Tarcocimab Tedromer for Diabetic Retinopathy: Primary Endpoint Efficacy and Safety Outcomes of the GLOW Phase 3 Pivotal Study

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on behalf of the GLOW Study Group

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Disclosures

This presentation will discuss IRB/IEC approved research of an investigational medicine.

Charles Wykoff has the following financial interests or relationships to disclose:

4DMT (C, R), Abbvie (C), Adverum (C,R), Aerie (C), AffaMed (R), AGTC (C), Alcon (C), Alexion (R), Alimera (R), Allgenesis (R), Amgen (R), Annexin (R), Annexon (C,R), Apellis (C, R), Arrowhead (C), Ascidian (C), Asclepix (R), Bausch + Lomb (C), Bayer (C, R), Boehringer Ingelheim (C,R), Chengdu Kanghong (R), Cholgene (C), Clearside (C,R), Curacle (C, R), Eyebiotech (C, R), EyePoint (C, R), Foresite (C), Frontera (C), Genentech (C,R), Gyroscope (C, R), IONIS (R), iRENIX (R), IVERIC Bio (C,R), Janssen (C, R), Kato (C), Kiora (C), Kodiak (C,R), LMRI (R), McMaster University (R), Merck (C), Nanoscope (C,R), Neurotech (C, R), NGM (C,R), Notal Vision (C), Novartis (C, R), Ocular Therapeutix (C, R), Ocuphire (C, R), OcuTerra (C, R), OliX (R), ONL (C, SO), Opthea (C,R), Oxurion (R), Oxular (C,R), Oyster Point (R), Palatin (C), PerceiveBio (C, R), PolyPhotonix (SO), Ray (C), RecensMedical (C, SO), Regeneron (C,R), RegenXBio (C,R), Resonance (C), Rezolute (R), Roche (C, R), SamChunDang (R), Sandoz (C,R), Sanofi (C), SciNeuro (C), Shanghai Henlius (R), Stealth (C), Surrozen (C), Suzhou Raymon (C), THEA (C), Therini (C), TissueGen (SO), UNITY (R), Valo (C), Verily, (R) Visgenx (SO), Vitranu (SO)

C= Consultant | R= Research Support | O= Ownership/Stock Options

KSI-301 (tarcocimab tedromer) and Antibody Biopolymer Conjugates (ABCs)

ANTIBODY

IgG1 Anti-VEGF Antibody

BIOPOLYMER

Branched, Optically Clear,
High Molecular Weight
Phosphorylcholine Polymer

CONJUGATE

KSI-301 (tarcocimab tedromer) is an anti-VEGF ABC that blocks all VEGF-A isoforms

GLOW – Study design – 4 total doses in Year 1
Unprecedented progressive extension of intervals to 6-month dosing

Randomized, double-masked, multi-center Phase 3 superiority study of tarcocimab tedromer 5 mg in moderately severe to severe non-proliferative diabetic retinopathy

Tarcocimab 5 mg Extended Interval Dosing

Sham

Primary endpoint – Week 48

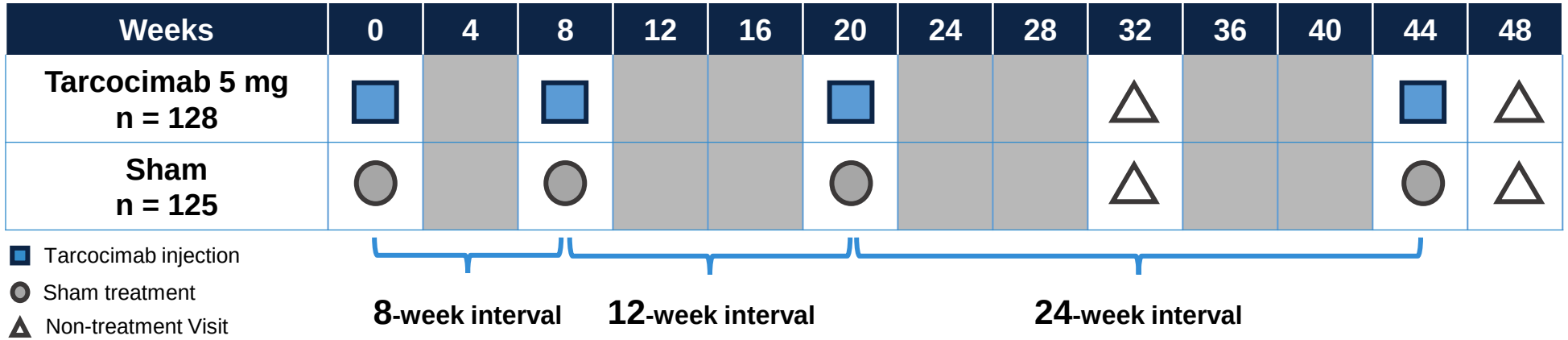
Proportion of eyes improving ≥2 steps on DRSS from baseline

Key Secondary endpoints

Proportion of eyes developing sight-threatening complications[a]

Proportion of eyes improving ≥3 steps on DRSS from baseline

End of Study at Week 100[b]



[a]Sight-threatening complications were defined as: diabetic macular edema, proliferative diabetic retinopathy, and anterior segment neovascularization.
[b]Study was terminated after all participants had completed the primary endpoint visit at Week 48.
DRSS: diabetic retinopathy severity score; GLOW Study KS301P106, NCT05066230. Tarcocimab tedromer also referred to as tarcocimab in this presentation.

GLOW: Key eligibility criteria

Key Inclusion Criteria

- Anti-VEGF treatment-naïve **moderately severe to severe NPDR (DRSS levels 47 and 53)** determined by the central reading center in whom PRP can safely deferred for at least 6 months
- BCVA ≥ 69 letters (≥20/40 Snellen equivalent)
- HbA1c of ≤12%

Key Exclusion Criteria

- Presence of center involving DME in the Study Eye (CST ≥ 320 microns)
- Prior PRP in the Study Eye
- Prior treatment with anti-VEGF therapy or intravitreal or peri-ocular steroid in the Study Eye
- Active or suspected ocular or periocular infection or inflammation in either eye
- Current anterior segment neovascularization, vitreous hemorrhage, or tractional retinal detachment in the Study Eye
- Recent history (within 6 months) of myocardial infarction, stroke, transient ischemic attack, acute congestive heart failure, or acute coronary event.

