Tarcocimab tedromer (KSI-301) 5 mg for the treatment of RVO: One-year primary efficacy, durability, and safety outcomes of the Phase 3 BEACON Study

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on behalf of the BEACON Investigators

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Disclosures

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

Ankoor Shah has the following financial interests or relationships to disclose:

Regeneron (C)
Notal Vision (C)
Apellis (O)
RegenexBio (C)

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

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

ANTIBODY

IgG1 Anti-VEGF Antibody

BIOPOLYMER

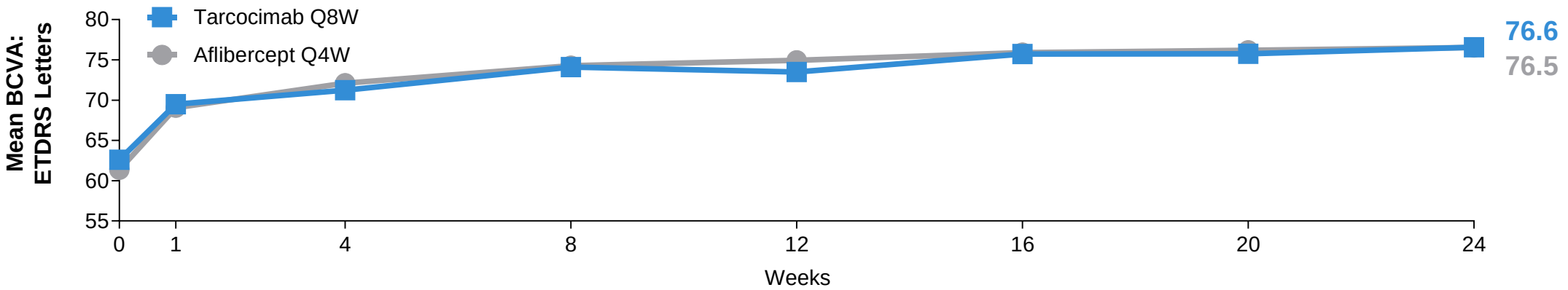
Branched, Optically Clear,
High Molecular Weight
Phosphorylcholine Polymer

CONJUGATE

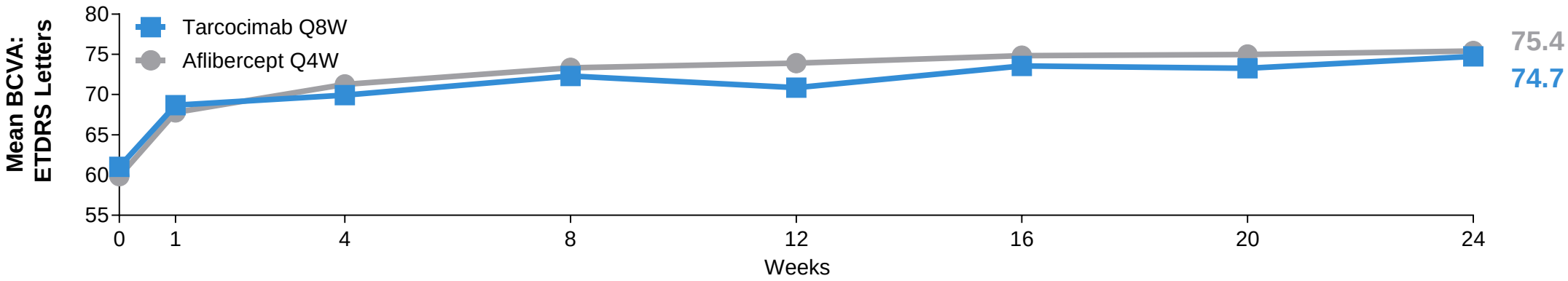
KSI-301 (tarcocimab tedromer) is an anti-VEGF ABC that blocks all VEGF-A isoforms

Tarcocimab Q8W demonstrated non-inferiority to aflibercept Q4W in change in BCVA from baseline to Week 24 in BRVO patients and all RVO patients, with 4 vs 6 doses

Mean BCVA Over Time in BRVO



Mean BCVA Over Time in all RVO



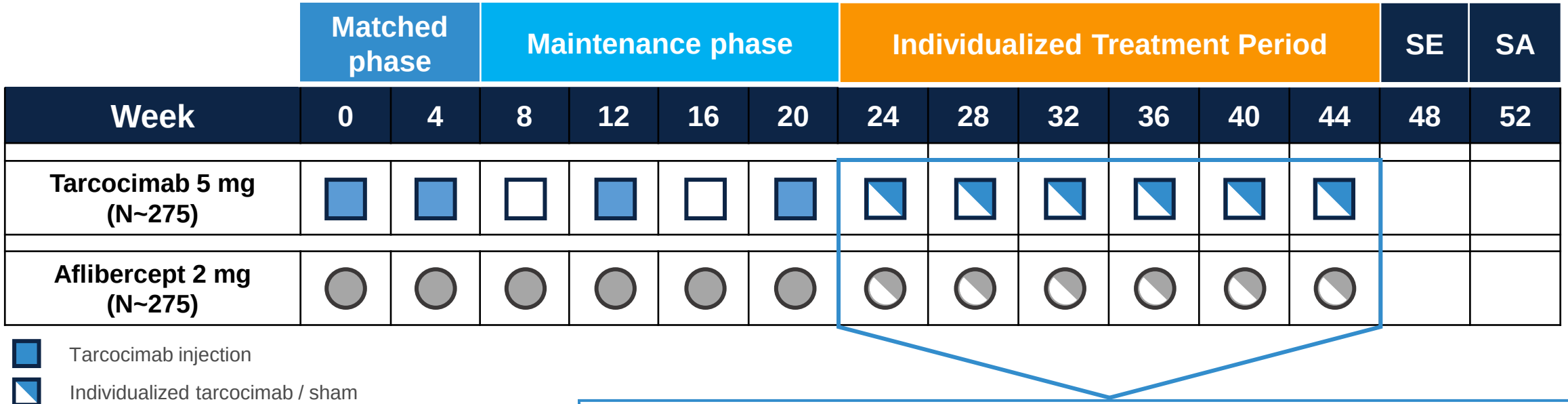
Results are based on a mixed model repeated measures (MMRM) analysis, with the change from baseline value as the dependent variable; treatment, visit (Week 1 through Week 24), and treatment by visit interaction as fixed effects; randomization stratification variables [baseline BCVA (≥70, 69-50 and ≤49 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.

BRVO: LS mean BCVA change from baseline at Week 24 (MMRM) was +14.2 letters for tarcocimab vs. +15.6 letters for aflibercept, with a p-value for non-inferiority of 0.0004.

