Appendix 4 Outcomes of included studies

GENEVA, 2010 [46-48] (DEX vs Sham)

Efficiency outcomes (changes from baseline at follow-up time points)			
6 months			
	DEX 0.7mg (n=136)	**DEX 0.35mg (n=154)**	**Sham (n=147)**
BCVA (ETDRS letters)	+0.1		-1.8
p value	<0.001 vs sham		
≥15 letters gained	25 (18.4%)	11 (17%)	18 (12.2%)
p value	NS vs sham	NS vs sham	
≥15 letters lost	19 (14.0%)		30 (20.4%)
p value	NS vs sham		
CRT (µm)	-118.2		-125.3
p value	NS vs sham		
12 months			
	DEX 0.7mg (n=136)	**DEX 0.35mg (n=154)**	**Sham (n=147)**
BCVA (ETDRS letters)	+2 (graph estimated)		-1.4 (ditto)
≥15 letters gained	37 (27%)		31 (21%)
Adverse events			
6 months			
	DEX 0.7mg (n=133)	**DEX 0.35mg (n=154)**	**Sham (n=147)**
Overall of ocular AEs	91 (68.4%)		73 (49.7%)
IOP increased	40 (30.1%)		2 (1.4%)
Cataract AEs	11 (8.3%)		7 (4.8%)

ROVO, 2013 [49] (Tria vs Sham)

Efficiency outcomes (changes from baseline at follow-up time points)			
12 months			
	Tria 4mg (n=25)	**RON (n=38)**	**Sham (n=20)**
BCVA (ETDRS letters)	-8	-35.5	0

p value	NS vs sham		
VA improvement	5 (20%)	18 (47.3%)	2 (10%)
p value	NS vs sham		
VA deterioration	NR	3 (7.9%)	7 (35%)
CRT (µm)	-235	-263	-206
p value	NS vs sham		
Adverse events			
12 months			
	Tria 4mg (n=25)	**RON (n=38)**	**Sham (n=20)**
IOP increased	8 (32%)		0
Cataract progression	6 (24%)	5 (13.2%)	3 (15%)
Neovscular glaucoma	3 (12%)	2 (5.3%)	3 (15%)
Rubeosis iridis	0		3 (15%)

SCORE, 2009 [50-66] (Tria vs sham)

Efficiency outcomes (changes from baseline at follow-up time points)			
6 months (weight mean and SD of 4 and 8 months)			
	Tria 4mg (n=85)	**Tria 1mg(n=84)**	**Obs (n=75)**
BCVA (letters)	-0.15±20.67	-3.93±23.42	-9.66±18.04
p value	NR	NR	
≥15 letters gained	17 (19.5%)	15(17.5%)	3 (4%)
p value	NR	NR	
≥15 letters lost	19 (20.5%)	21 (25.0%)	31 (35.5%)
p value	NR	NR	
12 months			
	Tria 4mg (n=82)	**Tria 1mg(n=83)**	**Obs (n=73)**
BCVA (letters, 95%CI)	-1.2±24.82 (-6.3 to +4.0)	-1.2±25.45 (-6.4 to +4.1)	-12.1±23.93 (-17.1 to -7.1)
p value	<0.05 vs obs	<0.05 vs obs	
≥15 letters gained	21 (25.6%)	22 (26.5%)	5 (6.8%)
p value	0.001 vs obs	0.001 vs obs	

