Tyrosine Kinase Inhibitors: A Suprachoroidal Perspective

Innovate Retina 2024

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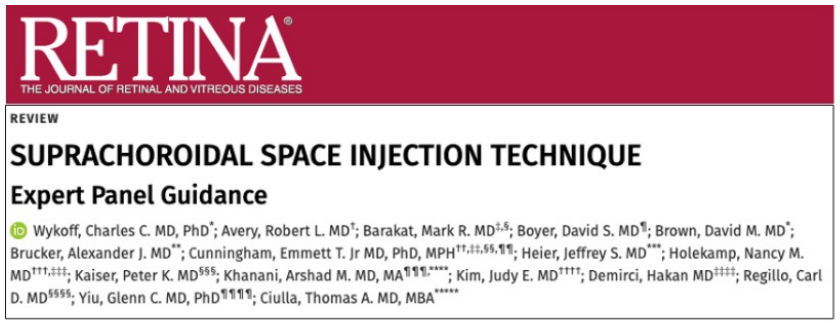
On behalf of the ODYSSEY investigators

Financial Disclosures

Straightforward Suprachoroidal Injection Technique


RETINA
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

REVIEW

SUPRACHOROIDAL SPACE INJECTION TECHNIQUE

Expert Panel Guidance

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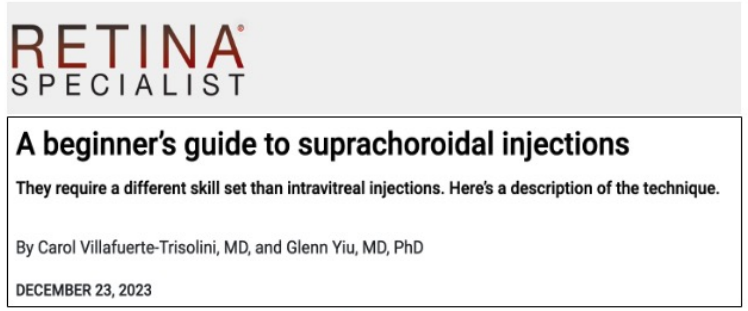
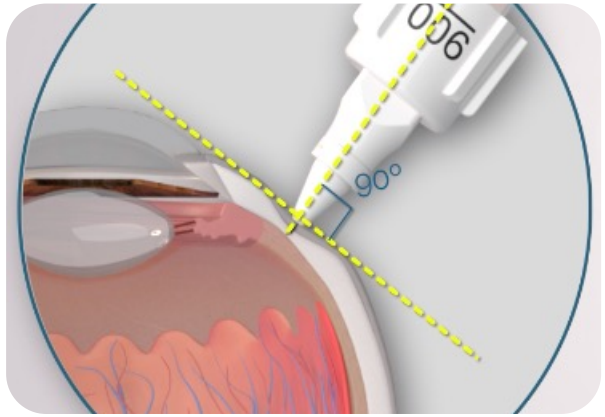

RETINA SPECIALIST

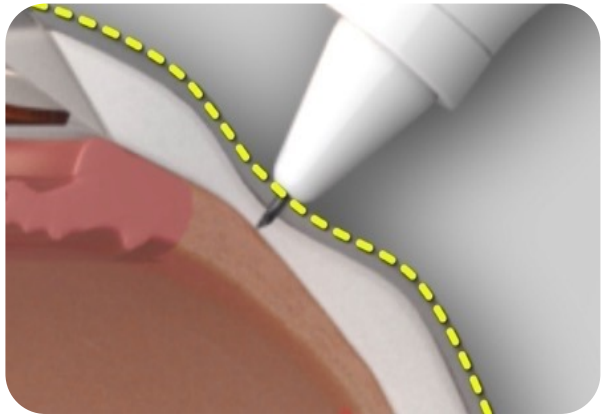
A beginner's guide to suprachoroidal injections

