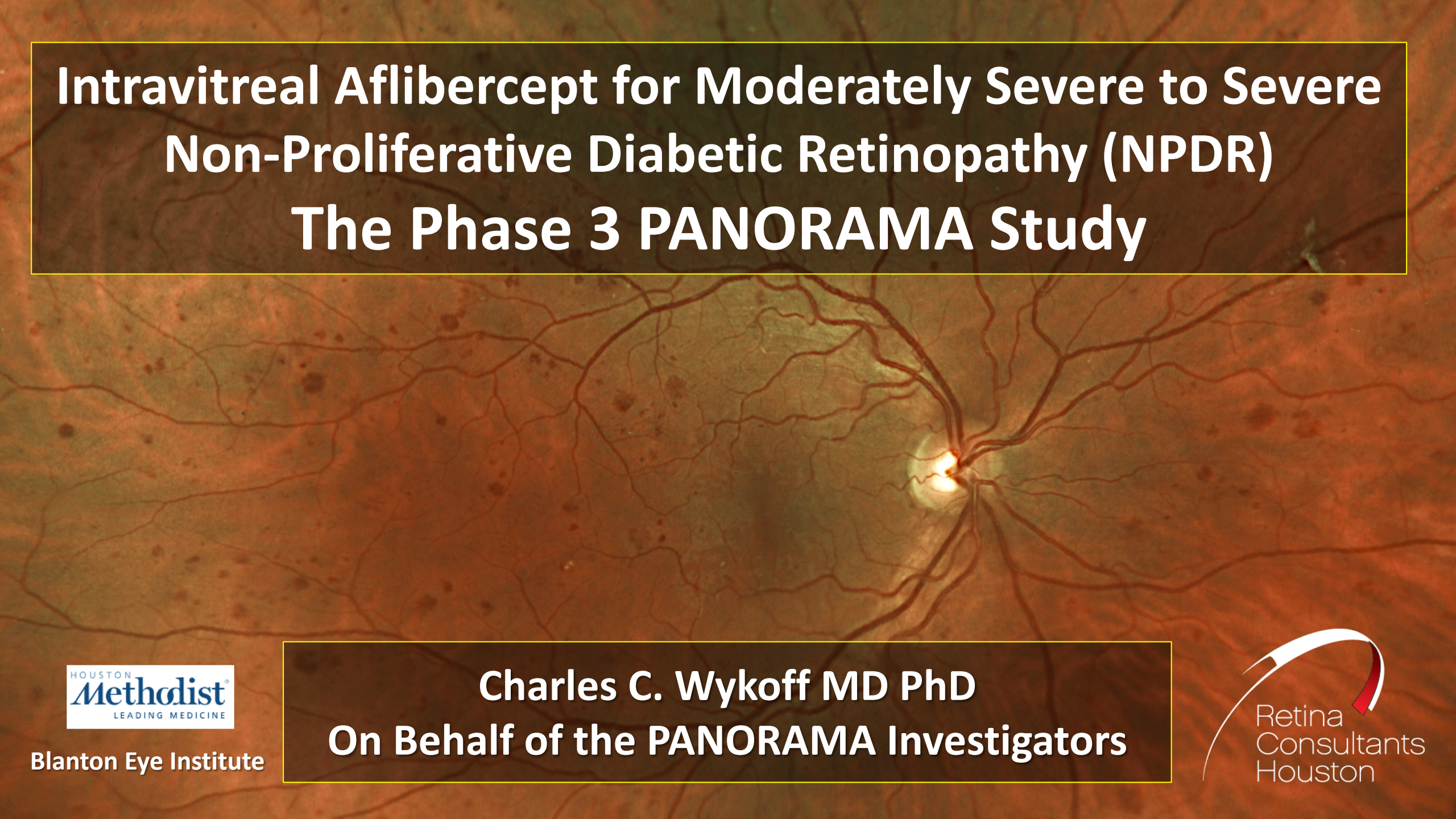
Intravitreal Aflibercept for Moderately Severe to Severe Non-Proliferative Diabetic Retinopathy (NPDR)
The Phase 3 PANORAMA Study



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On Behalf of the PANORAMA Investigators

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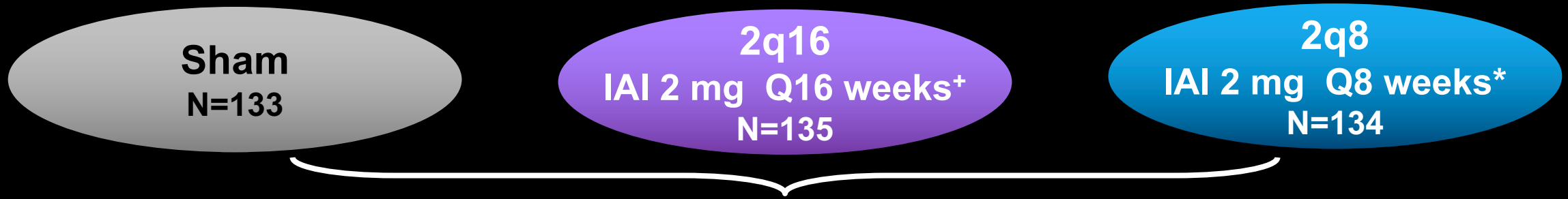
Disclosures

- Financial Disclosures
  - Adverum (R); Alimera Sciences (C); Allegro (C); Allergan(C, R); Alnylam (C); Apellis (C, R); Bayer (C); Clearside Biomedical (C, R); DORC (C); EyePoint (C, R); Genentech/Roche (C, R); Kodiak (C); Neurotech (R); Notal Vision (C); Novartis (C, R); ONL Therapeutics (C); Opthea (R); PolyPhotonix (C); Recens Medical (C); Regeneron(C, R, S); Regenxbio (C, R); Samsung (R), Santen (C, R)
- Study Disclosures
  - This study includes research conducted on human subjects. Institutional Review Board approval was obtained prior to study initiation.

