48-Week End of Study Results from BEHOLD Phase 2 Study of UBX1325 in Patients with DME

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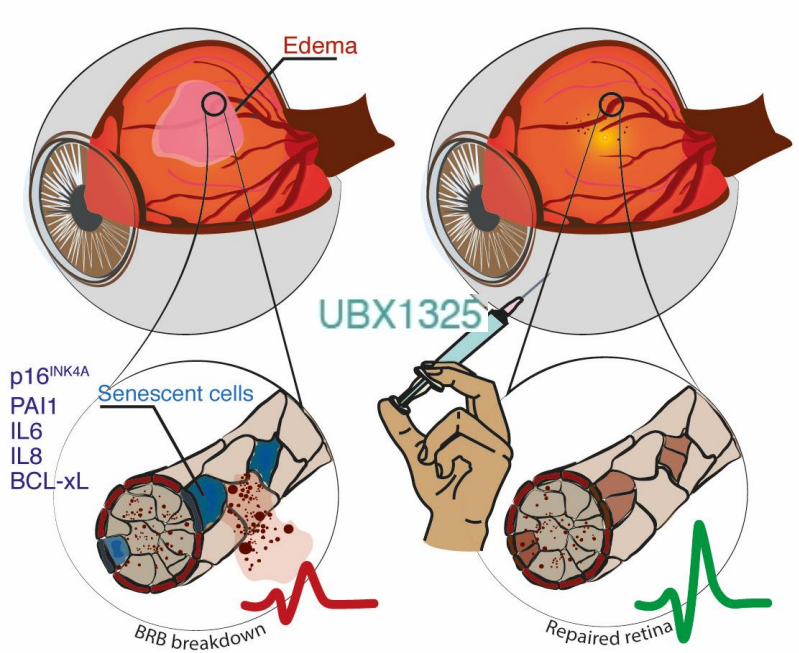
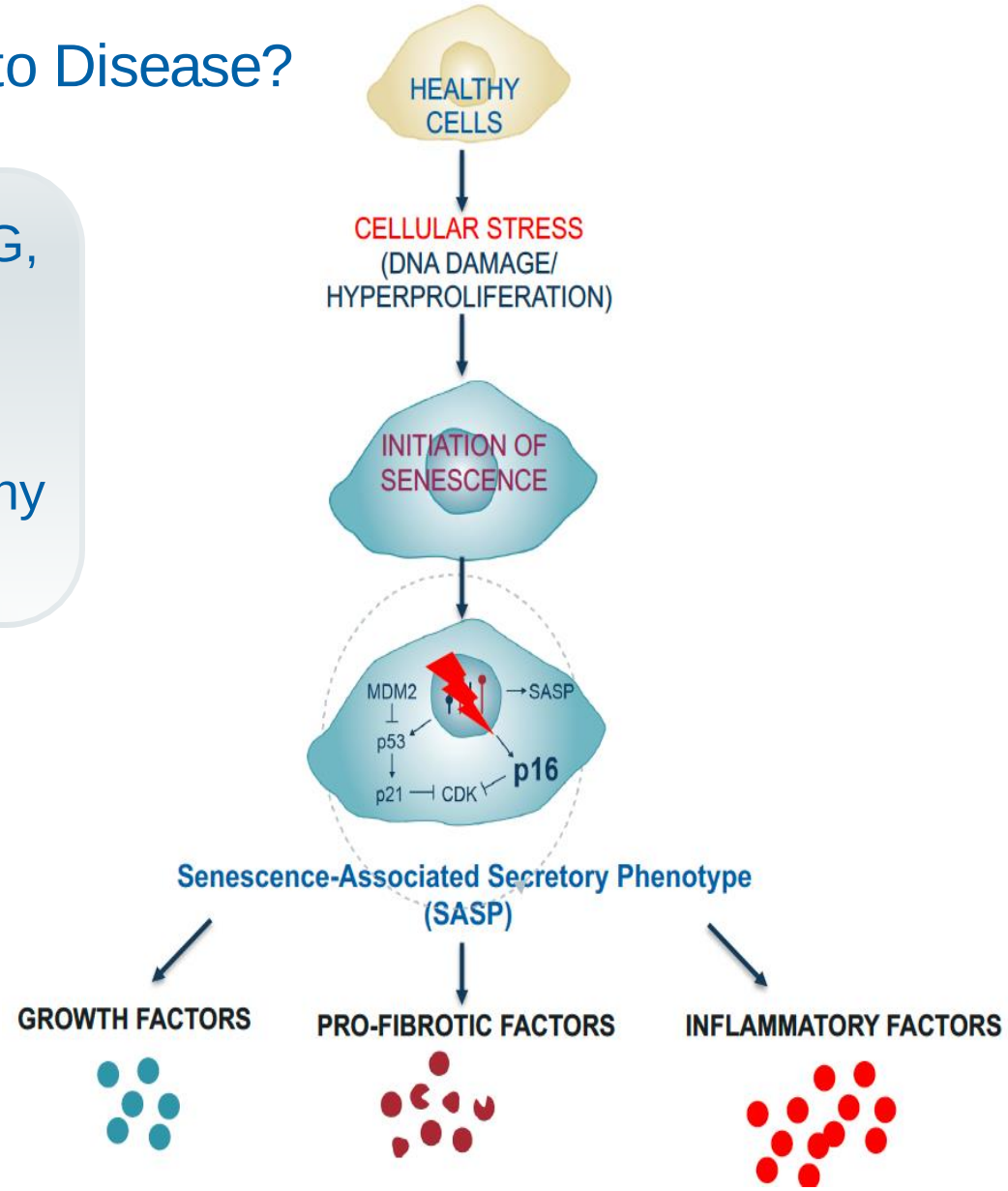
Equity: Aviceda, Oculis, PolyPhotonix, Recens Medical, Retrotope, RevOpsis, Vial

What is Cellular Senescence and How Can it Lead to Disease?

