

# **Ixoberogene Soroparvovec (Ixo-vec) IVT Gene Therapy for Neovascular AMD: 26-Week Interim Analysis Results from the Phase 2 LUNA Study**

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# Disclosures

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Allergan<sup>C</sup>  
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Apellis<sup>BC</sup>  
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Astellas<sup>BC</sup>  
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Genentech<sup>BCR</sup>  
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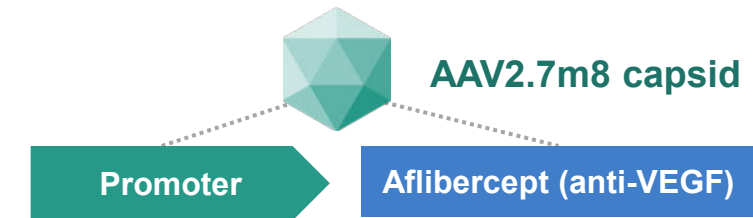
Harrow<sup>C</sup>  
Janssen<sup>C</sup>  
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Novartis<sup>BCR</sup>  
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Oculis<sup>CR</sup>  
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Outlook Therapeutics<sup>C</sup>  
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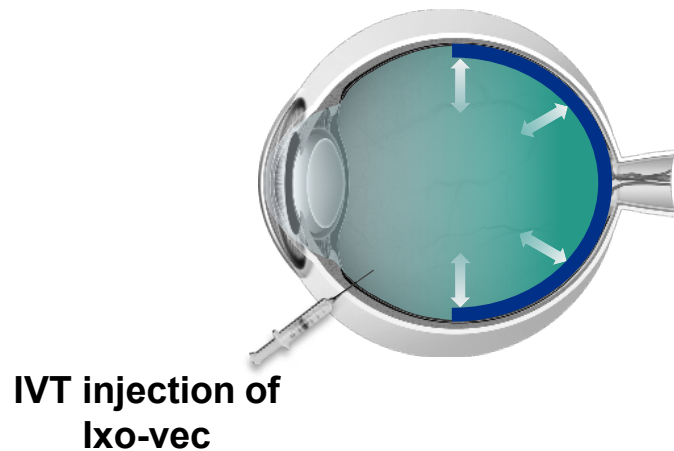
(B): Speakers' Bureau; (C): Consultant; (E): Equity; (R): Grants/Research Support

# Ixo-vec IVT Gene Therapy is Designed to Provide Continuous Delivery of Aflibercept for Long-term nAMD Management and Preservation of Vision

**AAV2.7m8 capsid engineered via directed evolution for enhanced transduction carrying a coding sequence for the anti-VEGF protein aflibercept**

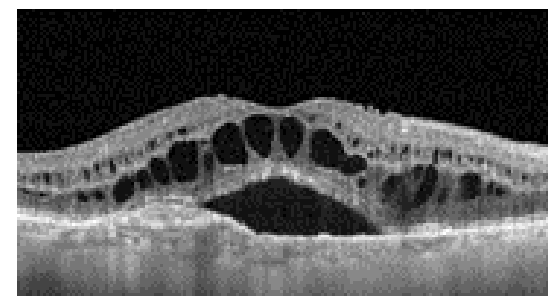


**Following a one-time IVT Ixo-vec injection, transduced retinal cells become the source of continual aflibercept production**

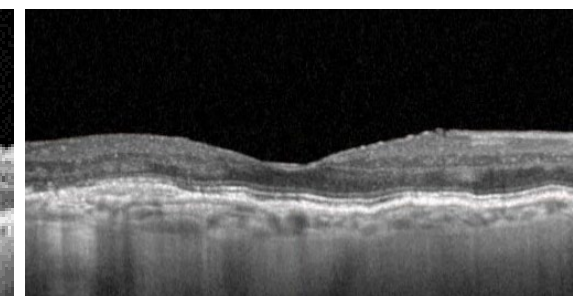


**115 participants dosed with Ixo-vec across 3 clinical trials with up to 5 years of follow-up**

**nAMD OPTIC 2x10<sup>11</sup> vg/eye Participant with No Supplemental anti-VEGF Injections Through 3 Years<sup>3</sup>**