All RVO: LS mean BCVA change from baseline at Week 24 (MMRM) was +13.0 letters for tarcocimab vs. +15.5 letters for aflibercept, with a p-value for non-inferiority of 0.0243.

Graphs show observed values, graphed as 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.

After receiving fixed dosing in the first 6 months of the BEACON study, patients transitioned to individualized treatment using identical criteria between the arms in the second 6 months

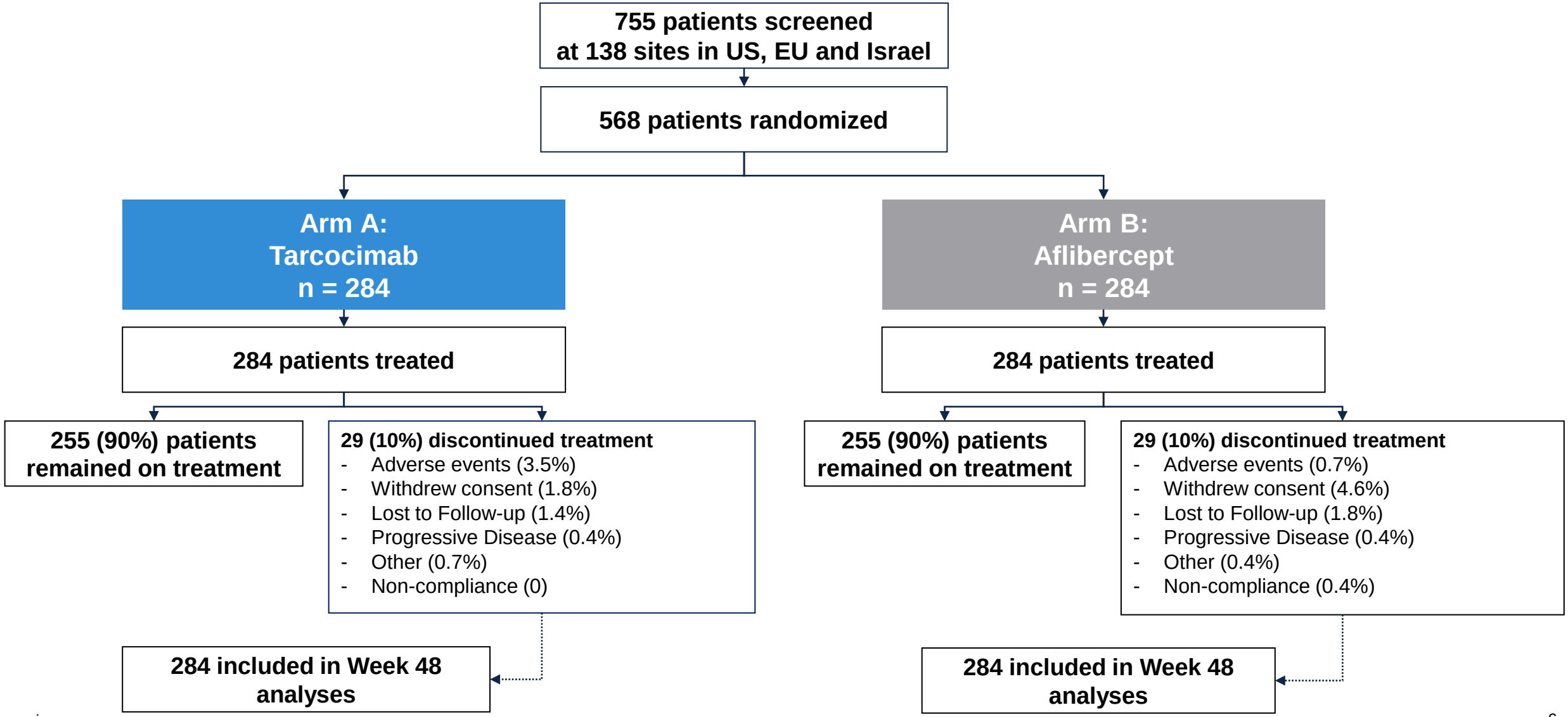


Matched Disease Activity Retreatment Criteria

- Increase in OCT **CST ≥ 50 µm compared to lowest** previous measurement ***and*** a decrease in **BCVA of ≥ 5 letters** compared to the average of the two best previous BCVA assessments, *or*
- Increase in OCT **CST ≥ 75 µm compared to lowest** previous measurement

SE: Secondary Endpoint; SA: Safety Assessment; OCT – CST: optical coherence tomography – central subfield thickness; BCVA: best corrected visual acuity.

Patient Disposition – discontinuations were low and balanced between groups, with 90% of patients remaining on treatment at Week 48



Baseline Patient Demographics and General Characteristics

	Tarcocimab n=284	Aflibercept n=284
Age, years, mean (SD)	66.0 (11.76)	64.7 (11.32)
Female, n (%)	141 (49.6)	134 (48.6)
Race, n (%)		
White	240 (84.5)	245 (86.3)
Black or African American	23 (8.1)	17 (6.0)
Asian	5 (1.8)	5 (1.8)
Other	5 (1.8)	6 (2.1)
Missing	11 (3.9)	11 (3.9)
Ethnicity, n (%)		
Not Hispanic or Latino	242 (85.2)	246 (86.6)
Hispanic or Latino	31 (10.9)	29 (10.2)
Choose not to respond	11 (3.9)	9 (3.2)
Medical history of diabetes, n (%)		
Yes	64 (22.5)	59 (20.8)
No	220 (77.5)	225 (79.2)

