KSI-301 Anti-VEGF Antibody Biopolymer Conjugate for Retinal Vein Occlusion: Primary 24-Week Efficacy and Safety Outcomes of the BEACON Phase 3 Pivotal Study

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on behalf of the BEACON Study Group

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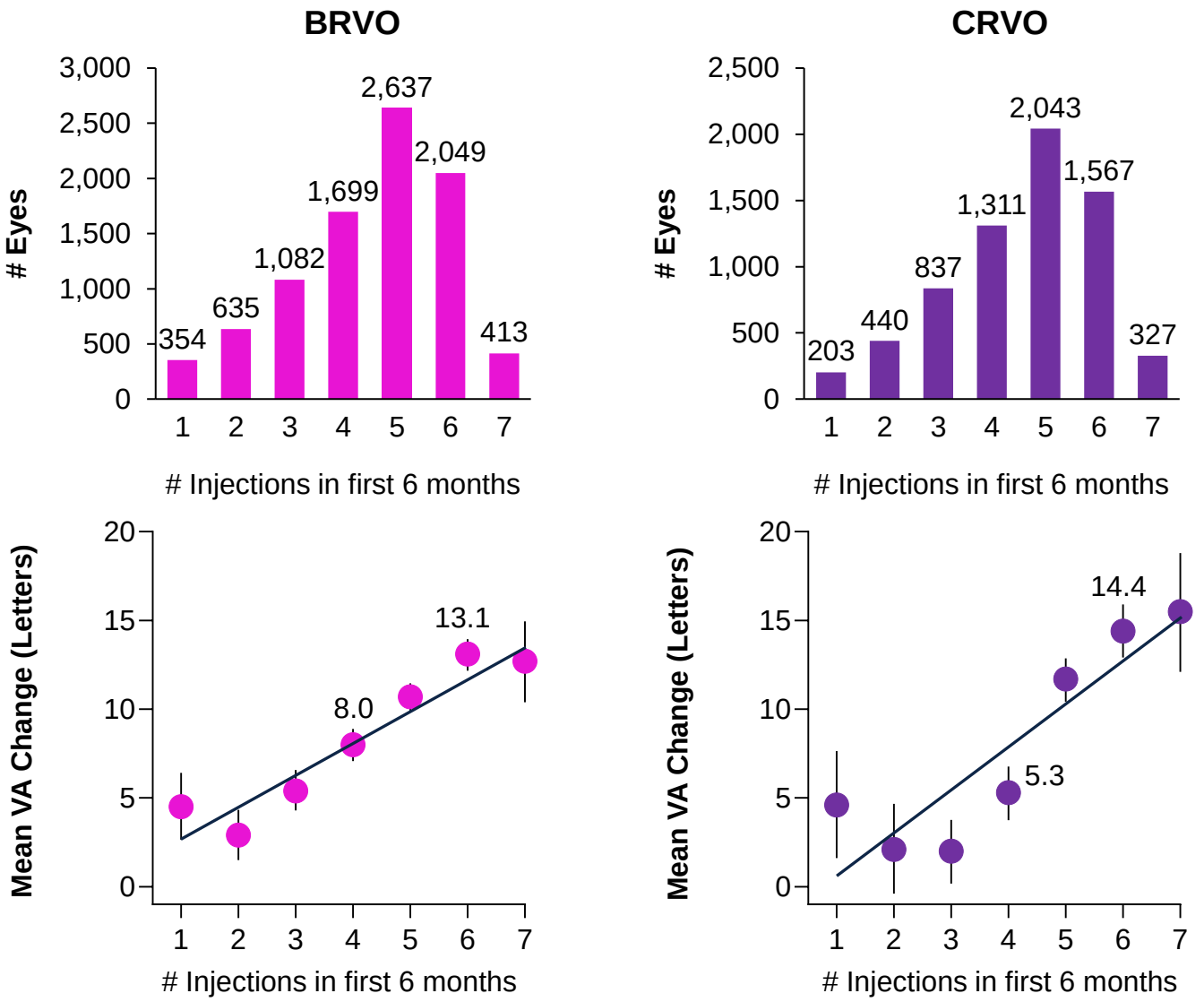
Disclosures

- Presenter's Financial Disclosures:
  - **Consultant**: Aerie, Allegro, Alimera, Allergan, Eyepoint, Genentech, Kodiak Sciences, Novartis, Regeneron, Santen
  - **Contracted Research**: Aerie, Alimera, Allegro, Allergan, DRCR.net, Genentech, Icon, Ionis, Kalvista, Kodiak Sciences, Novartis, Opthea, Optos, Regeneron, Santen, Senju, Sydnexis
  - **Equity**: Aviceda, Inflammasome, Nanoscope
  - **Speakers Bureau**: Allergan, Genentech, Mallinckrodt, Novartis, Regenerson, Spark
- This presentation will discuss IRB/IEC approved research of an investigational medicine.

RVO real-world anti-VEGF treatment outcomes fall short of clinical trial outcomes – more durable treatments are needed



Monthly dosing is difficult to achieve in clinical practice, where **72% of patients received less than monthly dosing**

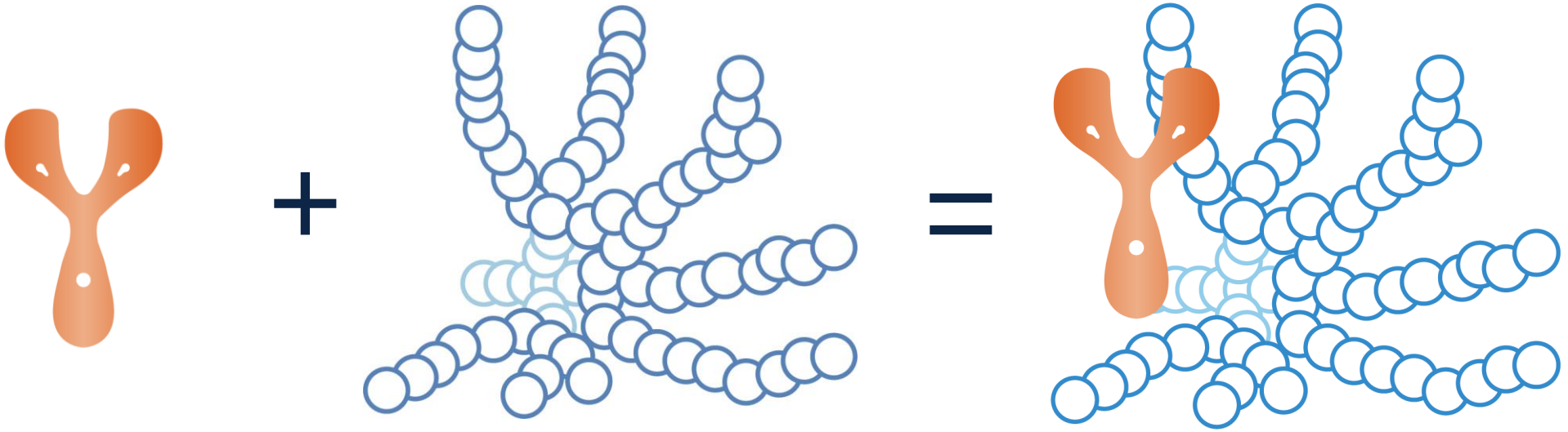
With currently available anti-VEGFs, treatment less often than monthly compromises vision outcomes in RVO

A less frequent therapy that achieves comparable outcomes would be an important advance

Adapted from Ciulla T, et al. Br J Ophthalmol 2021;105:1696–1704. doi:10.1136/bjophthalmol-2020-317337. Represents 8,876 BRVO eyes, 6,737 CRVO eyes from Vestrum database. Mean 4.5 and 4.6 anti-VEGF injections over first 6 months (aflibercept, ranibizumab, or bevacizumab) in BRVO and CRVO, respectively. VA, Visual acuity. RVO, retinal vein occlusion. BRVO, branch retinal vein occlusion. CRVO, central retinal vein occlusion.