**Baseline**  
BCVA (ETDRS): 75



**Year 3**  
BCVA (ETDRS): 80

# LUNA Phase 2 Trial in Previously Treated Patients with nAMD

## To Evaluate Lower Doses of Ixo-vec and Enhanced Corticosteroid Prophylaxis Regimens

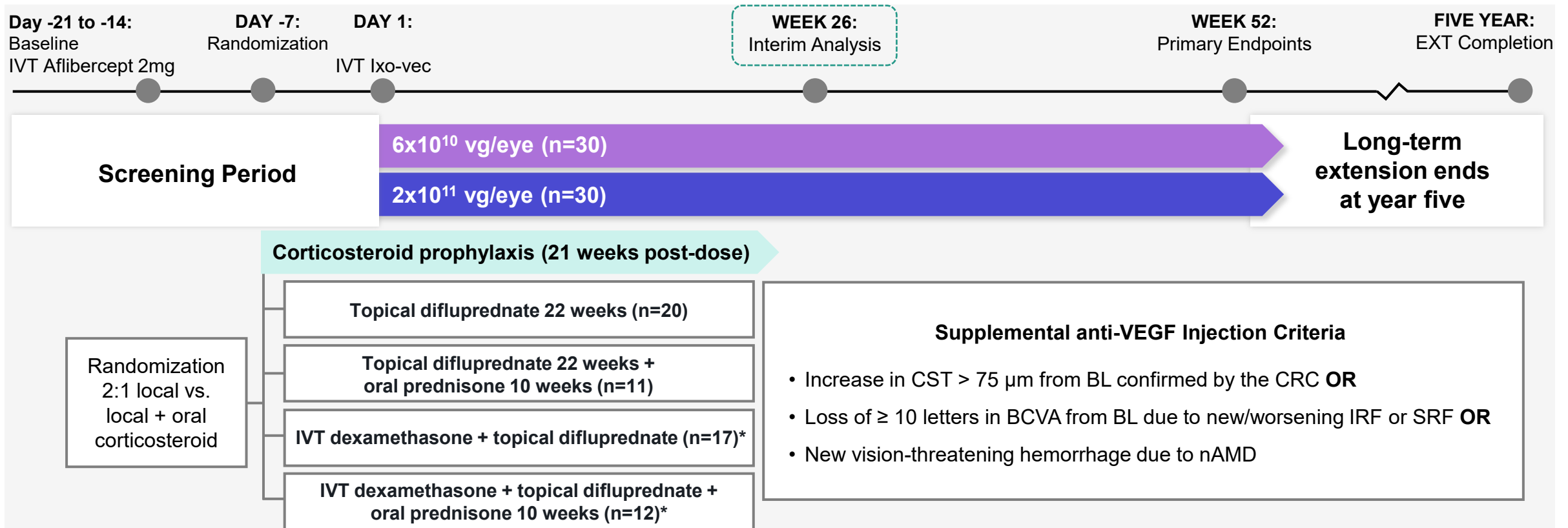
### Multicenter, double-masked, randomized, parallel-group Phase 2 study

#### Key inclusion criteria

- Demonstrated response to anti-VEGF therapy and under active treatment for choroidal neovascularization due to nAMD (minimum of 2 injections within 4 months of entry)
- Study eye BCVA in the range of 25 – 83 ETDRS letters

#### Primary endpoints

- Mean change in BCVA from baseline through Week 52
- Incidence and severity of adverse events through Week 52



Study timeline and length of arrows depicted are not to scale. Baseline is defined as the day screening aflibercept is administered. Investigators and participants are masked to the dose of Ixo-vec; they are not masked to the corticosteroid prophylaxis regimen. \*Protocol amended early in study to include difluprednate starting at week 4 to match the taper in difluprednate regimens; if initiated after week 4 visit difluprednate may be adjusted at the discretion of investigator in consult with medical monitors (6 participants did not receive difluprednate topical as part of prophylaxis). BCVA, best corrected visual acuity; CST, central subfield thickness; BL, baseline; CRC, central reading center; IRF, intraretinal fluid; SRF, subretinal fluid