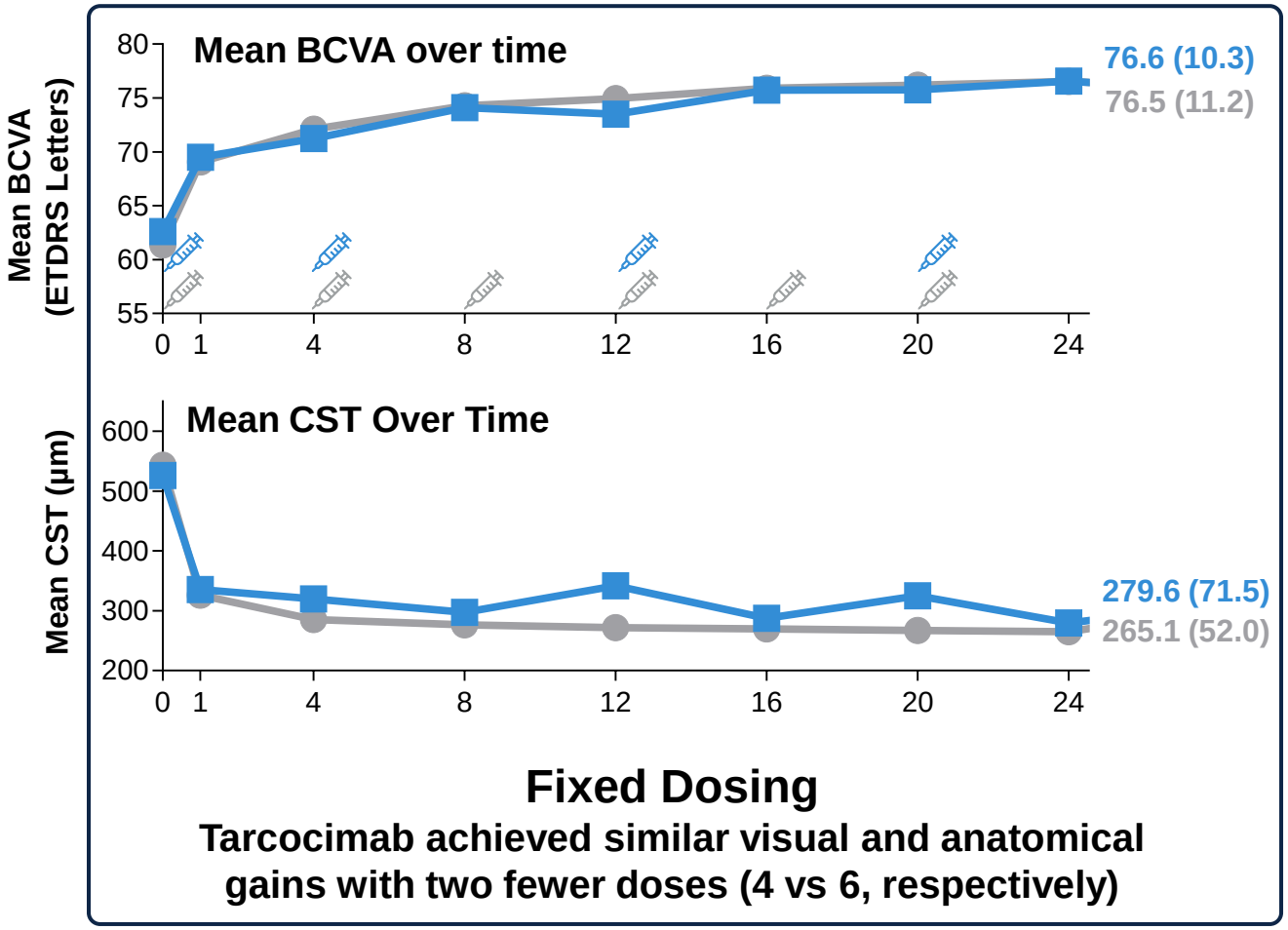
n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm.

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

Parameter	Tarcocimab n=284		Aflibercept n=284	
RVO Type, n (%)				
BRVO	220 (77.5)		218 (76.8)	
CRVO	64 (22.5)		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)**
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)
Lens Status, n (%)				
Phakic	185 (84.1)	230 (81.0)	180 (82.6)	234 (82.4)
Pseudophakic	35 (15.9)	54 (19.0)	38 (17.4)	50 (17.6)
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.
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

Tarcocimab achieved comparable visual and anatomical outcomes in BRVO patients, irrespective of the treatment paradigm used



Mean observed data; Week 24 datapoints are Mean (Standard Deviation).
BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; CST: central subfield thickness.

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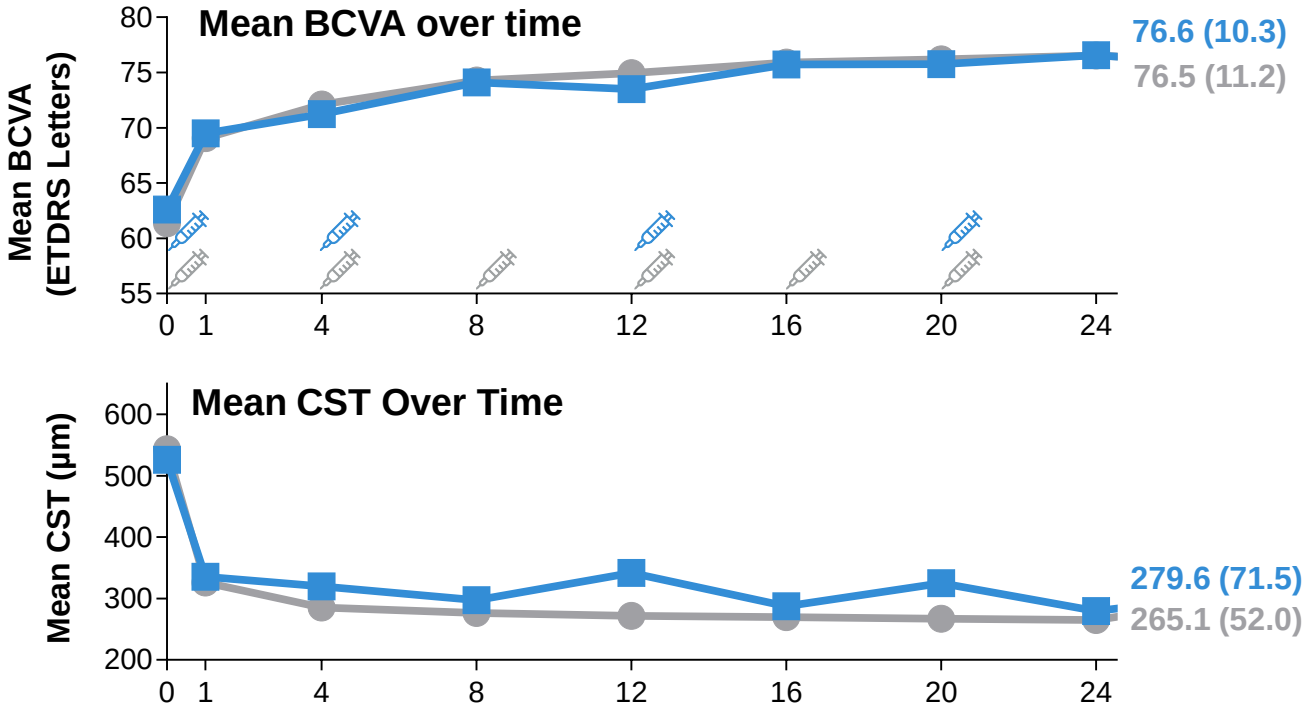
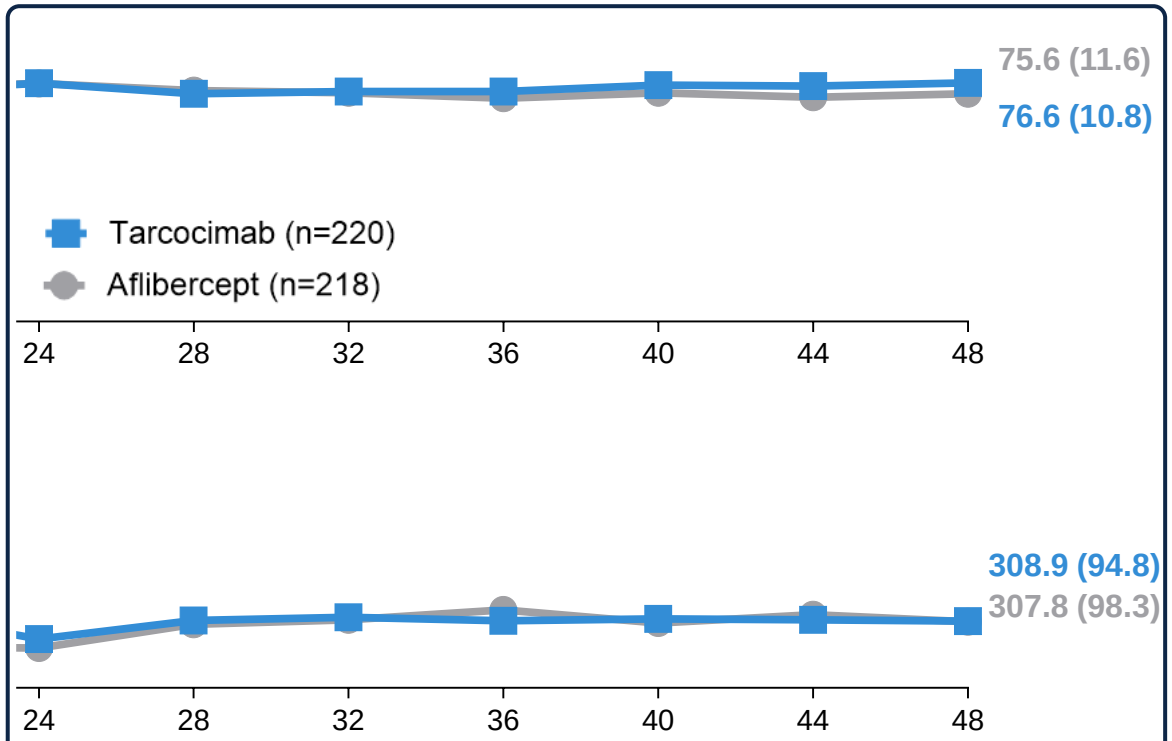