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

A novel class of biologics engineered for increased durability and efficacy



ANTIBODY

IgG1 Anti-VEGF Antibody
Immunologically inert

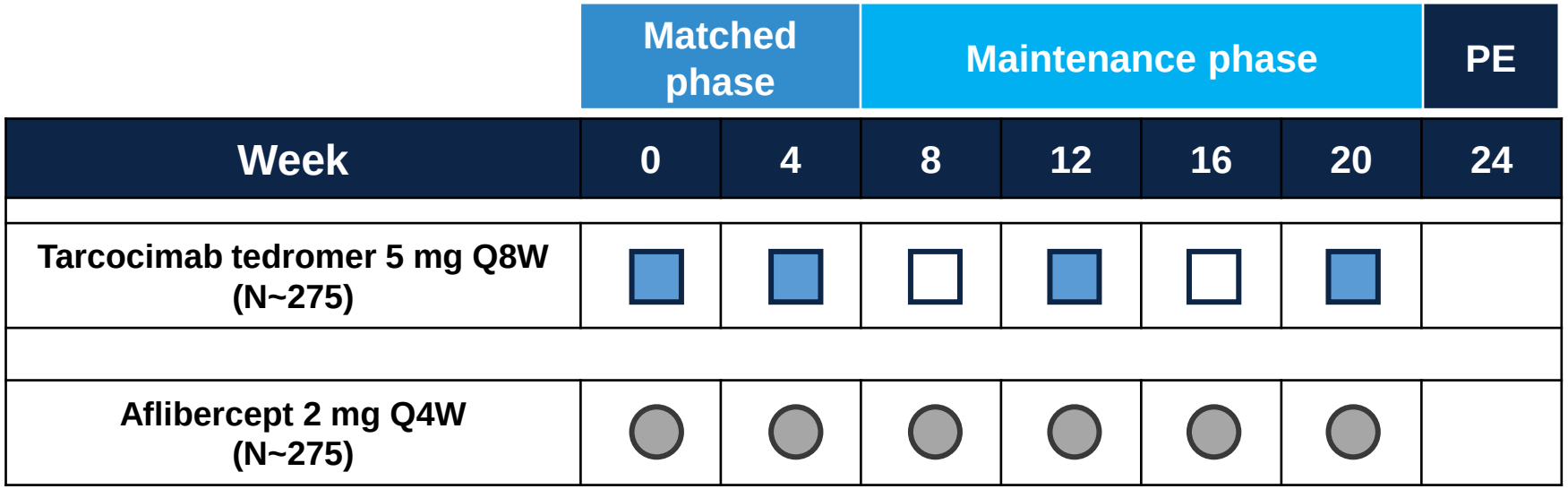
BIOPOLYMER

Branched, Optically Clear,
High Molecular Weight
Phosphorylcholine Polymer

CONJUGATE

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

BEACON: Phase 3 non-inferiority study of tarcocimab tedromer every 2 months after only two loading doses vs aflibercept every 1 month in treatment-naïve RVO patients



Months 6-12:
Individualized dosing in both arms

Months 12-18:
Open-label tarcocimab Individualized dosing

- Tarcocimab injection
- Aflibercept injection
- Sham injection

Primary Endpoint: Mean change in BCVA at Week 24

Hierarchical testing for control of type 1 error:

1. Test non-inferiority in BRVO patients
2. Test non-inferiority in all RVO patients (BRVO+CRVO)

Clinicaltrials.gov, study identifier: NCT04592419
RVO: retinal vein occlusion; PE: primary endpoint; BCVA: best-corrected visual acuity

Patient Eligibility Criteria

Key Ophthalmic Inclusion Criteria

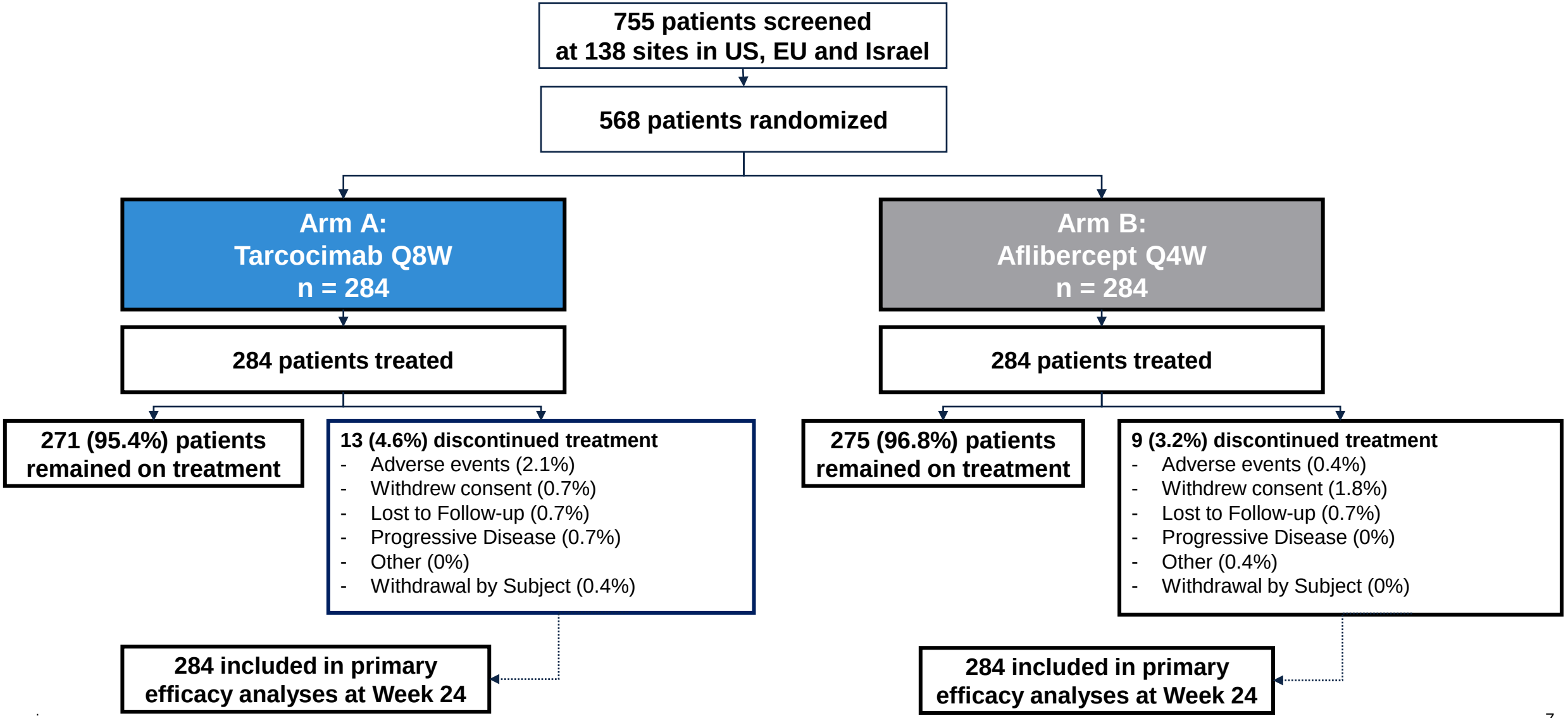
- Treatment-naïve macular edema secondary to RVO (BRVO or CRVO) of **≤ 6 months duration**
- **BCVA of 80 to 25 ETDRS letters** (≈20/25 to 20/320 Snellen)
- **CST of ≥320 microns** on SD-OCT

Key Ophthalmic Exclusion Criteria

- Macular edema in the Study Eye considered to be secondary to a cause other than RVO
- Active iris or angle neovascularization, neovascular glaucoma, neovascularization of the optic disc, retinal neovascularization or vitreous hemorrhage in the Study Eye
- Significant media opacities, including cataract, in the Study Eye that might interfere with visual acuity, assessment of safety, optical coherence tomography or fundus photography
- Prior vitrectomy in the Study Eye
- Active retinal disease other than the condition under investigation in the Study Eye
- Any history or evidence of a concurrent ocular condition that in the opinion of the Investigator could require either medical or surgical intervention or affect macular edema or alter visual acuity during the study (e.g. vitreomacular traction)
- **No specific exclusion for ischemic RVO**

ME: macular edema; RVO: retinal vein occlusion; BRVO: branch retinal vein occlusion; CRVO: central retinal vein occlusion; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; CST: central subfield thickness; SD-OCT: spectral domain optical coherence tomography.

Patient Disposition – discontinuations were low and balanced between groups; over 95% of patients remained on treatment



Baseline Ocular Characteristics – tarcocimab treated patients started at a slightly higher baseline BCVA

Parameter	Tarcocimab Q8W (n=284)		Aflibercept Q4W (n=284)	
RVO Type, n (%) BRVO CRVO	220 (77.5%) 64 (22.5%)		218 (76.8%) 66 (23.2%)	
	BRVO n=220	**All Patients** n=284	**BRVO** n=218	**All Patients** n=284
BCVA, ETDRS Letters, mean (SD)	**62.6 (12.24)**	**61.0 (13.19)**	**61.4 (13.33)**	**59.8 (14.18)**
≥20/40 Snellen equivalent, n (%)	81 (36.8%)	92 (32.4%)	75 (34.4%)	90 (31.7%)
≤20/200 Snellen equivalent, n (%)	12 (5.5%)	22 (7.7%)	17 (7.8%)	31 (10.9%)
BCVA Category, n (%)				
≤ 49 ETDRS Letters	27 (12.3%)	45 (15.8%)	30 (13.8%)	47 (16.5%)
50 – 69 ETDRS Letters	120 (54.5%)	155 (54.6%)	118 (54.1%)	155 (54.6%)
70 – 80 ETDRS Letters	73 (33.2%)	84 (29.6%)	70 (32.1%)	82 (28.9%)
Disease Duration, n (%)				
< 3 months	201 (91.4%)	262 (92.3%)	195 (89.4%)	256 (90.1%)
≥3 months	19 (8.6%)	22 (7.7%)	23 (10.6%)	28 (9.9%)
OCT Central Subfield Thickness (CST), µm, mean (SD)	526.0 (160.20)	568.4 (187.07)	543.5 (162.91)	587.5 (197.63)
Intraocular Pressure, mmHg, mean (SD)	15.3 (3.22)	15.1 (3.24)	15.3 (3.24)	15.2 (3.20)

n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm. Snellen equivalent of 20/40 is 69 ETDRS letters and of 20/200 is 38 ETDRS letters.
RVO: retinal vein occlusion; BRVO: branch retinal vein occlusion; CRVO: central retinal vein occlusion; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; OCT: optical coherence tomography