# LUNA Study Disposition

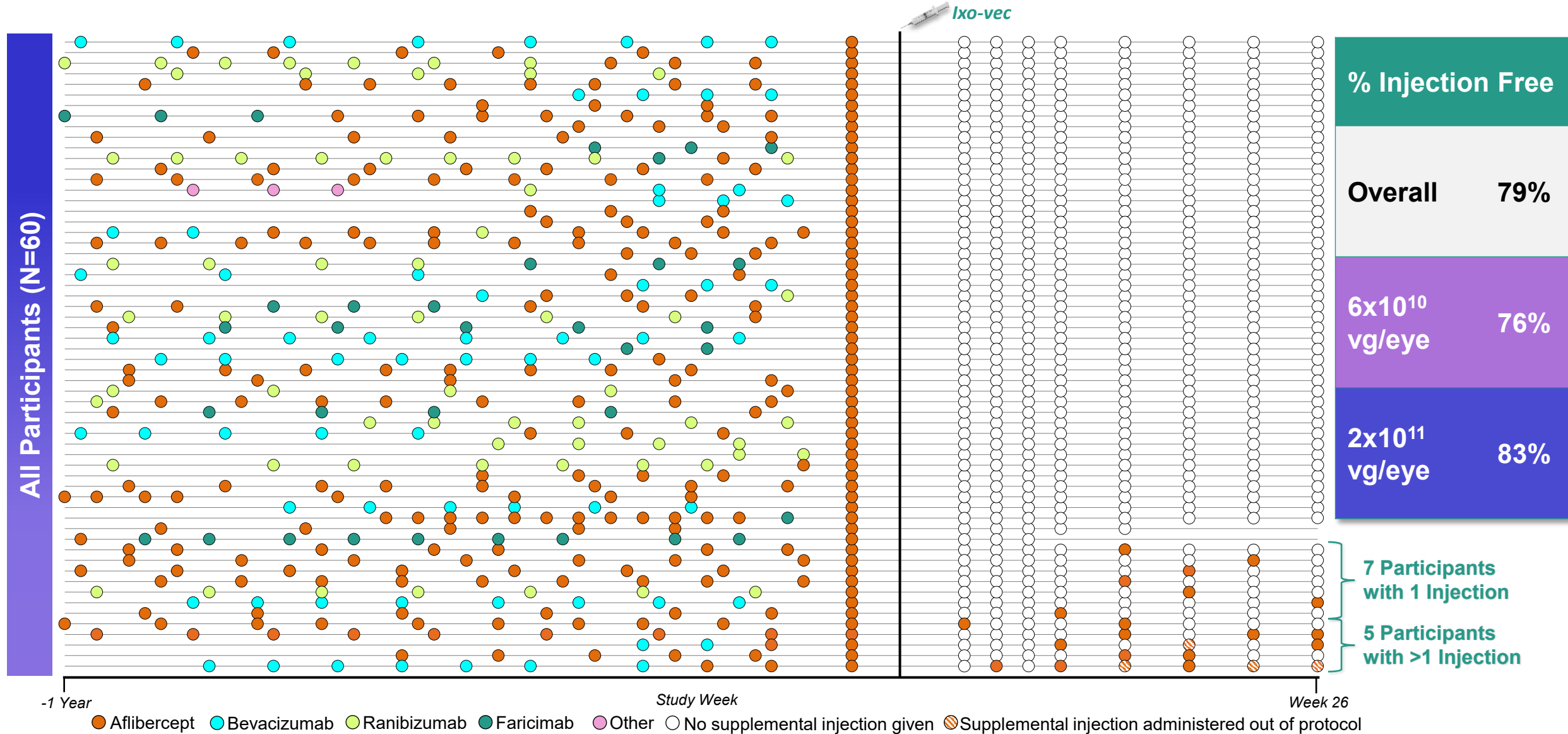
Participant Disposition	
<b>Number of participants randomized and dosed with Ixo-vec</b>	60
Number of participants who completed Week 26	58
<b>Number of participants who discontinued after Ixo-vec dosing</b>	2
<b>Reason for discontinuation (not related to Ixo-vec)</b>	
• Death (Abdominal mesenteric mass, multiple organ failure, and septic shock – not related to study drug)	1
• Adverse event (Dementia – not related to study drug)	1
<b>Mean follow-up duration in Weeks from Day 1</b>	35.2

Prespecified interim analysis performed when all participants completed the 26-week study visit