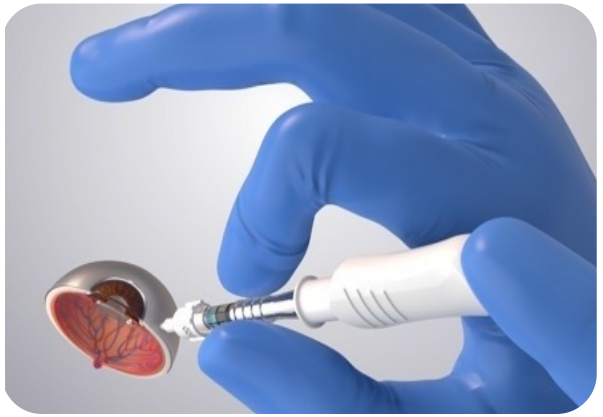
They require a different skill set than intravitreal injections. Here's a description of the technique.

By Carol Villafuerte-Trisolini, MD, and Glenn Yiu, MD, PhD

DECEMBER 23, 2023







Perpendicular

Hold the microinjector **perpendicular** to the ocular surface

Dimple

Ensure firm contact with sclera by maintaining a **dimple** throughout injection

Slow

Inject **slowly** over 5 – 10 seconds

Source: Clearside July 24, 2024 KOL Webinar

ODYSSEY Phase 2b Clinical Trial

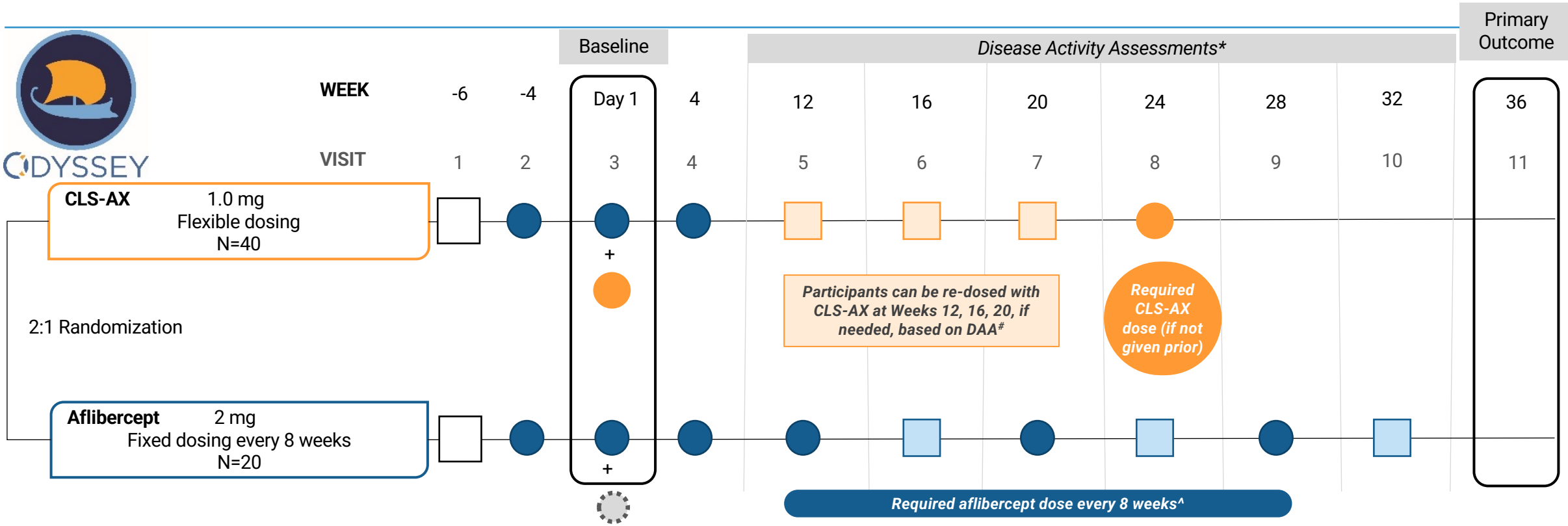
Trial Objectives:
Evaluate safety, efficacy & duration of CLS-AX in participants with wet AMD