Senescent cells are STRESSED, NO-LONGER DIVIDING, metabolically active cells that drive pathology:

- Accumulate in areas of disease activity
- Secrete inflammatory factors
- Do not form tight junctions with their neighboring healthy endothelial cells



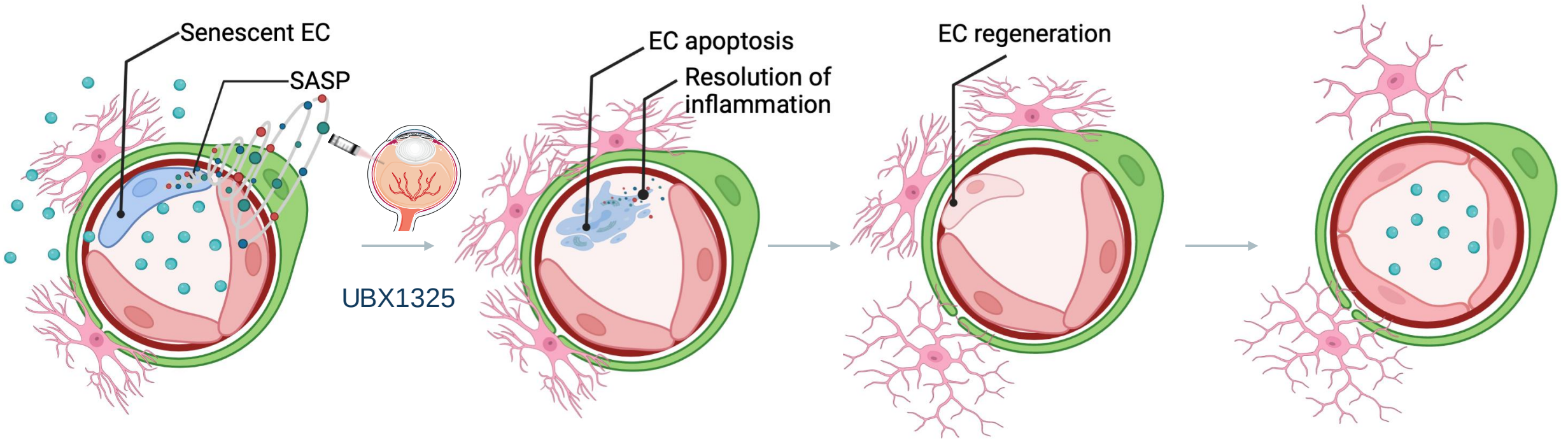


UBX1325: a Bcl-xL Inhibitor, Selectively Eliminates Senescent Cells

Diabetic blood vessel

Vessel remodeling

Repaired blood vessel

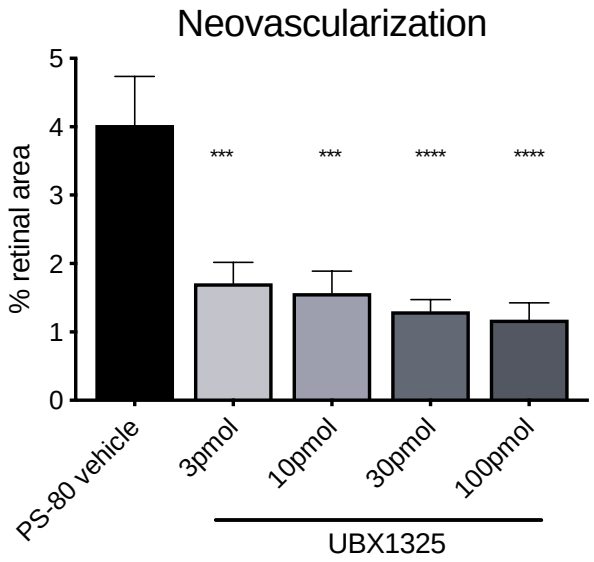


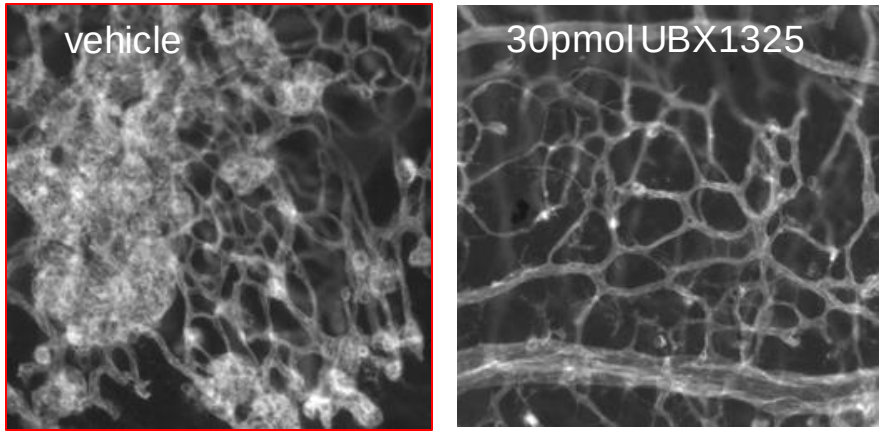
Senescent (Sn) ECs accumulate in diabetic retinas in areas of disease activity

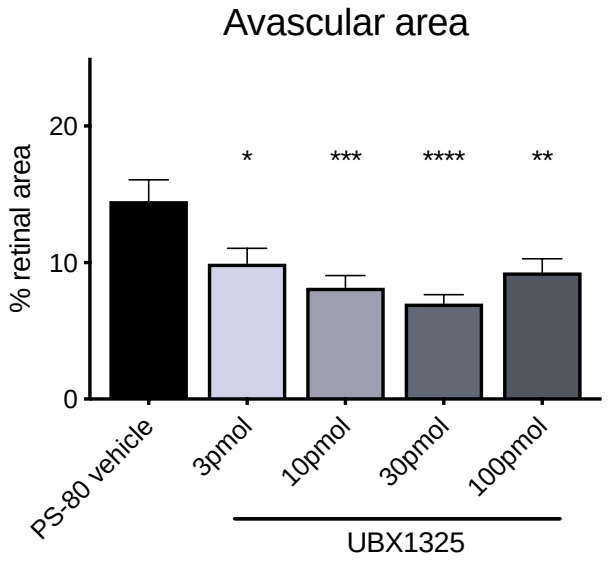
- UBX1325 selectively triggers cell death of Sn ECs
- UBX1325 reduces retinal inflammation and vascular leakage