# LUNA Demographics and Baseline Characteristics

Demographics and Baseline Characteristics	Ixo-vec 6x10 <sup>10</sup> vg/eye N = 30	Ixo-vec 2x10 <sup>11</sup> vg/eye N = 30	LUNA Total N = 60
Mean age, years (SD)	75.4 (8.2)	77.7 (7.4)	76.6 (7.8)
Female, n (%)	16 (53%)	18 (60%)	34 (57%)
Race, n (%)			
White	27 (90%)	28 (93%)	55 (92%)
Asian	2 (7%)	2 (7%)	4 (7%)
Mean years since nAMD diagnosis in the study eye (SD)	3.0 (2.9)	3.0 (3.1)	3.0 (2.9)
Mean annualized anti-VEGF injections in year prior to Day 1 (SD)	10.2 (1.7)	10.0 (3.3)	10.1 (2.6)
Mean BCVA, ETDRS letters (SD)	72.9 (8.8)	71.8 (6.4)	72.3 (7.7)
Mean CST, μm (SD)	360.6 (112.0)	340.5 (119.3)	350.6 (115.2)
Phakic lens status, n (%)	11 (37%)	11 (37%)	22 (37%)

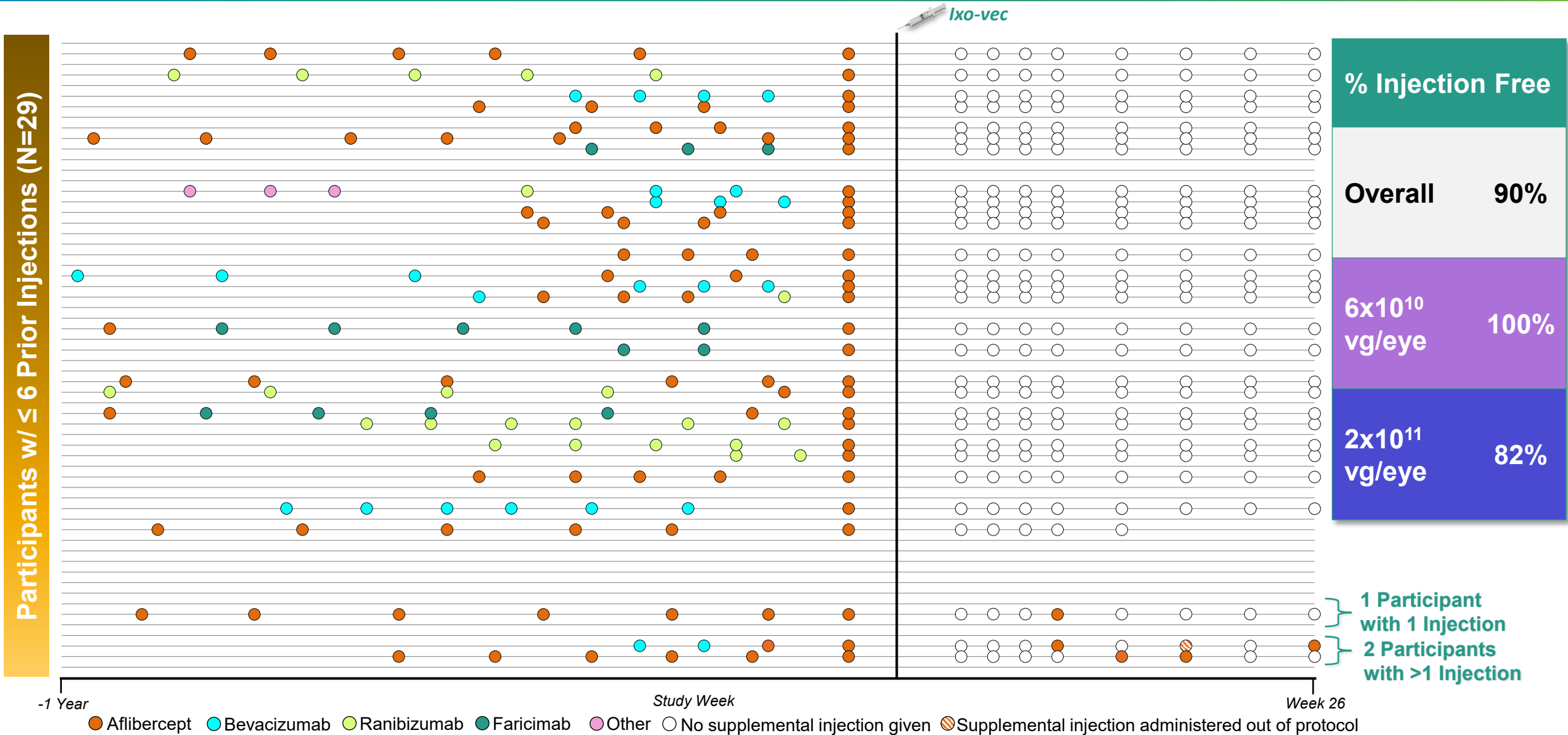
# 79% were Injection Free Across Both Ixo-vec Doses in Patients Previously Requiring Frequent Anti-VEGF Injections



