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

					Sample						
Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	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 o	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 syste	mic events at one y	ear)									
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 ocula	r events at one year	r)									
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	5										
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 ETDF	RS letters at two yea	ars (higher scores	s indicate bette	r 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 syste	mic events at two y	ears)									
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)											

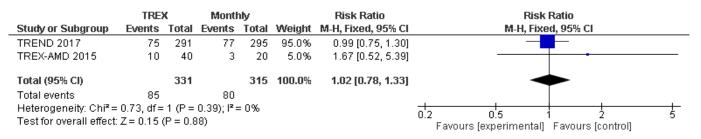
Macular Degeneration

Appendix H: Grade tables and meta-analysis results

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)

	TREX Monthly						Mean Difference		Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	
TREND 2017	6.2	12.522	320	8.1	12.5805	323	86.3%	-1.90 [-3.84, 0.04]	-	
TREX-AMD 2015	10.5	12.96534	40	9.2	6.26099	20	13.7%	1.30 [-3.57, 6.17]	-	
Total (95% CI)			360			343	100.0%	-1.46 [-3.26, 0.34]	•	
Heterogeneity: Chi² = 1.43, df = 1 (P = 0.23); l² = 30%									-10 -5 0 5 10	
Test for overall effect:	Z=1.59	(P = 0.11)							Favours monthly Favours TREX	

Adverse events (serious systemic events at one year)

	TRE	x	Monti	nly		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	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: $Chi^2 = 0.81$, $df = 1$ (P = 0.37); $I^2 = 0\%$							01 02 05 1 2 5 10
Test for overall effect: $Z = 0.96$ (P = 0.34)							Favours [experimental] Favours [control]

Adverse events (serious ocular events at one year)

	TRE	TREX Monthly				Risk Ratio	Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixe	ed, 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: Chi ² =	: 1.49, df=	1 (P=	0.22); l² :	= 33%			0.01 0.1	1 10	100
Test for overall effect	Z = 0.17	(P = 0.8)	37)				Favours [experimental]		100