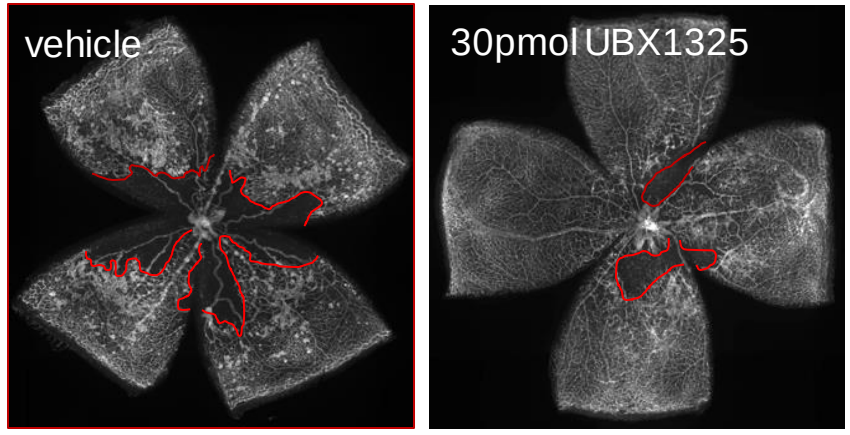
Preclinical data predicts progressive disease modification through vascular remodeling

UBX1325 Improves Retinal Vasculature in Mouse OIR Model









IVT UBX1325 decreases both neovascular and avascular areas in mouse OIR

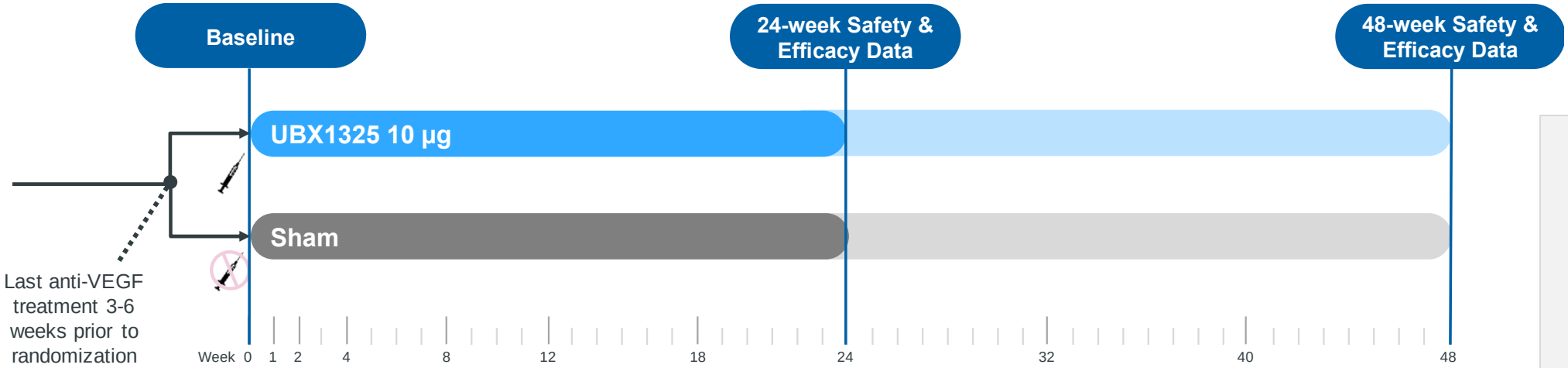
UBX1325 Ph2 BEHOLD Study
48-Week Data in Patients with DME

BEHOLD Study Design, Patient Population, and Endpoints

Patient Population

Individuals with **Diabetic Macular Edema**

- **Repeated anti-VEGF** treatments (≥2 injections/6 months) – Actual: 4.1 injections in prior 6 months
- **Residual retinal fluid** (≥300 µm) – Actual: 439.6 µm
- **Visual acuity deficit** (73 ETDRS letters or worse) – Actual: 61.4 ETDRS letters



	Sham	UBX	Total
Full Analysis Set	33	32	65
Completed to 24 Weeks only	4	5	9
Lost to follow-up	1	3	4
Site Closure	1	0	1
Patient withdrawal	1	0	1
Available through 48 Weeks	26	24	50

= UBX1325 injection

= Sham injection

Endpoints

- Safety and tolerability
- BCVA change from baseline
- Durability of response
- Sub- and intra-retinal fluid, CST changes
- Proportion of UBX1325 patients requiring 2 or more rescue treatments

- Source: t_14_1_1

Patient Characteristics at Baseline Were Well Balanced Between Groups

Parameter, Units (SD)	Sham	UBX1325
Age, Years	61.4 (9.09)	63.6 (9.33)
HBA1c, %	7.4 (1.36)	8.0 (1.68)
Diabetes Dx, Years	17.5 (10.53)	17.2 (11.41)
DME Dx, Years	3.0 (2.32)	3.5 (3.60)
BCVA, ETDRS letters	61.8 (9.61)	60.9 (9.97)
CST, µm	456.2 (98.07)	422.5 (84.16)
# anti-VEGF injections prior 190 days	4.1 (1.09)	4.1 (1.26)
Anti VEGF agent over prior 190 days (# of patients)		
Afilbercept	13	13
Aflibercept, bevacizumab	4	1
Bevacizumab	15	16
Ranibizumab	1	2