Doses pooled in swim lane plot to preserve investigator masking in an ongoing double masked study.

Data cut: 14Feb2024

# 90% were Injection Free Across Both Ixo-vec Doses in Patients with ≤ 6 Prior Injections in the Year Prior

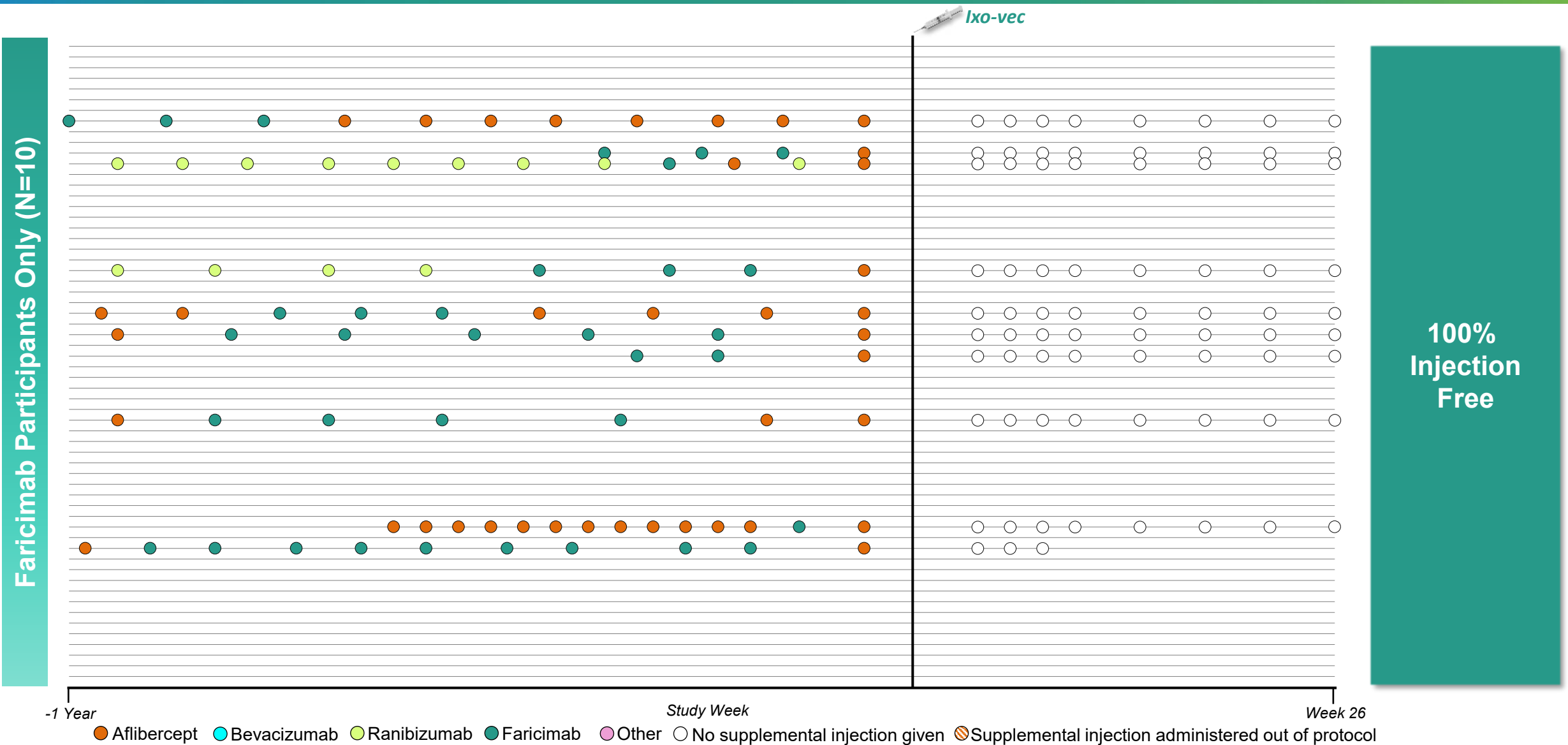


Patients received up to 6 injections in the year prior to entering the LUNA study excluding the LUNA aflibercept screening dose: 4.3 mean actual