H.6.1.8 Treatment frequency: PRN loading

Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
PRN (no loading vs loading)							
Gain of ≥15 letters at one year							
1 study (Barikian 2015)	Serious[1]	N/A	Not serious	Very serious[2]	60	RR 0.83 (0.43, 1.63)	VERY LOW
Gain of ≥10 letters at one year							
1 study (BeMoc 2013)	Serious[1]	N/A	Not serious	Very serious[2]	99	RR 0.93 (0.38, 2.25)	VERY LOW
Mean change in BCVA in ETDRS letters at one year (higher scores indicate better vision)							
2 studies (Barikian 2015, BeMoc 2013)	Serious[1]	Not serious	Not serious	Serious[3]	189	MD 1.20 (-2.51, 4.91)	LOW
Mean number of injections at one year							
2 studies (Barikian 2015, BeMoc 2013)	Serious[1]	Not serious	Not serious	Serious[3]	189	MD -0.30 (-1.92, 1.32)	LOW
Quality of life measures at one year (VFQ-25) (higher values indicate better QoL)							
1 studiy (BeMoc 2013)	Serious[1]	N/A	Not serious	Serious[4]	99	MD -0.06	LOW
PRN with 4 week vs 12 weeks loading phase							
Gain of ≥15 letters at one year							
1 study (CLEART-IT 2011)	Serious[1]	N/A	Not serious	Very serious[2]	126	RR 0.94 (0.51, 1.72)	VERY LOW
Loss of <15 letter at one year							
1 study (CLEART-IT 2011)	Serious[1]	N/A	Not serious	Not serious	126	RR 1.05 (0.94, 1.18)	MODERATE

Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Mean change in BCVA (ETDRS letters)							
1 study (CLEART-IT 2011)	Serious[1]	N/A	Not serious	Serious[5]	126	MD 3.41 (-0.16, 6.98)	LOW

1. Downgraded for risk of bias due to randomisation, allocation concealment, masking of participants, and selective report were unclear
2. Downgrade two levesl for imprecision due to 95%CI of the effect crossing 2 lines of a defined minimal important difference
3. Downgraded one level for imprecision as one of studies (BeMoc 2013) had no SD reported to estimate effect
4. Downgraded one level for imprecision due to SD was not reported with mean quality of life score
5. Downgraded one level for imprecision due to 95%CI of the effect crossing 1 line of a defined minimal important difference.

Visual acuity (mean change in visual acuity BCVA of ETDRS letters)

Study or Subgroup	no loading PRN Mean	SD	Total	loading PRN Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Barikian 2015	8.3	6.7	30	8	10.4	30	100.0%	0.30 [-4.13, 4.73]
BeMOc 2013	0.86	0	49	2.08	0	50		Not estimable
Total (95% CI)			79			80	100.0%	0.30 [-4.13, 4.73]

Heterogeneity: Not applicable
Test for overall effect: Z = 0.13 (P = 0.89)

Mean Difference
IV, Fixed, 95% CI

-20 -10 0 10 20
Favours loading PRN Favours no loading PRN