≥15 letters lost	21 (25.6%)	21 (25.3%)	32 (43.8%)
p value	NR	NR	
CRT (µm) (median, IQR)	-261 (-407 to -79) n=78	-196 (-390 to -62) n=72	-277 (-418 to -40) n=68
p value	NR	NR	
24 months			
	Tria 4mg (n=50)	**Tria 1mg(n=55)**	**Obs (n=46)**
BCVA (letters, 95%CI)	-2.4±24.89 (-9.3 to +4.4)	-4.4±26.87 (-11.5 to +2.8)	-10.7±22.84 (-17.4 to -4.1)
p value	NR		
≥15 letters gained	13 (26%)	17 (30.9%)	4 (8.7%)
p value	NR		
≥15 letters lost	13 (26%)	17 (30.9%)	22 (47.8%)
p value	NS, p=0.06 tria vs obs		
CRT (µm) (median, IQR)	-236 (-421 to -63) n=45	-286 (-458 to -119) n=48	-304 (-465 to -108) n=43
p value	NR		
Adverse events			
12 months			
	Tria 4mg (n=91)	**Tria 1mg(n=92)**	**Obs (n=88)**
Initiation of IOP-lowering medication	32 (35.2%)	18 (19.6%)	7 (8.0%)
Iris neovascularization or neovascular glaucoma	4 (4.4%)	9 (9.8%)	2 (2.3%)
Retinal neovascularization	2 (2.2%)	2 (2.2%)	4 (4.6%)
Vitreous hemorrhage	0	4 (4.3%)	4 (4.6%)
CRUISE, 2010 [67-69] (IVR vs sham)			
Efficiency outcomes (changes from baseline at follow-up time points)			
6 months			
	IVR 0.3mg (n=132)	**IVR 0.5mg (n=130)**	**Sham (n=130)**
BCVA (letters, 95%CI)	+12.7±15.9 (9.9, 15.4)	+14.9±13.2 (12.6, 17.2)	+0.8±16.2 (-2.0, 3.6)
p value	<0.0001 vs sham	<0.0001 vs sham	

≥15 letters gained	61 (46.2%)	62 (47.7%)	22 (16.9%)
p value	<0.0001 vs sham	<0.0001 vs sham	
≥15 letters lost	5 (3.8%)	2 (1.5%)	20 (15.4%)
p value	NR		
CRT (µm, 95%CI)	-433.7 (-484.9, -382.6) n=131	-452.3(-497.0, -407.6) n=130	-167.7 (-221.5, -114.0) n=129
p value	<0.0001 vs sham	<0.0001 vs sham	
NEI-VFQ (95%CI)	+7.1 (5.2, 9.0)	+6.2 (4.3, 8.0)	+2.8 (0.8, 4.7)
p value	<0.05 vs sham	<0.05 vs sham	
12 months (IVR PRN)			
	IVR 0.3mg (n=132)	**IVR 0.5mg (n=130)**	**Sham (n=130)**
BCVA (letters, 95%CI)	+13.9±15.2 (11.2, 16.5)	+13.9±14.2 (11.5, 16.4)	+7.3±15.9 (4.5, 10.0)
p value	0.0007 vs sham	0.0006 vs sham	
≥15 letters gained	62 (47.0%)	66 (50.8%)	43 (33.1%)
p value	NR		
≥15 letters lost	5 (3.8%)	3 (2.3%)	13 (10.0%)
p value	NR		
CRT (µm)	-462.1	-452.8	-427.2
p value	NS vs sham	NS vs sham	
NEI-VFQ	+7.1	+6.6	+5.0
p value	NR	NR	
Adverse events			
6 months			
	IVR 0.3mg (n=132)	**IVR 0.5mg (n=129)**	**Sham (n=129)**
Any intraocular inflammation event	3 (2.3%)	2 (1.6%)	5 (3.9%)
Cataract	2 (1.5%)	2 (1.6%)	0
Neovascular glaucoma	0	0	2 (1.6%)
Vitreous haemorrhage	5 (3.8%)	7 (5.4%)	9 (7.0%)
12 months			
	IVR 0.3mg (n=132)	**IVR 0.5mg (n=129)**	**Sham (n=110)**

Any intraocular inflammation event	3 (2.3%)	2 (1.6%)	2 (1.8%)
Cataract	5 (3.8%)	9 (7.0%)	2 (1.8%)
Neovascular glaucoma	0	1 (0.8%)	0
Vitreous haemorrhage	7 (5.3%)	7 (5.4%)	2 (1.8%)
Iris neovascularization	2 (1.5%)	5 (3.9%)	2 (1.8%)
Retinal tear	0	2 (1.6%)	2 (1.8%)

ROCC, 2010 [70] (IVR vs Sham)