injections in both 6E10 and 2E11 dose cohorts and 10.2 and 9.5 mean annualized injections in 6E10 and 2E11 dose cohorts, respectively; 6E10: N=12, 2E11: N=17. Doses pooled in swim lane plot to preserve investigator masking in an ongoing double masked study.

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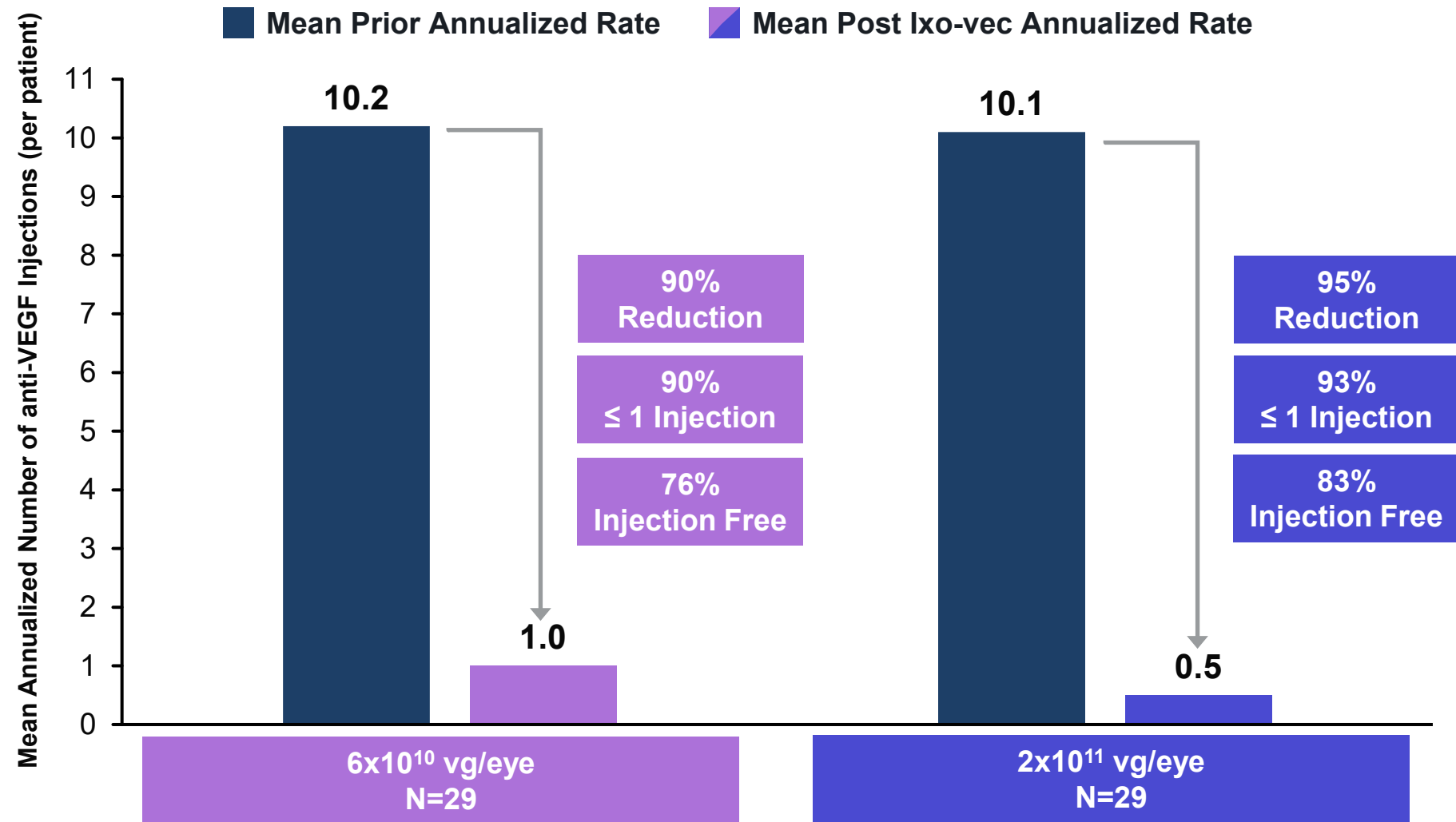
# 100% of Patients Previously Receiving Faricimab Remain Injection Free