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**



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

Key Secondary Endpoints
% developing PDR/ASNV
% developing CI-DME

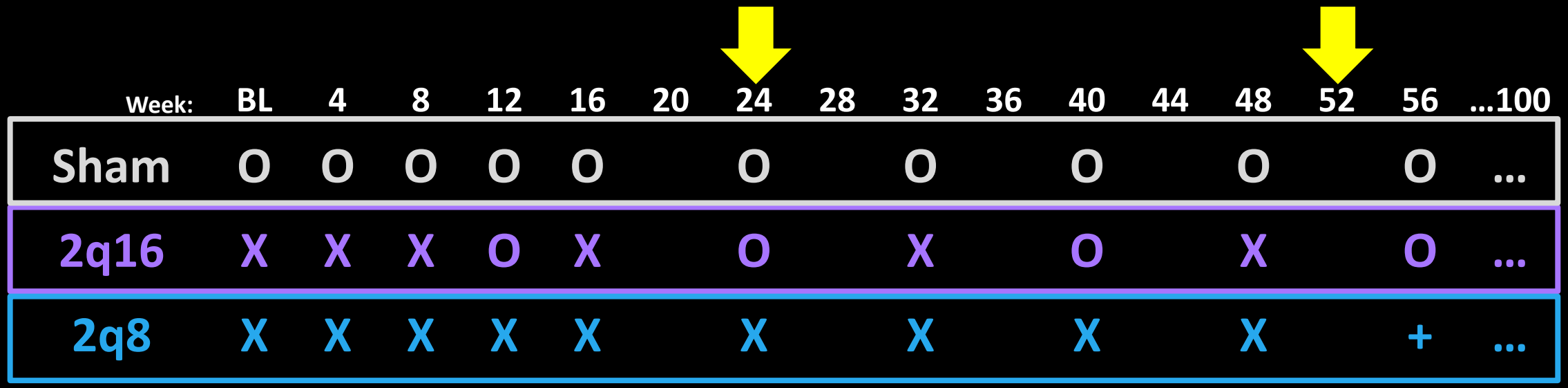
Follow up through Week 100

+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
2q8, 2 mg every 8 weeks; 2q16, 2 mg every 16 weeks; ASNV, anterior segment neovascularization; CI-DME, center-involved diabetic macular edema; DRSS, Diabetic Retinopathy Severity Score; IAI, intravitreal aflibercept injection; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Inclusion & Exclusion Criteria

- **Inclusion**
  - Anti-VEGF treatment naïve with moderately severe to severe NPDR (DRSS levels 47 or 53), confirmed by the central reading center, in whom PRP could be safely deferred for ≥6 months
  - BCVA ETDRS letter score of ≥69 letters (~ Snellen equivalent of ≥20/40)
- **Exclusion**
  - DME threatening the center of the macula
  - Evidence of retinal neovascularization
  - Any prior treatment with:
    - Focal or grid laser photocoagulation or PRP
    - Systemic or intravitreal anti-VEGF agents
    - Intraocular steroids
  - Current ASNV, vitreous hemorrhage, or traction retinal detachment
  - HbA1c >12% or HbA1c ≤12% with uncontrolled diabetes mellitus
  - Uncontrolled blood pressure
  - History of cerebrovascular accident or myocardial infarction within 6 months of study start

Dosing Schedule



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

= primary endpoints at weeks 24 and 52. X=active injection, O=sham injection

Baseline Demographics

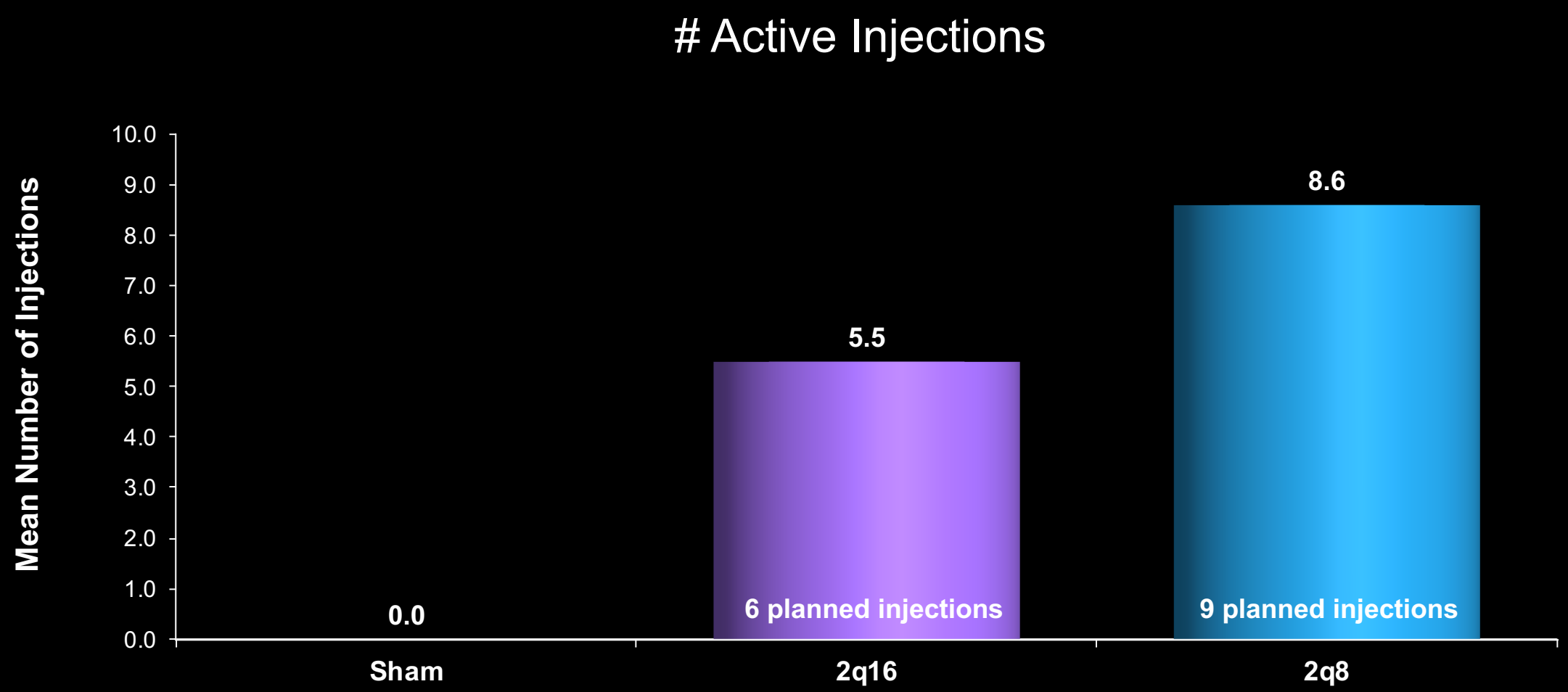
	Sham	2q16	2q8	Total
N (FAS/SAF)	133	135	134	402
Age (years (SD))	55.8 (10.31)	55.4 (11.13)	55.8 (10.19)	55.7 (10.53)
Women # (%)	64 (48.1%)	60 (44.4%)	53 (39.6%)	177 (44.0%)
Race # (%)				
White	107 (80.5%)	99 (73.3%)	104 (77.6%)	310 (77.1%)
Black or African American	13 (9.8%)	16 (11.9%)	12 (9.0%)	41 (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 (9.69)	14.4 (9.24)
Diabetes Type 2	123 (92.5%)	121 (89.6%)	124 (92.5%)	368 (91.5%)

Baseline Disease Characteristics and Disposition

	Sham	2q16	2q8	Total
N (FAS/SAF)	133	135	134	402
ETDRS BCVA (mean letters (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%)