- Primary Outcomes: Mean change in BCVA from Baseline to **Week 36**; Safety & tolerability
- Secondary Outcomes: Other changes in visual function and retinal imaging, including CST; Need for supplemental treatment; Treatment burden as measured by total injections

Participant Profile:
60 total with 2:1 randomization (40 in CLS-AX arm & 20 in aflibercept arm)

- Treatment experienced participants with reading center confirmation of **persistent active disease**
- Protocol required **re-dosing with CLS-AX** in study arm
  - Participants received at least 2 doses of CLS-AX
  - Provides important data to plan Phase 3 in chronic disease

ODYSSEY Trial Design



Screening visit

CLS-AX 1.0 mg Suprachoroidal Injection (SCS)

Sham Procedure

Aflibercept 2 mg Intravitreal Injection (IVT)

#Participants can be re-dosed with CLS-AX up to every 12 weeks; All arms are sham controlled

The determination of active disease will be made if any of the following are met:

- BCVA reduction of > 5 letters from Visit 3 (Baseline, Day 1) AND increase in CST of >75 microns on SD-OCT from Visit 3 (Baseline, Day 1)
- BCVA reduction of >10 letters from Visit 3 (Baseline, Day1)
- Increase in CST of >100 microns on SD-OCT from Visit 3 (Baseline, Day 1)
- Presence of new or worsening vision-threatening hemorrhage

* Disease Activity Assessments (DAA): Conducted at Week 12 through 32 to determine need for supplemental treatment.
# In CLS-AX arm, following 3 loading doses of aflibercept and initial dose of CLS-AX at Baseline, participants will receive CLS-AX at least every 24 weeks unless more frequently required based on DAA;
if disease is active and participant is <12 weeks since last CLS-AX injection, participant receives dose of aflibercept;
if disease is active and participant is >12 weeks since last CLS-AX injection, participant receives dose of CLS-AX.
^ In aflibercept arm, following 3 loading doses of aflibercept, participants will receive aflibercept on fixed dosing regimen every 8 weeks unless more frequently required based on DAA;
if disease is active, participant receives dose of aflibercept.

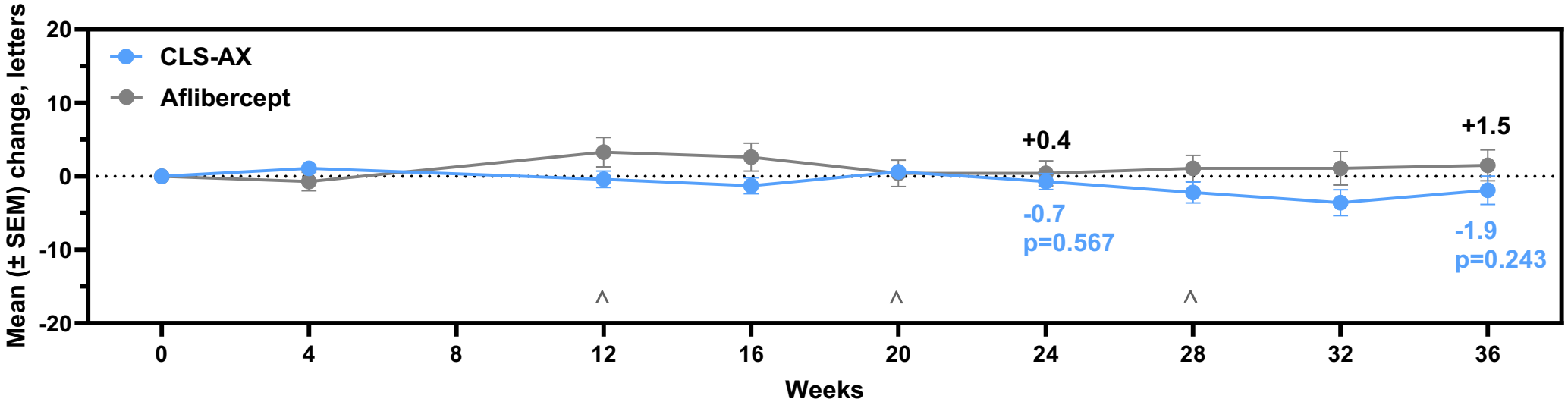
Demographics and Baseline Characteristics