Doses pooled in swim lane plot to preserve investigator masking in an ongoing double masked study. Patients who received faricimab in the year prior to receiving Ixo-vec. These received approximately 10 annualized injections in the year prior to Ixo-vec.

Data cut: 14Feb2024

# 90-95% Anti-VEGF Treatment Burden Reduction Across Both Ixo-vec Doses



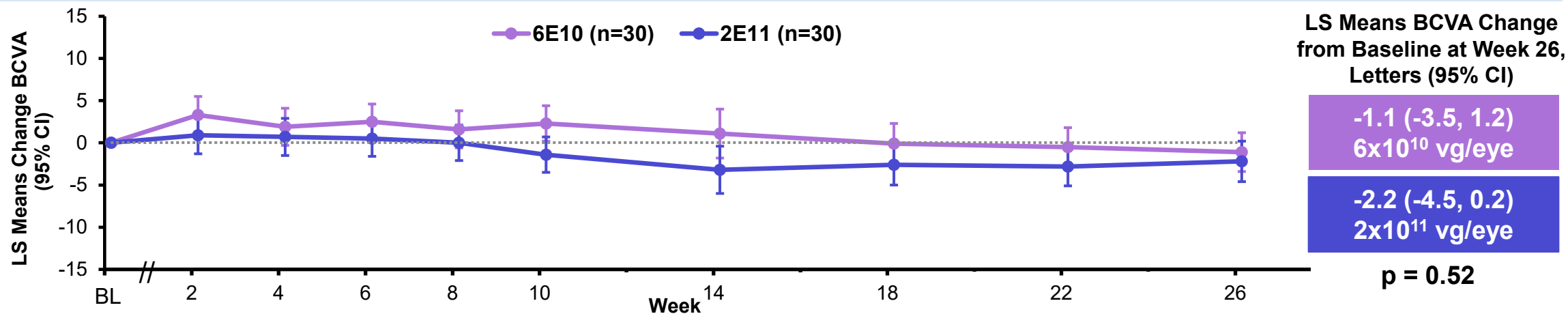
Annualized rate (Prior) = (number of IVTs in 12 months prior to Ixo-vec) / (days from the first IVT in the past 12 months to Ixo-vec / 365.25).

Annualized rate (Post) = (numbers of aflibercept IVTs since Ixo-vec) / (days from Ixo-vec to last follow-up within the interim analysis period / 365.25).

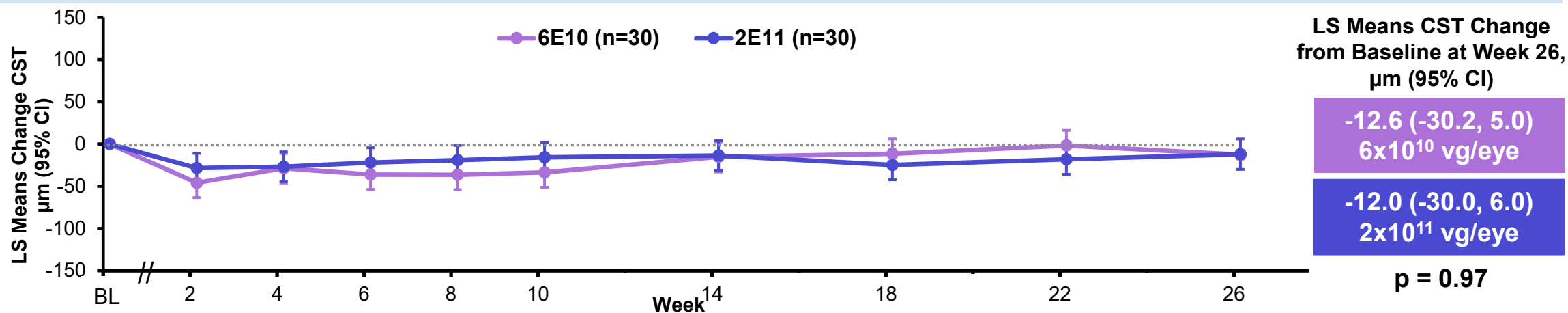
VEGF, vascular endothelial growth factor; IVT: intravitreal.

