H.6.1.3 Ranibizumab vs control (sham injection or PDT)

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	Control					
Gain of 15 letters or more visual acuity at one year	230 per 1000 (93 to 566)	59 per 1000	RR 3.25 (1.44 to 7.33)	1415 (4 studies)	⊕⊕⊕⊝ Moderate¹		
Loss of fewer than 15 letters visual acuity at one year	934 per 1000 (861 to 1000)	610 per 1000	RR 1.51 (1.41 to 1.63)	1415 (4 studies)	⊕⊕⊕⊕ High		
Mean change in visual acuity at one year (number of letters)	The mean change in visual acuity in the ranibizumab groups was on average 17.80 more letters gained (95%Cl 15.95 to 19.65 letters)	The mean change across control groups ranged from a loss 10 to 16 letter	MD 17.81 (15.94 to 19.67)	1322 (3 studies)	⊕⊕⊕⊕ High		
Mean change in vision-related quality of life vision related quality of life in the ranibizumab groups ranged from 5 to 7 points		The mean change across control groups in vision-related quality of life scores ranged from -3 to 2 points	MD 6.69 (3.38 to 9.99)	1134 (2 studies)	⊕⊕⊕⊕ High	Using the NEI-VFQ questionnaire with a 10-point difference considered as being clinically meaningful.	
Serious systemic adverse events at one year	Range of 0 to 55 per 1000	Range of 5 to 83 per 1000 for various systematic adverse events	Range of RR 0.17 (0.01 to 4.24) to 2.08 (0.23 to 18.45)	603 (2 studies)			
Myocardial infarction	10 per 1000	< 10 per 1000	RR 2.08 (0.23, 18.45)	603 (2 studies)	⊕⊕⊝⊝ Low²		

< 10 per 1000	< 10 per 1000	RR 1.04 (0.09, 11.38)	603 (2 studies)	⊕⊕⊖⊝ Low²
60 per 1000	80 per 1000	RR 0.67 (0.36, 1.24)	603 (2 studies)	⊕⊕⊕⊝ Moderate ³
60 per 1000	30 per 1000	RR 1.90 (0.78, 4.62)	603 (2 studies)	⊕⊕⊖⊖ Low²
Range of 3 to 118 per 1000	Range of 0 to 68 per 1000 for various systematic adverse events	Range of RR 0.52 (0.03 to 8.25) to 2.71 (1.36 to 5.42)	603 (2 studies)	
120 per 1000	40 per 1000	RR 2.71 (1.36 to 5.42)	603 (2 studies)	⊕⊕⊕⊕ High
80 per 1000	30 per 1000	RR 2.22 (0.99, 4.98)	603 (2 studies)	⊕⊕⊕⊝ Moderate ³
100 per 1000	70 per 1000	RR 1.48 (0.83, 2.66)		⊕⊕⊕⊖ Moderate³
	60 per 1000 60 per 1000 Range of 3 to 118 per 1000 120 per 1000 80 per 1000	60 per 1000 80 per 1000 Range of 3 to 118 per 1000 Range of 3 to 118 per 1000 for various systematic adverse events 120 per 1000 40 per 1000 80 per 1000 30 per 1000	10 per 1000 11.38 11.38	10 per 1000 11.38 11.38

^{*}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)

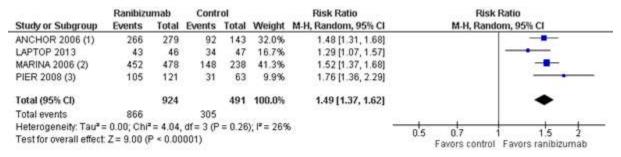
1. Downgrade one level for inconsistency due to heterogeneity (i2>=50%).

2. Downgrade two levels for serious imprecision.

^{3.} Downgrade one level for imprecision.

One year

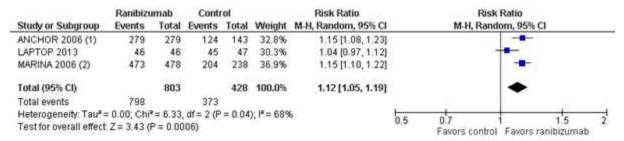
Visual acuity (loss of fewer than 15 letters)



Footnotes

- (1) Control group in the ANCHOR study received sham injections plus active verteporfin photodynamic therapy
- (2) Control group in the MARINA study received sham injections
- (3) Control group in the PIER study received sham injections

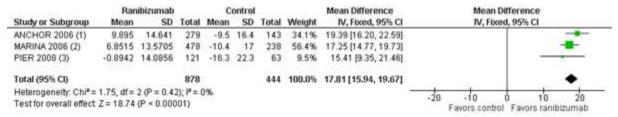
Visual acuity (loss of fewer than 30 letters)



Footnotes

- (1) Control group in the ANCHOR study received sham injections plus active verteporfin photodynamic therapy
- (2) Control group in the MARINA study received sham injections

