H.6 Pharmacological management

H.6.1 Anti-angiogenic therapies and frequency of administration

RQ12: What is the effectiveness of different anti-angiogenic therapies (including photodynamic therapy) for the treatment of late age-related macular degeneration (wet active)?

RQ18: What is the effectiveness of different frequencies of administration of antiangiogenic therapies for the treatment of late age-related macular degeneration (wet active)?

The GRADE tables for pairwise meta-analyses in this section were produced by the Cochrane Eyes and Vision group, as part of a collaboration with the NICE Internal Clinical Guidelines Team.

H.6.1.1 Photodynamic therapy versus placebo

Outcomes	**Illustrative comparative risks*** **(95% CI)**		**Relative effect**	**No of Participants**	**Quality of the evidence**
	Corresponding risk	**Assumed risk**	**(95% CI)**	**(studies)**	**(GRADE)**
	Intervention (photodynamic therapy with verteporfin)	Control (photodynamic therapy with 5% dextrose in water)			
Loss of 3 or more lines (15 or more letter) visual acuity ETDRS at 24 months	487 per 1000 (445 to 536)	609 per 1000	RR 0.8, 0.73 to 0.89	1381 (4 studies)	⊕⊕⊕⊖ Moderate[1]
Loss of 6 or more lines (30 or more letter) visual acuity ETDRS at 24 months	220 per 1000 (176 to 276)	333 per 1000	RR 0.66, 0.55 to 0.78	1381 (4 studies)	⊕⊕⊕⊕ High
Gain of 3 or more lines (15 or more	80 per 1000	36 per 1000	RR 2.59,	941	⊕⊕⊕⊕

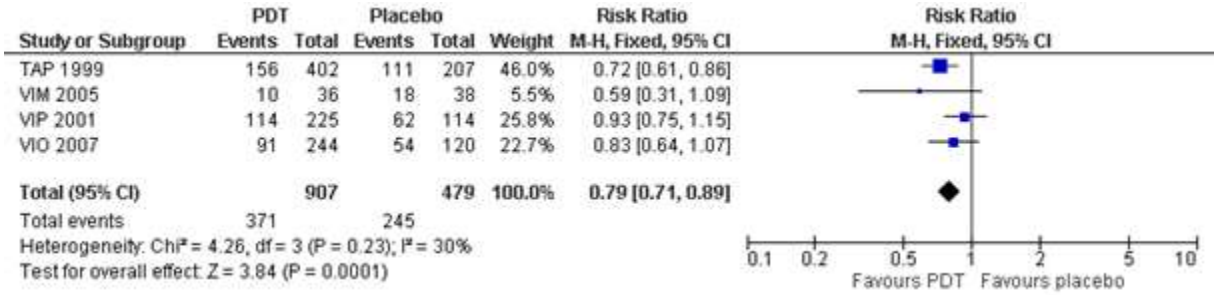
letter) visual acuity ETDRS at 24 months	(43 to 151)		1.33 to 5.06	(3 studies)	High
Adverse effects: acute severe visual acuity decrease (follow-up: 7 days)	11 per 1000 (3 to 48)	3 per 1000	RR 3.75 0.87 to 16.12	1075 (3 studies)	⊕⊕⊕⊖ Moderate[1]
Adverse effects: visual disturbance	270 per 1000	170 per 1000	RR 1.56 1.21 to 2.01	1075 (3 studies)	⊕⊕⊕⊖ Moderate[1]
Adverse effects: injection site	120 per 1000	60 per 1000	RR 1.36 0.50 to 3.71	1075 (3 studies)	⊕⊖⊖⊖ Very low[2]
Adverse effects: infusion-related back pain	20 per 1000 (6 to 70)	2 per 1000	RR 9.93 (2.82 to 35.02)	1439 (4 studies)	⊕⊕⊕⊕ High[3]
Adverse effects: allergic reactions	17 per 1000	19 per 1000	RR 0.94 (0.35 to 2.51)	948 (2 studies)	⊕⊕⊖⊖ Low[4]
Adverse effects: photosensitivity reactions	24 per 1000	3 per 1000	RR 2.73 (0.08 to 97.96)	948 (2 studies)	⊕⊖⊖⊖ Very low[2]

*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 of imprecision: 95%CI of the estimated effect across 1 line of defined minimal important difference.
2. Downgrade one level of heterogeneity (i2>=50%), and downgrade two levels of imprecision (wide confidence interval)
3. Not downgraded for imprecision: confidence interval wide however do not include 1 (no effect)
4. Downgrade two levels of serious imprecision.