Balanced on other parameters at baseline: ethnicity & race, BMI, DRSS score

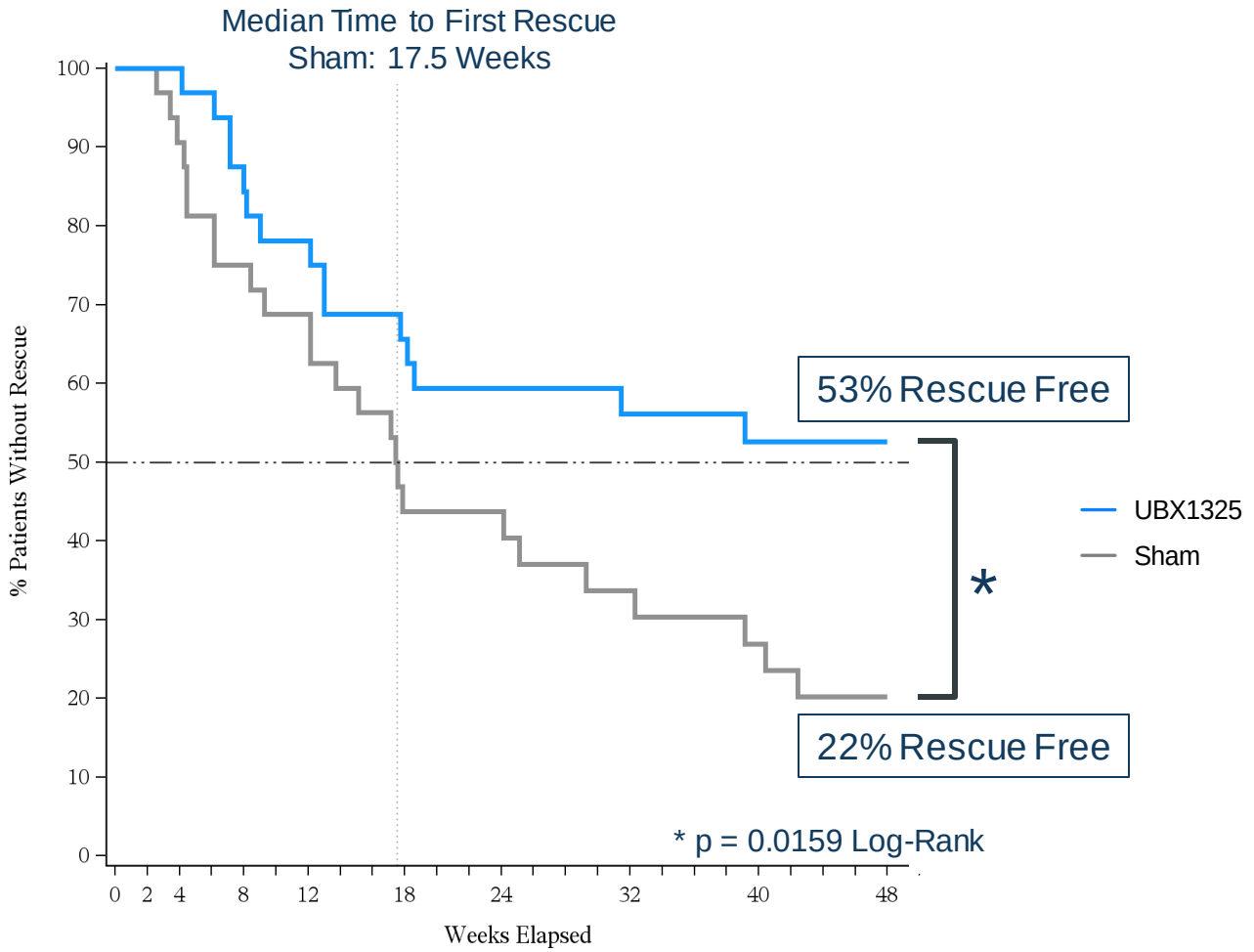
- Source: t_14_1_2

UBX1325-Treated Patients Had Marked Drop In Need For Anti-VEGF Rescue Beyond Week 18 Compared to Sham-Treated Patients Through 48 Weeks

- Median Time-To-First-Rescue in UBX arm was >48 weeks (at least 30 weeks greater than Sham arm)
- ~50% of UBX-treated patients went without rescue through 48 weeks
- ~80% of sham-treated patients required rescue before 48 weeks

Rescue Criteria (Either)

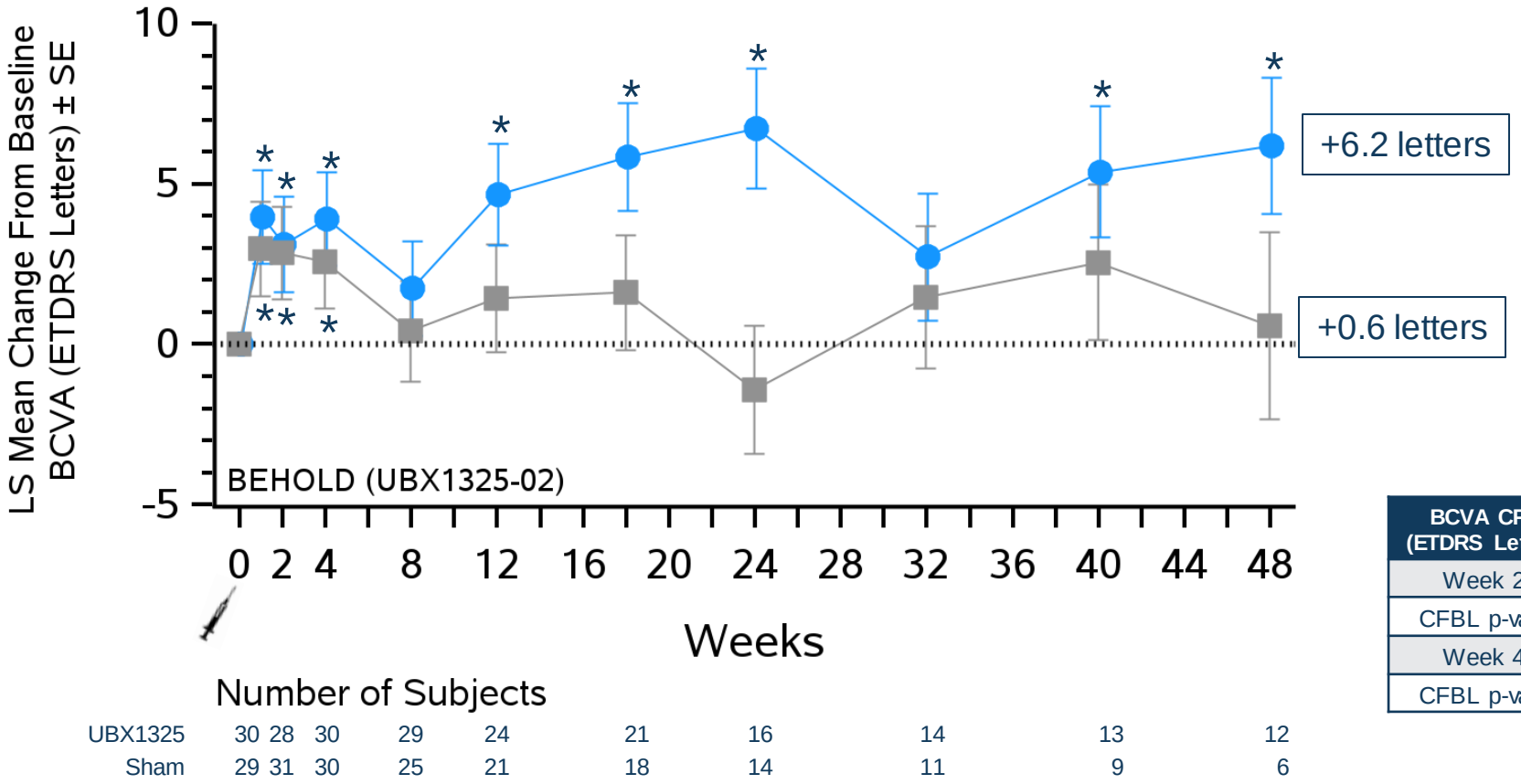
- Decrease of 10 ETDRS or more letters from any peak value
- Increase in CST of 75 µm or more from baseline