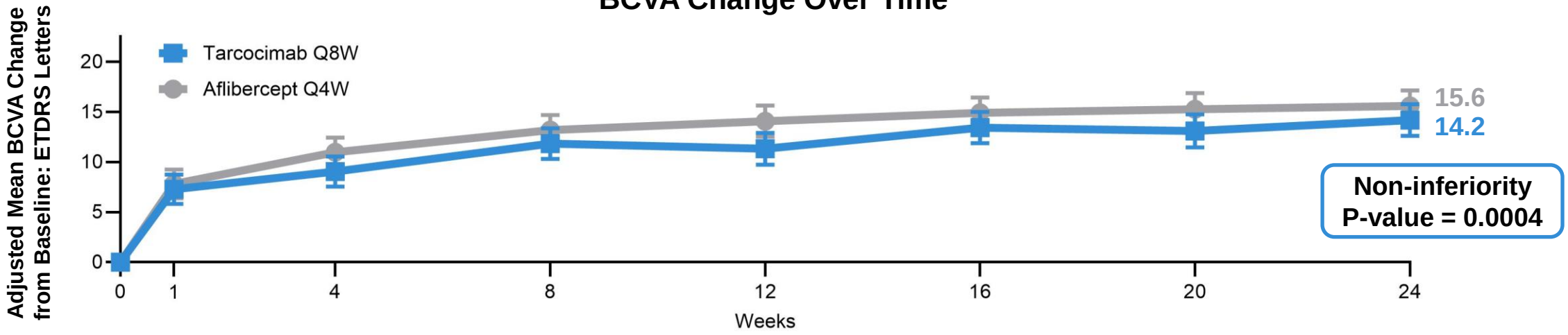
Results

Primary Endpoint Met

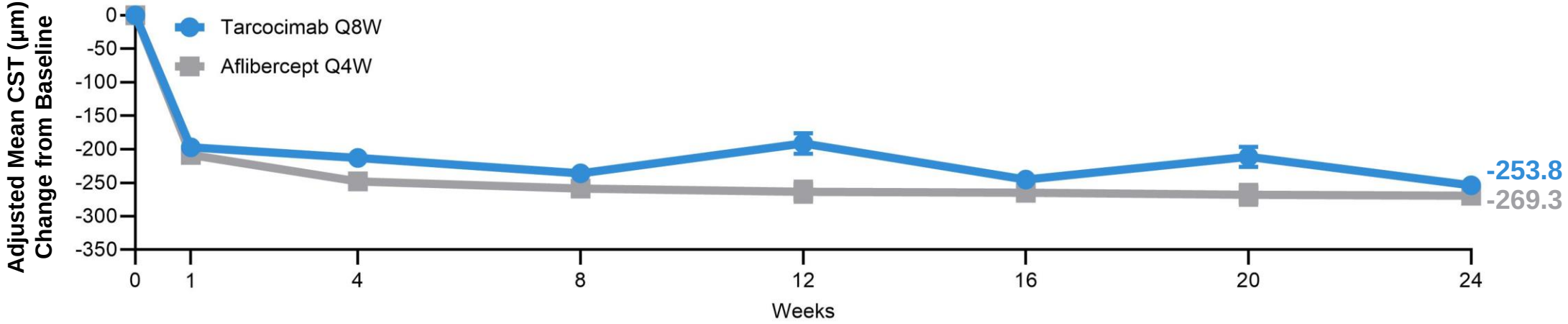
Tarcocimab Q8W was non-inferior to aflibercept Q4W in both BRVO and All RVO patients

Tarcocimab Q8W improved BCVA and OCT CST comparably to aflibercept Q4W from baseline to Week 24 in BRVO patients – non-inferiority to aflibercept demonstrated

BCVA Change Over Time

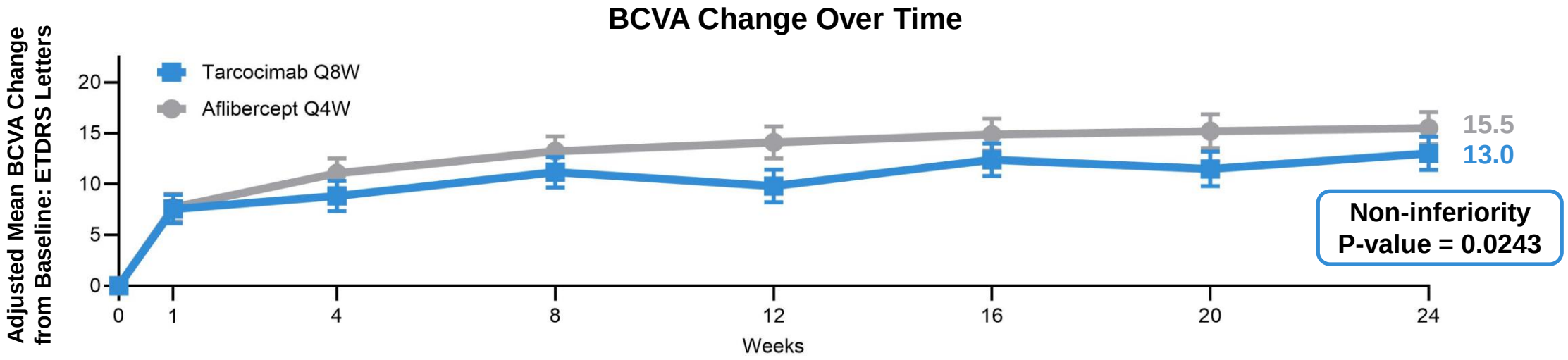


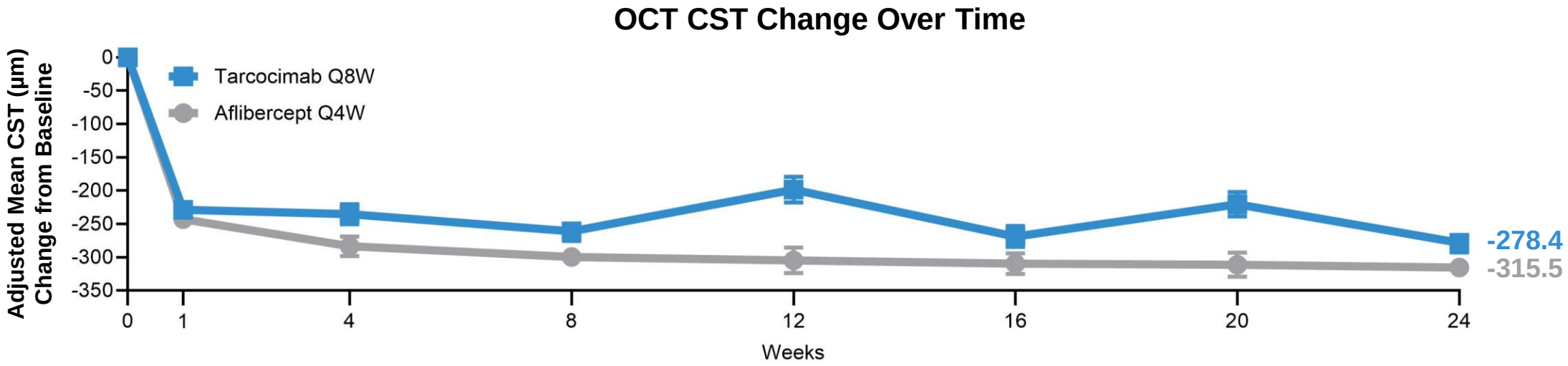
OCT CST Change Over Time



Results are based on a mixed model repeated measures (MMRM) analysis, with the change from baseline value as the dependent variable; treatment, visit (Week 1 through Week 24), and treatment by visit interaction as fixed effects; randomization stratification variables [baseline BCVA (≥70, 69-50 and ≤49 letters), disease duration (<3 months or ≥3 months), and geographical location (North America and Rest of World)] as covariates; and subject as a random effect. Non-inferiority margin = 4.5 ETDRS letters. Δ (95.02% CI): -1.4 (-3.11, 0.30) for tarcocimab - aflibercept. BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; OCT: optical coherence tomography; CST: central subfield thickness. 95% CI are displayed.