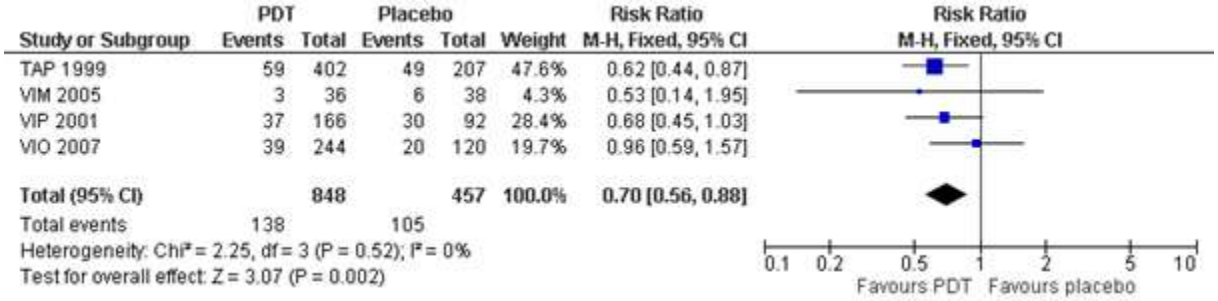
Visual acuity

One year

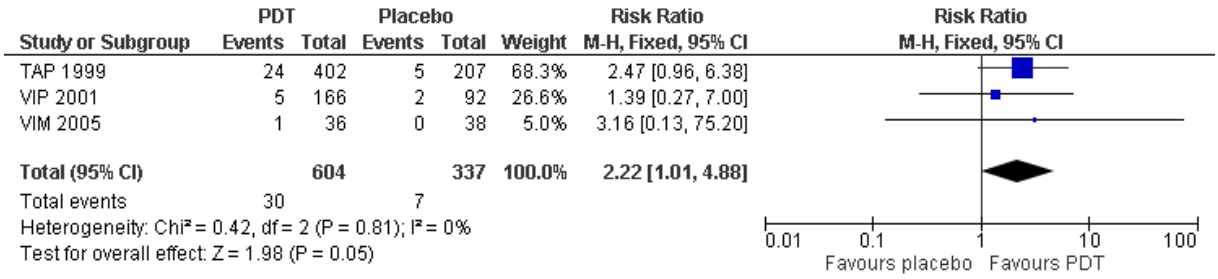
Visual acuity (loss of 3 or more lines ETDRS)



Visual acuity (loss of 6 or more lines ETDRS)



Visual acuity (gain of 3 or more line (15 or more letters) of visual acuity)

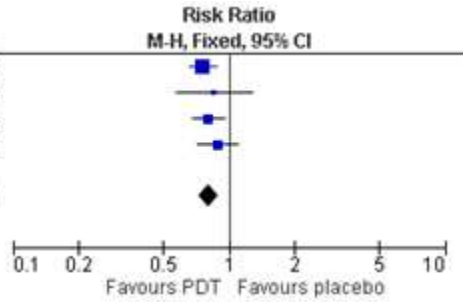


Two years

Visual acuity (loss of 3 or more line ETDRS)

Study or Subgroup	PDT Events	PDT Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
TAP 1999	189	402	129	207	45.2%	0.75 [0.65, 0.88]
VIM 2005	17	32	23	37	5.7%	0.85 [0.57, 1.29]
VIP 2001	121	225	76	114	26.8%	0.81 [0.68, 0.96]
VIO 2007	114	244	63	120	22.4%	0.89 [0.72, 1.11]
Total (95% CI)		**903**		**478**	**100.0%**	**0.80 [0.73, 0.89]**
Total events	441		291			