VEGF: vascular endothelial growth factor; NPDR: non-proliferative diabetic retinopathy; DRSS: diabetic retinopathy severity score; PRP: pan-retinal photocoagulation; BCVA: best-corrected visual acuity; DME: diabetic macular edema; CST: central subfield thickness

First Time Results

Baseline patient demographics and general characteristics

	Tarcocimab n = 128	Sham n = 125
Age, years, mean (SD)	56.4 (11.39)	57.0 (9.63)
Female, n (%)	51 (39.8)	56 (44.8)
Race, n (%)		
White	108 (84.4)	96 (76.8)
Black or African American	13 (10.2)	23 (18.4)
Asian	3 (2.3)	3 (2.4)
Other	4 (3.1)	3 (2.4)
Ethnicity, n (%)		
Not Hispanic or Latino	71 (55.5)	73 (58.4)
Hispanic or Latino	57 (44.5)	52 (41.6)
Hemoglobin A1c, % (SD)	8.33 (1.48)	8.45 (1.53)
Diabetes Type 2, n (%)	119 (93)	116 (92.8)

n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm.

Baseline ocular characteristics were well-matched between groups and typical of treatment-naïve NPDR patients. Most patients (≥92%) completed the study

Baseline ocular characteristics and patient disposition

	Tarcocimab n = 128	Sham n = 125
BCVA, ETDRS Letters, mean (SD)	**81.8 (5.79)**	**81.2 (5.76)**
Central Subfield Thickness (CST), µm, mean (SD)	**268.6 (26.3)**	**265.3 (25.05)**
Lens Status, n (%)		
Phakic	107 (83.6)	101 (80.8)
Pseudophakic	21 (16.4)	24 (19.2)
DR severity (ETDRS DRSS score), n (%)		
≤ Level 47	46 (35.9)	45 (36)
≥ Level 53	82 (64.1)	80 (64)
Intraocular Pressure, mmHg, mean (SD)	15.62 (3.21)	15.71 (3.35)

n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm.
BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; DRSS: diabetic retinopathy severity scale; CST: central subfield thickness; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy

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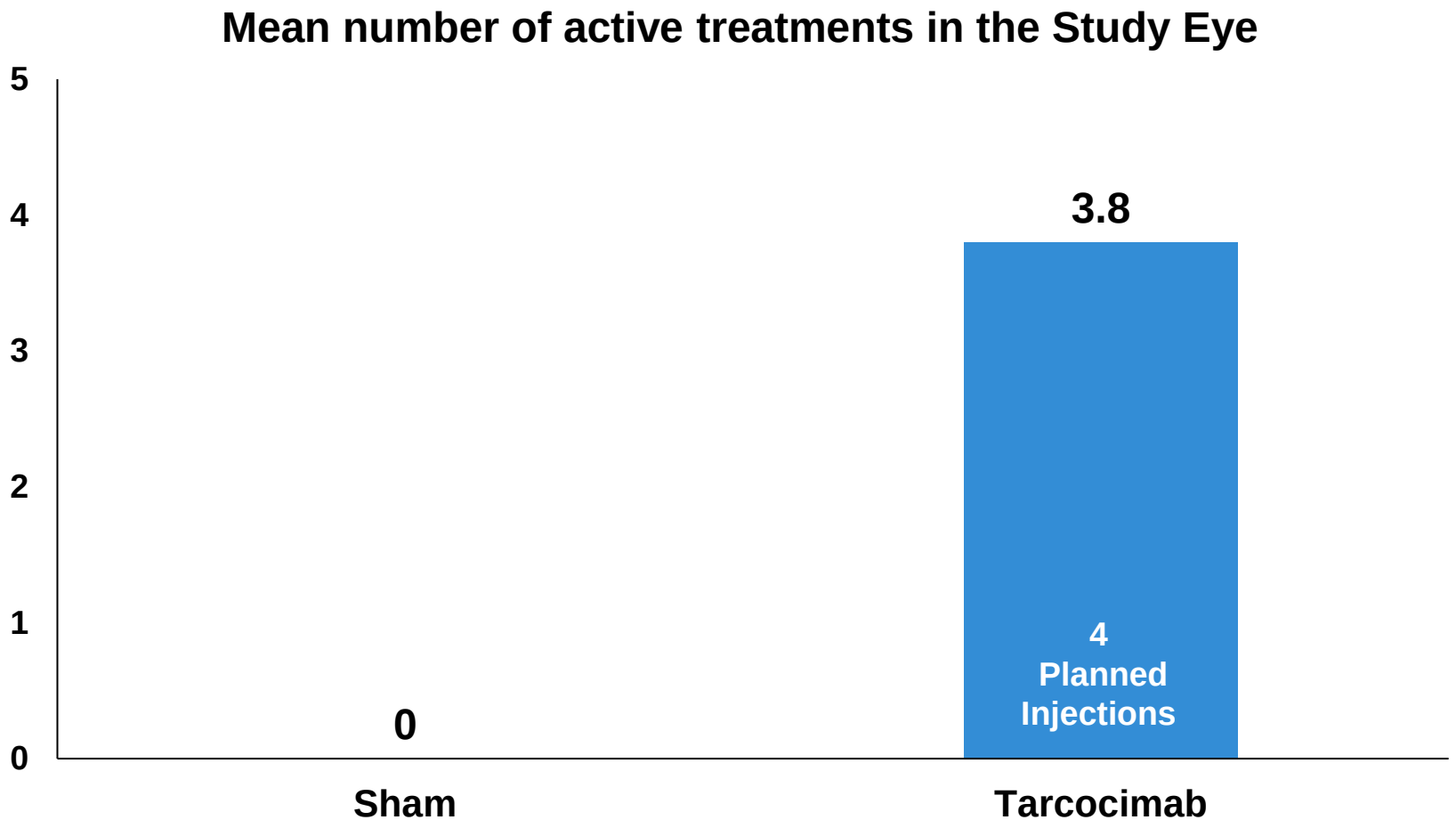
Patients treated, n (%)	**128 (100)**	**125 (100)**
Patients completing Week 48, n (%)	120 (93.8)	115 (92)
Discontinuations prior to Week 48, n (%)	8 (6.3)	10 (8)