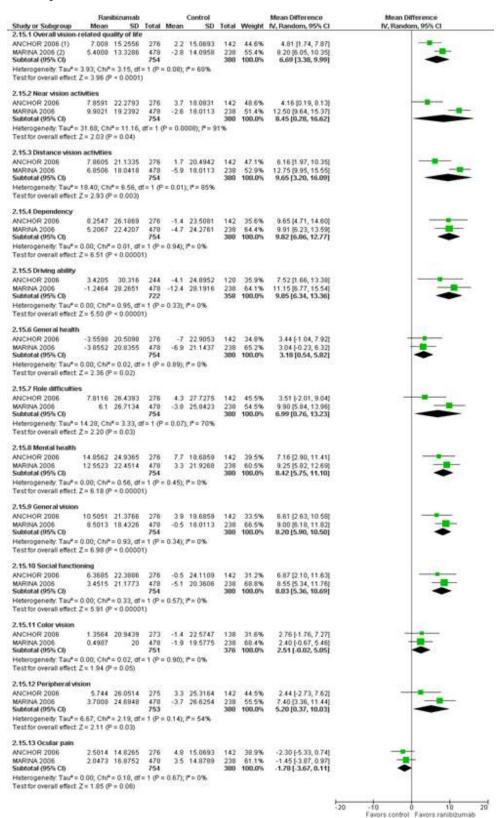
Mean change in visual acuity (number of letters)



Footnotes

- (1) Control group in the ANCHOR study received sharn injections plus active verteporfin photodynamic therapy
- (2) Control group in the MARINA study received sham injections
- (3) Control group in the PIER study received sham injections

Quality of life score



⁽¹⁾ Control group in the ANCHOR study received sham injections plus active verteportin photodynamic therapy (2) Control group in the MARINA study received sham injections

Two years

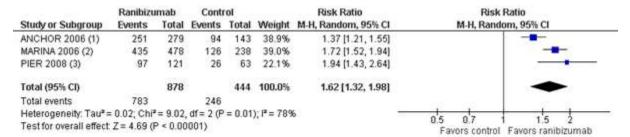
Visual acuity (gain of 15 letters or more ETDRS)



Footnotes

- (1) Control group in the ANCHOR study received sham injections plus active verteporfin photodynamic therapy
- (2) Control group in the MARINA study received sham injections
- (3) Control group in the PIER study received sham injections

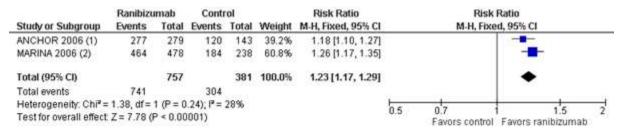
Visual acuity (loss of fewer than 15 letters or more ETDRS)



Footnotes

- (1) Control group in the ANCHOR study received sharm injections plus active verteporfin photodynamic therapy
- (2) Control group in the MARINA study received sham injections
- (3) Control group in the PIER study received sham injections

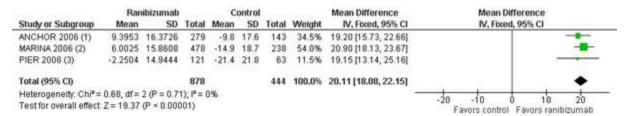
Visual acuity (loss of fewer than 30 letters or more ETDRS)



Footnotes

- (1) Control group in the ANCHOR study received sham injections plus active verteporfin photodynamic therapy
- (2) Control group in the MARINA study received sham injections

Mean change in visual acuity (number of letters)



cotnotes

- (1) Control group in the ANCHOR study received sham injections plus active verteporfin photodynamic therapy
- (2) Control group in the MARINA study received sham injections
- (3) Control group in the PIER study received sham injections

