Intravitreal Aflibercept Injection for Nonproliferative Diabetic Retinopathy: Results from the PANORAMA Study

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Disclosures

- Consultant: Acucela, Aerpio, Alcon, Allegro, Allergan, Amydis, Ascleptix, Bausch + Lomb, Bayer, BIoMotiv, Boehringer Ingelheim, Clearside Biomedical, CoDa Therapeutics, DigiSight, Eyepoint, Foresight Biotherapeutics, 4DMT, Genentech, GenSight Biologics, Glaukos, GlaxoSmithKline, Graybug Vision, Ionis Pharmaceutcials, Isarna Therapeutics, Kala, Notal Vision, Neurotech, Novartis, Ocular Therapeutix, Ohr, Optos, OptoVue, Ora, Ocular therapuetics, Ophthea, Oxurion, Polyactiva, pSivida Corp, Regeneron, Regulus Therapeutics, River Vision, Roche, Santen, Shire, Stealth Biotherapeutics, Sun Pharmaceuticals, Taiwan Liposome Company, Thea, ThromboGenics,
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Summary

- Aflibercept administered to high risk NPDR as infrequently as q 16 weeks caused a significant improvement in the DRSS score
- Vision threatening complications (PDR/ASNV) and CI-DME occurred in a substantially greater proportion of sham patients
- DR is a progressive disease and despite aflibercept therapy, some eyes still developed PDR or CI-DME

PANORAMA Study Design

Phase 3, Double-masked, Randomized, Study of Efficacy & Safety of IAI in Patients with moderately severe to severe NPDR (DRSS Level 47 and 53)
N=402**

Sham
N=133

2q16
IAI 2 mg Q16 weeks⁺
N=135

2q8►PRN
IAI 2 mg Q8 weeks*
N=134

Week 24
Primary Endpoint: **Proportion of patients improving ≥ 2 steps on DRSS**
All IAI Combined versus Sham

Week 52
Primary Endpoint: **Proportion of patients improving ≥ 2 steps on DRSS**
2q16 and 2q8 individually versus Sham

Follow up through Week 100

Key Secondary endpoints
- % developing PDR/ASNV
- % developing CI-DME
- Time to development of PDR/ASNV or CI-DME

⁺After 3 initial monthly doses and 1 q8 interval *After 5 initial monthly doses, flexible treatment schedule after week 52 **Patients were stratified by baseline DRSS level
ASNV, anterior segment neovascularization; CI-DME, center-involved diabetic macular edema; DRSS, Diabetic Retinopathy Severity Score; NPDR, nonproliferative diabetic retinopathy;

Dosing Schedule

Week:	BL	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88	92	96	100
Sham	O	O	O	O	O		O		O		O		O		O		O		O		O		O		O	-
2q16	X	X	X	O	X		O		X		O		X		O		X		O		X		O		X	-
2q8►PRN	X	X	X	X	X		X		X		X		X		+		+		+		+		+		+	-

+ = Aflibercept PRN:
Injection given unless DRSS is
Level 35 or better (mild NPDR)
as determined by the investigator

Patients progressing to PDR/ASNV or CI-DME were eligible for rescue treatment (IAI or laser) at the discretion of the investigator. Data for patients receiving rescue treatment was censored from the time of rescue.

X=active injection, O=sham injection

Baseline Demographics

	Sham	2q16	2q8▸PRN	Total
N (FAS/SAF)	133	135	134	402
Age (years (SD))	55.8 (10.31)	55.4 (11.13)	55.8 (10.19)	55.7 (10.53)
Women # (%)	64 (48.1%)	60 (44.4%)	53 (39.6%)	177 (44.0%)
Race # (%)				
White	107 (80.5%)	99 (73.3%)	104 (77.6%)	310 (77.1%)
Black or African American	13 (9.8%)	16 (11.9%)	12 (9.0%)	41 (10.2%)
Asian	4 (3.0%)	12 (8.9%)	7 (5.2%)	23 (5.7%)
Other	9 (6.8%)	8 (5.9%)	11 (8.2%)	28 (7.0%)
Hemoglobin A1C (%)	8.5 (1.54)	8.6 (1.69)	8.4 (1.64)	8.5 (1.62)
Duration of Diabetes (years (SD))	15.5 (9.34)	13.7 (8.61)	14.0 (9.67)	14.4 (9.23)
Diabetes Type 2	123 (92.5%)	121 (89.6%)	124 (92.5%)	368 (91.5%)