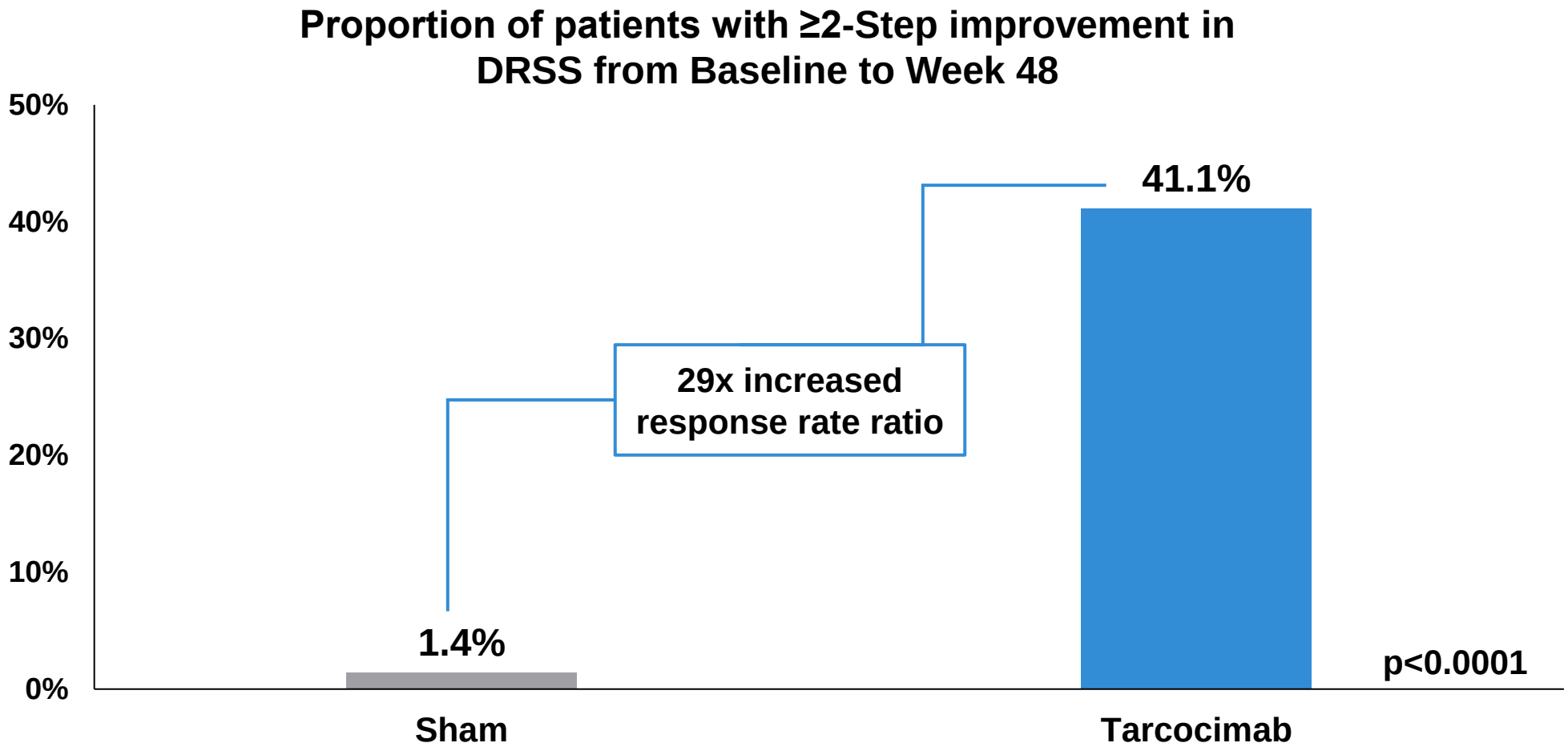
n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm.
BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; DRSS: diabetic retinopathy severity scale; CST: central subfield thickness; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy

Patients treated with tarcocimab received only 4 injections in Year 1



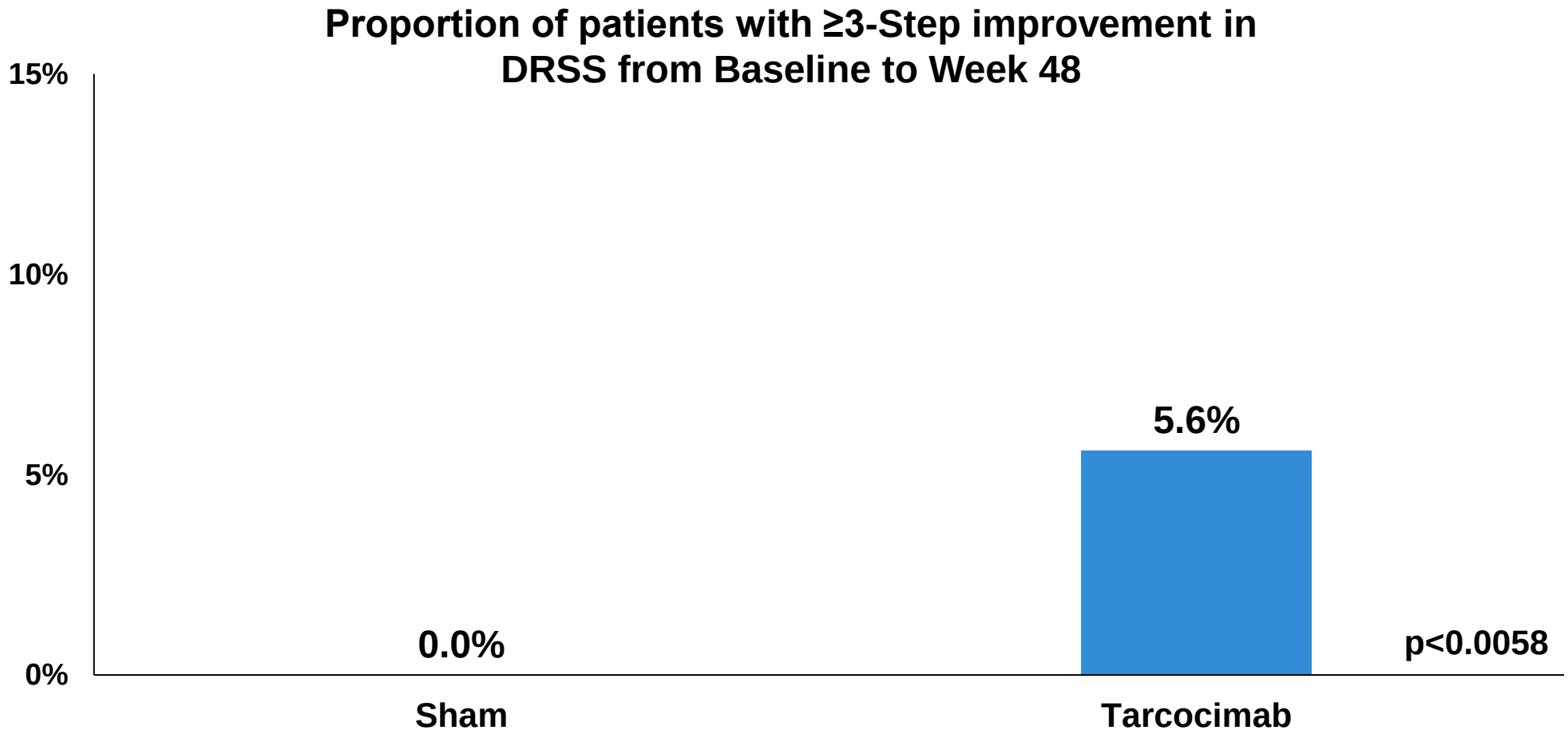
Sham (n=125); Tarcocimab (n=128)