Fixed Dosing

Tarcocimab achieved similar visual and anatomical gains with two fewer doses (4 vs 6, respectively)



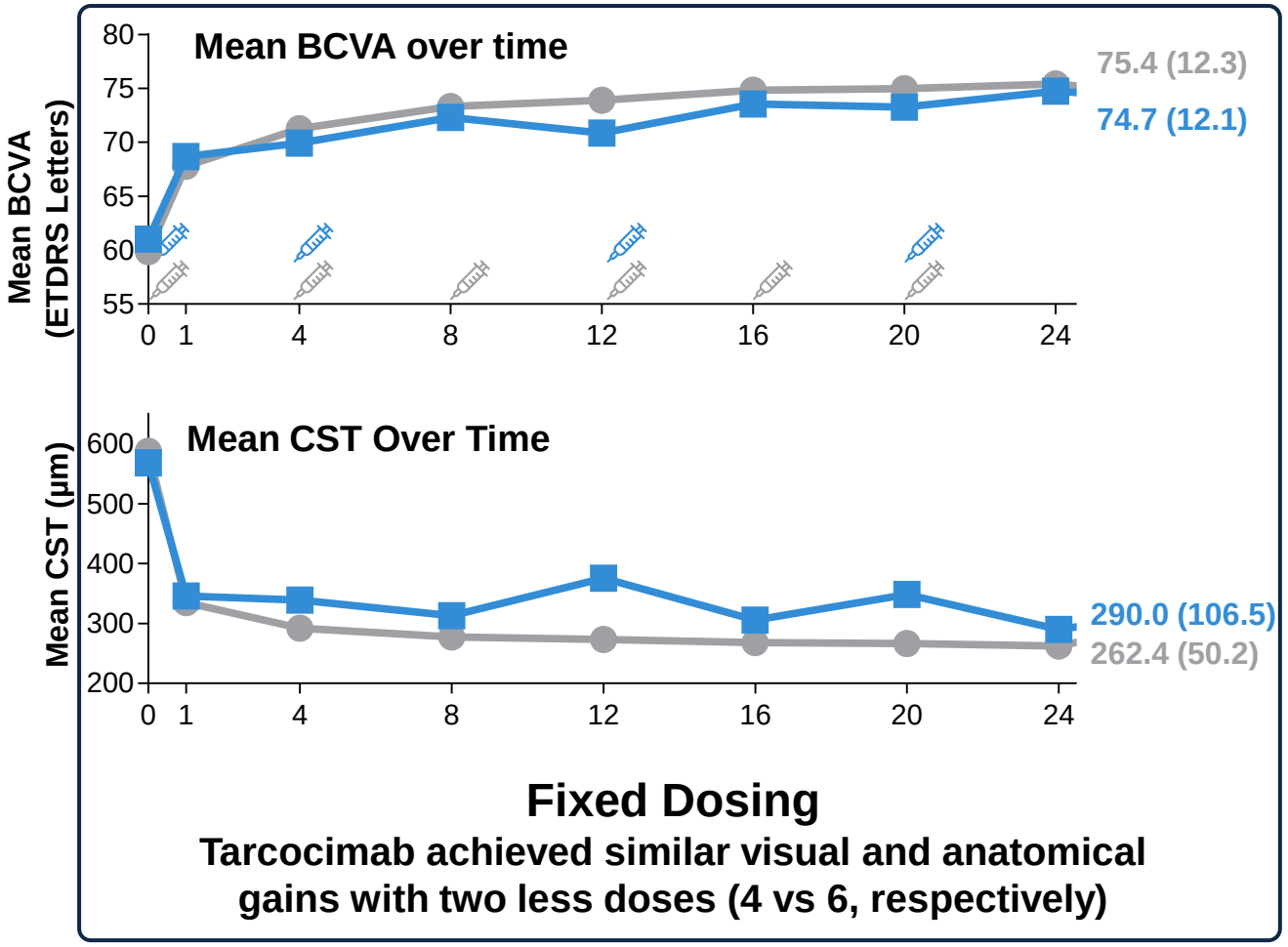
Head-to-head Individualized Dosing

Tarcocimab maintained similar visual and anatomical gains from Week 24 to 48

Mean observed data; Week 24 and 48 datapoints are Mean (Standard Deviation).
BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; CST: central subfield thickness.
Results for BCVA 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 48), 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 well as continuous covariates of baseline BCVA value and baseline OCT CMM value, as fixed effects; and subject as a random effect. Non-inferiority margin = 4.5 ETDRS letters.