Efficiency outcomes (changes from baseline at follow-up time points)		
6 months		
	IVR 0.5mg (n=15)	**Sham (n=14)**
BCVA (letters)	+12±20	-1±17
p value	0.067 vs sham	
CRT (µm)	-304±194	-151±205
p value	0.05 vs sham	

Adverse events		
6 months		
	IVR 0.5mg (n=15)	**Sham (n=14)**
Vitreous hemorrhage	2 (13.3%)	0
Retinal tear	0	1 (7.1%)
Neovascular disease	0	1 (7.1%)

COPERNICUS, 2012 [71-72] (IAI vs Sham)

Efficiency outcomes (changes from baseline at follow-up time points)		
6 months		
	IAI 2mg (n=114)	**Sham (n=73)**
BCVA (letters)	+17.3±12.8	-4.0±18
p value	<0.001	
≥15 letters gained	64 (56.1%)	9 (12.3%)
p value	<0.001	

≥15 letters lost	2 (1.8%)	20 (27.4%)
p value	NR	
CRT (µm)	-457.2	-144.8
p value	<0.001	
NEI VFQ-25	+7.2±12.1	+0.8±9.8
p value	0.001	
12 months (all IAI PRN)		
	IAI 2mg (n=114)	**Sham (n=73)**
BCVA (letters)	+16.2	+3.8
p value	<0.001	
≥15 letters gained	63 (55.3%)	22 (30.1%)
p value	<0.001	
≥15 letters lost	6 (5.3%)	11 (15.1%)
p value	NR	
CRT (µm)	-413.0	-381.8
p value	NS	
NEI VFQ-25	+7.5	+5.1
p value	NS	
Adverse events		
6 months		
	IAI 2mg (n=114)	**Sham (n=74)**
Patients with at least one serious adverse events	4 (3.5%)	10 (13.5%)
Vitreous hemorrhage	0	4 (5.4%)
Neovascular glaucoma	0	2 (2.7%)
Iris neovascularization	0	2 (2.7%)
Retinal hemorrhage	0	2 (2.7%)
Retinal tear	0	1 (1.4%)
Endophthalmitis	1 (0.9%)	0
6 to 12months		

	IAI 2mg + PRN (n=110)	Sham + PRN (n=60)
Patients with at least one serious adverse events	3 (2.7%)	2 (3.3%)
Vitreous hemorrhage	1 (0.9%)	1 (1.7%)
Glaucoma	0	1 (1.7%)
Retinal tear	0	1 (1.7%)
Cataract	1 (0.9%)	1 (1.7%)

GALILEO, 2013 [73-74] (IAI vs Sham)

Efficiency outcomes (changes from baseline at follow-up time points)		
6 months		
	IAI 2mg (n=103)	**Sham (n=68)**
BCVA (letters)	+18.0±12.2	+3.3±14.1
p value	<0.0001	
≥15 letters gained	62 (60.2%)	15 (22.1%)
p value	<0.0001	
≥15 letters lost	8 (7.8%)	15 (22.1%)
p value	0.0033	
CRT (µm)	-448.6	-169.3
p value	<0.0001	
NEI-VFQ-25	+7.5	+3.5
p value	0.0013	
Adverse events		
6 months		
	IAI 2mg (n=104)	**Sham (n=68)**
Eye pain	12 (11.5%)	3 (4.4%)
Conjunctival haemorrhage	9 (8.7%)	3 (4.4%)
Ocular hyperaemia	5 (4.8%)	4 (5.9%)
Vitreous floaters	5 (4.8%)	0
Macular ischaemia	4 (3.8%)	3 (4.4%)

Eye irritation	3 (2.9%)	7 (10.3%)
Retinal ischaemia	1 (1.0%)	3 (4.4%)
IOP increased	10 (9.6%)	4 (5.9%)

Epstein, 2012 [75-76] (IVB vs Sham)