Primary Endpoint Met – tarcocimab established superiority in ≥2-step improvement in DRSS



Sham (n=125); Tarcocimab (n=128); Week 48 (LOCF) represents the last available observation while on randomized treatment, within the Week 48 visit window. Note: Percentages are 100*n/N. Weighted percentages are based on weighted average of observed estimates across strata using CMH weights. p-values are based on the difference in response rates

Key Secondary Endpoint Met – tarcocimab also demonstrated superiority in ≥3-Step improvement in DRSS



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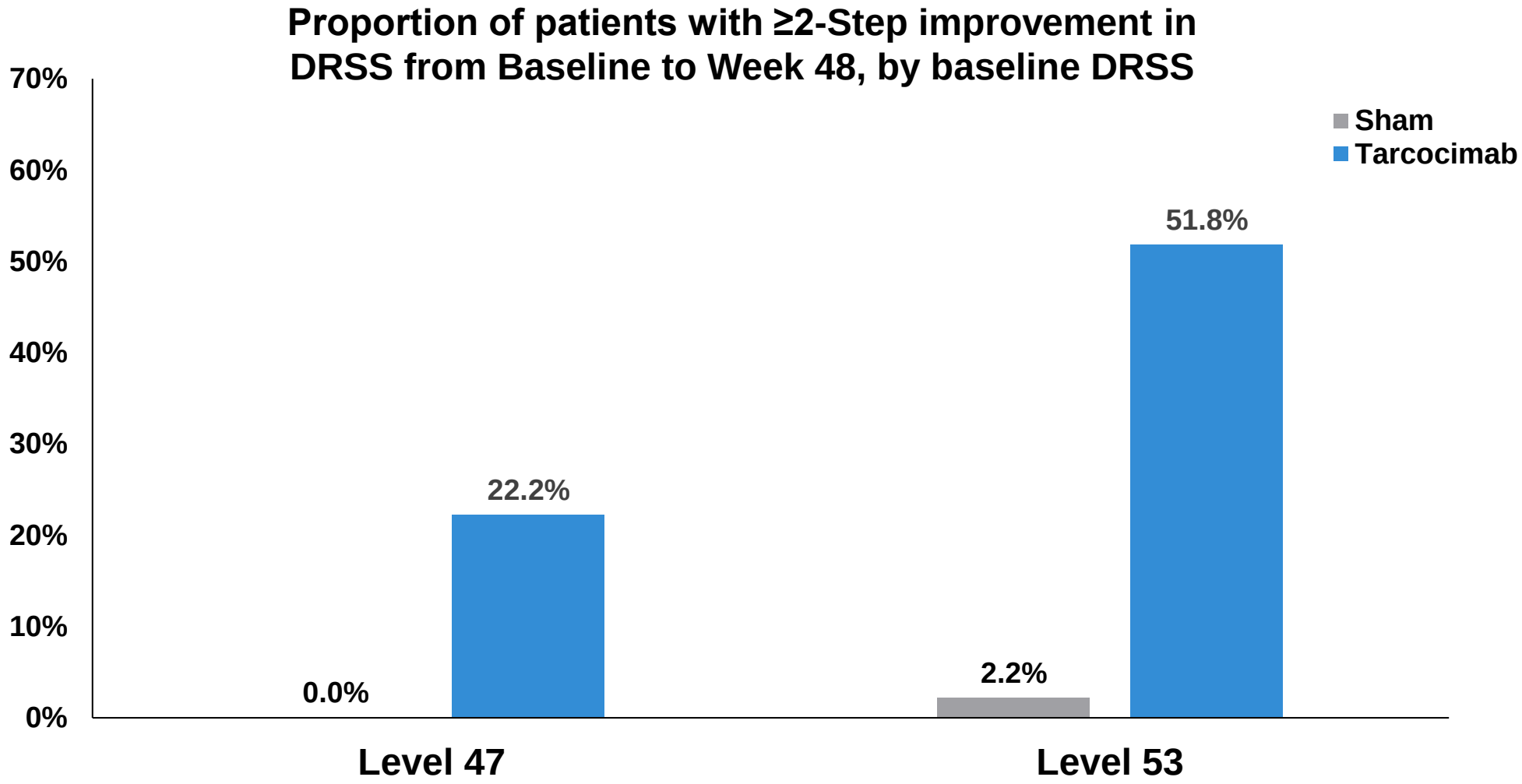
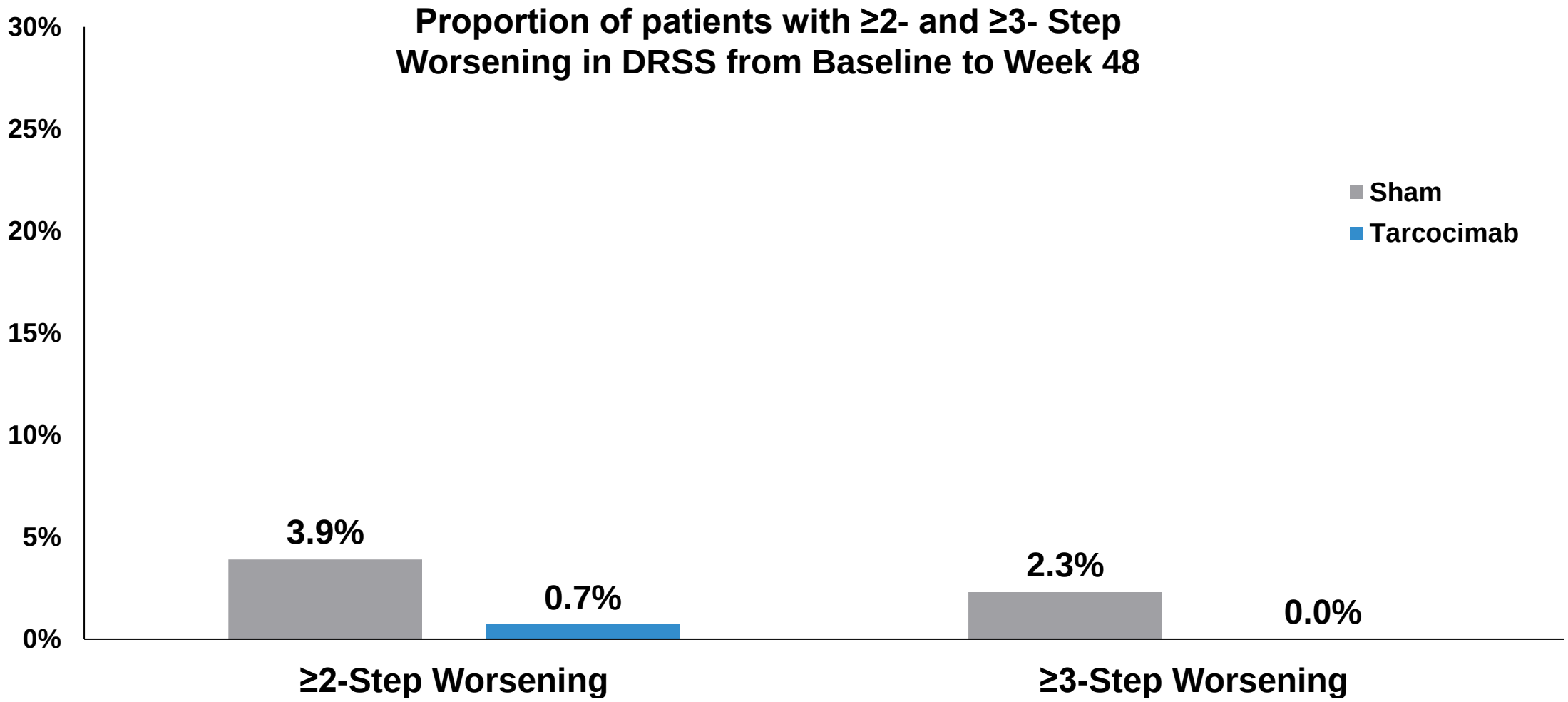
Tarcocimab improved the DRSS score irrespective of the baseline diabetic retinopathy level, showing excellent control in more severe disease