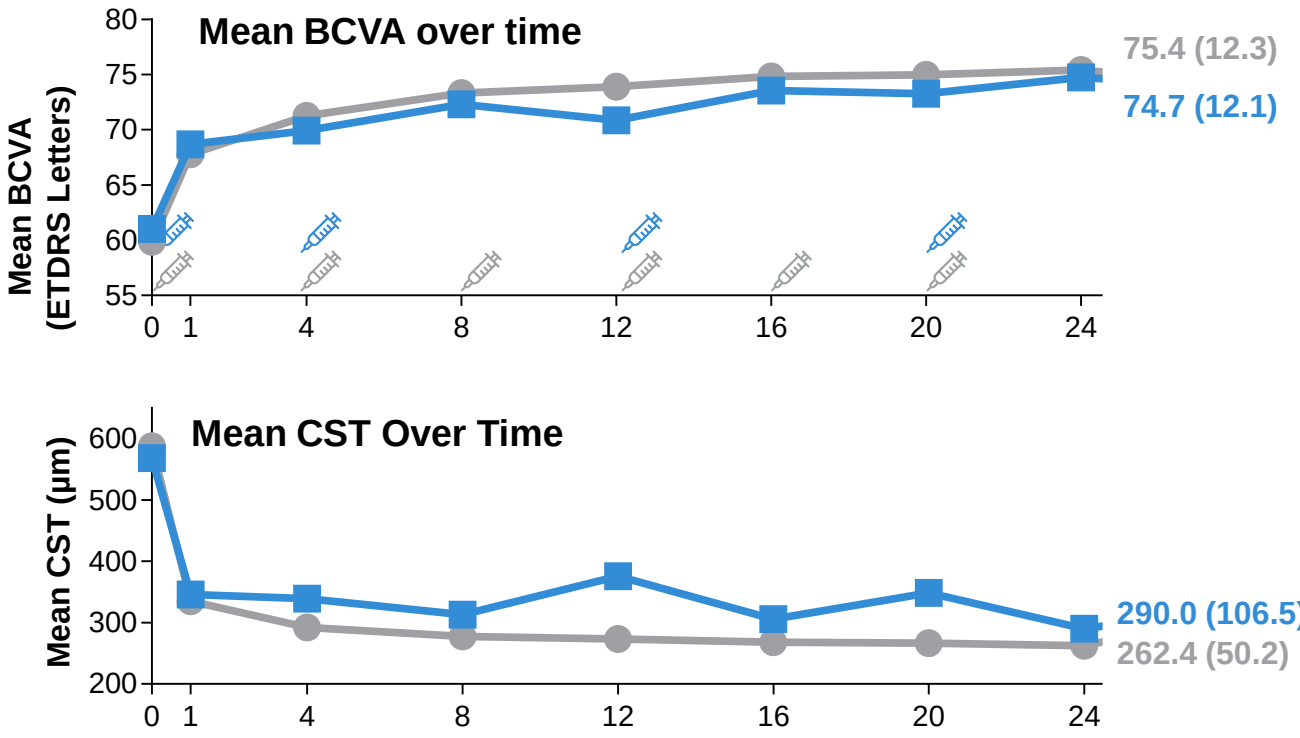
	LSM change from BL BCVA at Week 48 (MMRM)[a]	95% CI for LSM difference	P-value for non-inferiority[a]
Tarcocimab	13.0	-1.91, 1.96	p <0.0001
Aflibercept	13.0		

Similarly, tarcocimab achieved comparable visual and anatomical outcomes in <u>All RVO patients</u>, irrespective of the treatment paradigm used



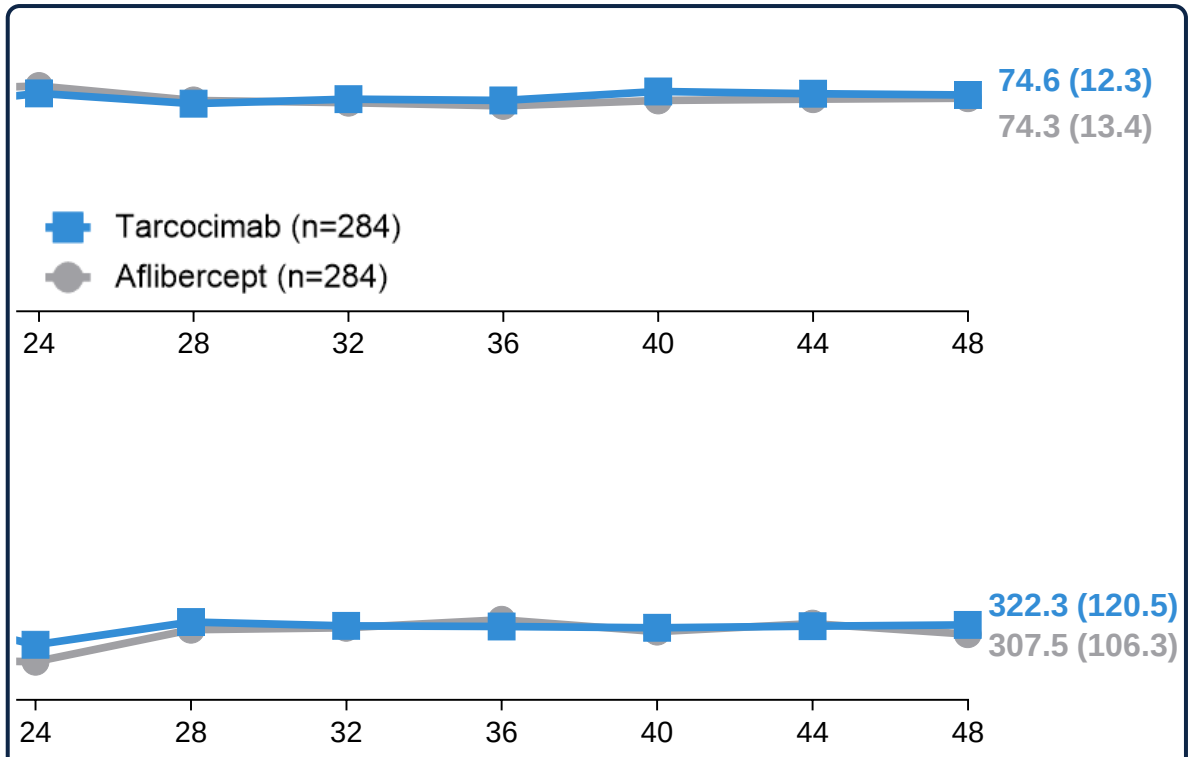
Mean observed data; Week 24 datapoints are Mean (Standard Deviation).
BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; CST: central subfield thickness.