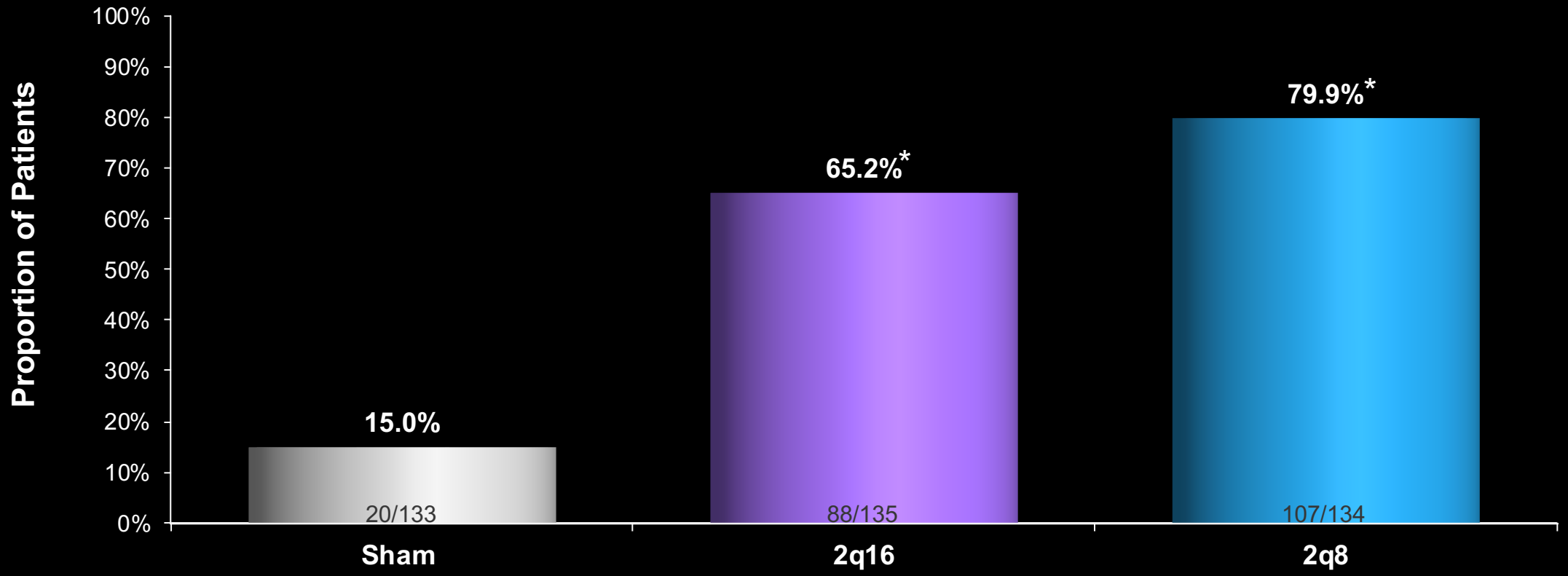
# of Patients Completing Week 24	119 (89.5%)	129 (95.6%)	132 (98.5%)	380 (94.5%)
# of Patients Completing Week 52	109 (82.0%)	122 (90.4%)	124 (92.5%)	355 (88.3%)

Treatment Experience through Week 52



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

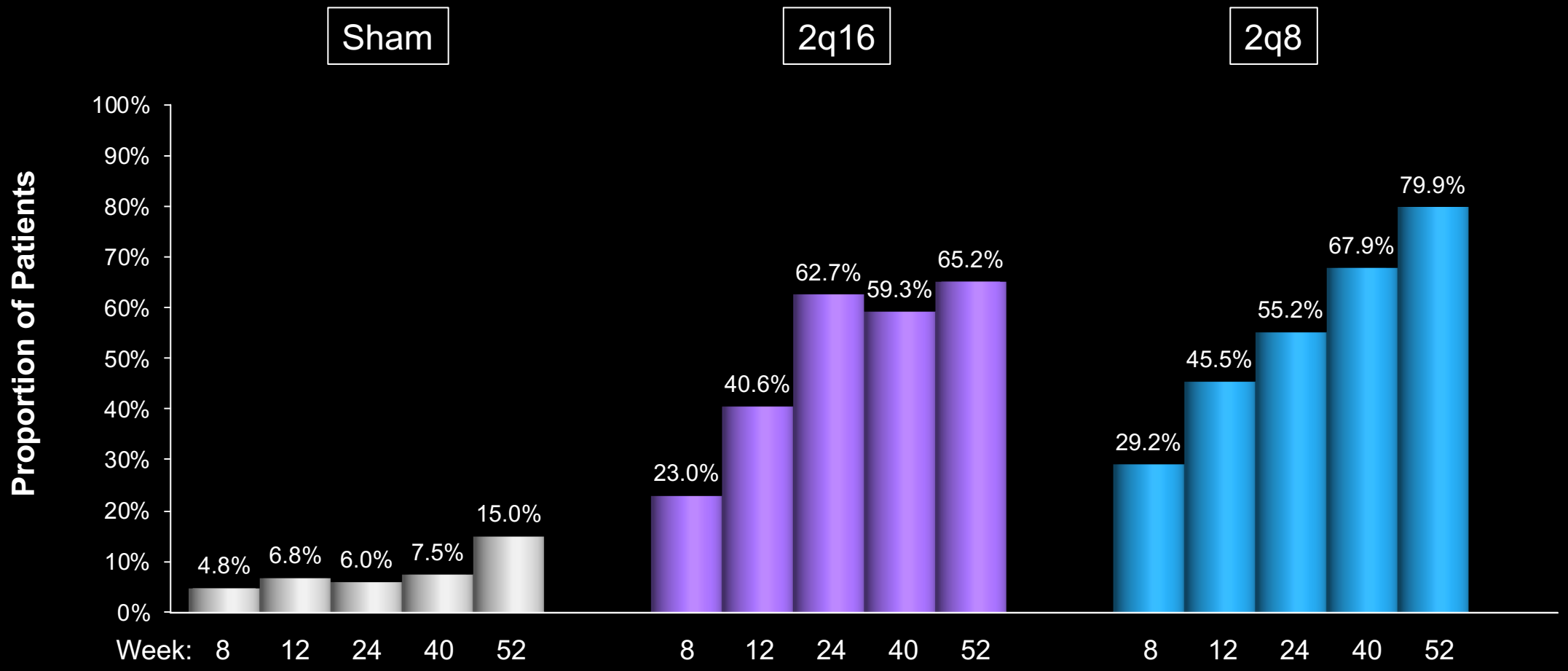
Proportion of Patients with ≥2-Step Improvement from Baseline in DRSS at Week 52