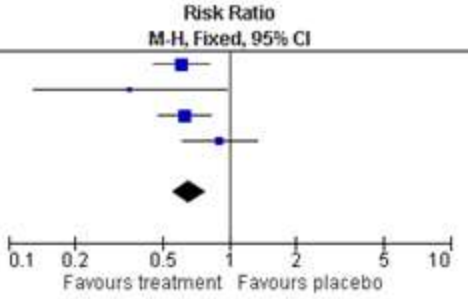
Heterogeneity: Chi² = 1.64, df = 3 (P = 0.65); I² = 0%
Test for overall effect: Z = 4.34 (P < 0.0001)



Visual acuity (loss of 6 or more lines ETDRS)

Study or Subgroup	Treatment Events	Treatment Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
TAP 1999	73	402	62	207	39.8%	0.61 [0.45, 0.81]
VIM 2005	4	32	13	37	5.9%	0.36 [0.13, 0.98]
VIP 2001	67	225	54	114	34.8%	0.63 [0.48, 0.83]
VIO 2007	55	244	30	120	19.5%	0.90 [0.61, 1.33]
Total (95% CI)		**903**		**478**	**100.0%**	**0.66 [0.55, 0.78]**
Total events	199		159			

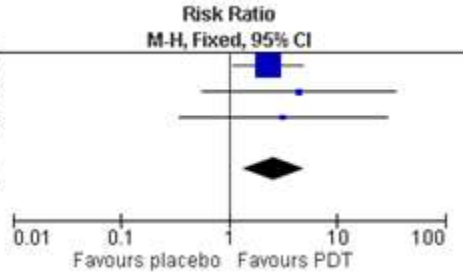
Heterogeneity: Chi² = 4.35, df = 3 (P = 0.23); I² = 31%
Test for overall effect: Z = 4.64 (P < 0.00001)



Visual acuity (gain of 3 or more lines ETDRS)

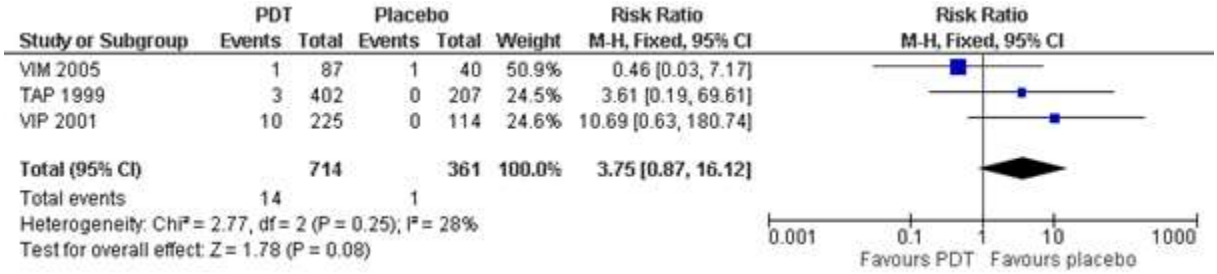
Study or Subgroup	PDT Events	PDT Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
TAP 1999	36	402	8	207	82.4%	2.32 [1.10, 4.89]
VIP 2001	8	166	1	92	10.0%	4.43 [0.56, 34.90]
VIM 2005	3	36	1	38	7.6%	3.17 [0.35, 29.06]
Total (95% CI)		**604**		**337**	**100.0%**	**2.59 [1.33, 5.06]**
Total events	47		10			

Heterogeneity: Chi² = 0.38, df = 2 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.80 (P = 0.005)

