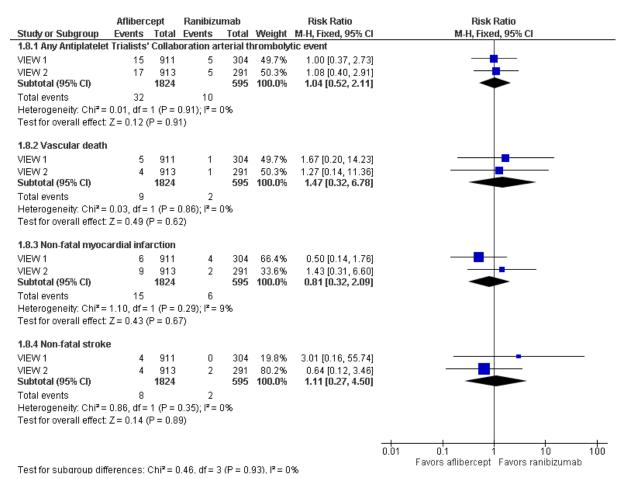
Loss of ≥15 letters of BCVA



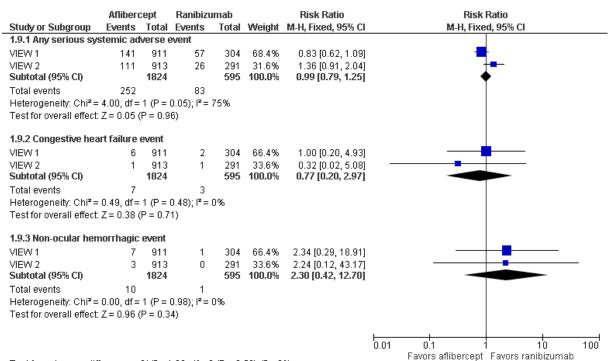
Mean change in BCVA in ETDRS letters



Arterial thrombotic events

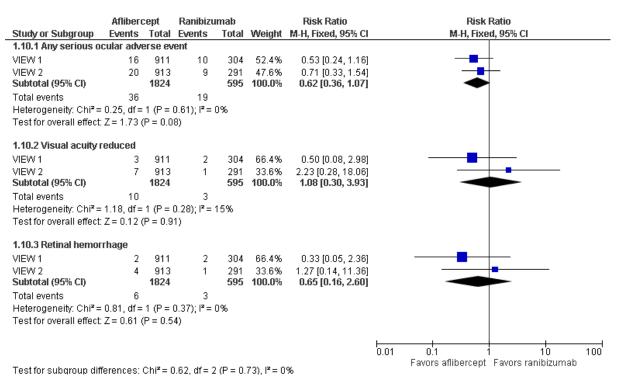


Serious systemic events

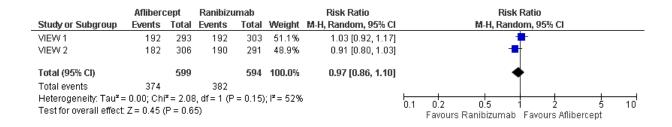


Test for subgroup differences: Chi² = 1.06, df = 2 (P = 0.59), I^2 = 0%

Serious ocular events



Proportion of people had gain more than 5 ETDRS letters and had clinical improvement in NEI-VFQ compsite score (more than 6-point)