FAS, Full analysis set; SAF, Safety analysis set; SD, standard deviation

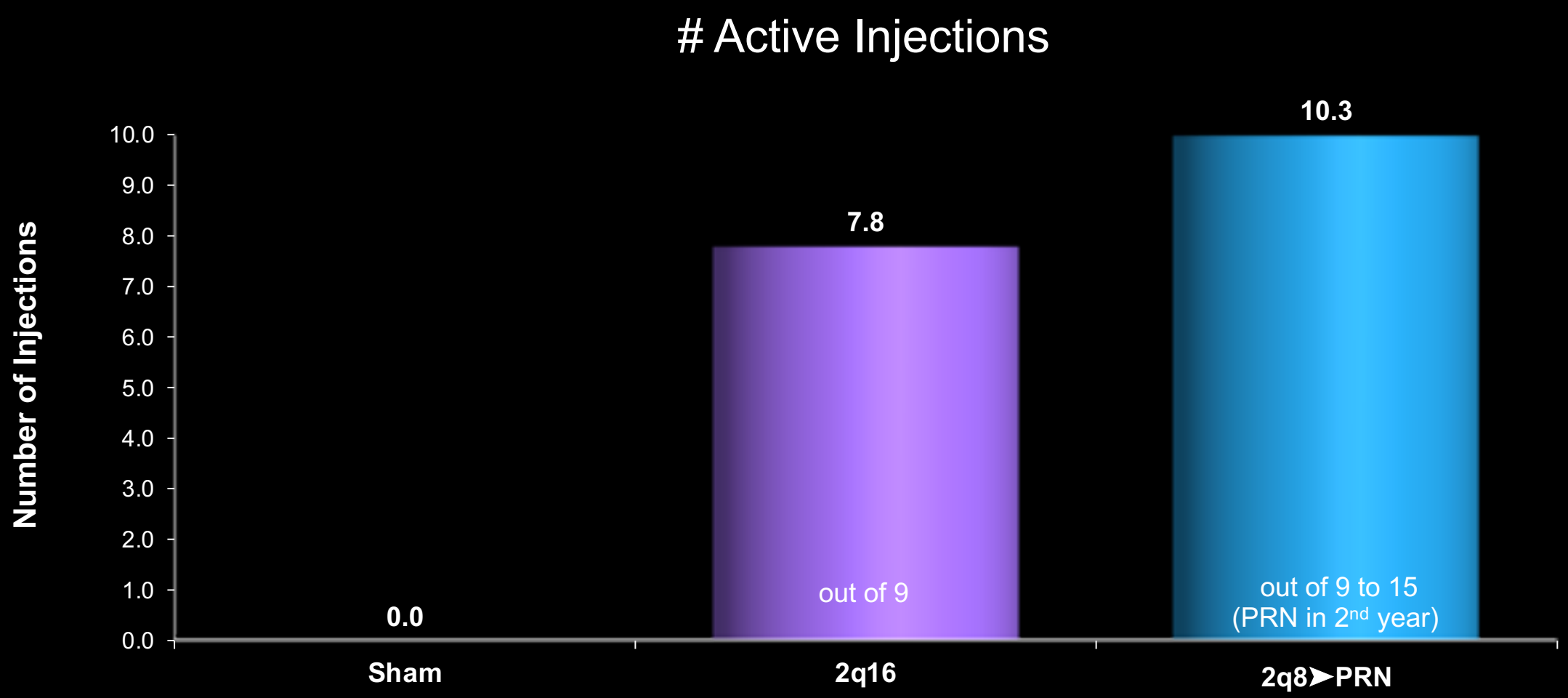
Baseline Disease Characteristics and Disposition