Efficacy analyses *excluding* and *including* data post anti-VEGF rescue show a treatment benefit of UBX1325

- Source: f_km_plots_listings; f_km_plots

UBX1325-treated Patients Had a Significant Improvement in BCVA from Baseline† of 6.2 letters at 48 weeks (*excluding* data post-rescue)



* p < 0.05 vs. baseline

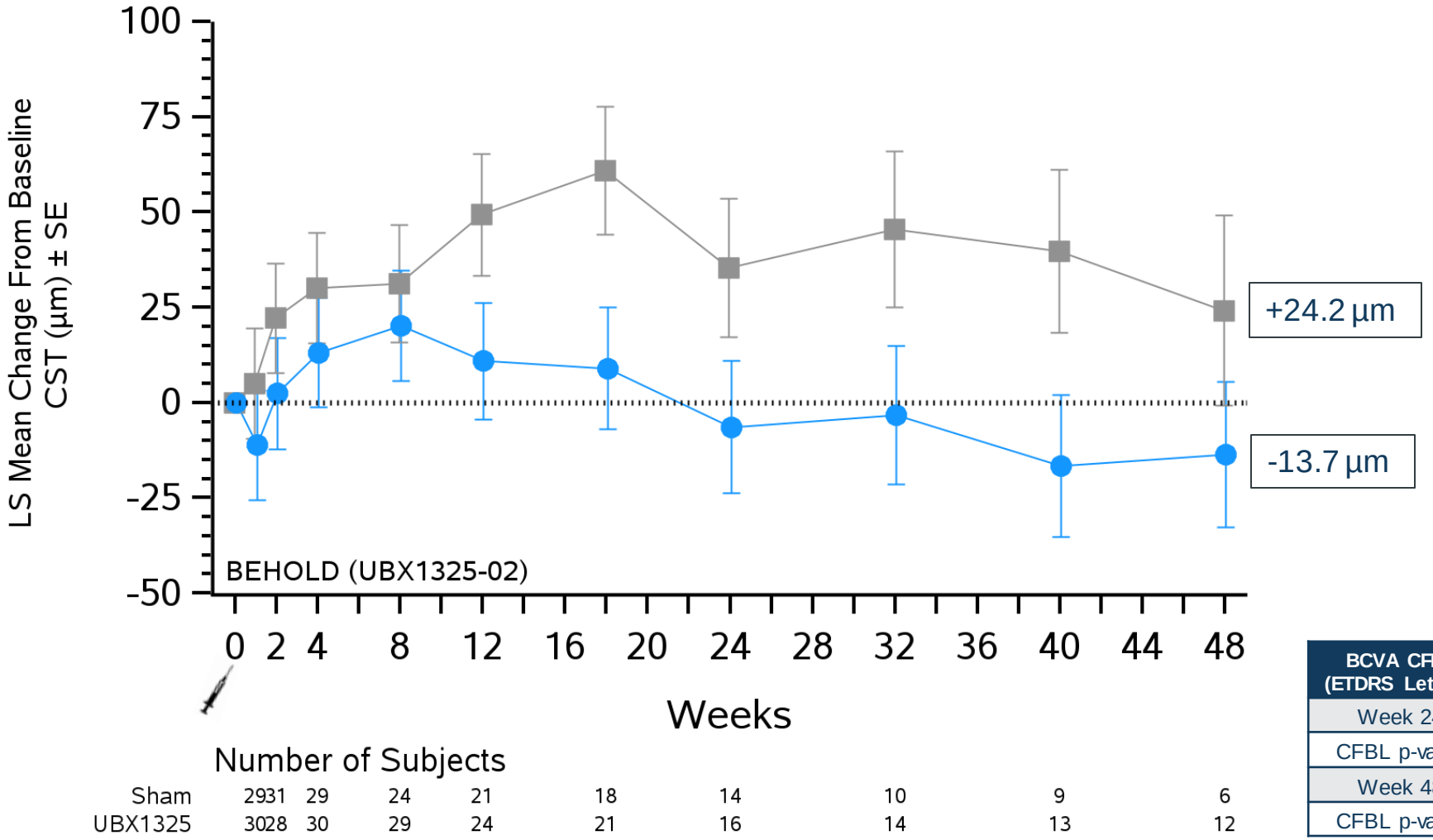
BCVA CFBL (ETDRS Letters)	UBX1325	Sham	Delta	Between Group p-value
Week 24	6.7	-1.4	8.1	0.0031
CFBL p-value	0.0004	NS		
Week 48	6.2	0.6	5.6	0.1198
CFBL p-value	0.0037	NS		

NS: not significant

† MMRM Analysis

- Source: f_14_2_1_1;t_14_2_1_1

CST Remained Stable In UBX1325-Treated Patients Compared to Worsening In Sham Patients (*Excluding* Post-Rescue Data)