Tarcocimab Q8W improved BCVA and OCT CST comparably to aflibercept Q4W from baseline to Week 24 in all RVO patients – non-inferiority to aflibercept demonstrated





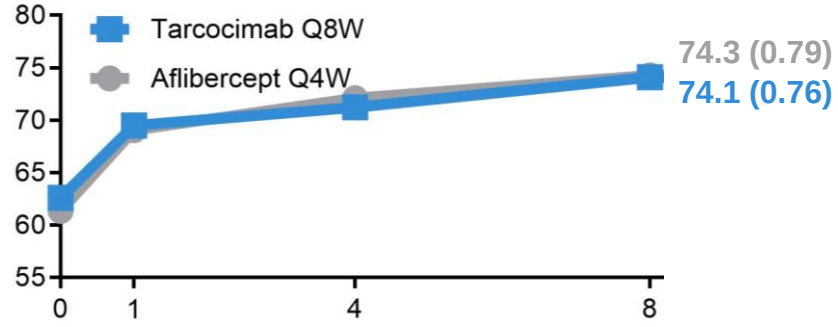
Results are based on a mixed model repeated measures (MMRM) analysis, with the change from baseline value as the dependent variable; treatment, visit (Week 1 through Week 24), and treatment by visit interaction as fixed effects; randomization stratification variables [RVO subtype (CRVO and BRVO), baseline BCVA (≥70, 69-50 and ≤49 letters), disease duration (<3 months or ≥3 months), and geographical location (North America and Rest of World)] as covariates; and subject as a random effect. Non-inferiority margin = 4.5 ETDRS letters. Δ (95.02% CI): -2.5 (-4.24, -0.71) for tarcocimab - aflibercept. BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; OCT: optical coherence tomography; CST: central subfield thickness. 95% CI are displayed.

Tarcocimab achieved comparable visual and anatomical outcomes in BRVO patients, in both the matched phase and the maintenance phase

Matched Phase

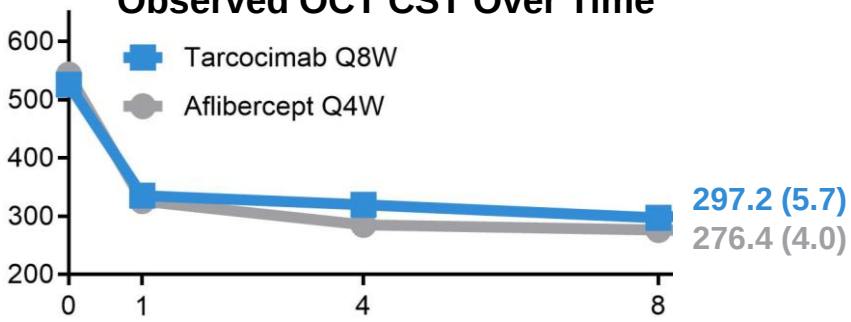
Strong immediate improvements are seen as early as Week 1

Observed BCVA over time



Sample size (n)				
Tarcocimab Q8W	220	216	215	212
Aflibercept Q4W	218	209	213	215

Observed OCT CST Over Time

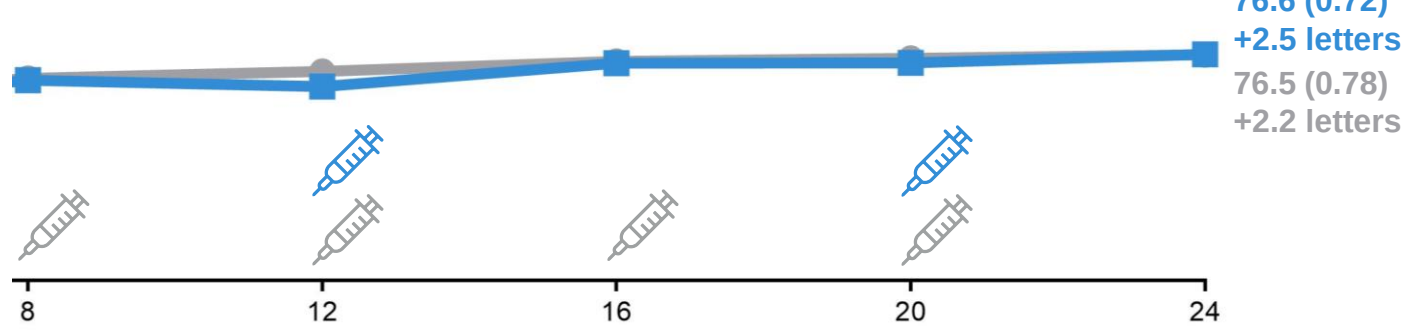


Sample size (n)				
Tarcocimab Q8W	220	214	215	212
Aflibercept Q4W	218	208	214	214

Maintenance Phase

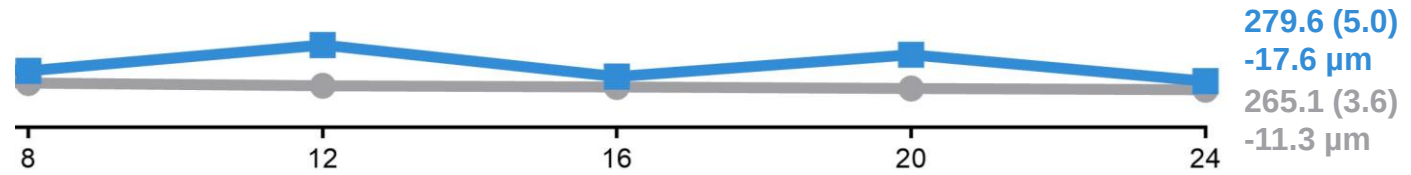
Similar visual and anatomical gains are achieved by tarcocimab from Week 8 to Week 24, with half the doses

Observed BCVA over time



Tarcocimab Q8W	212	214	209	202	204
Aflibercept Q4W	215	212	208	207	205

Observed OCT CST Over Time



Tarcocimab Q8W	212	213	208	202	204
Aflibercept Q4W	214	212	208	207	205

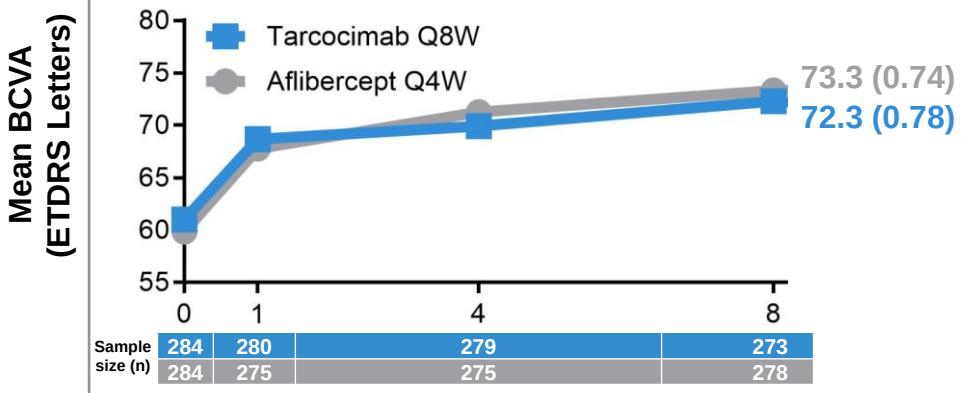
Observed data, graphed as Mean ± Standard Error of the Mean; Week 8 and 24 datapoints are Mean (Standard Error of the Mean). Standard errors are not visible on the graphs
BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; OCT: optical coherence tomography; CST: central subfield thickness.

Similarly, tarcocimab achieved comparable visual and anatomical outcomes in <u>all RVO patients</u>, in both the matched phase and the maintenance phase

Matched Phase

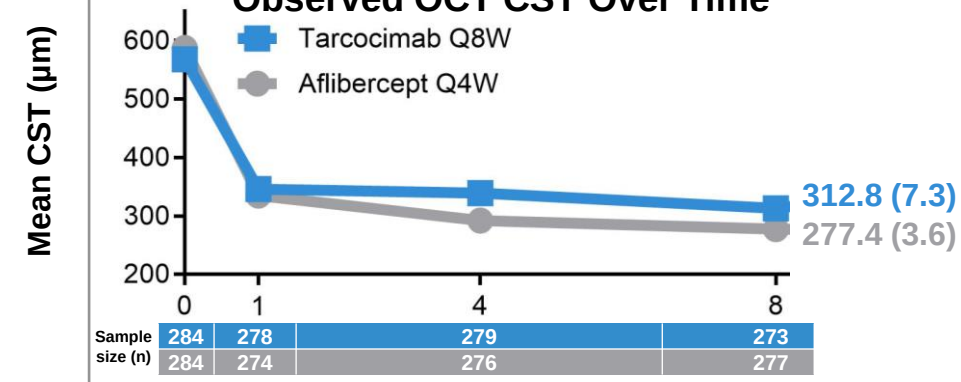
Strong immediate improvements are seen as early as Week 1

Observed BCVA over time



Sample size (n)				
Tarcocimab Q8W	284	280	279	273
Aflibercept Q4W	284	275	275	278