	Sham	2q16	2q8▸PRN	Total
N (FAS/SAF)	133	135	134	402
ETDRS BCVA (letters) Mean (SD) Snellen Equivalent	82.7 (6.03) 20/25	82.2 (6.63) 20/25	82.3 (5.15) 20/25	82.4 (5.96) 20/25
CRT(microns) Mean (SD)	249.4 (38.41)	246.0 (34.34)	246.8 (31.59)	247.4 (34.82)
Diabetic Retinopathy Severity Score (DRSS)				
Level 47	99 (74.4%)	102 (75.6%)	101 (75.4%)	302 (75.1%)
Level 53	34 (25.6%)	33 (24.4%)	33 (24.6%)	100 (24.9%)

# of Patients Completing Week 100	97 (72.9%)	111 (82.2%)	112 (83.6%)	320 (79.6%)
# of Patients Completing Week 52	109 (82.0%)	122 (90.4%)	124 (92.5%)	355 (88.3%)

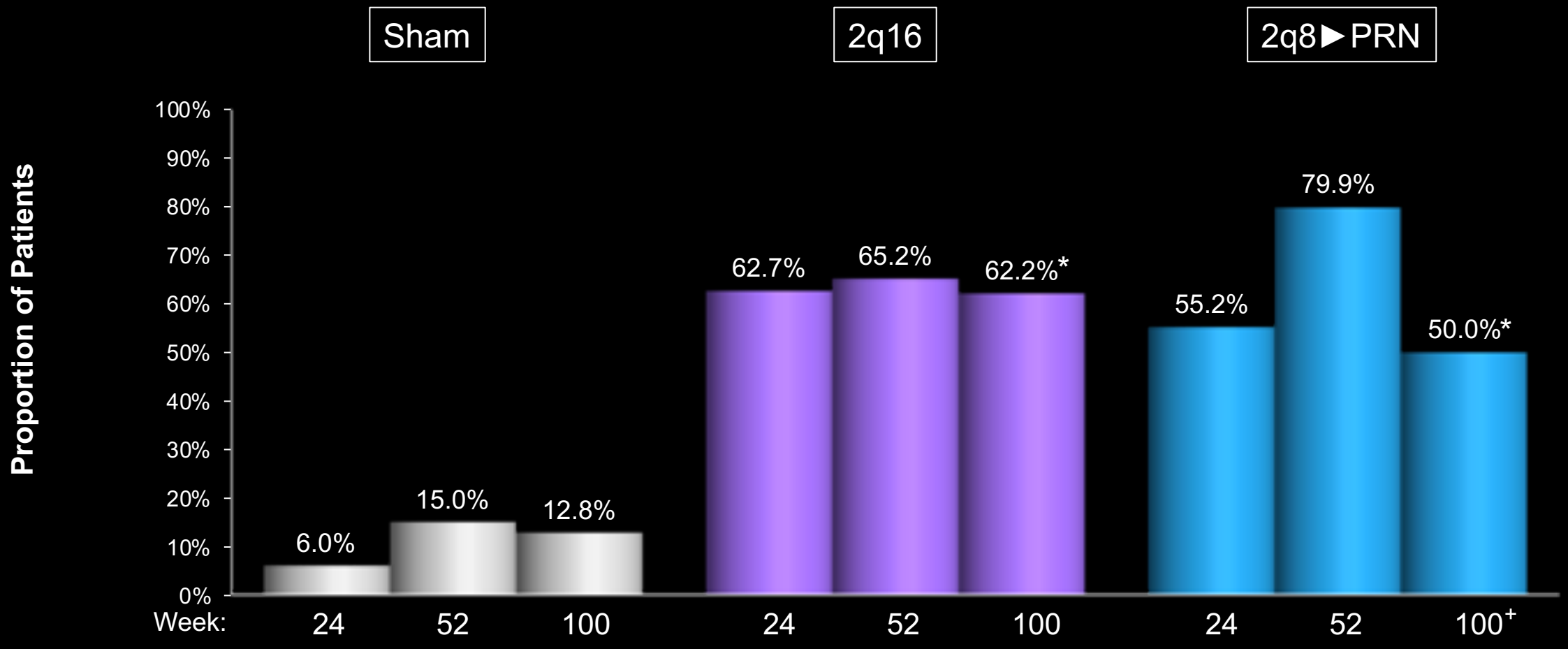
CRT, central retinal thickness.