Similarly, tarcocimab achieved comparable visual and anatomical outcomes in All RVO patients, irrespective of the treatment paradigm used



Fixed Dosing

Tarcocimab achieved similar visual and anatomical gains with two less doses (4 vs 6, respectively)



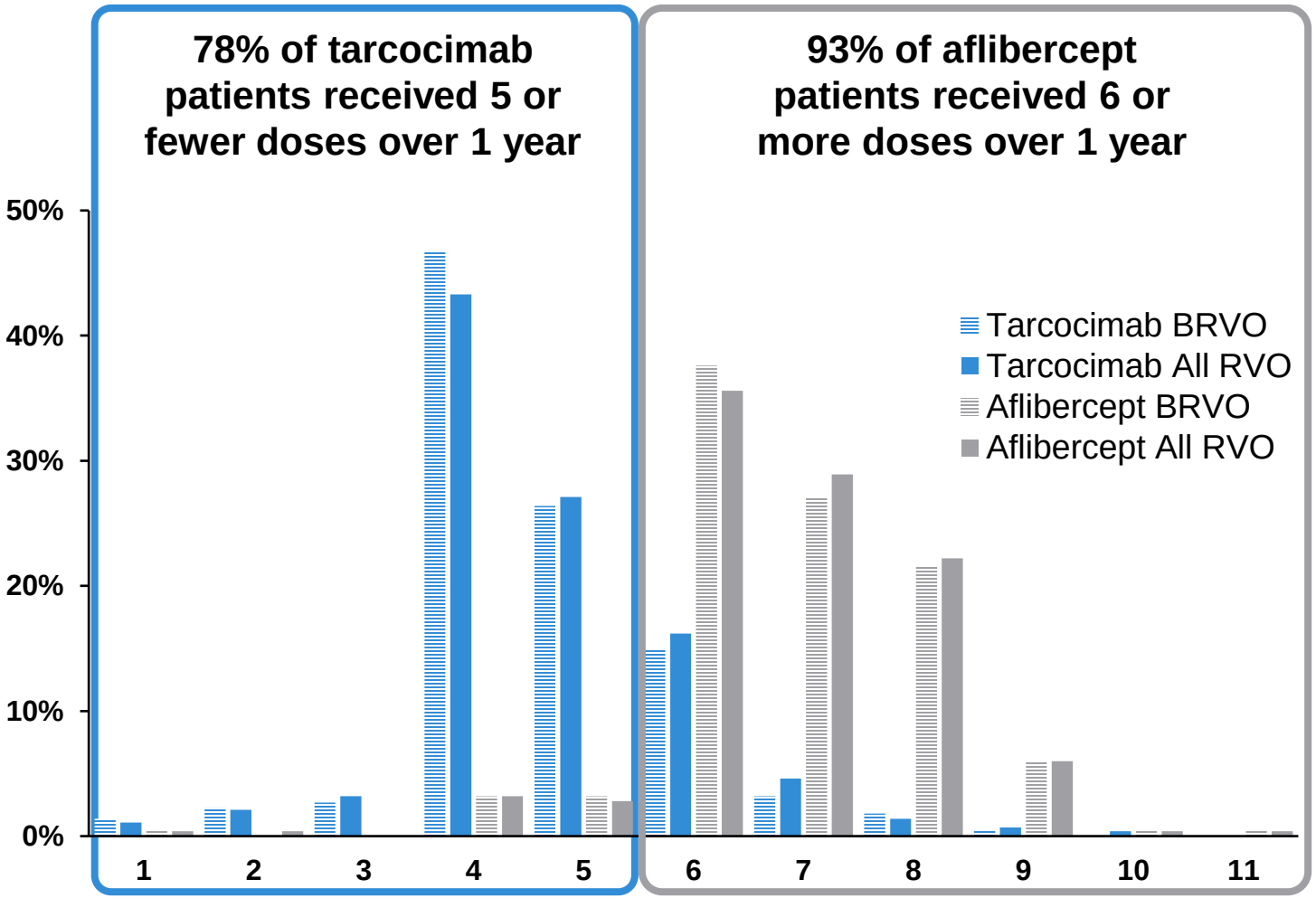
Head-to-head Individualized Dosing

Tarcocimab maintained similar visual and anatomical gains from Week 24 to 48

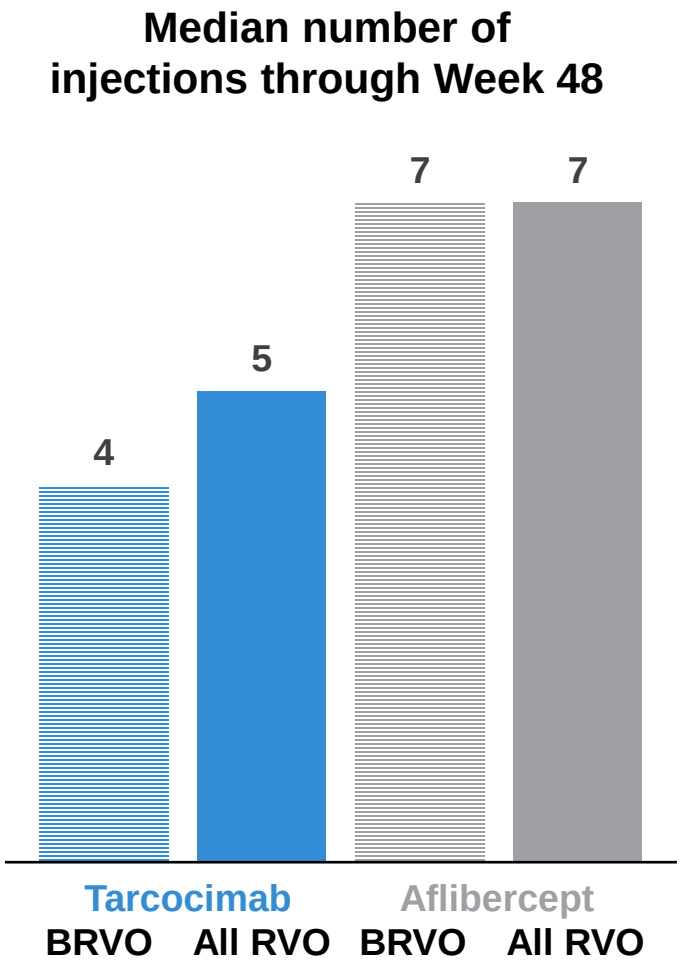
Mean observed data; Week 24 and 48 datapoints are Mean (Standard Deviation).
BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; CST: central subfield thickness.
Results for BCVA are based on a mixed model repeated measures (MMRM) analysis, with the change from baseline value as the dependent variable; treatment, visit (Week 1 through Week 48), 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), RVO type (BRVO or CRVO) and geographical location (North America and Rest of World)], as well as continuous covariates of baseline BCVA value and baseline OCT CMM value, as fixed effects; and subject as a random effect. Non-inferiority margin = 4.5 ETDRS letters.