Observed OCT CST Over Time

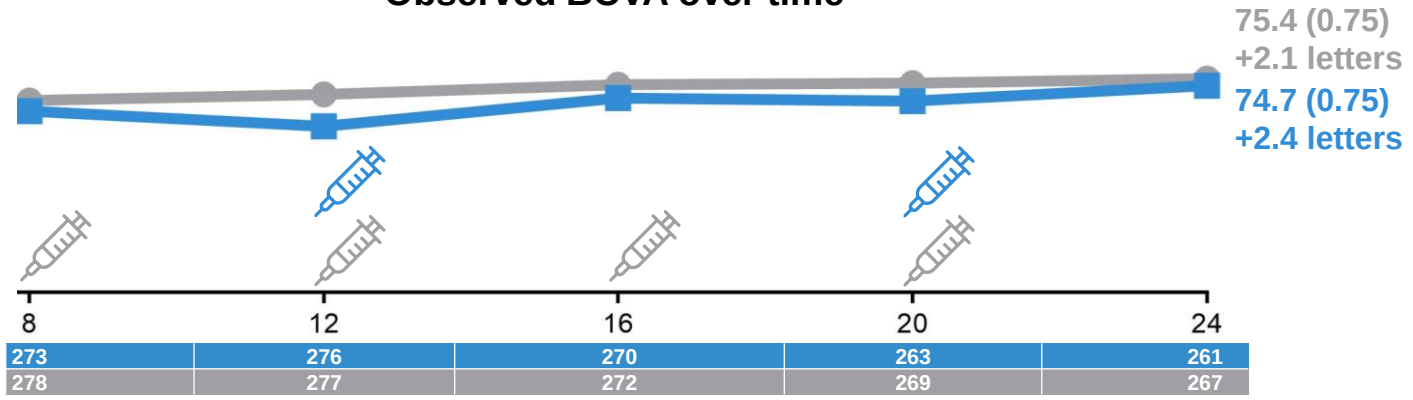


Sample size (n)				
Tarcocimab Q8W	284	278	279	273
Aflibercept Q4W	284	274	276	277

Maintenance Phase

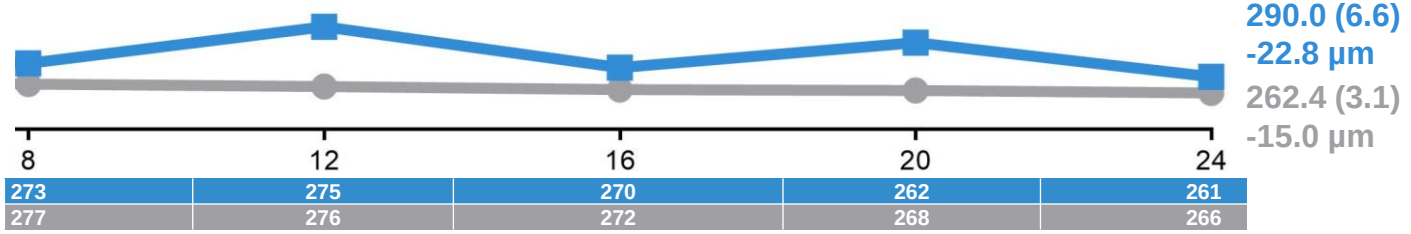
Similar visual and anatomical gains are achieved by tarcocimab from Week 8 to Week 24, with half the doses

Observed BCVA over time



Tarcocimab Q8W	273	276	270	263	261
Aflibercept Q4W	278	277	272	269	267

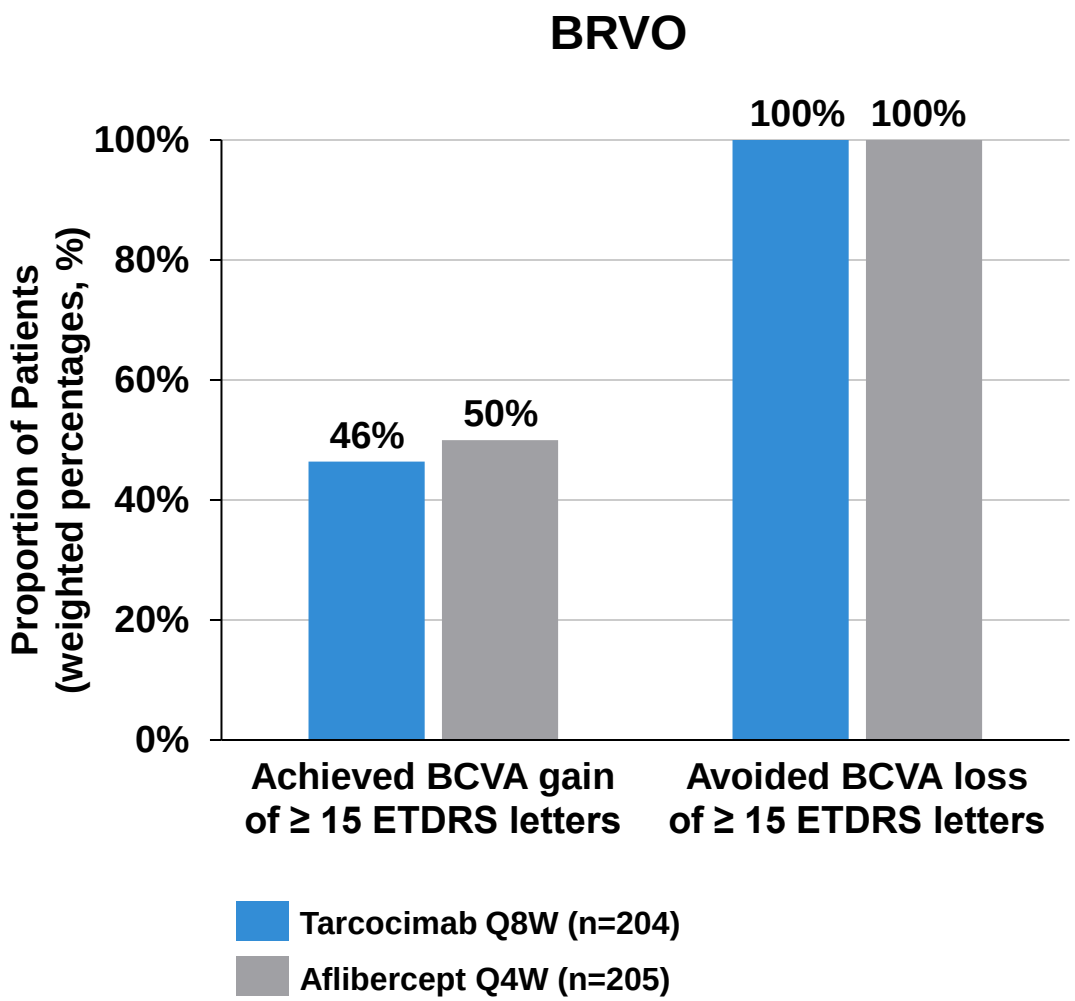
Observed OCT CST Over Time

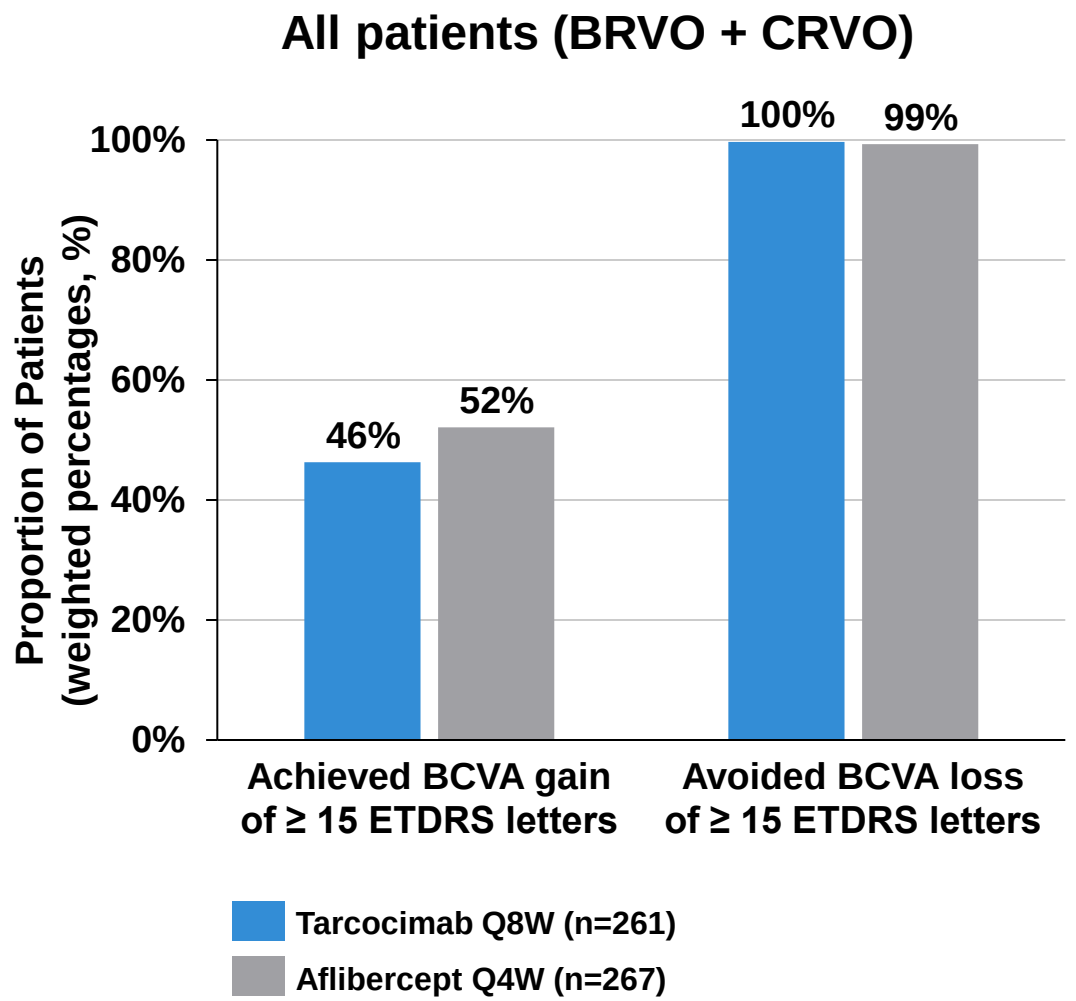


Tarcocimab Q8W	273	275	270	262	261
Aflibercept Q4W	277	276	272	268	266

Observed data, graphed as Mean ± Standard Error of the Mean; Week 8 and 24 datapoints are Mean (Standard Error of the Mean). Standard errors are not visible on the graphs
BCVA: best corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; OCT: optical coherence tomography; CST: central subfield thickness.