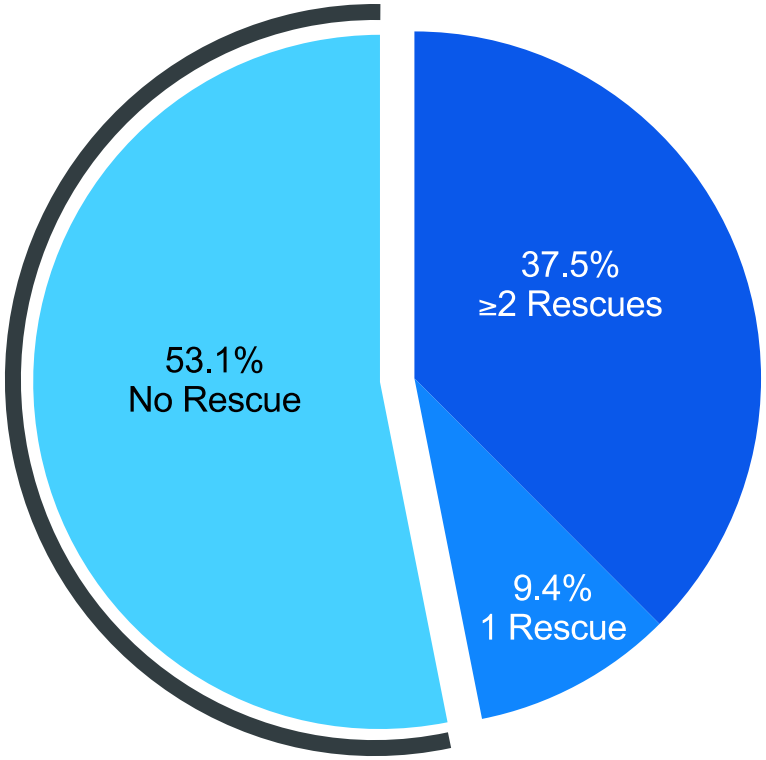
Sham: p < 0.15 vs BL all points *except* Weeks 1 and 48
UBX: All points not significantly different from baseline

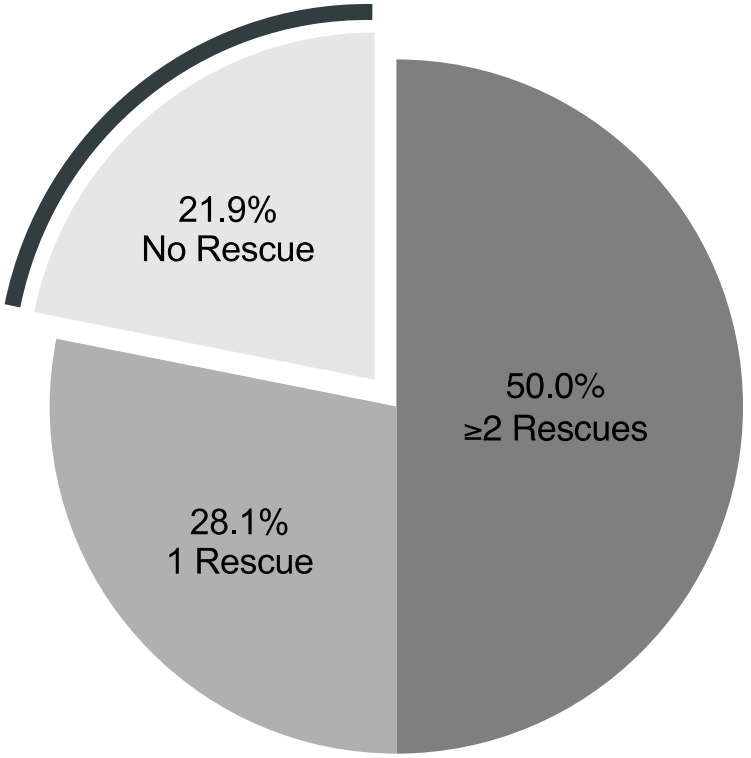
BCVA CFBL (ETDRS Letters)	UBX1325	Sham	Delta	Between Group p-value
Week 24	-6.4	35.4	-41.8	0.0985
CFBL p-value	NS	0.0534		
Week 48	-13.7	24.2	-37.9	NS
CFBL p-value	NS	NS		

NS: not significant

- Source: f_14_2_1_2;t_14_2_1_3

53.1% of UBX1325-Treated Patients In the Study Did Not Require Anti-VEGF Rescue Compared to 21.9% of Sham Patients at 48 Weeks





Rescue Criteria (Either)

- Decrease of 10 ETDRS or more letters from any peak value
- Increase in CST of 75 µm or more from baseline

UBX vs. Sham
p = 0.0096

n = 32
UBX1325

n = 32
Sham

- Source: f_14_2_4_1; t_14_2_2_1

UBX1325 Demonstrated a Favorable Overall Safety and Tolerability Profile With **No Instances of Intraocular Inflammation, Endophthalmitis, Retinal Artery Occlusion or Vasculitis**

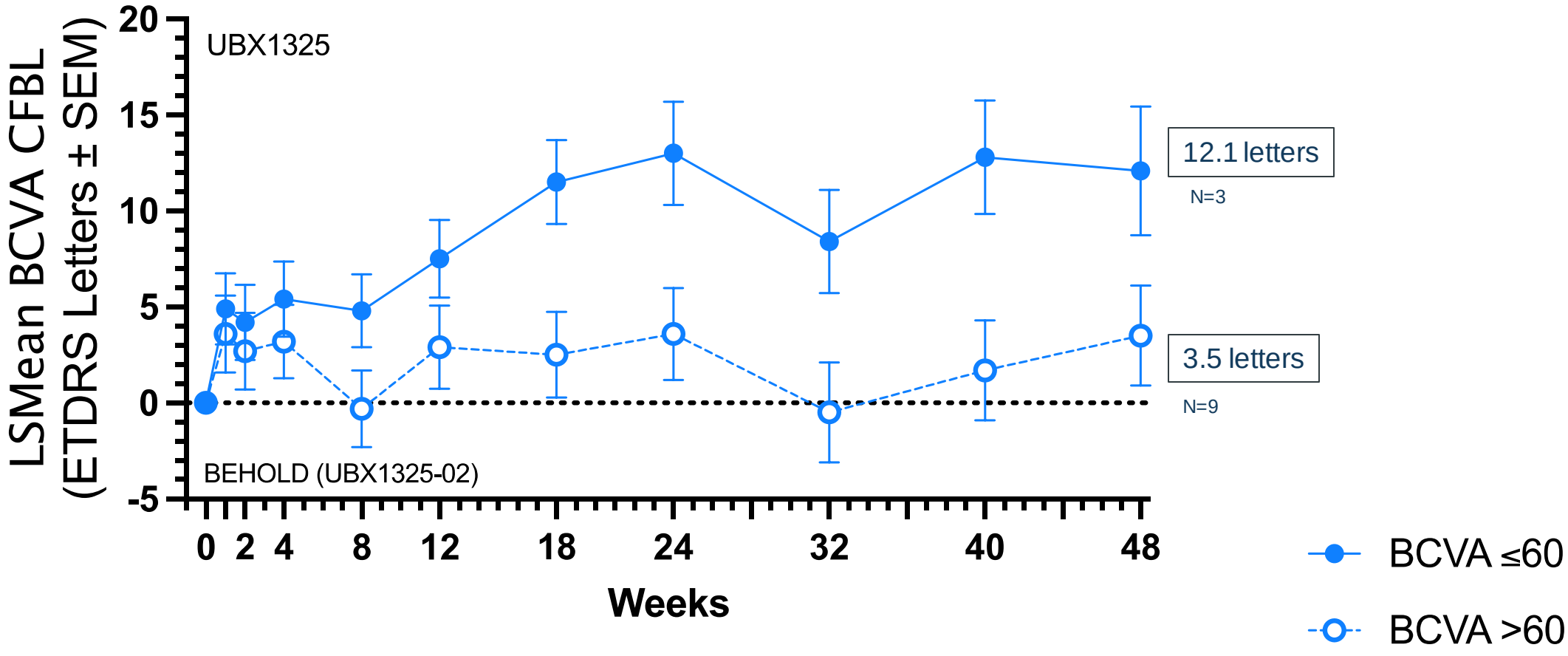
Parameter, No. of Patients	Sham (N = 33)	UBX1325 10 µg (N = 32)
Subjects with at least one TEAE	31 (93.9)	26 (81.3)
Related TEAE	3 (9.1)	6 (18.8)
Grade >=3 TEAE	4 (12.1)	5 (15.6)
Serious TEAE	3 (9.1)	5 (15.6)
Ocular TEAE for Study Eye	28 (84.8)	23 (71.9)
Treatment-related Ocular TEAE for Study Eye	3 (9.1)*	6 (18.8)*
TEAE leading to death	0	0
Intraocular inflammation, endophthalmitis, retinal artery occlusion, or vasculitis	**0**	**0**