Characteristics	CLS-AX	Aflibercept	Overall
No. of participants	40	20	60
Mean age (range), years	76.9 (51-90)	80.3 (54-96)	78.0 (51-96)
Women, no. (%)	25 (62.5)	14 (70.0)	39 (65.0)
Race, no. (%) White Asian	 37 (92.5) 3 (7.5)	 20 (100) 0	 57 (95.0) 3 (5.0)
Median duration of wet AMD diagnosis (range), months	9.65 (1.4-31.1)	10.2 (1.4-20.8)	9.9 (1.4-31.1)
Mean BCVA (range) at screening, ETDRS letters	69.1 (37-80)	69.1 (51-80)	69.1 (37-80)
Mean CST (range) at screening, µm	266.8 (175-378)	294.3 (209-592)	276.0 (175-592)
Mean Total Area of CNV (range) at screening, mm^2	6.8 (1.6-26.9)	6.5 (0.5-20.8)	6.7 (0.5-26.9)
Bilateral wet AMD, n	17	6	23
Mean annualized number of prior wet AMD treatments (injections/year) [a] (range)	9.5 (3.2-17.2)	9.2 (4.1-17.2)	9.4 (3.2-17.2)

Abbreviations: AMD = age-related macular degeneration; BCVA = best corrected visual acuity; CNV = choroidal neovascularization; CST = central subfield thickness; ETDRS = Early Treatment Diabetic Retinopathy Study.
[a]Annualized number of prior wet AMD treatments defined as the total number of prior wet AMD treatments divided by the duration of wet AMD diagnosis in years.

Stable Best Corrected Visual Acuity (BCVA) Over 36 Weeks

BCVA Within 2 Letters From Baseline at Both Week 24 and Week 36 in CLS-AX Arm

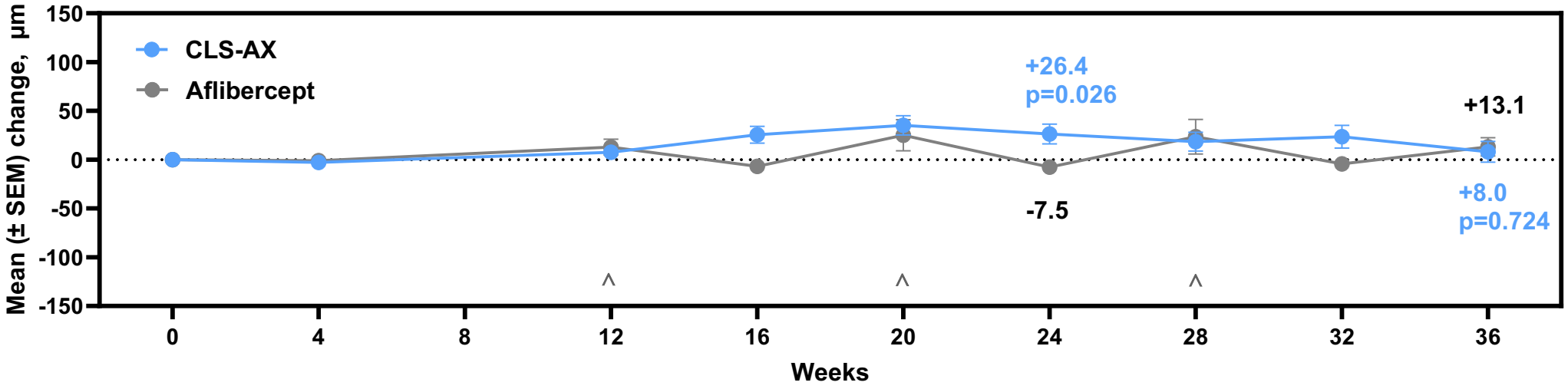


CLS-AX results do not include supplemental therapy with aflibercept

^Study drug administration for aflibercept participants given at Weeks 12, 20 and 28.
Abbreviations: BCVA = best corrected visual acuity; SEM = standard error of the mean.
P-value based on a 2-sample t-test between treatment groups .