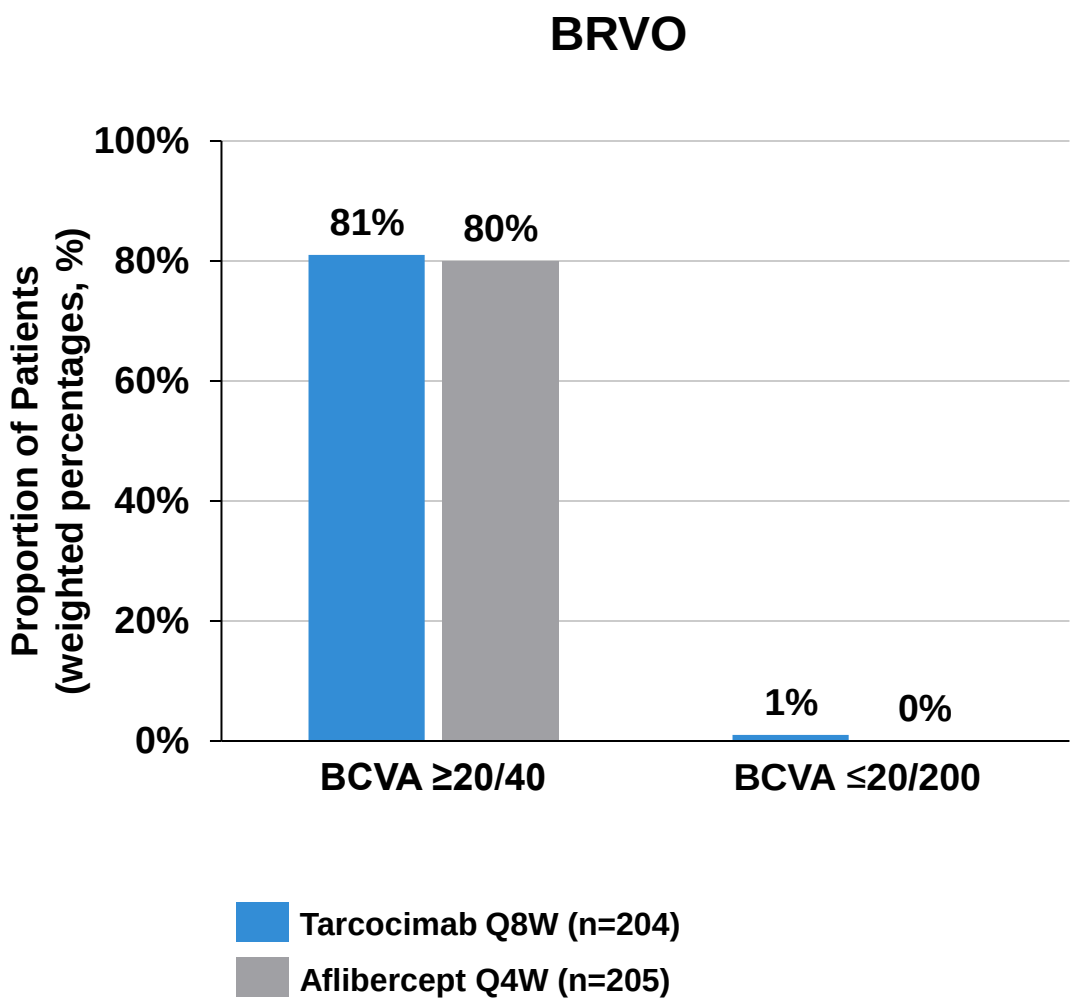
Secondary endpoints: Comparable proportions of tarcocimab Q8W and aflibercept Q4W patients gained or maintained vision at Week 24

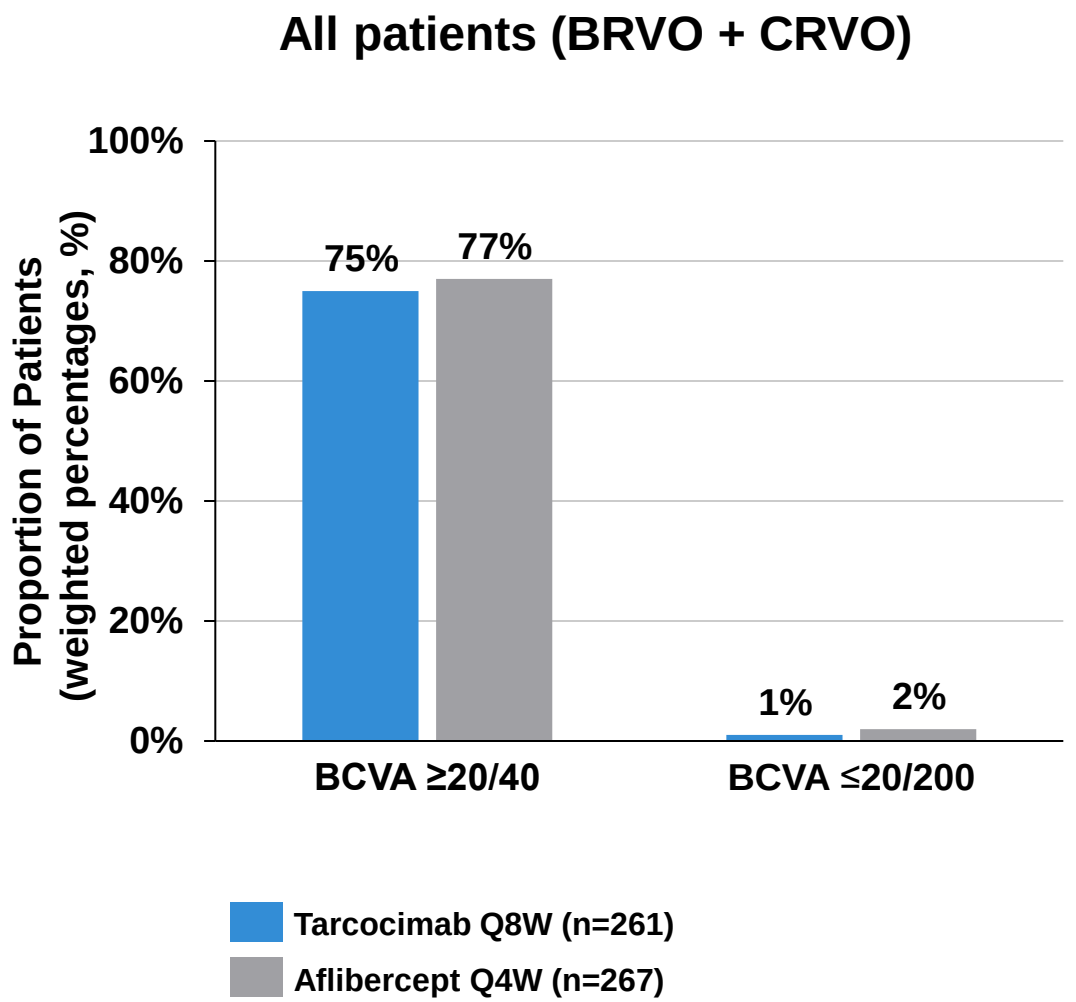




Prespecified secondary endpoints. ETDRS: Early Treatment Diabetic Retinopathy Study. Weighted percentages are based on the CMH statistic.