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

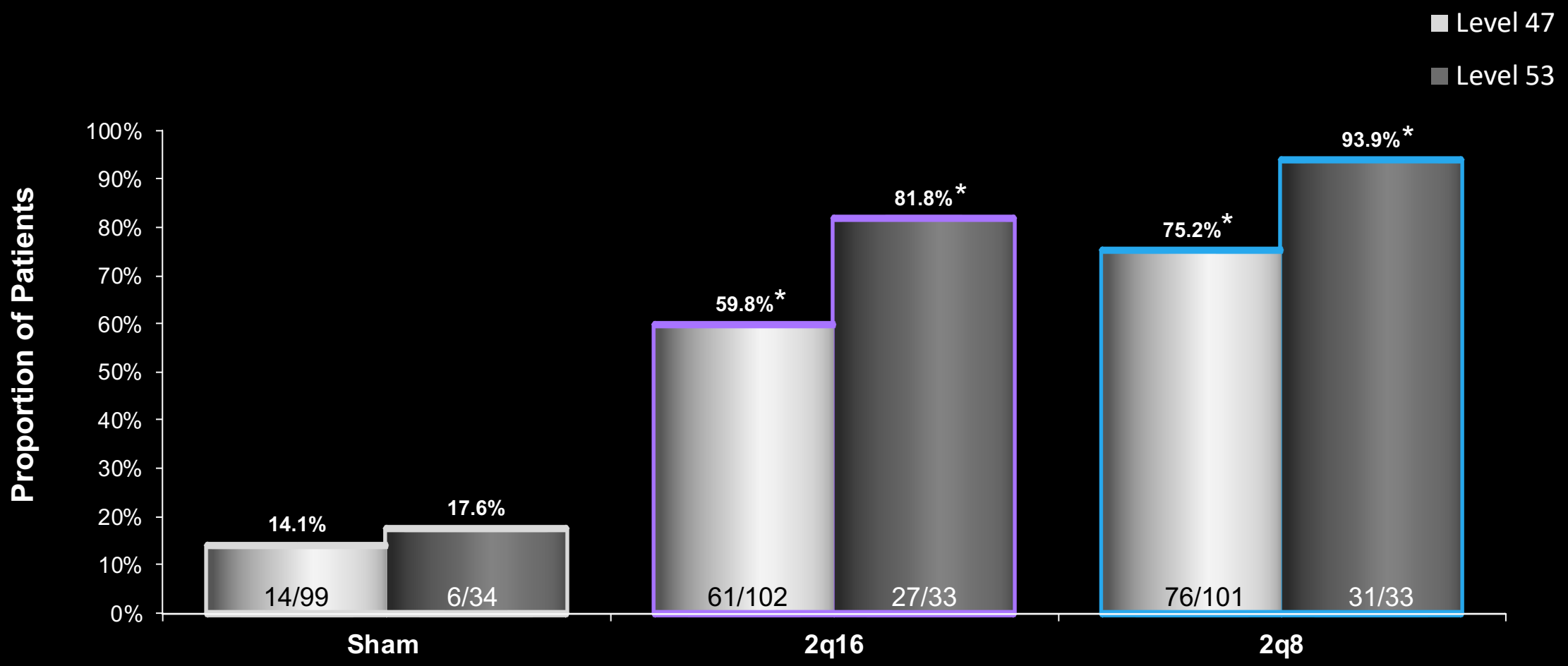
*p < 0.0001 vs. sham

Proportion of Patients with ≥2-Step Improvement from Baseline in DRSS at Week 52



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

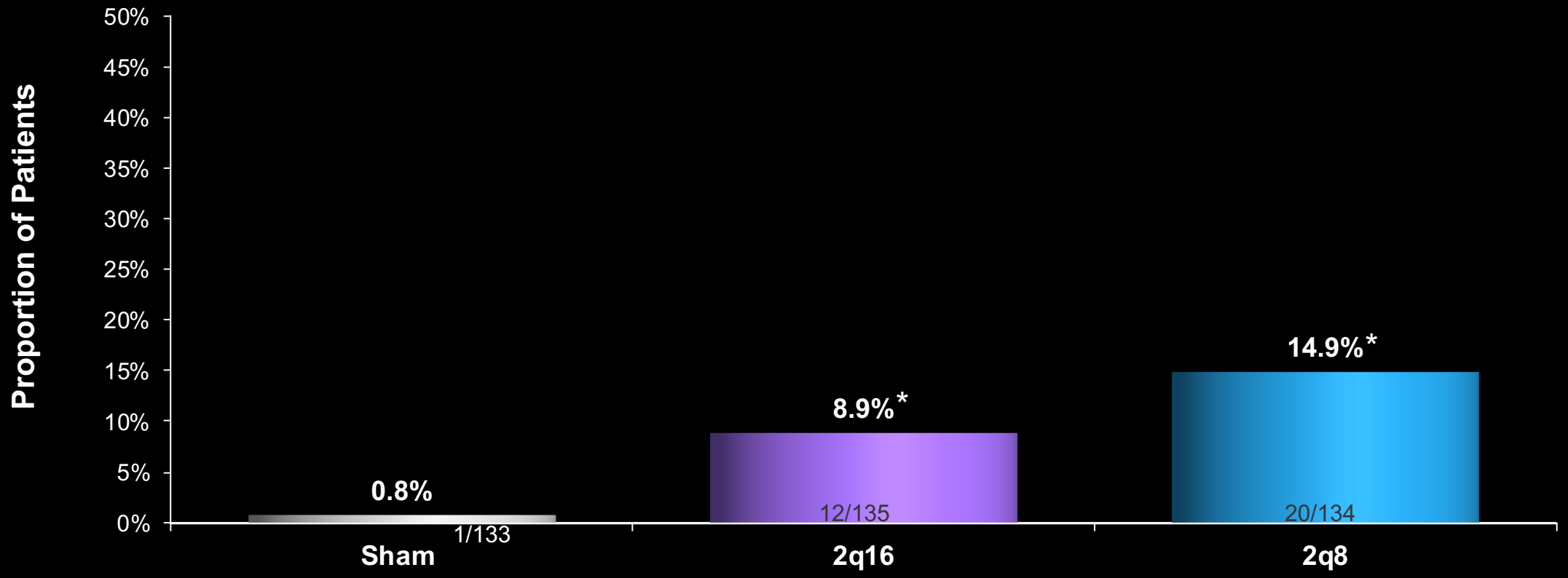
Proportion of Patients with ≥2-Step Improvement in DRSS by Baseline DRSS Score at Week 52