Sham Level ≤47 (n=45); Sham Level ≥53 (n=80); Tarcocimab Level ≤47 (n=46); Tarcocimab Level ≥53 (n=82); Note: Percentages are 100*n/N. Weighted percentages are based on weighted average of observed estimates across strata using CMH weights.

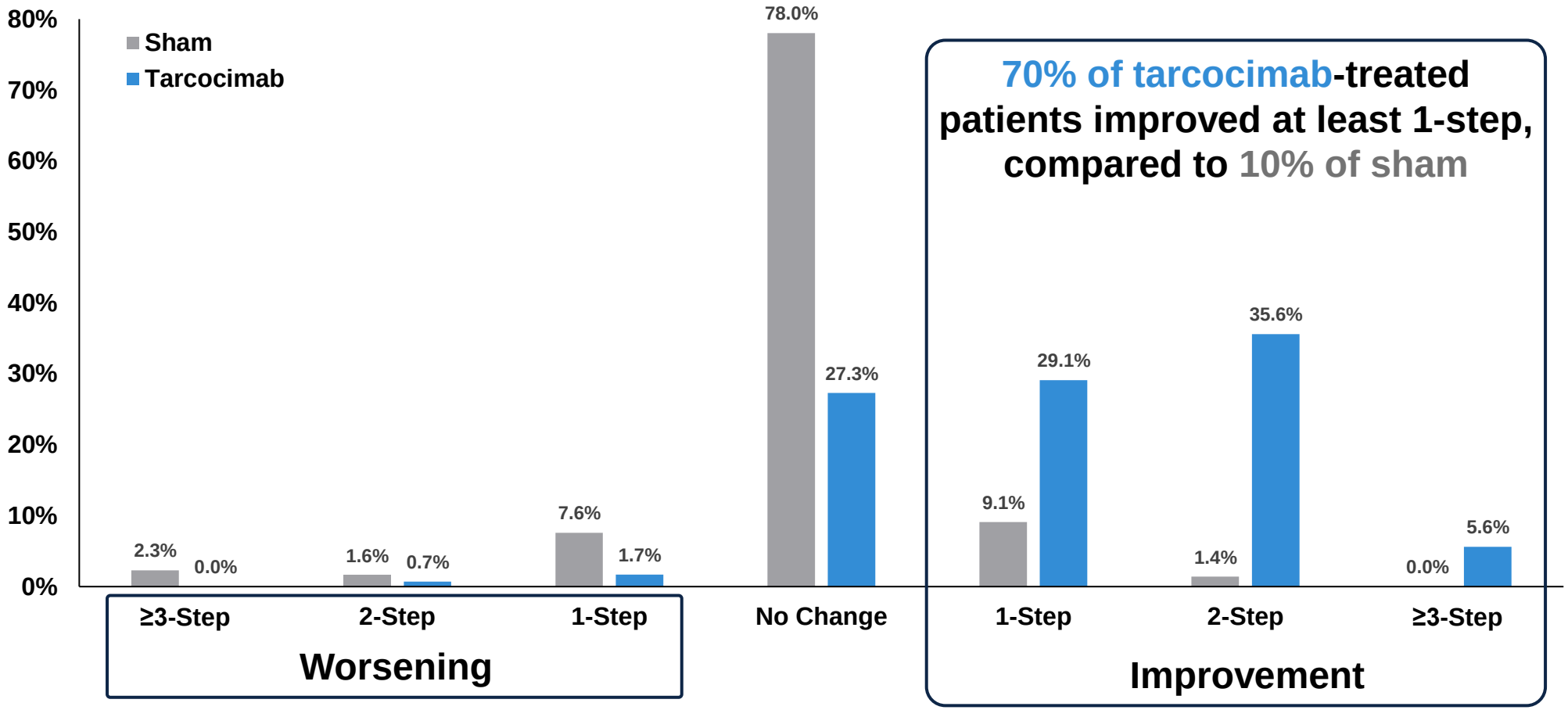
Treatment with tarcocimab resulted in a meaningful risk reduction of 2- and 3-step worsening in DRSS



DRSS: diabetic retinopathy severity score;
Weighted percentages are based on weighted average of observed estimates across strata using CMH weights.