Stable Central Subfield Retinal Thickness (CST) Over 36 Weeks as Verified by Independent Reading Center

CLS-AX Demonstrates Stable Anatomical Control and Reduces Fluctuation

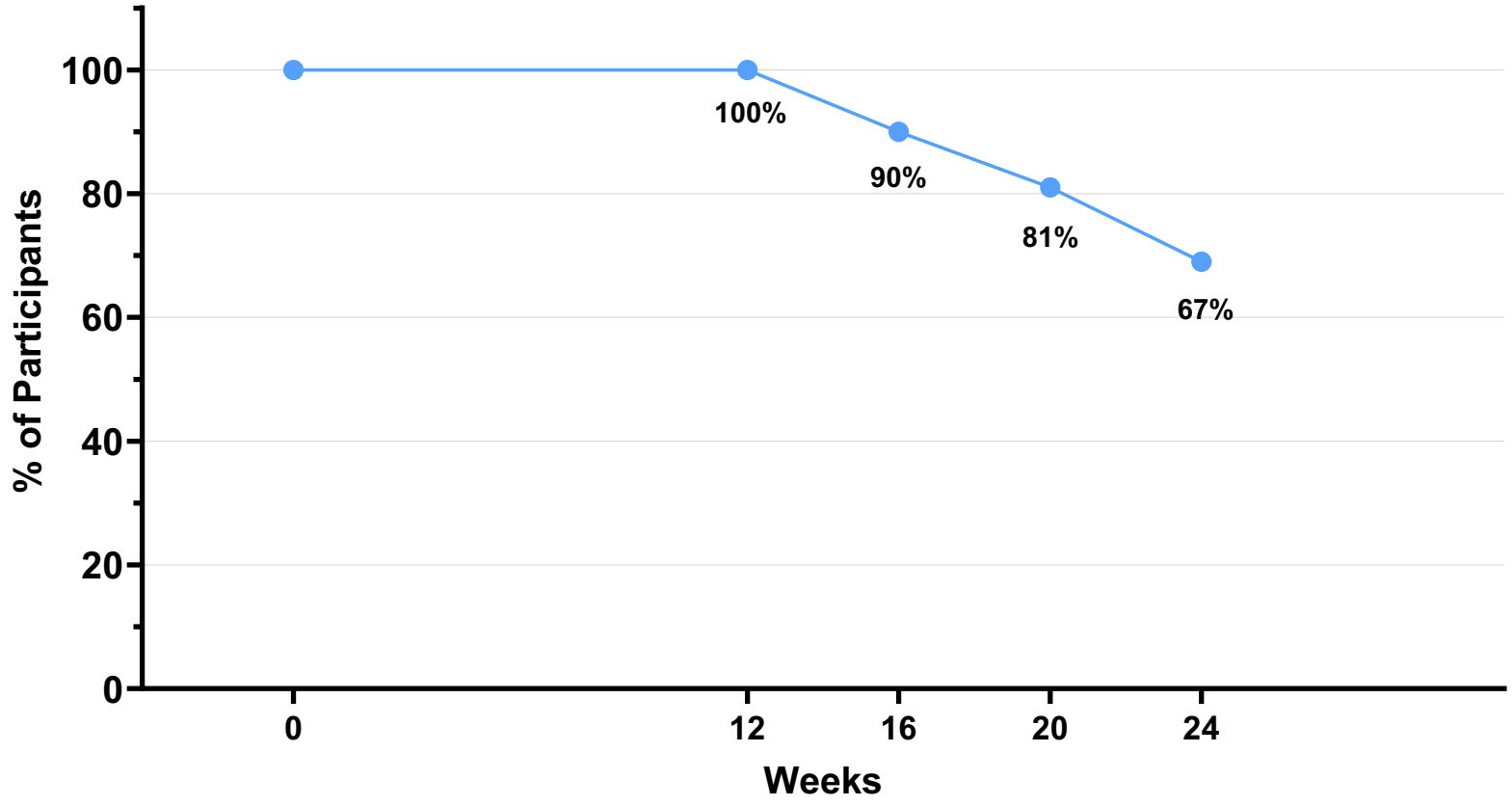


CLS-AX results do not include supplemental therapy with aflibercept

^Study drug administration for aflibercept participants given at Weeks 12, 20 and 28.
Abbreviations: CST = central subfield thickness – as reported by the reading center; SEM = standard error of the mean.
P-value based on a 2-sample t-test between treatment groups .