* Most are likely procedural related, all were mild-mod, and self-limited:
Sham: 1 conj. hemorrhage, 1 conj. hyperemia, 1 diabetic macular edema
UBX: 5 conj. hemorrhage, 1 ant. chamber pigmentation, 1 eye irritation

- Source: t_14_3_1_1

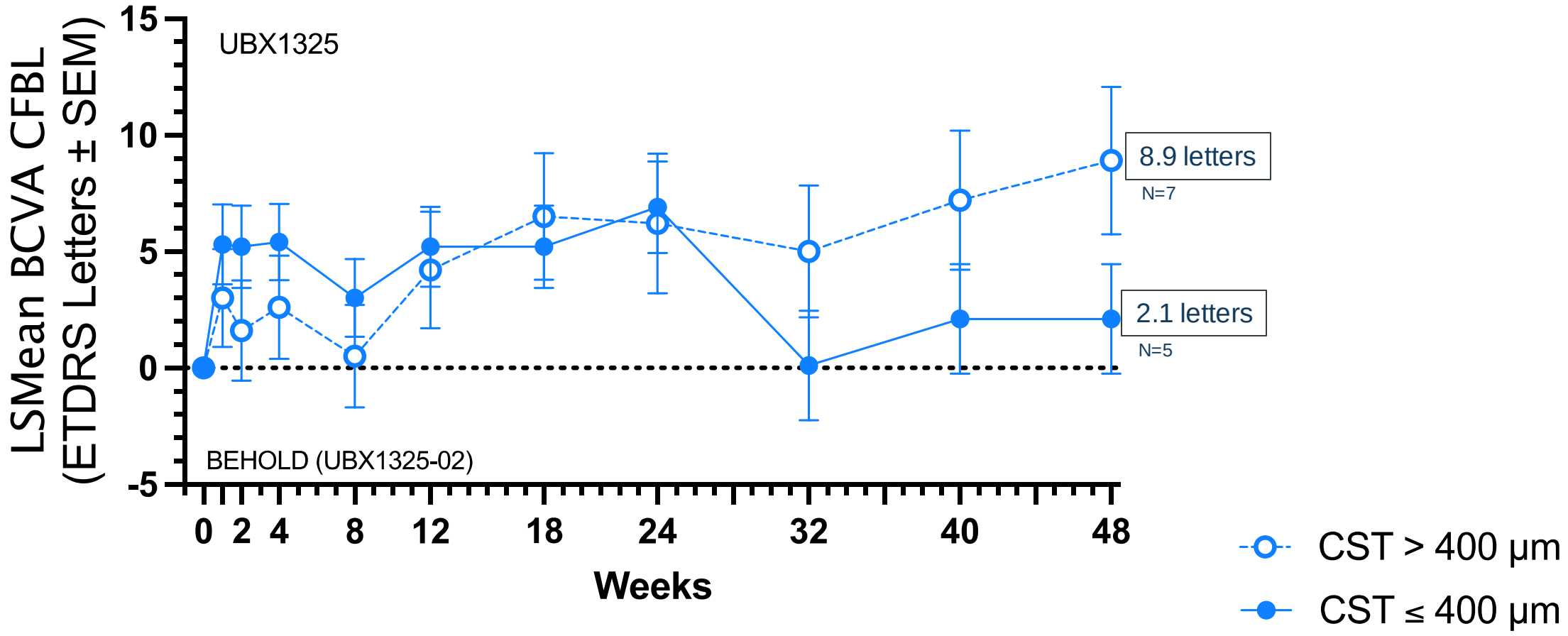
Pre-specified Subgroup Analyses

Higher BCVA Gain in UBX1325-Treated Patients With Baseline BCVA ≤60 Letters at 48 Weeks