Efficiency outcomes (changes from baseline at follow-up time points)		
6 months		
	IVB 1.25mg (n=30)	**Sham (n=30)**
BCVA (letters)	+14.1±18.7	-2.0±20.5
p value	<0.01	
≥15 letters gained	18 (60%)	6 (20%)
p value	0.003	
≥15 letters lost	2 (6.7%)	7 (23.3%)
p value	NS, 0.146	
CRT (µm)	-426	-102
p value	<0.0001	
12 months		
	IVB 1.25mg (n=30)	**Sham (n=30)**
BCVA (letters)	+16.1	+4.6
p value	<0.05	
≥15 letters gained	18 (60%)	10 (33.3%)
p value	<0.05	
≥15 letters lost	2 (6.7%)	2 (6.7%)
p value	NS	
CRT (µm)	-435	-404
p value	>0.05	
Adverse events		
6 months		
	IVB 1.25mg (n=30)	**Sham (n=30)**
Iris rubeosis	0	5 (16.7%)

Wroblewski, 2009 [23, 77-83] (IVP vs Sham)

Efficiency outcomes (changes from baseline at follow-up time points)			
6 months (~30weeks)			
	IVP 0.3mg (n=33)	**IVP 1mg (n=33)**	**Sham (n=32)**
BCVA (letters)	+7.1	+9.9	-3.2
p value	0.09 vs sham	0.02 vs sham	
≥15 letters gained	12 (36.4%)	13 (36.1%)	9 (28.1%)
p value	0.48		
≥15 letters lost	3 (9.1%)	2 (6.1%)	10 (31.3%)
p value	0.03 vs sham	0.01 vs sham	
CRT (µm)	-243	-179	-148
p value	0.13	0.06	
12 months			
	IVP 0.3mg (n=33)	**IVP 1mg (n=33)**	**Sham (n=32)**
BCVA (letters)	+7.5	+6.3	-2.4
p value	NS vs sham	NS vs sham	
CRT (µm)	-295	-216	-183
p value	<0.05 vs sham		
Adverse events			
No serious ocular adverse events up to 30 weeks. No evidence of increased risk of systemic adverse events up to 30 weeks.			

Ramezani, 2014 [84] (IVB vs Tria)

Efficiency outcomes (changes from baseline at follow-up time points)		
6 months		
	IVB (n=43)	**Tria (n=43)**
BCVA (letters)	+23±11.5	+9.5±11.5
p value	<0.001	<0.001
CRT (µm)	-151±122	-75±89
p value	<0.001	<0.001

Adverse events		
6 months		
	IVB (n=43)	**Tria (n=43)**
IOP changes (mmHg)	-1.0±2.2	+2.2±2.7

COMRADE-C, 2016 [85] (IVR vs DEX)

Efficiency outcomes (changes from baseline at follow-up time points)		
6 months		
	IVR (n=124)	**DEX (n=119)**
BCVA (letters)	+16.9±13.6	-0.7±22.5
p value	<0.0001 vs DEX	
≥15 letters gained	73 (58.9%)	22 (18.5%)
p value	<0.0001 vs DEX	
≥15 letters lost	1 (0.8%)	31 (26.1%)
p value	<0.0001 vs DEX	
CRT (µm)	-376.7±274.9	-168.7±288.3
p value	NR	
Adverse events		
6 months		
	IVR (n=124)	**DEX (n=119)**
IOP increased	7 (5.6%)	38 (31.9%)
Macular edema	14 (11.3%)	21 (17.6%)
Eye pain	15 (12.1%)	15 (12.6%)
VA reduced	8 (6.5%)	22 (18.5%)
Conjunctival hemorrhage	16 (12.9%)	13 (10.9%)
Vitreous floaters	5 (4.0%)	11 (9.2%)
Iris neovascularization	0 (0.0%)	9 (7.6%)
Dry eye	4 (3.2%)	4 (3.4%)
Glaucoma	0 (0.0%)	8 (6.7%)
Visual impairment	2 (1.6%)	6 (5.0%)

Vitreous detachment	5(4.0%)	3 (2.5%)
Eye irritation	4(3.2%)	3 (2.5%)
Retinal ischemia	1(0.8%)	6 (5.0%)
Retinal vascular disorder	2(1.6%)	5 (4.2%)
Ocular hypertension	0	6 (5.0%)
Retinal exudates	2(1.6%)	4 (3.4%)
Optic disc vascular disorder	5(4.0)	0