Two-Thirds of Participants Dosed with CLS-AX Reached Six Months Without Additional Treatment

Intervention–Free Rates By Week Up to Each Visit

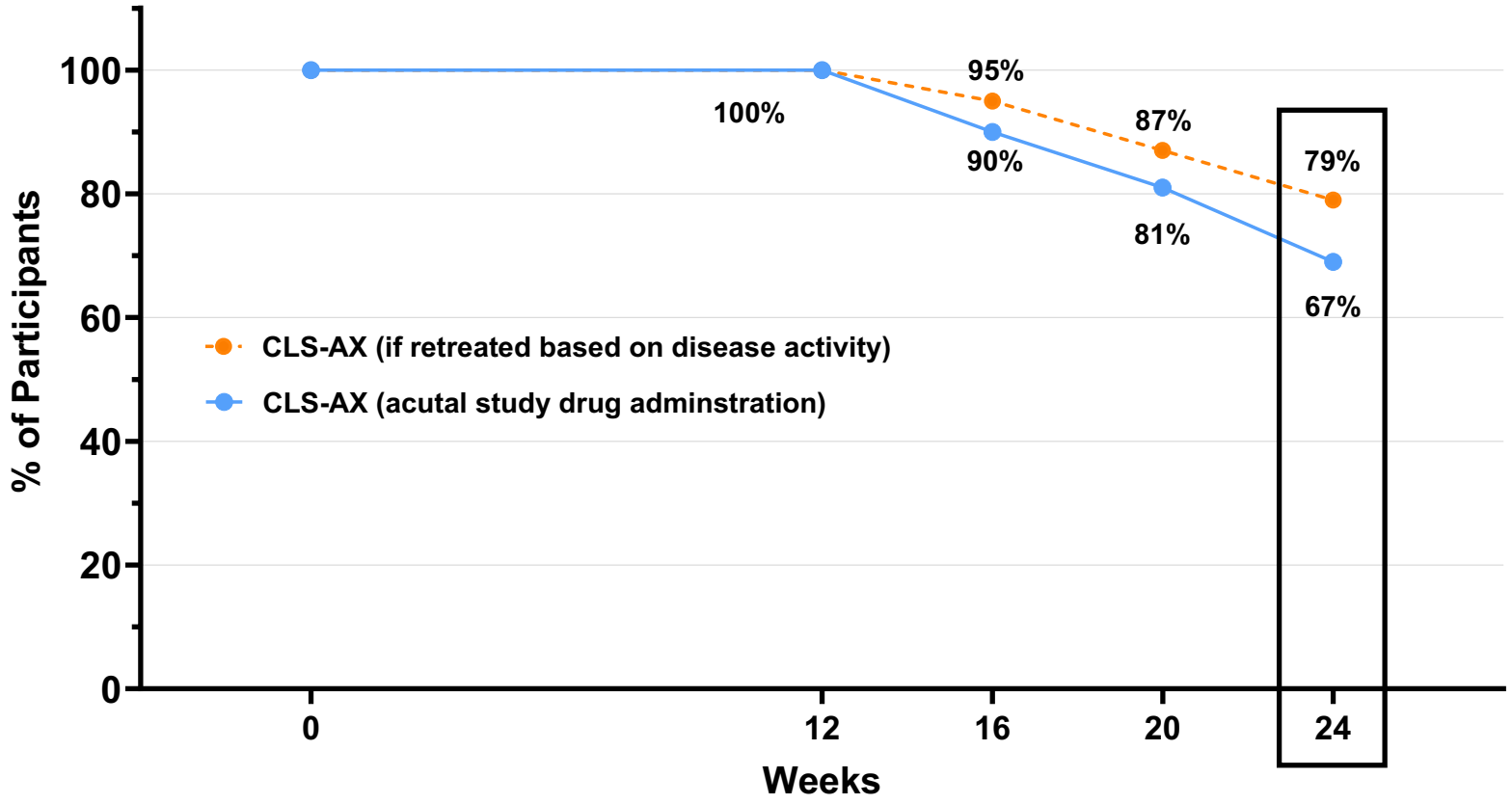


Week 12: 40/40 (100%)
Week 16: 35/39 (89.7%)
Week 20: 30/37 (81.1%)
Week 24: 26/39 (66.7%)

Calculation accounts for missed treatments; time of initial administration of study drug shown as month 0 on figure. Intervention-free rate calculation: if participant received intervention at a study visit, those were reflected in the count at the following study visit.

More Participants May Have Been Intervention Free at Every Time Point if DAA Criteria Strictly Applied

No Participants Met the DAA Criteria Per Reading Center Confirmation at Week 24, but They Received Mandatory Re-Dosing Per the Protocol



Based on disease activity
Week 12: 40/40 (100%)
Week 16: 37/39 (94.9%)
Week 20: 32/37 (86.5%)
Week 24: 30/38 (78.9%)

DAA = Disease Activity Assessment. Actual treatments compared to reading center confirmation. Active disease-free rate calculation: if participant had active disease at a study visit, those were reflected in the count at the following study visit. N = number of participants assessed at a study visit; n = number of participants active disease-free up to a visit. Active disease presence based on BCVA and CST as graded by the central reading center.

CLS-AX Consistently Reduced the Frequency of Injections

Comparison of Wet AMD Treatments Pre- and Post- Randomization

24 Weeks Before and After

Average number of treatments
24 Weeks prior to Screening Visit:
2.95 injections

Average number of treatments
up to 24 Weeks after Baseline Visit:
0.475 injections

Reduced injection frequency by

84%

Injection post Baseline includes re-dosing with CLS-AX and/or supplementary treatment with aflibercept.
Injection frequency reduction calculated by the average number of treatments 24 Weeks prior to Screening Visit as compared to average number of treatments up to 24 Weeks after Baseline Visit.