Treatment Experience through Week 100



Sham n=133, 2q16 n=135, 2q8 n=134

Proportion of Patients with ≥2-step Improvement from Baseline in DRSS

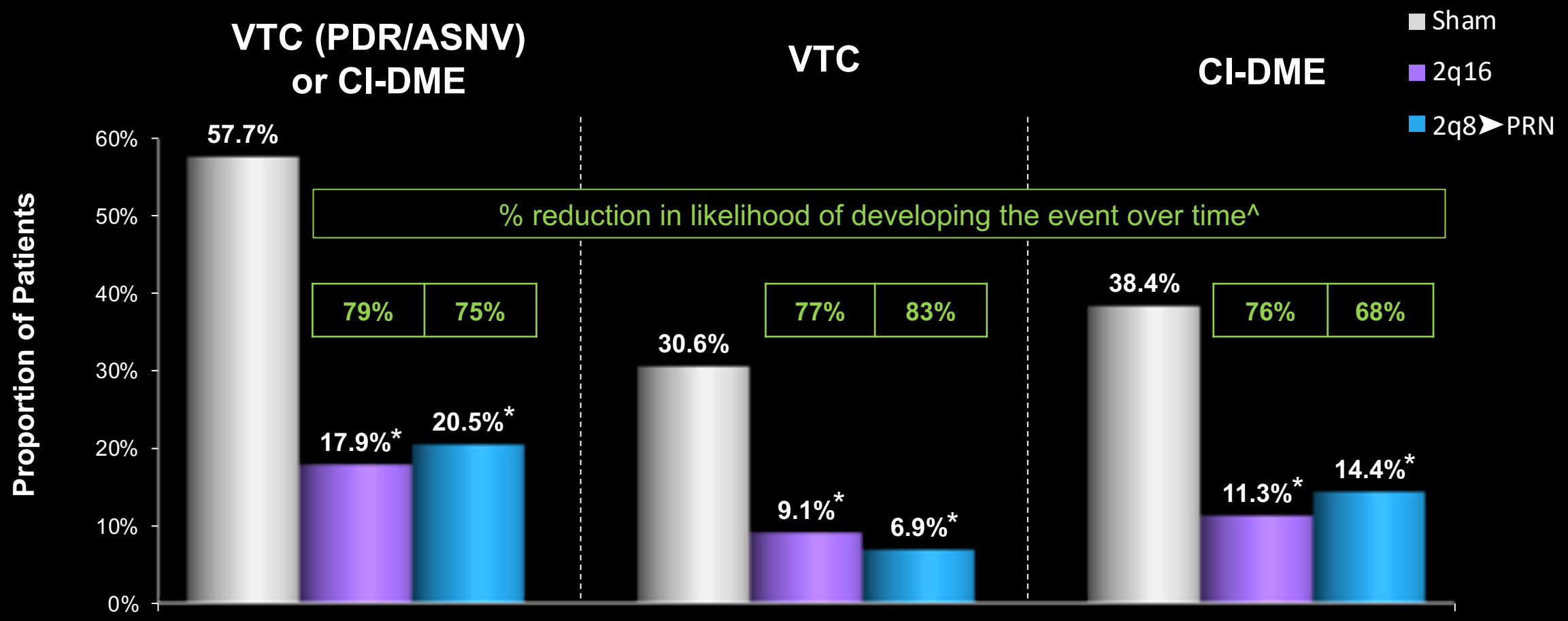


+Independent reading center review of investigator PRN decisions suggests under treatment during Year 2

Nominal p < 0.0001 vs. sham

Last observation carried forward (LOCF); Sham n=133, 2q16 n=135, 2q8 n=134

Proportion of Patients Developing a VTC or CI-DME through Week 100
Kaplan-Meier Analysis