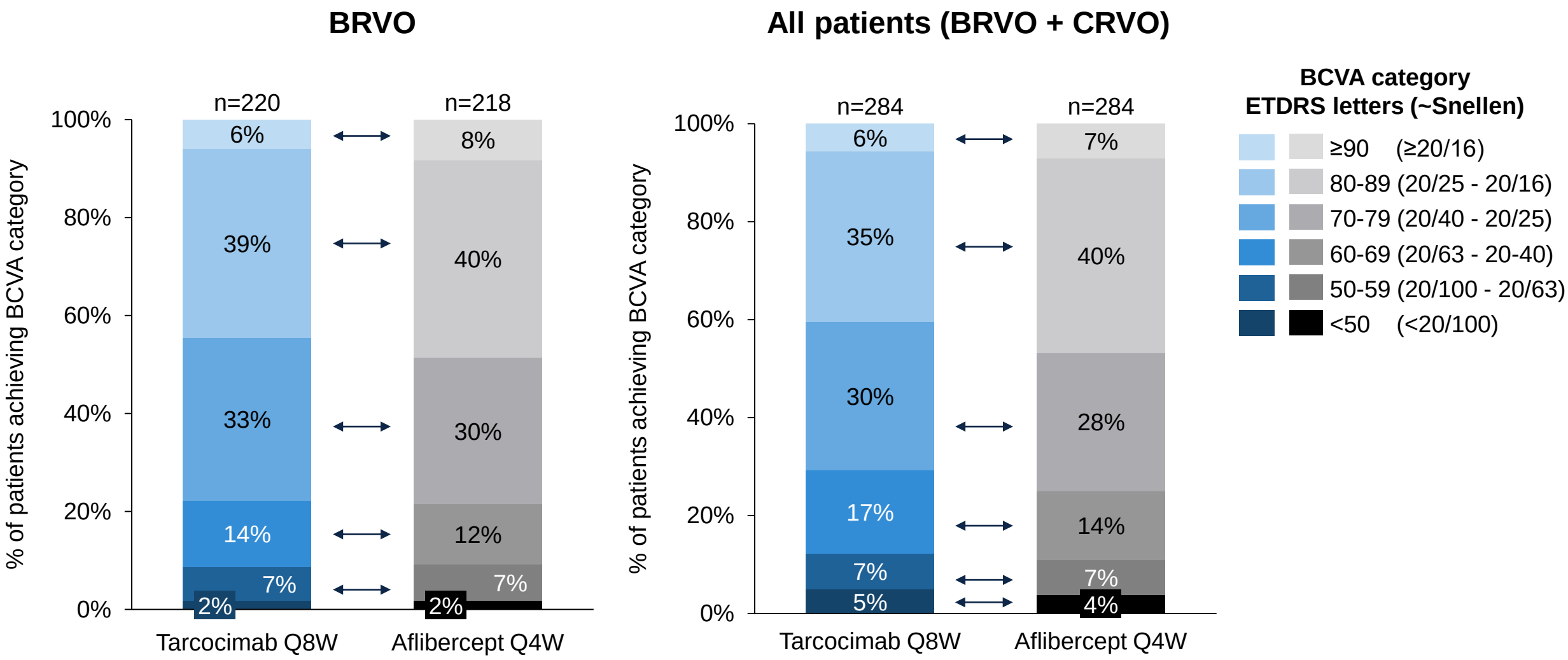
Secondary endpoints: Comparable proportions of tarcocimab Q8W and aflibercept Q4W achieved good vision (≥20/40) and avoided poor vision (≤20/200) at Week 24





Prespecified secondary endpoints. ETDRS: Early Treatment Diabetic Retinopathy Study. Weighted percentages are based on the CMH statistic.

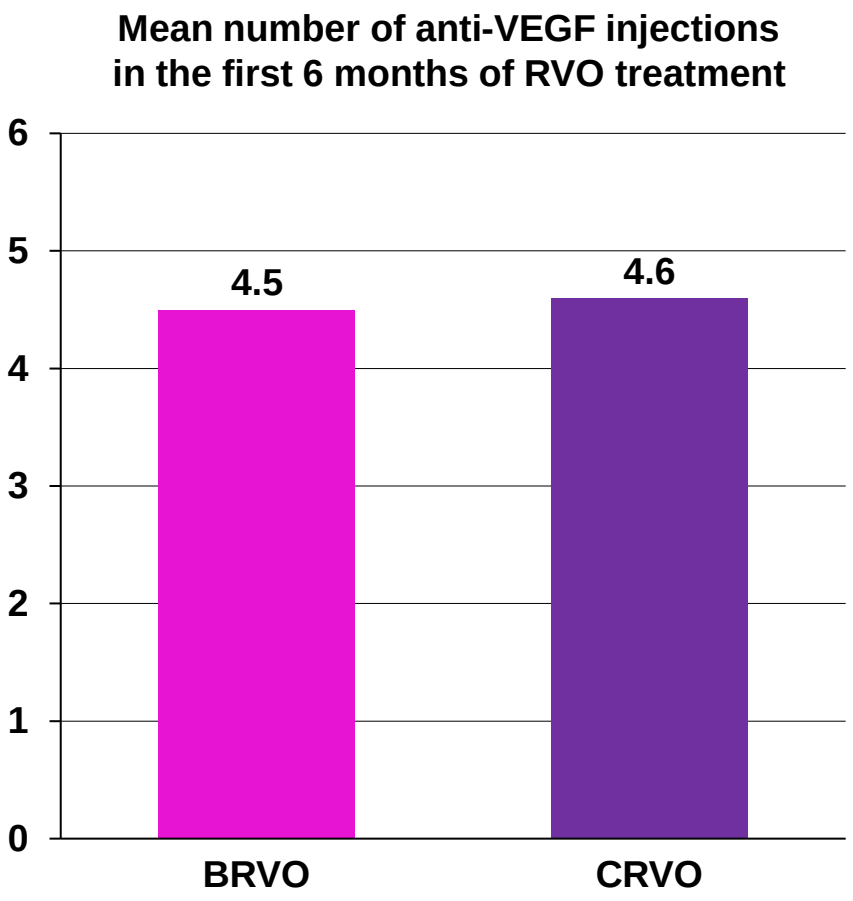
Tarcocimab Q8W and aflibercept Q4W had similar distribution of vision outcomes both among BRVO and all RVO patients at Week 24



* Observed data. For patients with missing data at Week 24, the last value observed was used. BCVA: best corrected visual acuity; ETDRS: early treatment diabetic retinopathy study

Tarcocimab is the first anti-VEGF therapy to demonstrate non-inferior vision outcomes with fewer doses than the average used in clinical practice

Real World Evidence[1]



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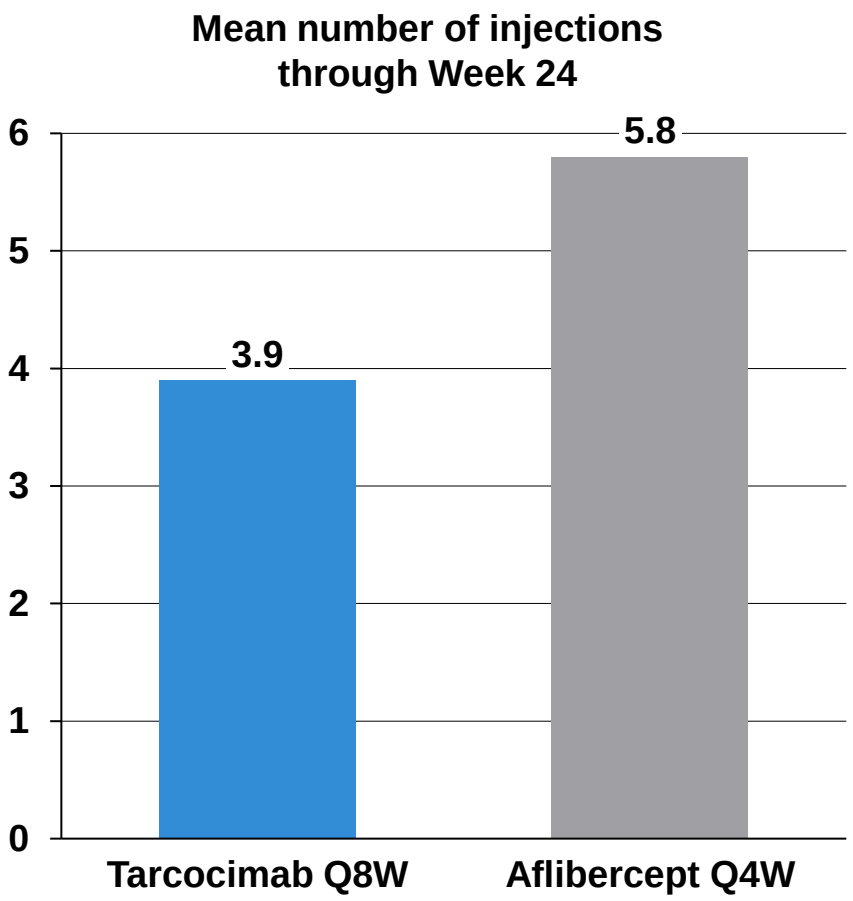


1. Ciulla T, et al. Br J Ophthalmol 2021;105:1696–1704. doi:10.1136/bjophthalmol-2020-317337. Represents 8,876 BRVO eyes, 6,737 CRVO eyes from Vestrum database. Mean 4.5/4.6 anti-VEGF injections over first 6 months (aflibercept, ranibizumab, or bevacizumab).