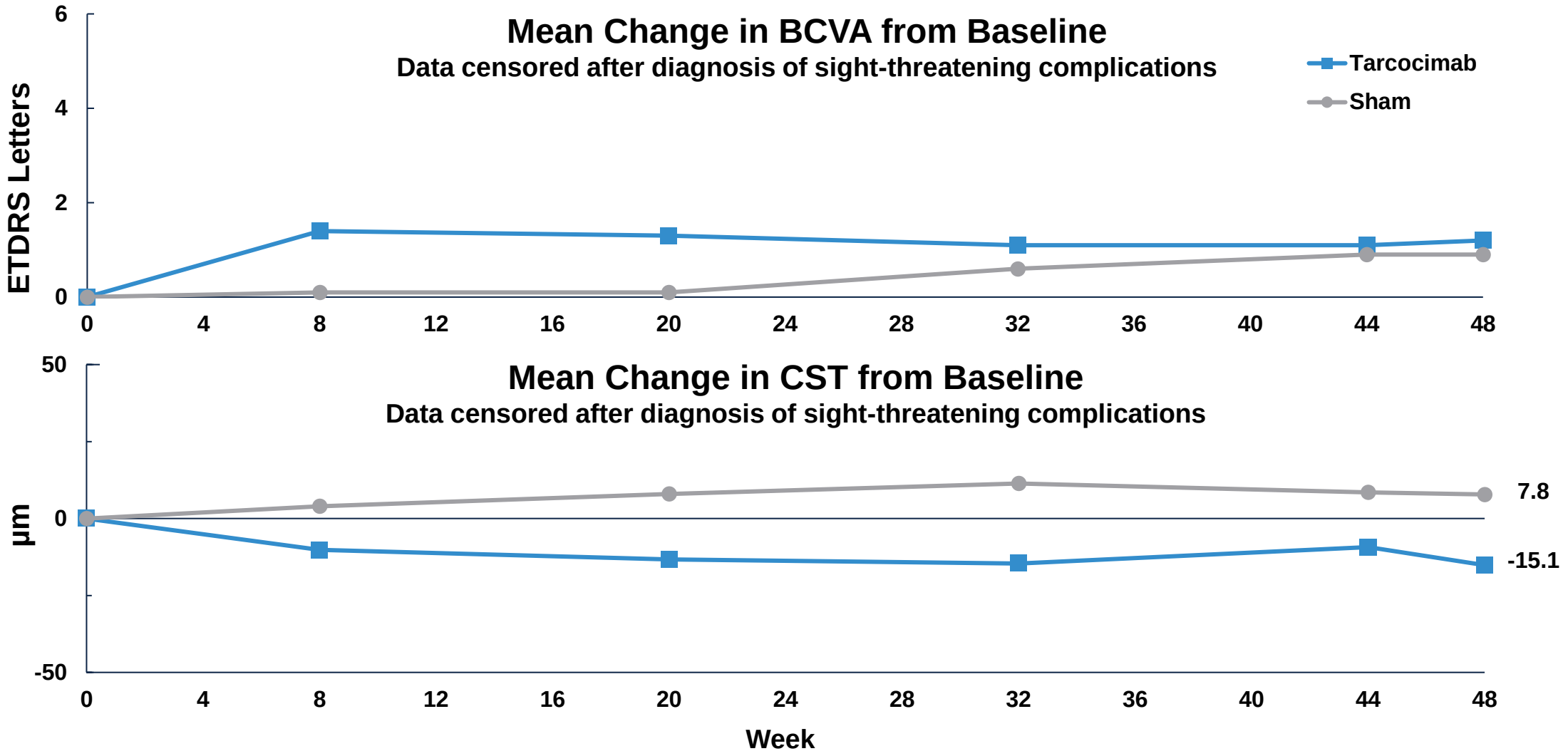
The majority of patients treated with tarcocimab demonstrated at least 1-step improvement in DRSS

Distribution of DRSS-step changes at Week 48



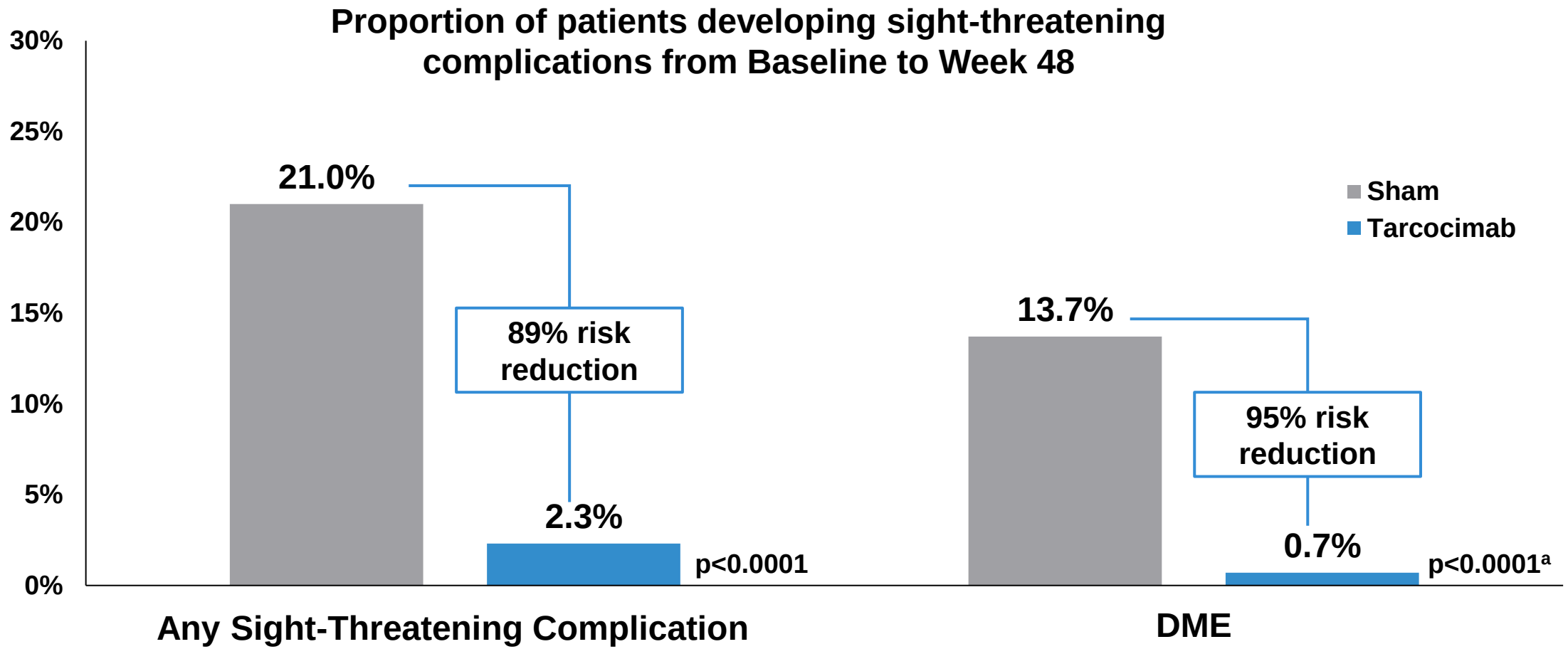
Sham (n=125); Tarcocimab (n=128); Week 48 (LOCF) represents the last available observation while on randomized treatment, within the Week 48 visit window. Note: Percentages are 100*n/N. Weighted percentages are based on weighted average of observed estimates across strata using CMH weights.