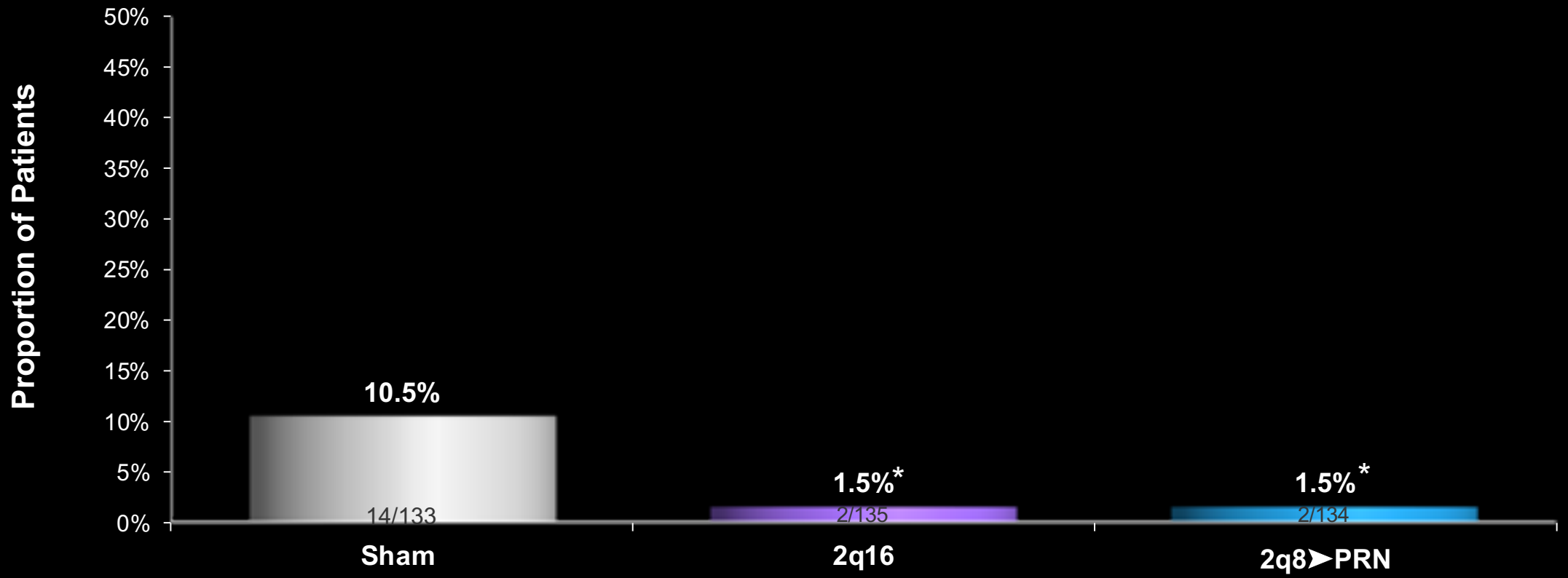


Nominal p < 0.001 vs. sham

VTC = Vision threatening complication defined as PDR/ASNV
CI-DME = center-involved DME
FAS; Sham n=133, 2q16 n=135, 2q8 n=134

^Percentage reductions in risk derived from hazard ratios from Kaplan-Meier estimates.