*nominal p < 0.001 vs. sham

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

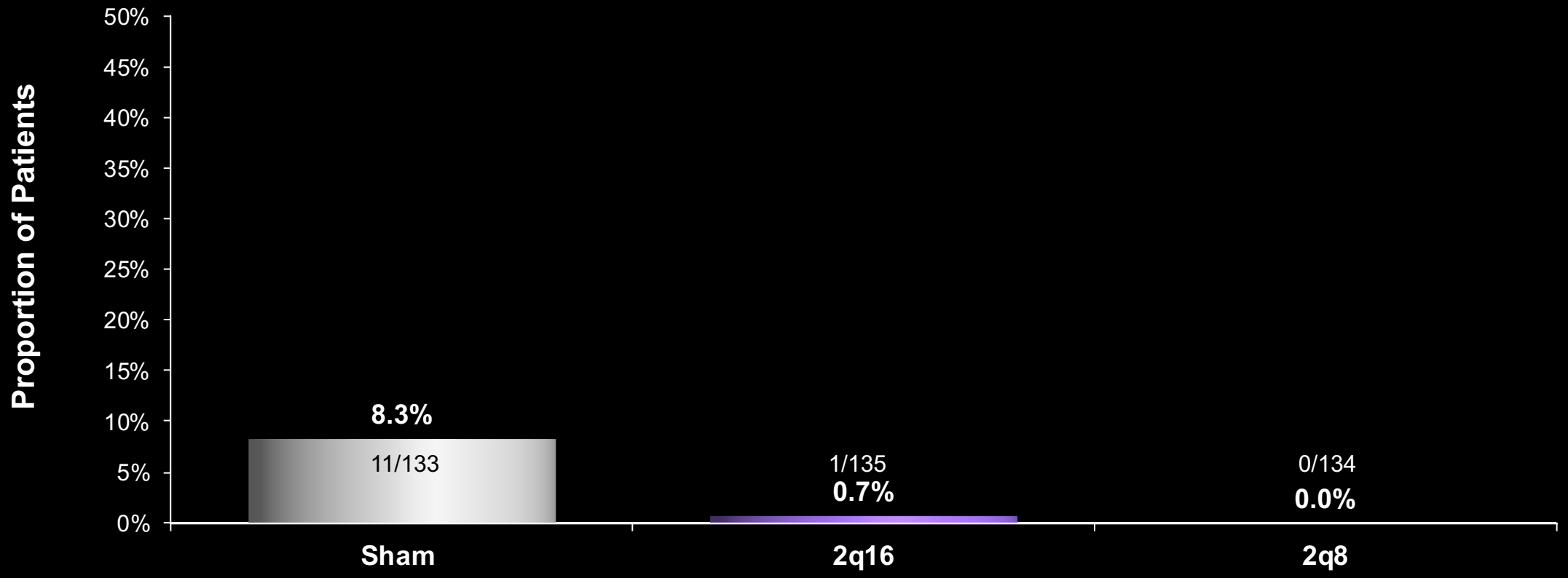
Proportion of Patients with ≥3-Step Improvement from Baseline in DRSS at Week 52



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

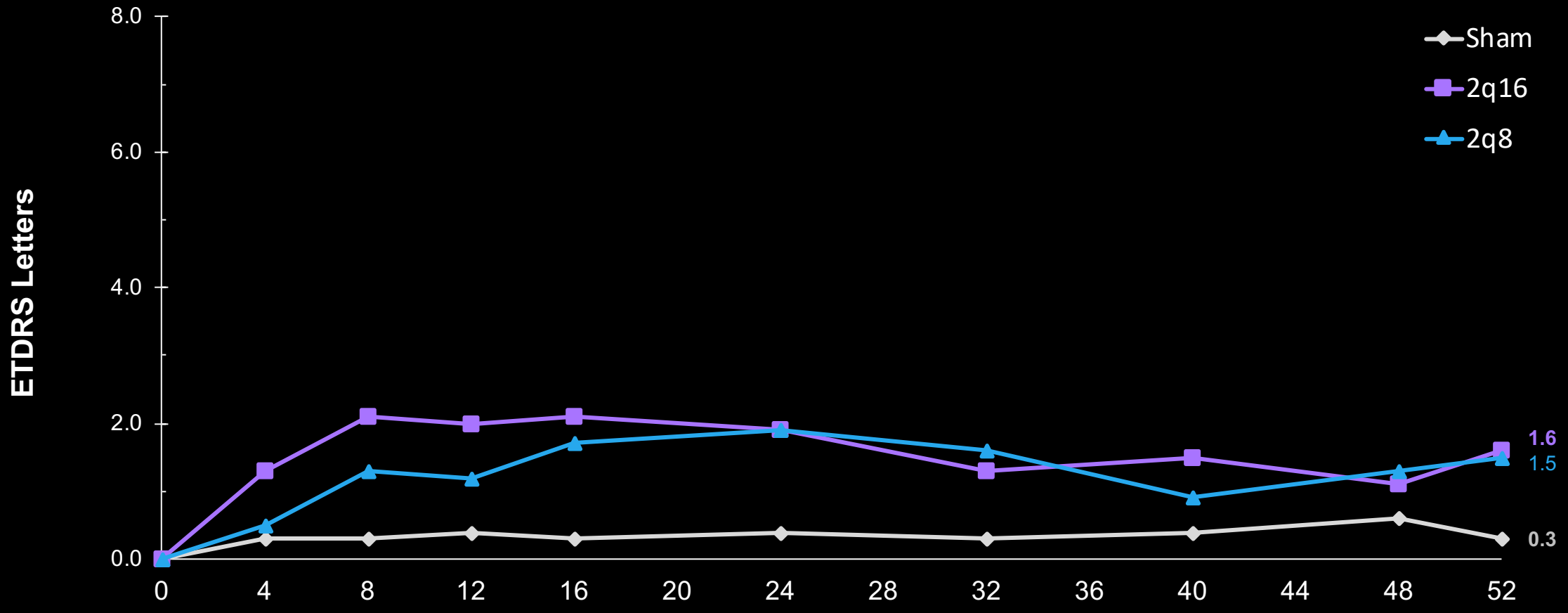
**nominal p < 0.001 vs. sham*

Proportion of Patients with ≥2-Step Worsening from Baseline in DRSS at Week 52



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

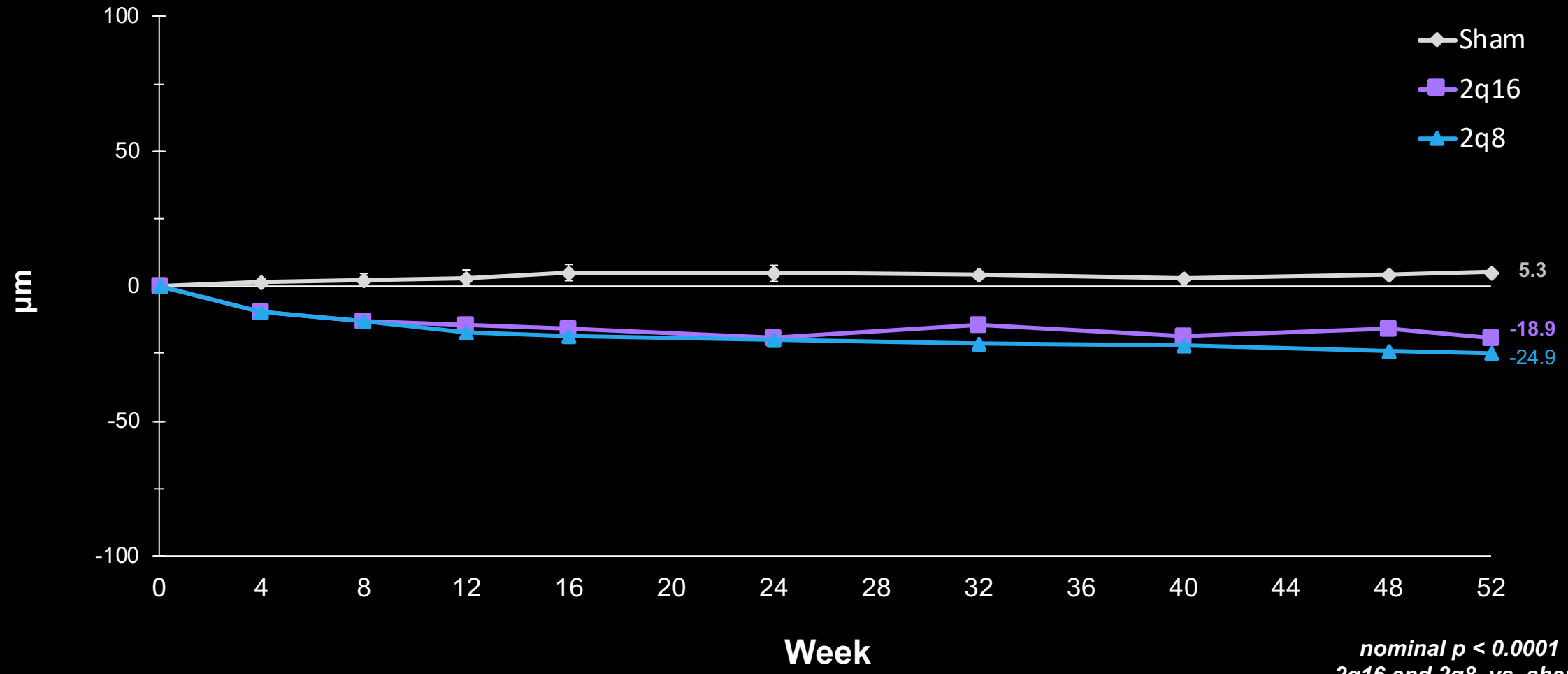
Mean Change in Best Corrected Visual Acuity