Visual acuity and retinal anatomy were improved and stable with tarcocimab on extended-dosing intervals



BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; CST: central subfield thickness; µm: microns
Sham (n=125); Tarcocimab (n=128); Results are based on a MMRM model including the change from baseline value as the dependent variable.
Patients that developed sight-threatening complications in either arm were treated with open-label tarcocimab and all subsequent data was censored.

Key Secondary Endpoint Met – tarcocimab reduced the risk of developing pre-specified sight-threatening complications by ~90%

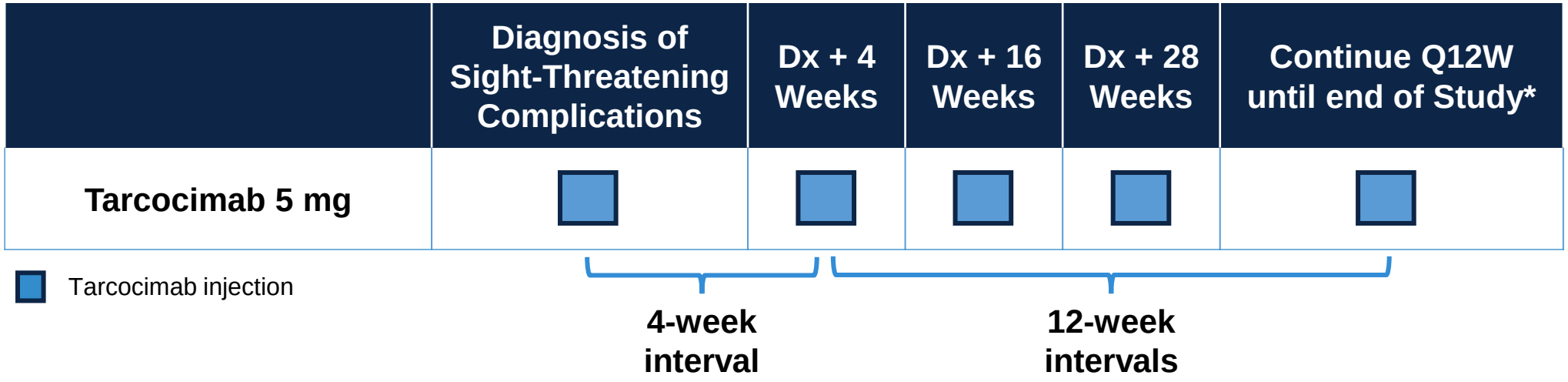


DME	CST of ≥320 and a 5-letter decrease in BCVA from Day 1; *or* CST of ≥350
PDR	NVD or NVE; or VH
ANSV	ASNV; or NVG

DME; diabetic macular edema; PDR; proliferative diabetic retinopathy; ASNV: anterior segment neovascularization; CST; central subfield thickness; BCVA; best corrected visual acuity; NVD: neovascularization of the disc; NVE; neovascularization elsewhere; VH: vitreous hemorrhage; NVG; neovascular glaucoma.
Weighted percentages are based on weighted average of observed estimates across strata using CMH weights. p-values are based on the difference in response rates
a. nominal p-value

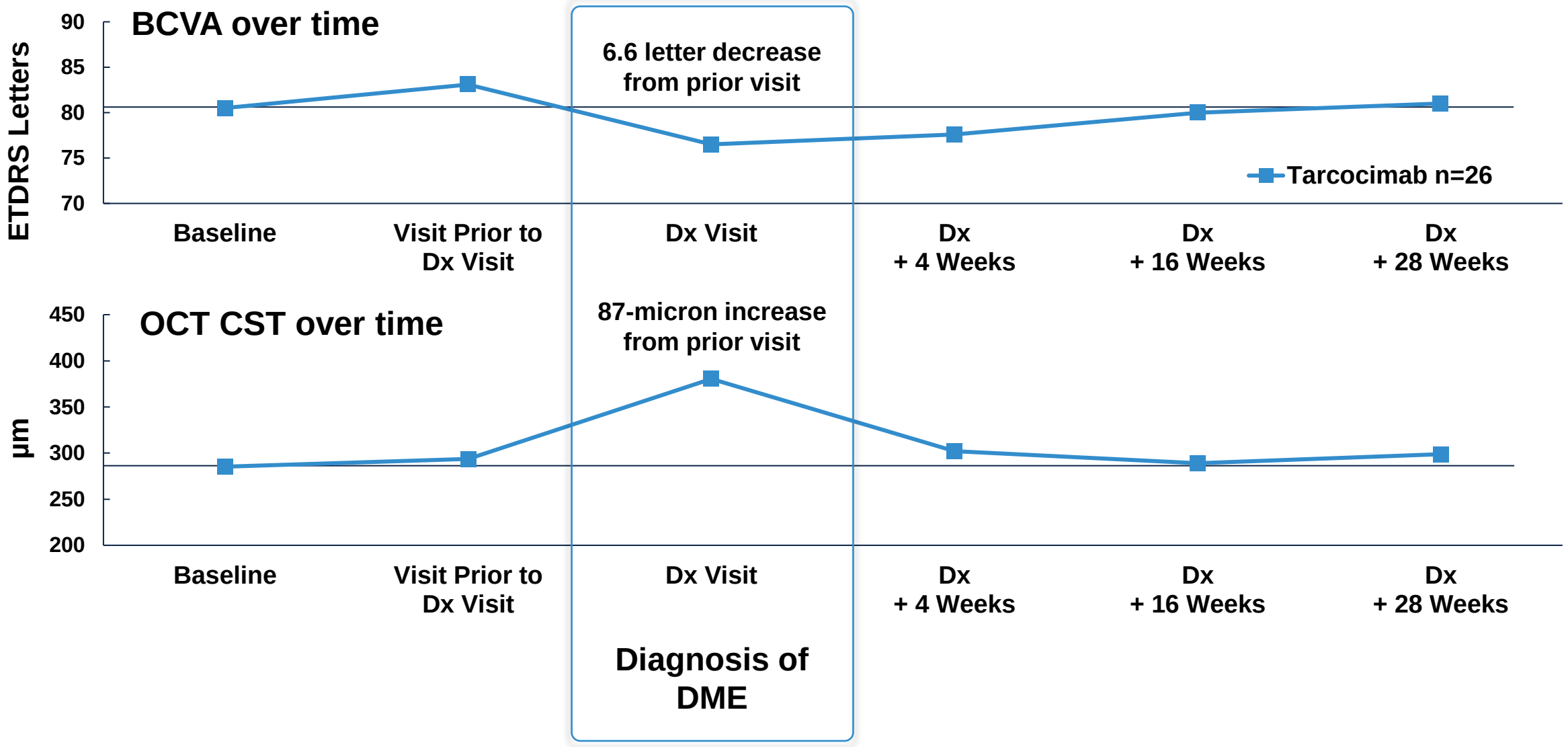
Participants developing sight-threatening complications in both groups were treated with open-label tarcocimab, starting with two monthly loading doses and then Q12W dosing