Safety: tarcocimab Q8W was well-tolerated, with low rates of adverse events

Adverse Events (AEs) up to Week 24	Tarcocimab Q8W (n=284)	Aflibercept Q4W (n=284)
Ocular - Study Eye		
Subjects with any ocular AE	86 (30.3%)	71 (25.0%)
Subjects with any ocular serious AE (SAE)	4 (1.4%)	0
Subjects with any Injection Procedure Related AEs	41 (14.4%)	32 (11.3%)
Subjects with any Injection Procedure Related SAE	1 (0.4%)	0
Non-Ocular		
Subjects with any Non-Ocular AE	123 (43.3%)	108 (38.0%)
Subjects with at Least One Non-Ocular SAE	15 (5.3%)	15 (5.3%)
Subjects with any APTC-classified ATE events	4 (1.4%)	3 (1.1%)
Any Deaths	2 (0.7%)	0

Results presented for the Week 24 Safety Population. Events are investigator reported and relatedness of an event to study drug or injection procedure is investigator assessed.. APTC was used to classify all ATE events; Treatment emergent adverse events are events with start date ≥first study drug date and ≤last study drug date + 28 days. SAE: serious adverse event; APTC: anti-platelet trialists' collaboration; ATE: Arteriothromboembolic

Rates of intraocular inflammation were low and comparable between treatment groups, and there were no cases of endophthalmitis

Intraocular Inflammation in Study Eye up to Week 24	Tarcocimab Q8W (n=284)	Aflibercept Q4W (n=284)
Subjects Reporting at Least 1 Intraocular Inflammation AE	4 (1.4%)	1 (0.4%)
Uveitis	2 (0.7%)	0
Keratic precipitates	1 (0.4%)	0
Vitritis	1 (0.4%)*	1 (0.4%)

Endophthalmitis (Procedure-Related) in Study Eye up to Week 24	Tarcocimab Q8W (n=284)	Aflibercept Q4W (n=284)
Endophthalmitis (Procedure-Related)	0	0

No cases of intraocular inflammation with vasculitis or vascular occlusion were observed

Results presented for the Week 24 Safety Population. Events are investigator reported. Adverse events are events with start date ≥first study drug date and ≤last study drug date + 28 days.
***** The vitritis case reported in the tarcocimab group was grade 2+ out of 4+. It was considered a serious adverse event because the patient was hospitalized per local standard of care for a workup.

Rates of common ocular adverse events (≥1.5% in either study arm) and ocular serious adverse events were low

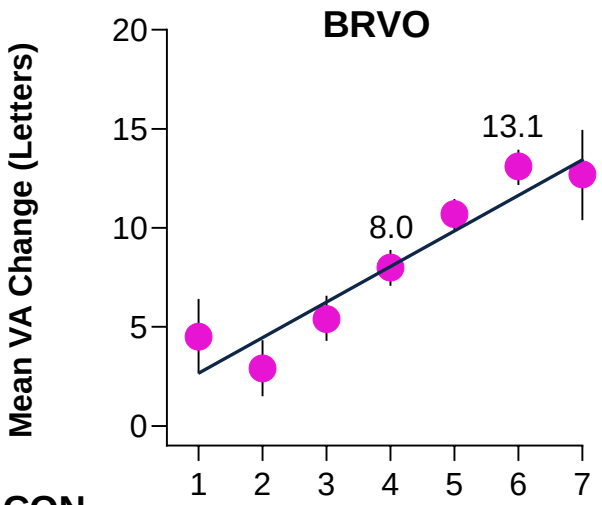
Common Ocular Adverse Events (AEs) up to Week 24	Tarcocimab Q8W (n=284)	Aflibercept Q4W (n=284)
Subjects with any AE in the Study Eye	86 (30.3%)	71 (25.0%)
Conjunctival haemorrhage	25 (8.8%)	21 (7.4%)
Eye Pain	11 (3.9%)	3 (1.1%)
Vitreous floaters	7 (2.5%)	5 (1.8%)
Dry eye	6 (2.1%)	3 (1.1%)
Eye irritation	5 (1.8%)	2 (0.7%)
Intraocular pressure increased	5 (1.8%)	3 (1.1%)
Vitreous detachment	5 (1.8%)	5 (1.8%)

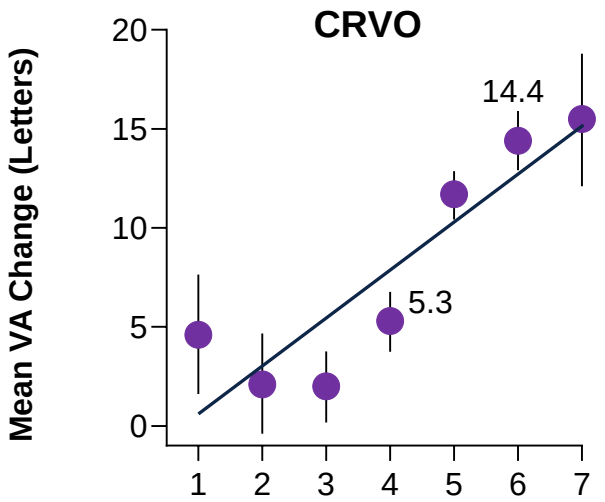
Other Ocular Serious Adverse Events (SAEs) in Study Eye up to Week 24	Tarcocimab Q8W (n=284)	Aflibercept Q4W (n=284)
Glaucoma	1 (0.4%)	0
Intraocular pressure increased	1 (0.4%)	0
Rhegmatogenous retinal detachment	1 (0.4%)	0

Results presented for the Week 24 Safety Population. Events are investigator reported. Adverse events are events with start date ≥first study drug date and ≤last study drug date + 28 days.

Relevance: reducing the treatment burden from 6 to 4 doses/injections/visits while maintaining vision outcomes is highly meaningful for patients

Real World Evidence[1]





Real world evidence showed that **reducing doses from 6 to 4 results in reduction of visual acuity gains of 39% and 63%** in BRVO and CRVO patients, respectively

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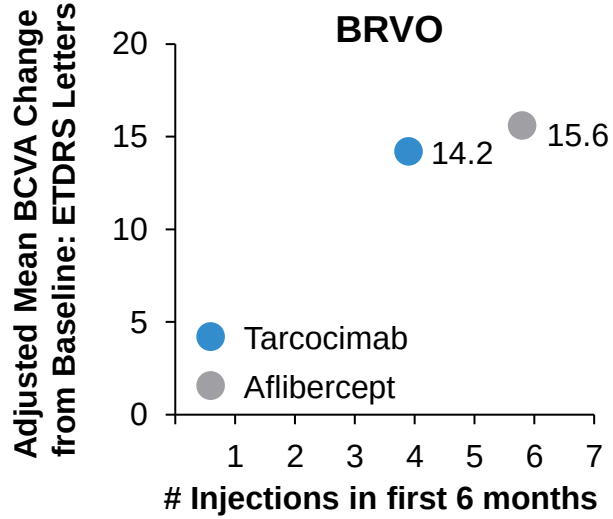

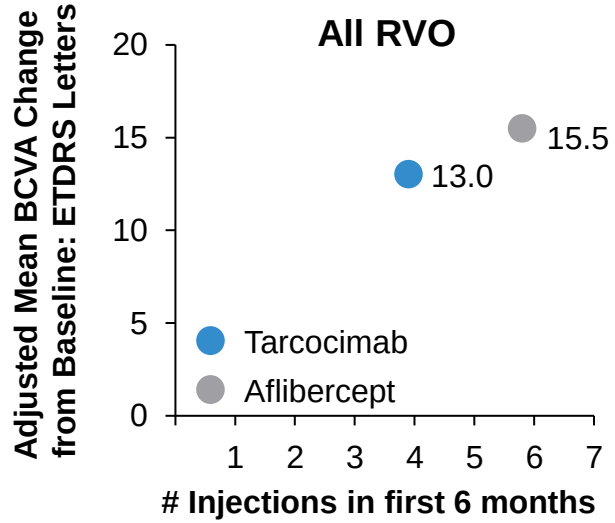

Tarcocimab is the first anti-VEGF therapy to demonstrate comparable vision gains while doubling the treatment interval from monthly to every-other-month dosing

1. Ciulla T, et al. Br J Ophthalmol 2021;105:1696–1704. doi:10.1136/bjophthalmol-2020-317337. Represents 8,876 BRVO eyes, 6,737 CRVO eyes from Vestrum database. Mean 4.5/4.6 anti-VEGF injections over first 6 months (aflibercept, ranibizumab, or bevacizumab).

Conclusions

BEACON met primary endpoint

Mean change in BCVA with **tarcocimab Q8W was non-inferior to aflibercept Q4W** in RVO

Similar efficacy, meaningfully fewer doses

Tarcocimab is the **first anti-VEGF therapy to show comparable visual acuity outcomes** to monthly aflibercept **while doubling the treatment interval**

- Matched phase: **strong efficacy** with comparable vision and anatomic improvement as early as Week 1
- Maintenance phase: similar BCVA, OCT gains from Week 8 to Week 24 with **half the doses**

Safe and well-tolerated

Favorable safety profile with 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

Ongoing tarcocimab Phase 3 program

Successful outcomes from BEACON **lend confidence to ongoing studies** across indications (wet AMD, DME, NPDR)

Thank you to all BEACON investigators and site staff!

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