nominal p =
0.0494 2q16 vs. sham
0.0895 2q8 vs. sham

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

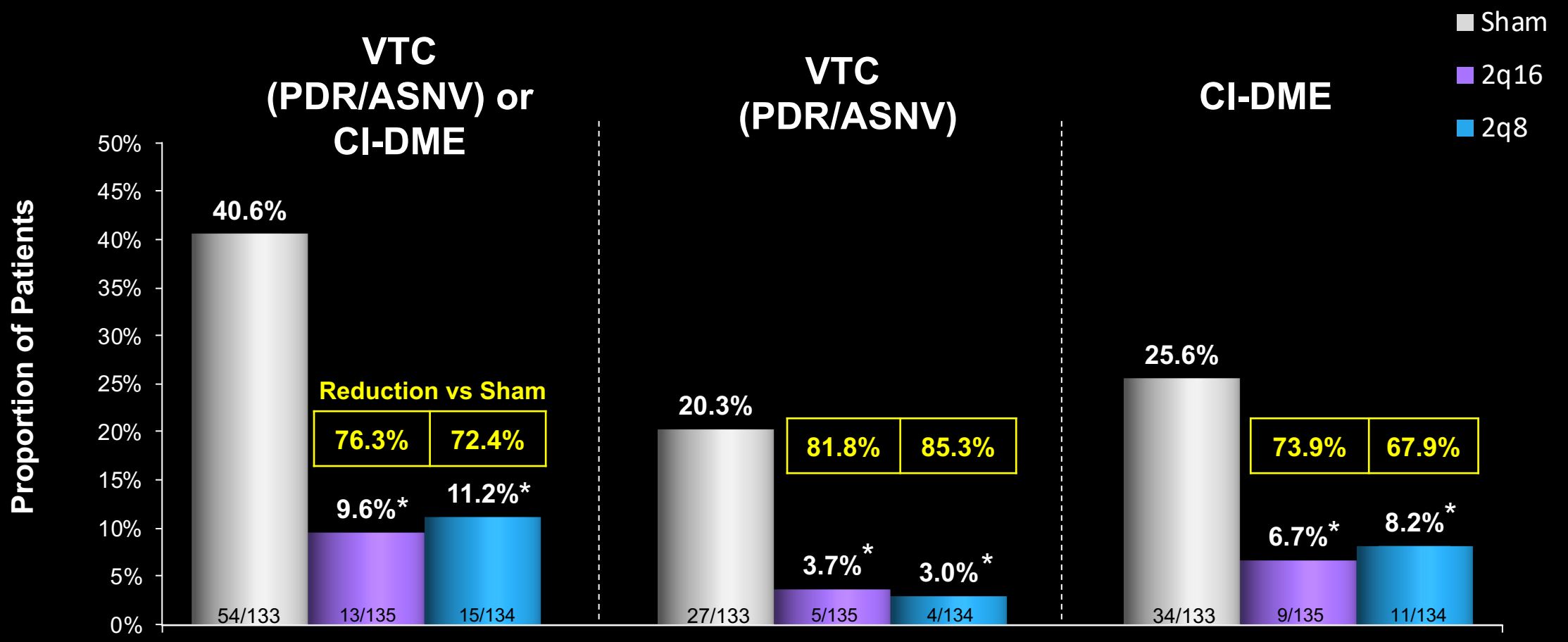
Mean Change in Central Retinal Thickness



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

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

Proportion of Patients Developing a Vision Threatening Complication (VTC) or Center Involved (CI)-DME through Week 52