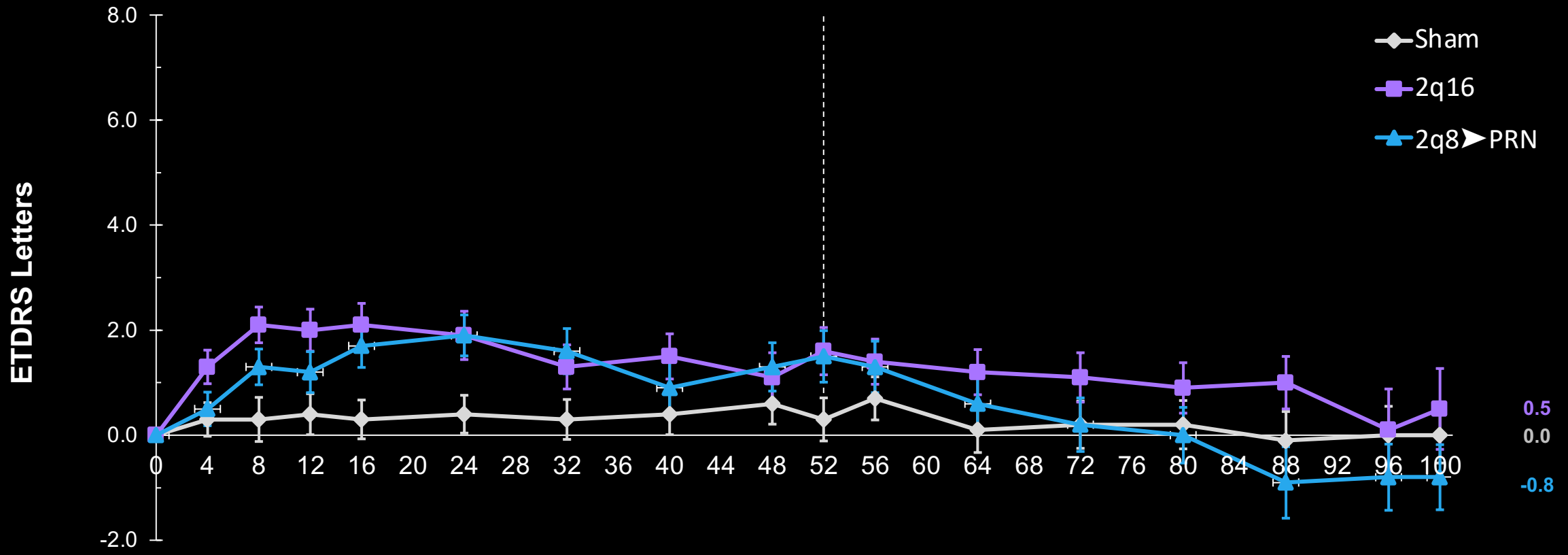
Proportion of Patients Receiving PRP or Vitrectomy through Week 100



*Nominal p < 0.002 vs. sham

Sham n=133, 2q16 n=135, 2q8 n=134

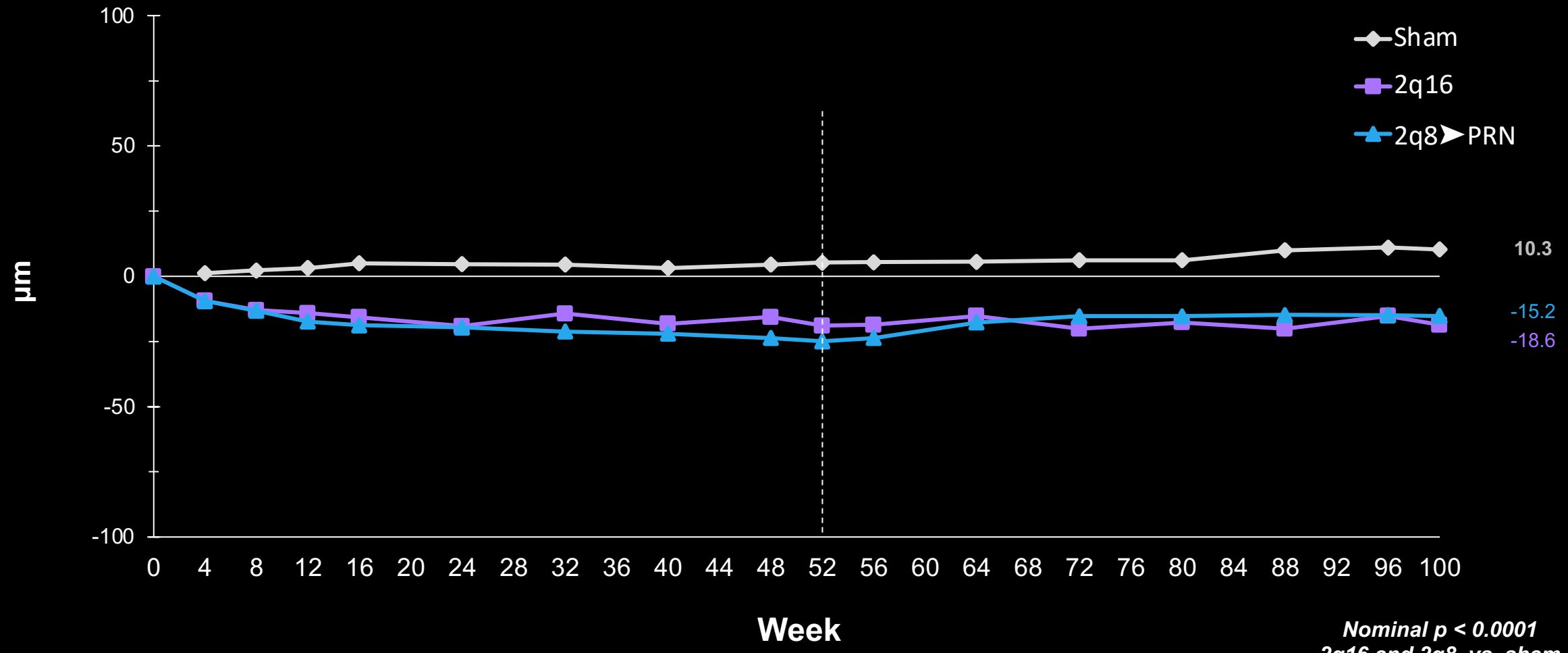
Mean Change in Best Corrected Visual Acuity