Mean change in NEI-VFQ subscale score

	Mean	bercept SD	Total		bizumi SD		Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
Study or Subgroup 1.13.1 General vision	MEGII	30	rucai	antign)	30	2008	aveignt	19, FIXER, SON CI	iv, rived, 20% Ci
/IEW 1	10.1	19	293	9.5	18.8	303	46.3%	0.60 [2.44, 3.64]	
/IEW 2	9.1	17	306		18.1	291	53.7%	-0.48 [-3.22, 2.42]	-
iulototal (95% CI)			599			594	100.0%	0.06 [-2.00, 2.13]	•
Heterogeneity: Chi*= I Fest for overall effect 2		100		l*= 0%					Î
1.13.2 Near activities									
/IEW 1	6.1	22.2	293	7.2	23.1	303	46.4%	-1.18 [-4.74, 2.54]	
VIEW 2		21.03	306		21.1	291		-0.20 [-3.58, 3.18]	-
Subtotal (95% CI)		Market .	599					-0.62 [-3.09, 1.86]	•
Heterogeneity: Chi ^a = I Test for overall effect 2				P= 0%					
1.13.3 Distance activi	ies								
VIEW 1	6.2	21.8	293	2.5	23.1	303	48.3%	3.70 (0.10, 7.30)	-
VIEW 2		21.8	306		21.6	291		-3.30 [-6.78, 0.18]	-
Subtotal (95% CI)			599			594	100.0%	0.08 [-2.43, 2.58]	•
Heterogeneity: Chi*= 1 Fest for overall effect 2				i = 87	%				
.13.4 Mental health		W. 1-1751	2250.00						
/EW 1	10.1	24.1	293	9.8	21.8	303	47.7%	0.30 [-3.39, 3.99]	
VIEW 2	10.4	22	306	10.4	22	291	52.3%	0.00 [-3.53, 3.53]	
Subtotal (95% CI)	0.27		599	2510	7.5	594	100.0%	0.14 [-2.41, 2.70]	•
Heterogeneity: ChP = 0 Test for overall effect 2				P=0%				englishmetten Stock Gill B	
1.13.5 Role difficulitie	8								2-
/IEW 1	7.1	28.7	293		29.4	303	48.5%	1.30 [3.21, 5.81]	-
VIEW 2	7.8	24.1	306	5.9	29.9	291	51.5%	0.90 [3.47, 5.27]	
Subtotal (95% CI)	122300	1999120	599	garden i		594	100.0%	1.09 [-2.04, 4.23]	-
Heterogeneity: Chi ^a = (Test for overall effect: i				r= 0%					
1.13.6 Dependency									
VIEW 1	3.4	22.9	293		22.6	303		-2.00 [-5.65, 1.65]	
/IEW 2	4.1	25.2	306	4.5	25.5	291		-0.40 [-4.47, 3.57]	
Subtotal (95% CI)	e in the Court	100	599	market and		594	100.0%	-1.29 [-4.00, 1.43]	
Heterogeneity: Chi ² = 0 Test for overall effect 2				C=090					
1.13,7 Social function	177.15			_					ro <u>l</u>
VIEW 1		22.1	293	3	20			-0.40 [-3.79, 2.99]	
VIEW 2 Subtotal (95% CI)	40	24	306 599	0.1	23.2	291 594	100.0%	0.90 [-2.89, 4.69]	
Heterogeneity: Chi*= (125 df	1 (P =		P = 0%		304	1001011	2.10[2.00]2.70]	T
Test for overall effect 2									
1.13.8 Driving									Service Control of the Control of th
VIEW 1	2.2	24.4	293	0.1	22	303	50.7%	2.10 [1.63, 5.83]	
VIEW 2	1	24	306	0.1	23.2	291	49.3%	0.90 [-2.89, 4.69]	
Sulototal (95% CI) Heterogeneity: Chi* = (Test for overall effect:)				P = 0%		594	100.0%	1.51 [-1.15, 4.17]	
		0 - 4.2							
1.13.9 Colour vision	n e	22.2	202	1.0	19.1	202	47.3%	-1.30 [-4.64, 2.04]	
VIEW 2	0.6	22.3	293 306					-2.70 [-5.98, 0.46]	
Subtotal (95% CI)	0.9	41.4	599	- 100	102			-2.04 [-4.33, 0.26]	•
Heterogeneity: Chi*= (Test for overall effect 2			0.55);	1*= 0%					3.
1.13.10 Ocular pain									
VIEW 1	1.2	20	293	1.3	17.7	303	55.6%	-0.10 [-3.14, 2.94]	
VIEW 2	3.1	19.4	306	5.1	22.7			-2.00 [-5.40, 1.40]	
Subtotal (95% CI)	ROSUL	29.0	599	12301		594	100.0%	-0.94 [-3.21, 1.32]	•
Heterogeneity: Chi ^a = (Test for overall effect 2				= 0%					
1.13.11 Peripheral vis	ion								
/IEW 1		23.9	293	5.5	25.3	303	52.7%	-1.10 [-5.05, 2.85]	
/IEW 2		25.7	306		26.2	291		-0.60 [-4.77, 3.57]	
Subtotal (95% CI)			599					-0.86 [-3.73, 2.00]	•
Heterogenetly: ChP = 0 Fest for overall effect 2				P=0%					
1.13.12 General health	ti.								
VIEW 1	-4.9	22.1	293	-3.6	20.4	303	46.5%	-1.30 [4.72, 2.12]	-
VIEW 2	1.5	19	306		20.6	291	53.5%	0.70 [-2.48, 3.88]	
			599			594	100.0%	-0.23 [-2.56, 2.10]	-
Subtotal (95% CI)	CONTRACTOR OF		A 400	III WARREN					
				P = 0%					