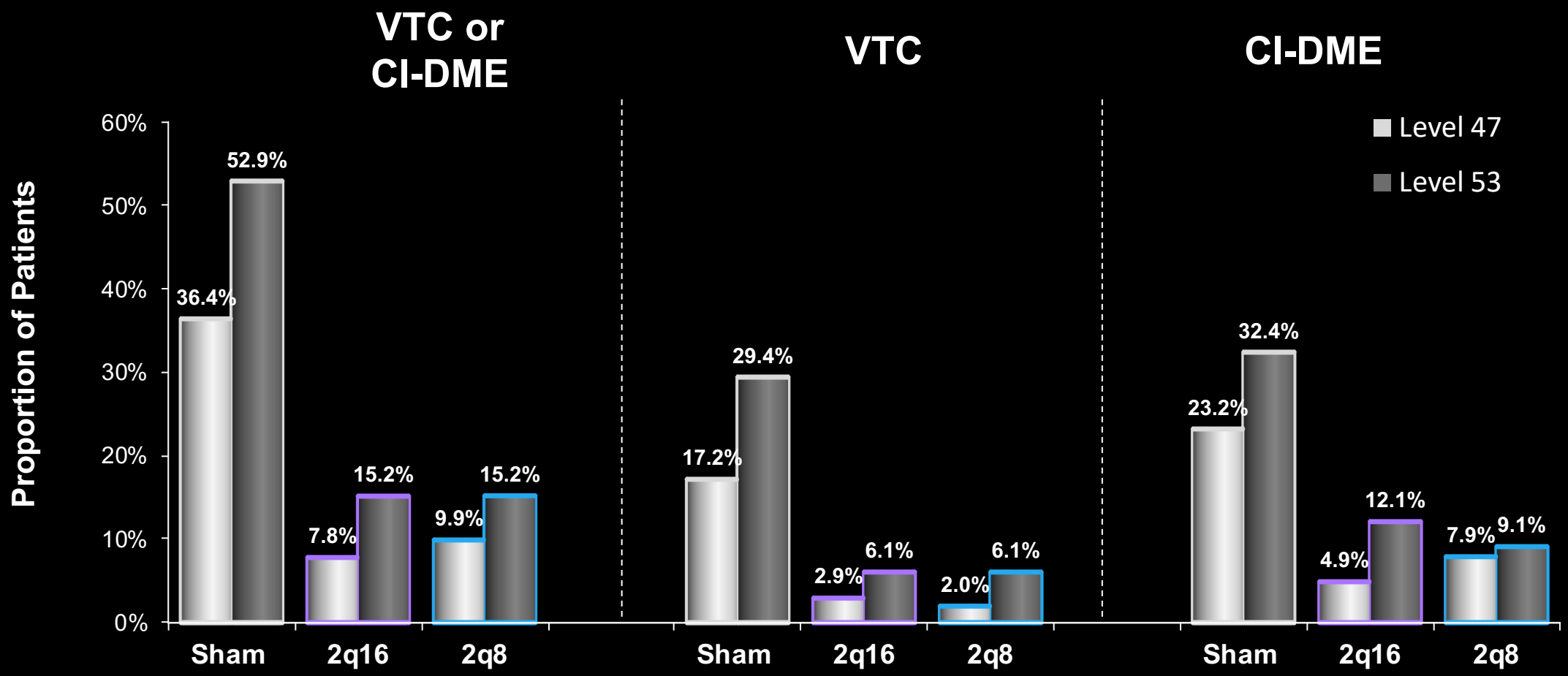


Number needed to treat = 3 patients in order to prevent 1 prespecified VTC or CI-DME event

VTC = Vision threatening complication, PDR/ASNV; FAS; Sham n=133, 2q16 n=135, 2q8 n=134

p < 0.0003 vs. sham

Proportion of Patients Developing a VTC or CI-DME through Week 52 by Baseline DRSS



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

Ocular TEAEs in Study Eye through Week 52
(≥3%)

	Sham	2q16	2q8
N (FAS/SAF)	133	135	134
Number of Patients ≥ 1 AE, n (%)	67 (50.4%)	58 (43.0%)	60 (44.8%)
Eye disorders	64 (48.1%)	57 (42.2%)	59 (44.0%)
Conjunctival haemorrhage	7 (5.3%)	16 (11.9%)	23 (17.2%)
Diabetic retinal oedema	32 (24.1%)	8 (5.9%)	12 (9.0%)
Vitreous floaters	3 (2.3%)	6 (4.4%)	12 (9.0%)
Eye pain	4 (3.0%)	10 (7.4%)	5 (3.7%)
Retinal exudates	5 (3.8%)	5 (3.7%)	7 (5.2%)
Blepharitis	1 (0.8%)	2 (1.5%)	6 (4.5%)
Vitreous detachment	1 (0.8%)	4 (3.0%)	4 (3.0%)
Cataract	1 (0.8%)	3 (2.2%)	4 (3.0%)
Dry eye	4 (3.0%)	3 (2.2%)	4 (3.0%)
Diabetic retinopathy	13 (9.8%)	2 (1.5%)	3 (2.2%)
Visual impairment	0	1 (0.7%)	4 (3.0%)

Serious Ocular Events, APTC Events and Deaths through Week 52

Serious Ocular AEs

One patient had an SAE of Iris neovascularization, and one patient had 2 SAEs of vitreous hemorrhage and visual acuity reduced.

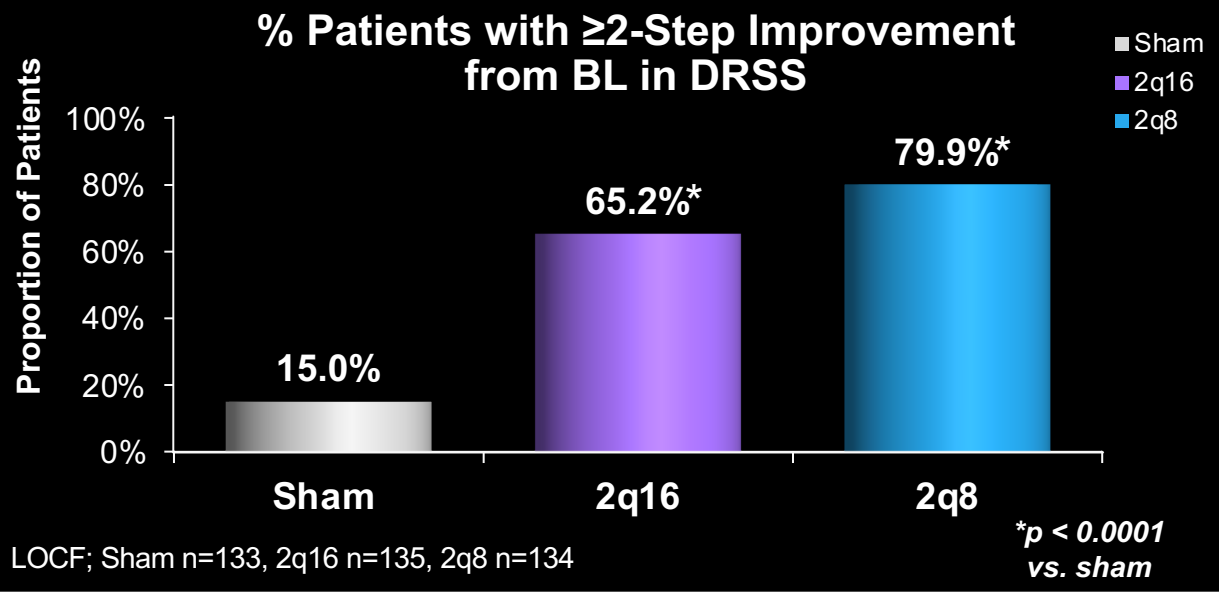
APTC EVENTS

	Sham	2q16	2q8
N (FAS/SAF)	133	135	134
Number of Patients with at Least One Such AE, n (%)	5 (3.8%)	4 (3.0%)	2 (1.5%)

Deaths

Deaths	6 (4.5%)	0	1 (0.75%)

