**H.6.1.9   Treatment frequency: treat-and-extend vs routine month injection**

| Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
Gain of ≥15 letters at one year							
2 studies (TREX-AMD 2015; TREND 2017)	Serious[1]	Not serious	Not serious	Very serious[2]	646	RR 1.02 (0.78, 1.33)	VERY LOW
Mean change in BCVA in ETDRS letters at one year (higher scores indicate better vision)							
2 studies (TREX-AMD 2015; TREND 2017)	Serious[1]	Not serious	Not serious	Not serious[3]	703	MD -1.46 (-3.26, 0.34)	MODERATE
Mean number of injections at one year							
1 study (TREND 2017)	Not serious	N/A	Not serious	Not serious	643	MD -2.40 (-2.80, -2.00)	HIGH
Adverse events (serious systemic events at one year)							
2 studies (TREX-AMD 2015; TREND 2017)	Serious[1]	Not serious	Not serious	Very serious[2]	709	RR 1.04 (0.68, 1.58)	VERY LOW
Adverse events (serious ocular events at one year)							
2 studies (TREX-AMD 2015; TREND 2017)	Serious[1]	Not serious	Not serious	Very serious[2]	709	RR 1.61 (0.61, 4.22)	VERY LOW
Gain of ≥15 letters at two years							
1 study (TREX-AMD 2015)	Serious[1]	N/A	Not serious	Very serious[2]	60	RR 1.50 (0.55, 4.06)	VERY LOW
Mean change in BCVA in ETDRS letters at two years (higher scores indicate better vision)							
1 study (TREX-AMD 2015)	Very serious[1,4]	N/A	Not serious	Very serious[2]	41	MD -1.80 (-10.48, 6.88)	VERY LOW
Adverse events (serious systemic events at two years)							
1 study (TREX-AMD 2015)	Serious[1]	N/A	Not serious	Not serious	60	RR 9.50 (1.37, 65.97)	MODERATE
Adverse events (serious ocular events at two years)							

Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect (95%CI)	Quality
1 study (TREX-AMD 2015)	Serious[1]	N/A	Not serious	Very serious[2]	60	RR 5.63 (0.33, 97.10)	VERY LOW

1. Downgraded one level for risk of bias due to masking of participants (method of random sequence generation was not reported) in TREX-AMD.
2. Downgraded two levels of serious imprecision due to 95% confidence interval of estimated effect crossing 2 lines of a defined minimal important difference
3. 95% confidence interval of estimated effect within bounds of a defined minimal important difference
4. Substantial, asymmetric, unexplained attrition between year 1 and year 2

Gain of ≥15 letters at one year
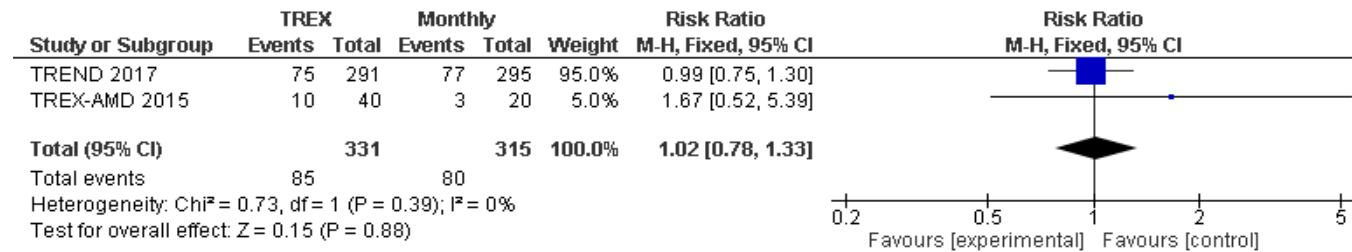
Mean change in BCVA in ETDRS letters at one year (higher scores indicate better vision)
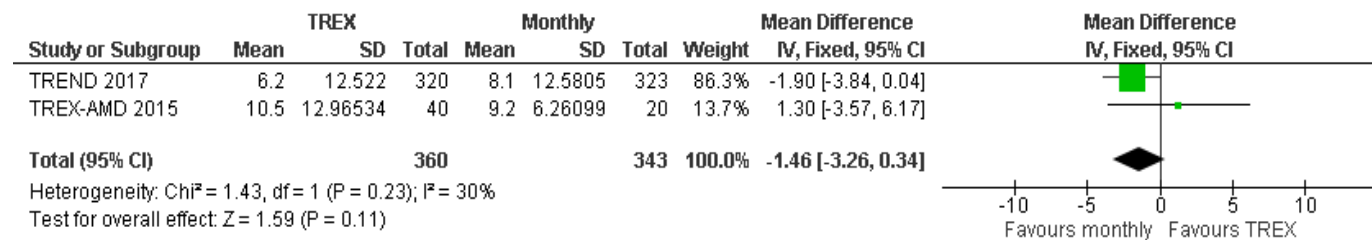
Adverse events (serious systemic events at one year)

Study or Subgroup	TREX Events	Total	Monthly Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
TREND 2017	4	323	4	326	59.9%	1.01 [0.25, 4.00]	
TREX-AMD 2015	10	40	2	20	40.1%	2.50 [0.60, 10.34]	
Total (95% CI)		363		346	100.0%	1.61 [0.61, 4.22]	
Total events	14		6				

Heterogeneity: Chi² = 0.81, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)
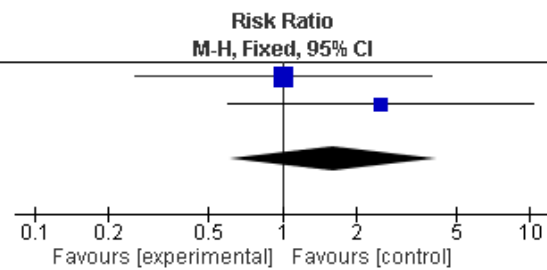
Favours [experimental]   Favours [control]

Adverse events (serious ocular events at one year)

Study or Subgroup	TREX Events	Total	Monthly Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
TREND 2017	36	323	38	326	98.3%	0.96 [0.62, 1.47]	
TREX-AMD 2015	5	40	0	20	1.7%	5.63 [0.33, 97.10]	
Total (95% CI)		363		346	100.0%	1.04 [0.68, 1.58]	
Total events	41		38				

Heterogeneity: Chi² = 1.49, df = 1 (P = 0.22); I² = 33%
Test for overall effect: Z = 0.17 (P = 0.87)

Favours [experimental]   Favours [control]