Nominal p = NS 2q16 vs. sham
Nominal p = NS 2q8 vs. sham

LOCF; Sham n=133, 2q16 n=135, 2q8 n=134

Mean Change in Central Retinal Thickness



Nominal p < 0.0001
2q16 and 2q8 vs. sham

LOCF; Sham n=133, 2q16 n=135, 2q8 n=134

Ocular TEAEs in Study Eye through Week 100
(≥3%)

	Sham	2q16	2q8▸PRN
N (FAS/SAF)	133	135	134
Number of patients ≥ 1 AE, n (%)	76 (57.1%)	77 (57.0%)	81 (60.4%)
Conjunctival hemorrhage	8 (6.0%)	18 (13.3%)	25 (18.7%)
Diabetic retinal edema	43 (32.3%)	14 (10.4%)	19 (14.2%)
Vitreous floaters	3 (2.3%)	7 (5.2%)	13 (9.7%)
Cataract	5 (3.8%)	8 (5.9%)	8 (6.0%)
Vision blurred	1 (0.8%)	1 (0.7%)	5 (3.7%)
Eye pain	6 (4.5%)	11 (8.1%)	5 (3.7%)
Retinal exudates	6 (4.5%)	5 (3.7%)	9 (6.7%)
Vitreous detachment	4 (3.0%)	7 (5.2%)	7 (5.2%)
Blepharitis	1 (0.8%)	2 (1.5%)	7 (5.2%)
Cataract subcapsular	1 (0.8%)	5 (3.7%)	4 (3.0%)
Diabetic retinopathy	22 (16.5%)	3 (2.2%)	5 (3.7%)
Dry eye	6 (4.5%)	3 (2.2%)	5 (3.7%)
Cataract nuclear	0	0	6 (4.5%)

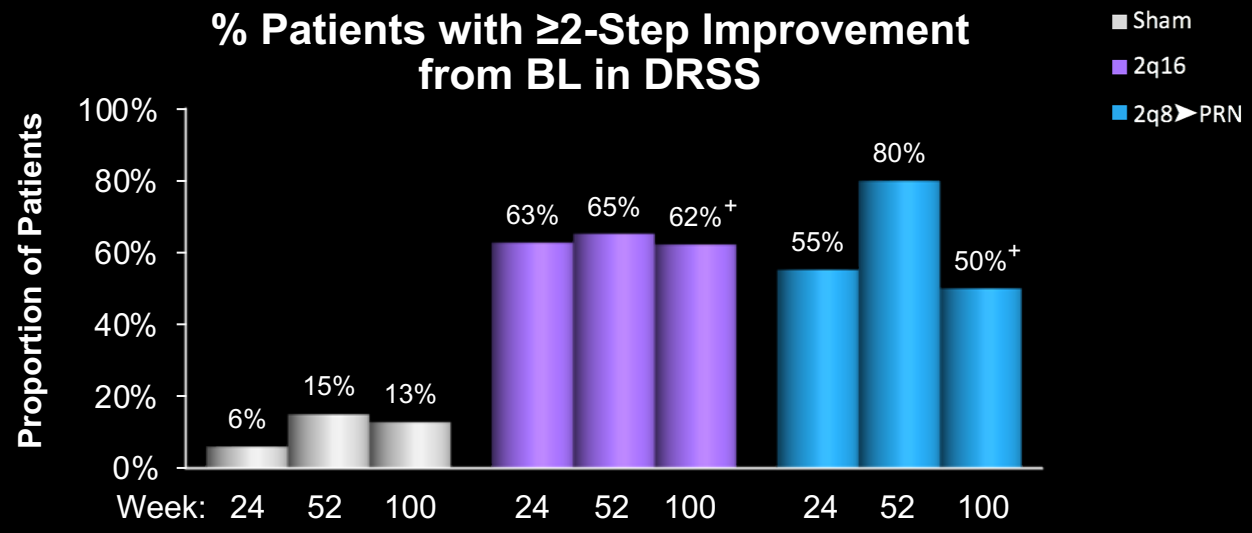
AE, adverse event; TEAE, treatment-emergent AE