PANORAMA 52 Week Results



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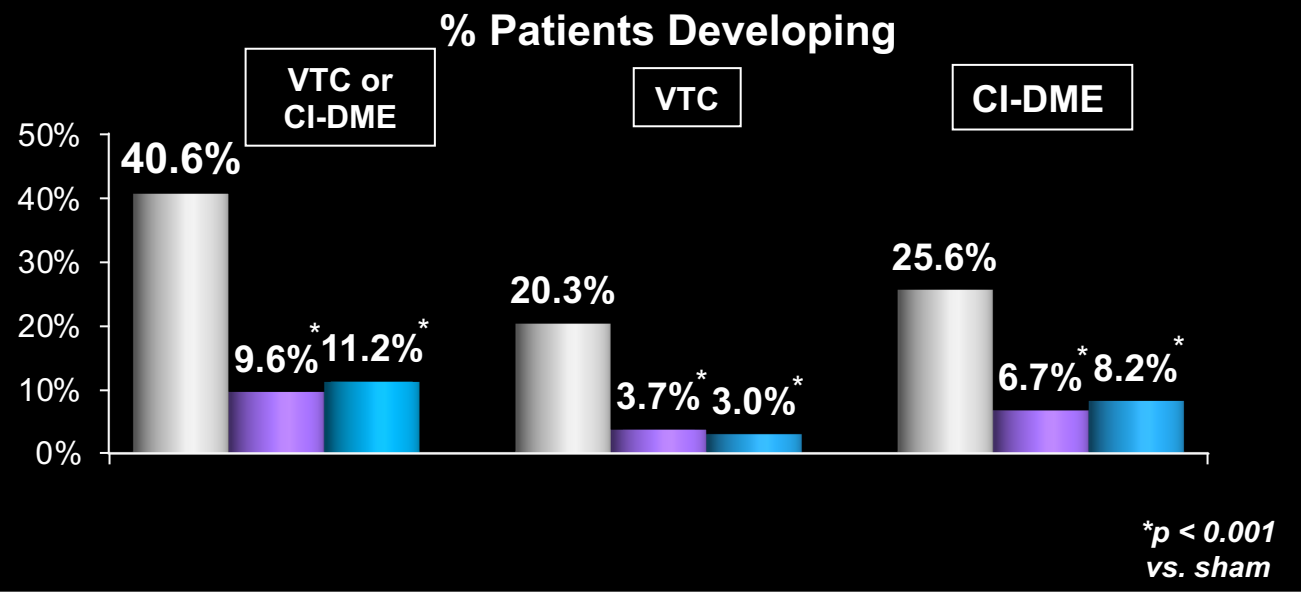
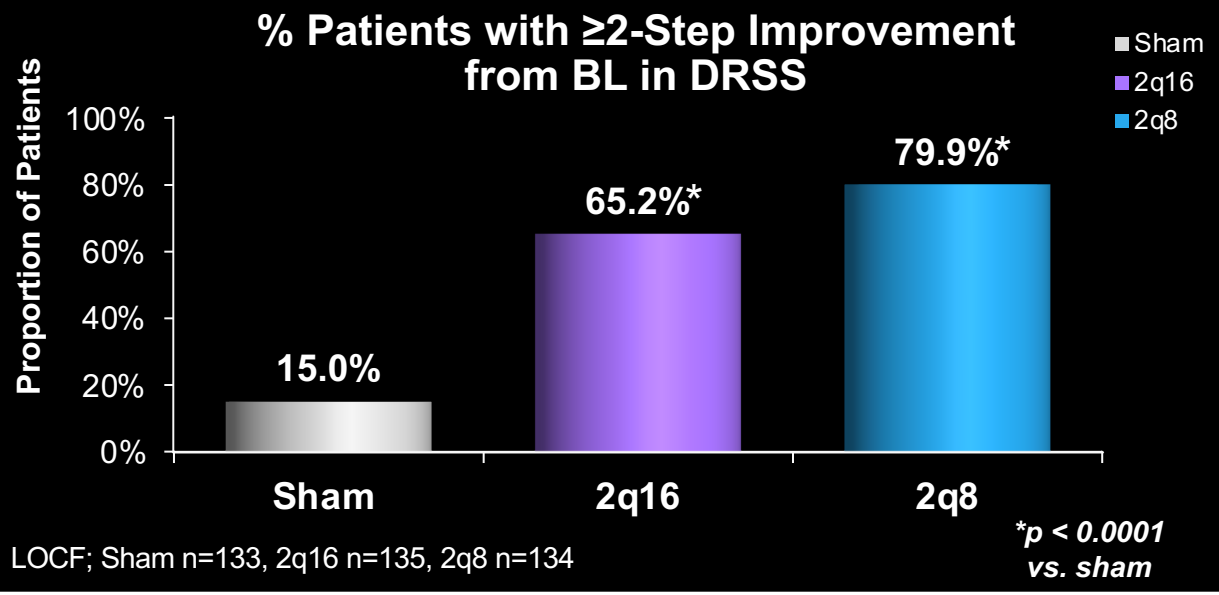
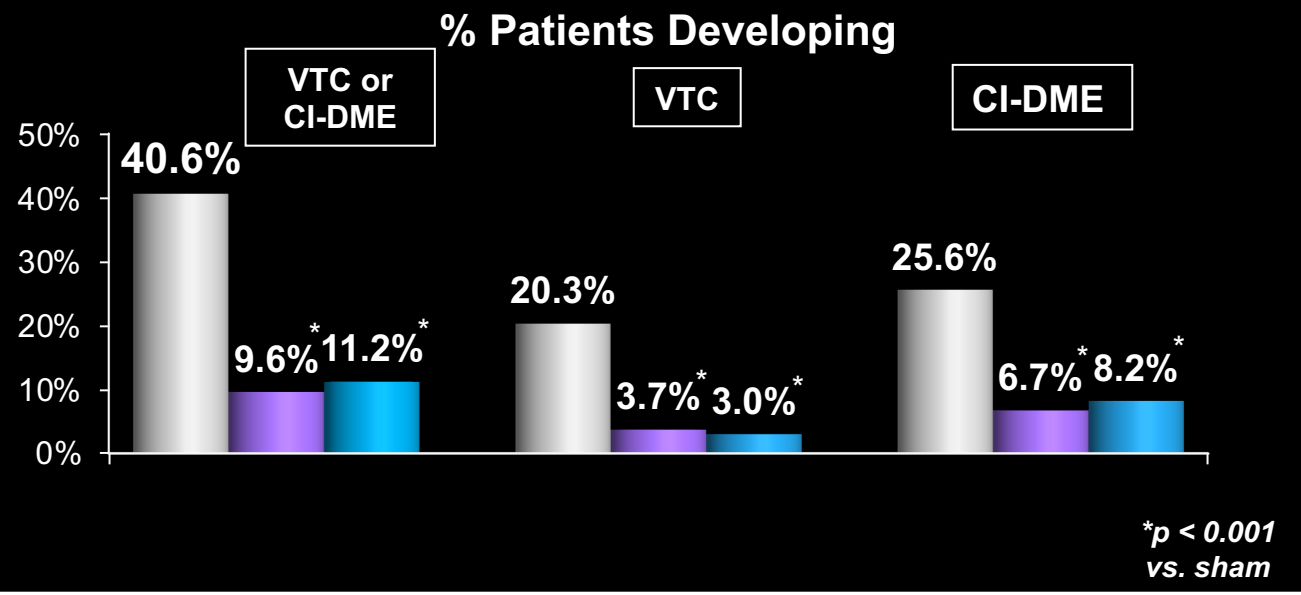


- First large, prospective trial of high-risk NPDR eyes (moderately severe & severe NPDR) without DME since the ETDRS
- The proportion of patients with ≥ 2-step improvements in DRSS significantly greater with aflibercept
- PDR/ASNV & CI-DME occurred in a substantially greater proportion of sham patients
- No new safety signals identified

PANORAMA 52 Week Results





- PANORAMA provides high-quality data to inform management of eyes with moderately severe and severe NPDR without DME
- PANORAMA is a 100-week study

Thank You


Japan (6 sites)
Europe
Germany (3 sites)
Hungary (5 sites)
United Kingdom (2 sites)
USA
(71 sites)
PANORAMA Study Sites