	LSM change from BL BCVA at Week 48 (MMRM)[a]	95% CI for LSM difference	P-value for non-inferiority[a]
Tarcocimab	11.7	-3.11, 0.94	p = 0.001
Aflibercept	12.8		

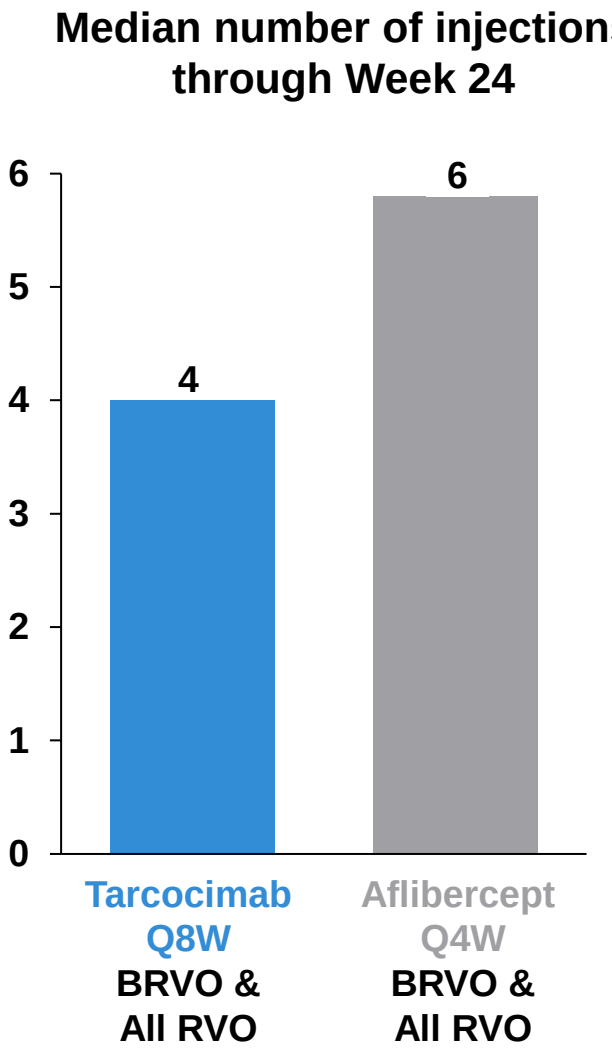
Treatment burden distribution through 48 weeks had minimal overlap, favoring tarcocimab in both BRVO and All RVO patients



Treatment distribution through Week 48



After only 4 initiating doses in the first 6 months, approximately half of tarcocimab-treated patients required no additional injections in the second 6 months



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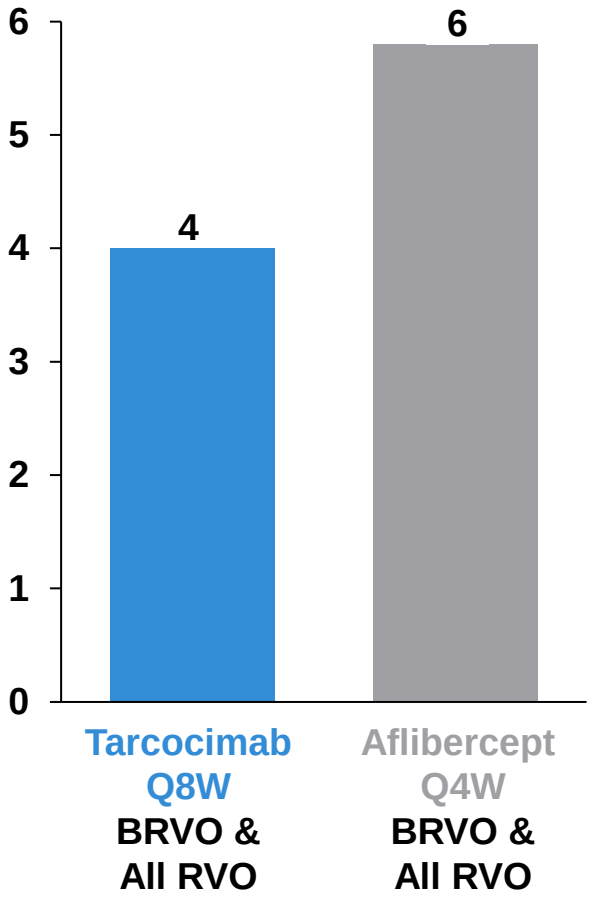
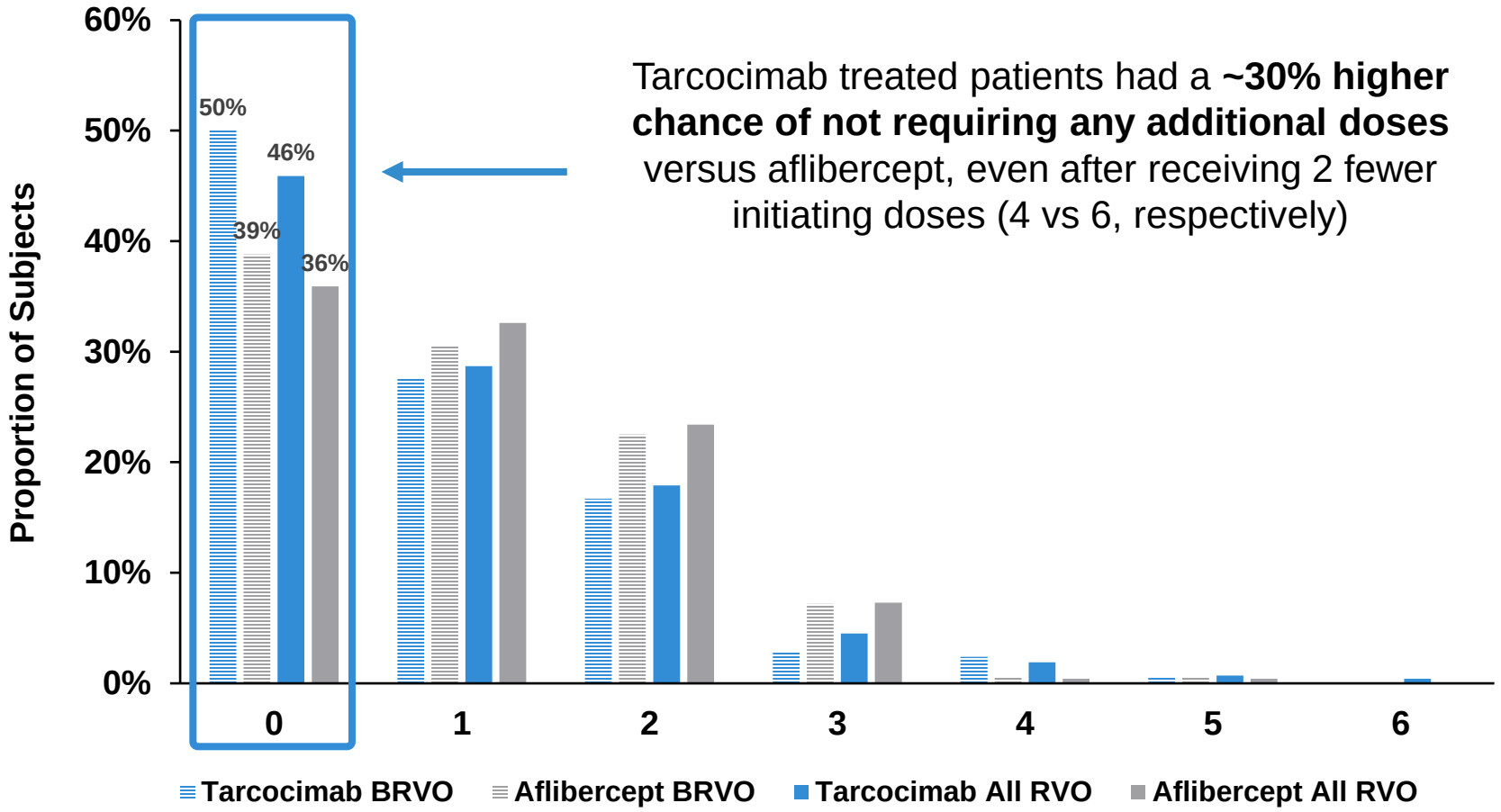
Median number of injections through Week 24