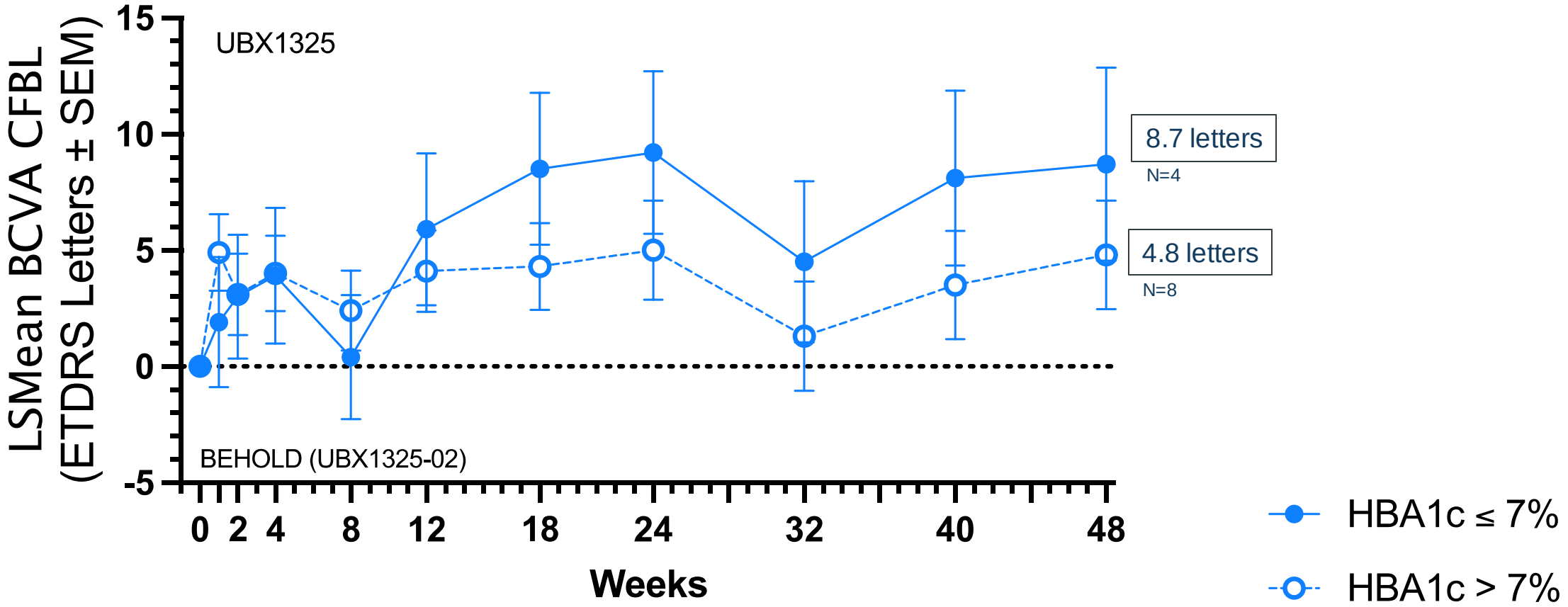
- Source: t_14_2_3_3

Higher BCVA Gain in UBX1325-Treated Patients With Baseline CST > 400 at 48 Weeks



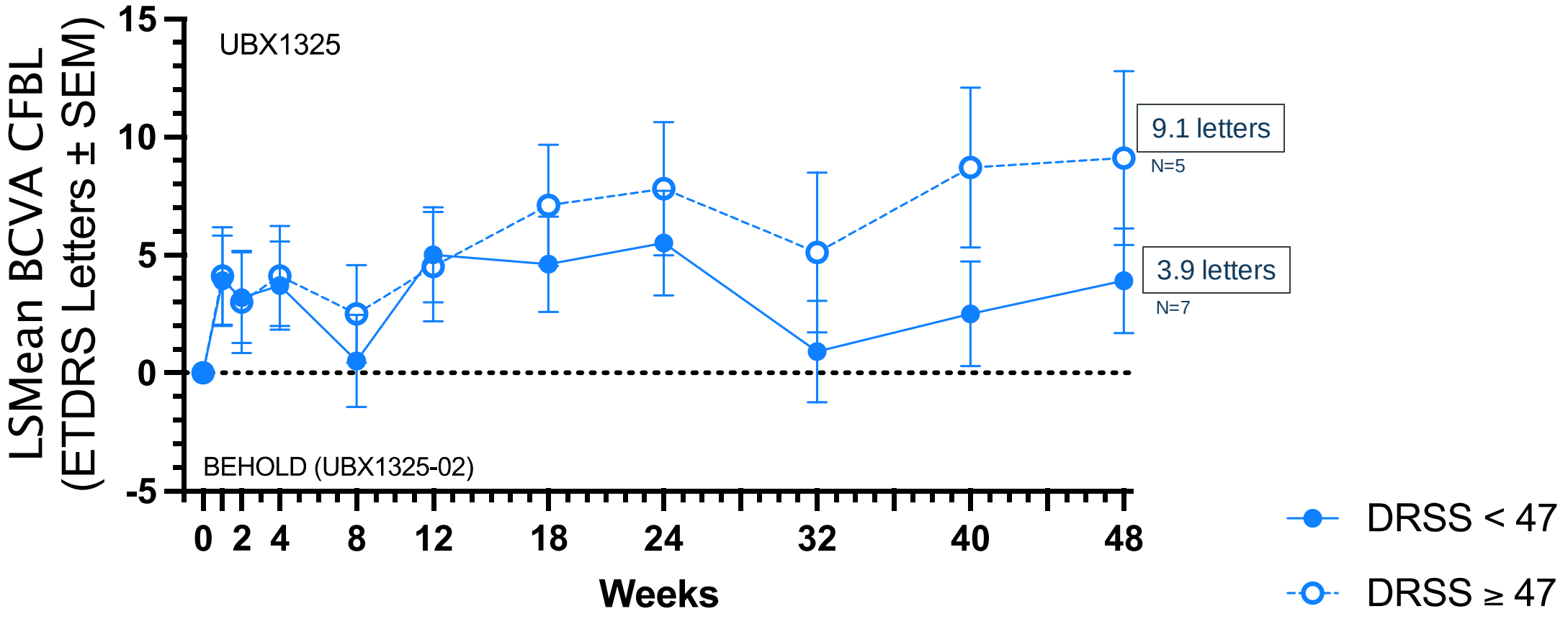
- Source: t_14_2_3_5

Trend Towards Higher BCVA Gain in UBX1325-Treated Patients With Baseline HBA1c ≤ 7% at 48 Weeks



- Source: t_14_2_3_9

Trend Towards Higher BCVA Gain in UBX1325-Treated Patients With Baseline DRSS ≥47 at 48 Weeks



- Source: t_14_2_3_1

Conclusions

In the BEHOLD Phase Study, UBX1325:

- Improved visual acuity at 48 weeks by **6.2 letters from baseline after a single injection**
- Led to ~50% of patients achieving a **rescue-free interval of at least 48 weeks** and may represent the **potential for disease modification**
- **Maintained retinal structure** throughout the duration of the study without the need for anti-VEGF rescue
- Had a **generally favorable safety and tolerability profile** with no intraocular inflammation