APTC Events and Deaths through Week 100

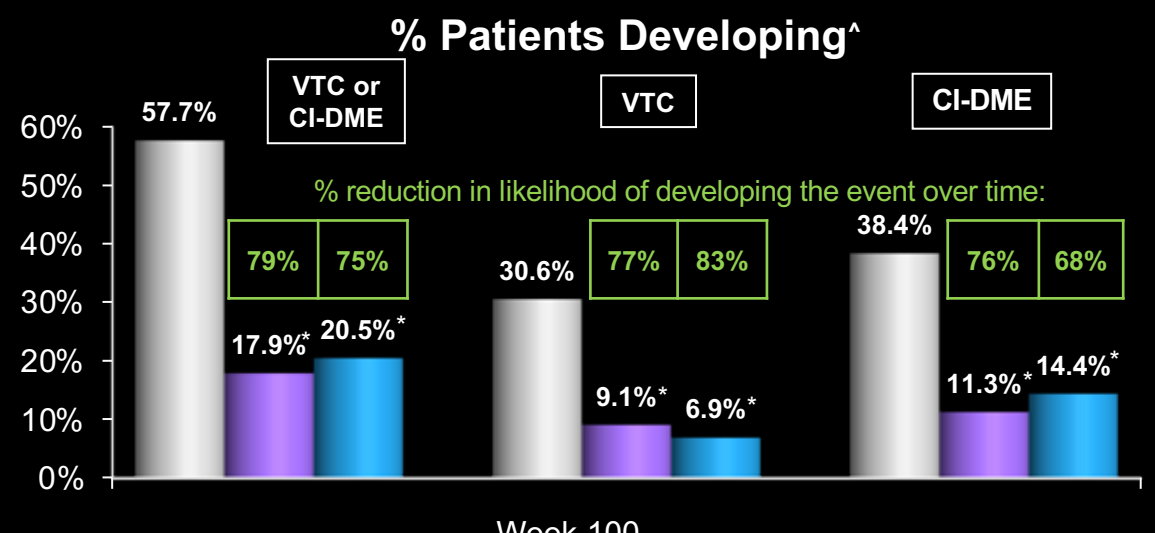
	Sham	2q16	2q8▸PRN
N (FAS/SAF)	133	135	134
Number of patients with at least one such AE, n (%)	7 (5.3%)	8 (5.9%)	4 (3.0%)
Non Fatal Stroke	3 (2.3%)	5 (3.7%)	1 (0.7%)
Non Fatal MI	0	3 (2.2%)	2 (1.5%)
Vascular Death	4 (3.0%)	0	1 (0.7%)
All Deaths	8 (6.0%)	1 (0.7%)	3 (2.2%)

APTC, Antiplatelet Trialists' Collaboration; MI, myocardial infarction.

PANORAMA 100 Week Conclusions



LOCF; Sham n=133, 2q16 n=135, 2q8 n=134



^Derived from hazard ratios from Kaplan-Meier estimates.

- Proportion of patients with a ≥2-step DRSS improvement remained significantly greater with aflibercept vs sham
- Vision threatening complications (PDR/ASNV) and CI-DME occurred in a substantially greater proportion of sham patients
- DR is a progressive disease and despite aflibercept therapy, some eyes still developed PDR or CI-DME