Quality of life score

Study or Subgroup 2.16.1 Overall vision a	Mean	doministration of the	Total		Control SD	Total	Weight	Mean Difference N, Random, 95% CI	Mean Difference IV, Raeutom, 95% CI
ANCHOR 2006 (1) MARINA 2006 (2) Subtotal (95% CI) Hetorogenethy Taul* = Test for overall effect.	5.4029 4.6494 12.30; Ch	21 2708 15 296 *= 5.86, d	276 478 754	-6.5	16.8776 14.8789 (P=83%		46.2% 53.8% 100.0%	5.70 [1.96, 9.44] 11.15(8.81, 13.48] 8.63 [3.31, 13.95]	-
2.16.2 Near vision act		- 0.0017							
ANCHOR 2006 MARINA 2006 Subnotal (95% CI) Heterogeneity: Tau* = Test for overall effect	7.4475 8.7506 29.12, Ch		276 478 754 f = 1.0P	-6.7	22.9053 21.9268 8); #= 87%	238 380		7.25 (2.47, 12.03) 15.45 (12.00, 18.90) 11.52 (3.49, 19.55)	
2.16.3 Distance vision									
ANCHOR 2006 MARINA 2006 Subtotal (95% CI) Heterogeneity: Tau*=	5.9525 5.8494 21.79, Ch	23.1462 21.5659 P= 6,30, d	276 478 754 r=1 (P	-8.4	22.9053 19.5775 P=84%	142 238 380	52.9%	7.05 (2.40, 11.71) 14.25 (11.10, 17.40) 10.86 (3.82, 17.90)	-
Test for overall effect.	2 = 3.02 ()	= 0.002)							
2.16.4 Dependency ANCHOR 2006 MARINA 2006 Subtotal (95% CI) Heterogenety: Tau*= Test for overall effect.	4 2573 25.10, Ch		270 478 754 f = 1 (P	-10.5	29.3303 25.8423 (F= 80%	142 238 380		6.81 [1.04, 12.58] 14.76 [10.71, 18.80] 11.06 [3.29, 18.83]	
2.16.5 Driving ability									
ANCHOR 2006 MARINA 2006 Subtotal (95% CI) Heterogeneity: Tau* =	-2.1523 0.00, CHP		722 1 (P =	-17.1	30.4275 32.1071 P=0%	120 238 358	32.5% 67.4% 100.0%	10.60 (3.56, 17.64) 14.95 (10.05, 19.85) 13.53 (9.51, 17.55)	-
Test for overall effect	Z = 8.60 (F	· + 0.0000	1).						
2.16.6 General health ANCHOR 2006 MARINA 2006 Subtotal (95% CI) Heterogenedy Tau* =	-6.2021	22.7857 22.7399 = 0.04. df	276 478 754	-9	22 9053 21 9268 P= 0%	142 238 360	35.7% 64.3% 100.0%	2 19 [-2 43, 6.82] 2 80 [-0.65, 6.25] 2.59 [-0.18, 5.35]	±
Test for overall effect.					(11.5%				
2.16.7 Role difficultier ANCHOR 2006 MARINA 2008 Subtotal (95% CD	5.7159	31.5034 29.0658	276 470 754		29.5358 29.1916	239	46.6% 53.4% 100.0%	5.02 § 1.10, 11.13 13.30 (8.67, 17.73) 9.44 [1.34, 17.54]	
Heterogenetic Tau* = Test for overall effect				= 0.03	; 1°= 78%		-1600EN	.5177.458538.2557.18.	
2,16.8 Mental health		- 0.02							
ANCHOR 2006 MARINA 2006 Subtotal (95% CI) Heterogenety: Tau* = Test for overall effect	12.2515 14.41; Ch		276 478 754 f= 1 (P	-0.7	24.1109 23.493 (P×74%	142 238 380	46.1% 53.9% 100.0%	6.71 (1.69, 11.74) 12.95 (9.26, 16.65) 10.07 (3.98, 16.17)	-
2.16.9 General vision									
ANCHOR 2006 MARINA 2006	10.9518 0.1025	22.27 19.2233	276 479		21.097	142 238	42.3% 57.7%	7.15 (2.80, 11.50) 11.40 (8.54, 14.27)	
Subtotal (95% Cl) Heterogeneity: Tau*=				0.11);	P=61%	380	100.0%	9.61 [5.49, 13,72]	-
Test for overall effect.		4 0.0000	.,						2.00
2,16,10 Social functio ANCHOR 2006 MARINA 2006 Subtobal (95% CI)	4.2547 1.649	25.81 23.5197	276 478 754	-9.5	23.5081 23.493	142 238 380	46.6% 53.4% 100.0%	4.65 [-0.27, 9.58] 11.15 [7.49, 14.80] 8.12 [1.77, 14.47]	-
Heterogeneity: Tau* = Test for overall effect :			f= 1 (P	= 0.04)	P= 77%				
Z.16.11 Color vision ANCHOR 2006 MARINA 2006		21.3391 22.5383			24 951 21 9268		33.3% 66.7%	3.80 [-1.07, 8.68] 6.64 (3.20, 10.08)	-
Subtotal (95% CI) Heterogeneity: Tau*= Test for overall effect	0.00, CMP	= 0.87, af	751 -1 P =				100.0%	5.70 [2.89, 8.51]	-
2.16.12 Peripheral vis		99.000	200	22	33 43 47	- 4-	40.00	2801467.000	
ANCHOR 2006 MARINA 2006 Subtotal (95% CI) Hetorogeneity: Tau* «	2.0469	27.9811 25.0974 = 2.49, df	275 478 753 +1 (P+	-7.1	27,1247 25,0592 P= 60%	238	43.2% 56.8% 100.0%	3.68 [-1.87, 9.23] 9.15 [5.25, 13.05] 6.79 [1.48, 12.09]	-
Test for overall effect.									
2.16.13 Ocular pain ANCHOR 2006 MARINA 2006 Subtotal (95% CI)	1.9477	15.7608 16.4841	276 478 754	3.2	18.0831 15.862	238	33.3% 66.7% 100.0%	-0.80 [-4.31, 2.70] -1.25 [-3.73, 1.23] -1.10 [-3.13, 0.92]	*
Heterogeneity: Tau* = Test for overall effect:			=1 (P=	0.84),	r* = 0%				

Footsobes
(1) Control group in the ARCHOR study received sharm injections plus active verteportin photodynamic therapy
(2) Control group in the MARRIAA study received sharm injections