Treatment schedule for patients developing STCs



*The end of the study for any patient was approximately 100 weeks after the baseline visit
Q12W: every 12 weeks;

In patients developing DME, the initial VA decrease and CST increase were both rapidly controlled and then stabilized with Q12W dosing



Includes 8 patients that developed DME (diabetic macular edema) after the Primary Endpoint

Safety: tarcocimab was safe and well-tolerated, with low rates of common ocular adverse events

Common Ocular Adverse Events (AEs) up to Week 48	Tarcocimab n = 128	Sham n = 125
Subjects with any AE in the Study Eye, n (%)	42 (32.8)	43 (34.4)
Total number of AEs, n (%)[a]		
Cataract	13 (10.2)	5 (4.0)
Conjunctival hemorrhage	9 (7.0)	4 (3.2)
Dry eye	4 (3.1)	2 (1.6)
Vitreous floaters	3 (2.3)	1 (0.8)
Diabetic macular edema	2 (1.6)	18 (14.4)
Diabetic retinopathy	2 (1.6)	8 (6.4)

Cataract AE up to Week 48[b]	Tarcocimab n = 128	Sham n = 125
Subjects with Cataract AE in the Study Eye	15 (11.7%)	5 (4.0%)
Subjects with Cataract AE in the Fellow Eye	8 (6.3%)	3 (2.4%)

Results presented for the Safety Population (≥2.0% in either study arm). Events are investigator reported. Adverse events are events with start date ≥first study drug date and ≤last study drug date + 28 days.

a. Includes all adverse events (AE) reported. A single patient can have multiple events of the same AE term reported and can be counted in different AE terms.

b. Total number of patients with one or more events of cataract (AE terms: cataract, cataract cortical, cataract nuclear, posterior subcapsular cataract and lenticular opacities). A patient with multiple events of the same AE term reported are only counted once.

Rates of intraocular inflammation were low in both treatment groups

Intraocular Inflammation in Study Eye up to Week 48	Tarcocimab n = 128	Sham n = 125
Subjects with at Least 1 Intraocular Inflammation AE*, n (%)	2 (1.6)	0

Endophthalmitis in Study Eye up to Week 48	Tarcocimab n = 128	Sham n = 125
Subjects with at Least 1 Endophthalmitis AE	0	0

No cases of vasculitis or vascular occlusion were observed in any tarcocimab-treated patient, including sham patients treated with tarcocimab for sight threatening complications

*Reported AE terms: anterior chamber cell, anterior chamber flare, vitritis. Both cases: 1+, resolved with standard of care steroid therapy, retreated with tarcocimab without inflammation recurrence.
Results presented for the Week 48 Safety Population. Events are investigator reported. Adverse events are events with start date ≥first study drug date and ≤last study drug date + 28 days.

Tarcocimab can provide a clinically meaningful reduction in treatment burden for the management of diabetic retinopathy

Currently approved anti-VEGF therapies for Diabetic Retinopathy

Weeks	0	4	8	12	16	20	24	28	32	36	40	44	48	Doses in Year 1
Ranibizumab 0.3 mg Every month	●	●	●	●	●	●	●	●	●	●	●	●	●	13
Aflibercept 2 mg Every 8 weeks	●	●	●	●	●		●		●		●		●	9
Aflibercept 8 mg Every 8 to 12 weeks	●	●	●			●			●			●		6-8

Tarcocimab extended intervals to 6-month dosing

Weeks	0	4	8	12	16	20	24	28	32	36	40	44	48	Doses in Year 1
Tarcocimab 5 mg Every 6 months	■		■			■						■		4

8-week **12-week** **24-week**

Lucentis US prescribing information; Eylea US prescribing information; Eylea HD US prescribing information

Glow Study Conclusions

Tarcocimab met superiority in NPDR	• Primary Endpoint met: superiority in ≥2-step improvement (29x over sham) • Key Secondary Endpoint met: superiority in ≥3-step improvement • Key Secondary Endpoint met: superiority in reduction of development of sight-threatening complications (90% risk reduction)
Tarcocimab continues to demonstrate 6-month durability	• Superiority was achieved with only 4 total doses in Year 1 • With no loading doses, all tarcocimab-treated patients reach 6-month dosing in the first year due to an unprecedented progressive extension of intervals
Safe and well-tolerated	• Low rates of intraocular inflammation and no cases of intraocular inflammation with vasculitis or vascular occlusion • No new or unexpected ocular or non-ocular safety signals
An enhanced formulation of tarcocimab is available	An enhanced commercial formulation of tarcocimab with a combination of free and conjugated antibody has been manufactured for improved usability, decreasing the injection time from 7-10 seconds to 2-3 seconds
What is the future?	Three successful phase 3 pivotal trials in RVO, wAMD and now NPDR provide strong evidence for the benefit of Kodiak's ABC Platform and platform-derived medicines

Thank you to all GLOW investigators, site staff and patients

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