Treatment distribution from Week 24 to Week 48



Tarcocimab treated patients had a **~30% higher chance of not requiring any additional doses** versus aflibercept, even after receiving 2 fewer initiating doses (4 vs 6, respectively)

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

Adverse Events (AEs) up to Week 48	Tarcocimab n=284	Aflibercept n=284
Ocular - Study Eye		
Subjects with any ocular AE	119 (41.9%)	113 (39.8%)
Subjects with any ocular serious AE (SAE)	6 (2.1%)	1 (0.4%)
Subjects with any Injection Procedure Related AEs	50 (17.6%)	37 (13.0%)
Subjects with any Injection Procedure Related SAE	2 (0.7%)	0
Non-Ocular		
Subjects with any Non-Ocular AE	165 (58.1%)	155 (54.6%)
Subjects with at Least One Non-Ocular SAE	31 (10.9%)	22 (7.7%)
Subjects with any APTC-classified ATE events	7 (2.5%)	4 (1.4%)
Any Deaths	3 (1.1%)	1 (0.4%)

Results presented for the Week 48 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 common ocular adverse events were low. Cataract events were low and comparable between groups.

Common Ocular Adverse Events (AEs) up to Week 48[a]	Tarcocimab n=284	Aflibercept n=284
Subjects with any AE in the Study Eye	119 (41.9%)	113 (39.8%)
Conjunctival haemorrhage	24 (8.5%)	22 (7.7%)
Eye Pain	13 (4.6%)	6 (2.1%)
Vitreous detachment	12 (4.2%)	9 (3.2%)
Vitreous floaters	10 (3.5%)	6 (2.1%)
Cataract	10 (3.5%)	3 (1.1%)
Dry eye	9 (3.2%)	5 (1.8%)
Retinal vein occlusion	7 (2.5%)	14 (4.9%)
Macular edema	6 (2.1%)	10 (3.5%)
Intraocular pressure increased	6 (2.1%)	3 (1.1%)

Cataract in Study Eye up to Week 48[b]	Tarcocimab n=284	Aflibercept n=284
Subjects with Cataract AE in the Study Eye	14 (4.9%)	8 (2.8%)

Results presented for the Week 48 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. Each patient can have multiple events of the same AE term

b. Total number of patients with one or more events of cataract. Each patient could have multiple adverse events with the same AE preferred term

Rates of intraocular inflammation were low in both treatment groups

Intraocular Inflammation in Study Eye up to Week 48	Tarcocimab n=284	Aflibercept n=284
Subjects with at Least 1 Intraocular Inflammation AE*	7 (2.5%)	2 (0.7%)

Endophthalmitis in Study Eye up to Week 48	Tarcocimab n=284	Aflibercept n=284
Subjects with at Least 1 Endophthalmitis AE	0	0

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

*Reported AE terms: anterior chamber cell, keratic precipitates, uveitis, vitreal cells, vitritis. A 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 (previously reported at the primary endpoint).
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.

Conclusions

Dosed head-to-head, tarcocimab demonstrated the same efficacy	After transitioning to as needed retreatment using identical criteria between the arms, tarcocimab matched the efficacy of aflibercept while maintaining tarcocimab's signature durability advantage
Tarcocimab continues to demonstrate strong durability	Treatment burden distribution through 48 weeks had minimal overlap favoring tarcocimab, with 80% of tarcocimab patients receiving 5 or fewer doses vs 93% of aflibercept patients receiving 6 or more doses over 1 year After only 4 initiating doses in the first 6 months, approximately half of tarcocimab-treated patients required no additional injections through 12 months of treatment
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
KSI-501, a clinical stage anti-IL-6/VEGF bispecific, is progressing	Successful outcomes from BEACON provide additional supportive evidence for the development of Kodiak's ABC Platform and platform-derived medicines.

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