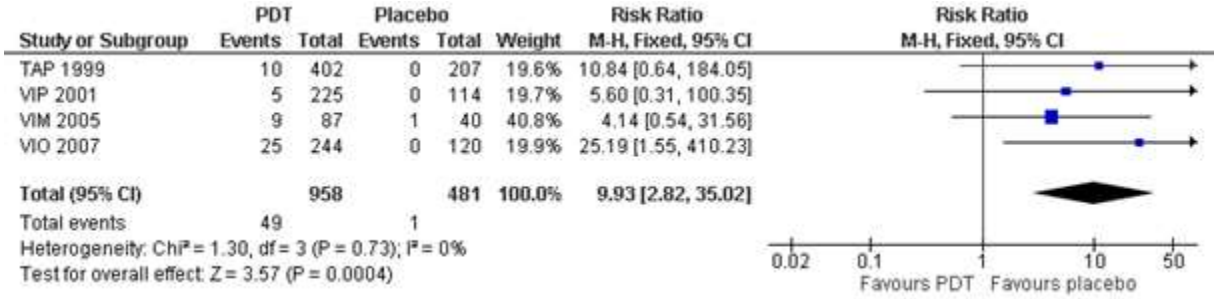


Adverse effects

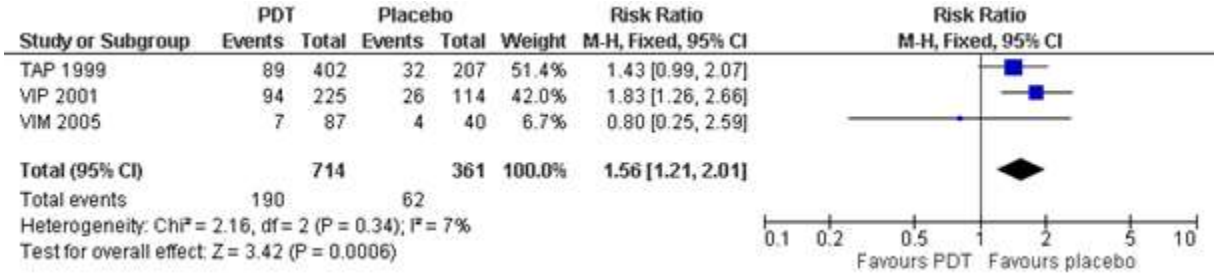
Acute severe visual acuity decrease



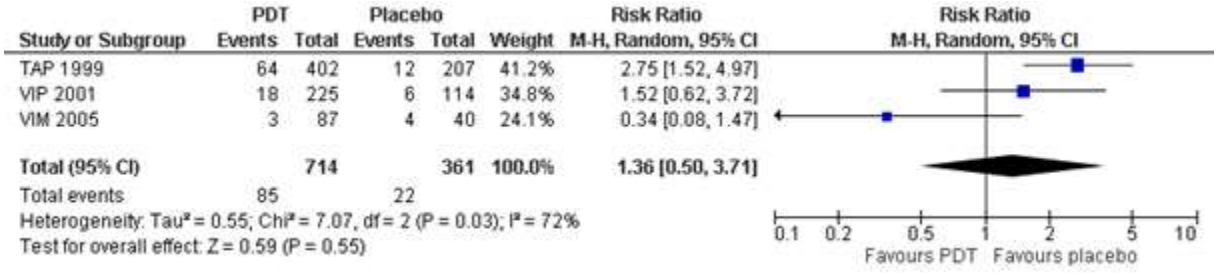
Infusion-related back pain



Visual disturbance



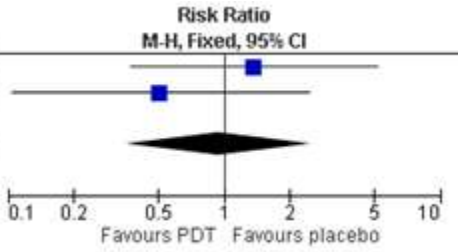
Injection site



Allergic reactions

Study or Subgroup	PDT Events	PDT Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
TAP 1999	8	402	3	207	49.9%	1.37 [0.37, 5.12]
VIP 2001	3	225	3	114	50.1%	0.51 [0.10, 2.47]
Total (95% CI)		**627**		**321**	**100.0%**	**0.94 [0.35, 2.51]**
Total events	11		6			

Heterogeneity: Chi² = 0.90, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 0.13 (P = 0.90)



Photosensitivity reactions

Study or Subgroup	PDT Events	PDT Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
TAP 1999	14	402	0	207	49.7%	14.97 [0.90, 249.66]
VIP 2001	1	225	1	114	50.3%	0.51 [0.03, 8.03]
Total (95% CI)		**627**		**321**	**100.0%**	**2.73 [0.08, 97.96]**
Total events	15		1			

Heterogeneity: Tau² = 4.65; Chi² = 3.30, df = 1 (P = 0.07); I² = 70%
Test for overall effect: Z = 0.55 (P = 0.58)