CLS-AX Demonstrated Positive Safety Profile

No Ocular SAEs and No Treatment-Related SAEs

- No drug or procedure-related ocular SAEs
- No reported drug or procedure-related systemic SAEs
- No endophthalmitis
- No retinal vasculitis
- Four cases of intraocular inflammation all deemed clinically mild by the Safety Review Committee
  - Two cases had minimal clinical signs that resolved
  - Two cases were potentially related to drug administration
  - In all four cases, the inflammation was no longer detected at or before Week 36

Abbreviations: AE = adverse event; SAE = serious adverse event; TEAE = treatment-emergent adverse event.

CLS-AX Now Phase 3 Ready Based on Positive ODYSSEY Data

- Achieved Primary Objective: Stable BCVA to Week 36
  Difficult-to-treat Wet AMD participants with confirmed activity
- Compelling injection free rates up to 6 months
  Injection frequency reduced by nearly 84%
- Positive safety profile
  No ocular SAEs or treatment-related SAEs
  CLS-AX was well-tolerated after re-dosing
- Only Phase 2 trial in wet AMD with repeat TKI dosing data to better inform and potentially de-risk Phase 3 design

Preliminary Topline Results
Subject to Change

Thank You ODYSSEY Investigators!

Retinal Research Institute - Phoenix
Retina Consultants of Orange County
Northern California Retina Vitreous Associates
Retina Research Institute of Texas
Texas Retina Associates - Plano
Southeast Retina Center
Western Carolina Retinal Associates
Vitreo-Retinal Associates
Retinal Consultants Medical Group
Retina Consultants of Texas
California Retina Consultants
Austin Retina
Tennessee Retina PC
Retina Group of Florida
Associated Retina Consultants
Sierra Eye Associates
Illinois Retina Associates
Spokane Eye Clinical Research
Retinal Consultants of Southern California
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