# Both Doses of Ixo-vec Maintained Visual & Anatomic Outcomes

Least Squares Means Change in Best Corrected Visual Acuity (BCVA) Over Time by Dose

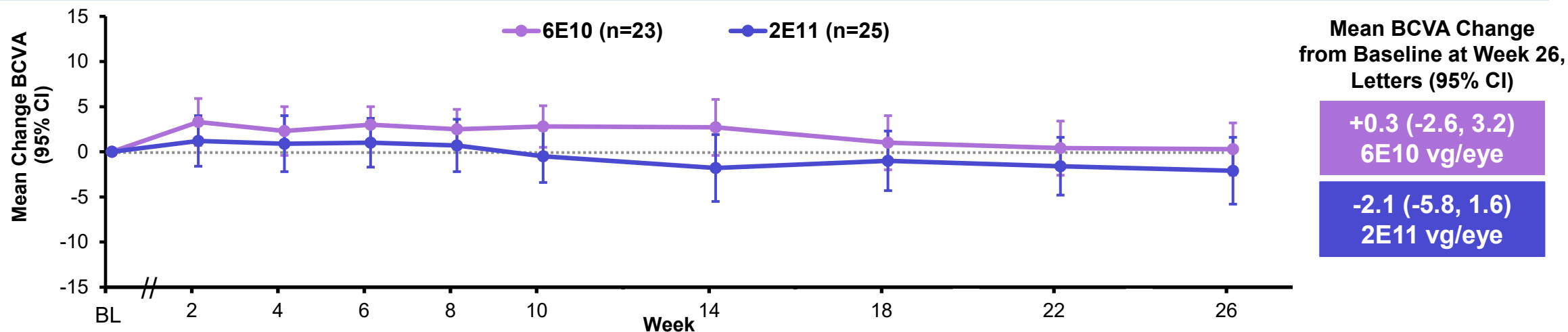


Least Squares Means Change in Central Subfield Thickness (CST) Over Time by Dose

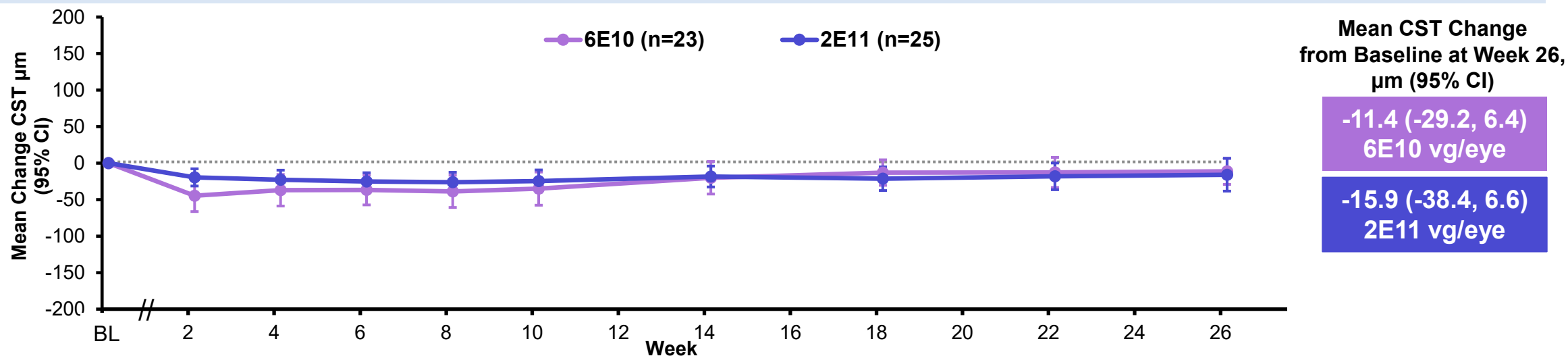


# Both Doses of Ixo-vec Maintained Visual and Anatomic Outcomes in Supplemental Injection-Free Participants

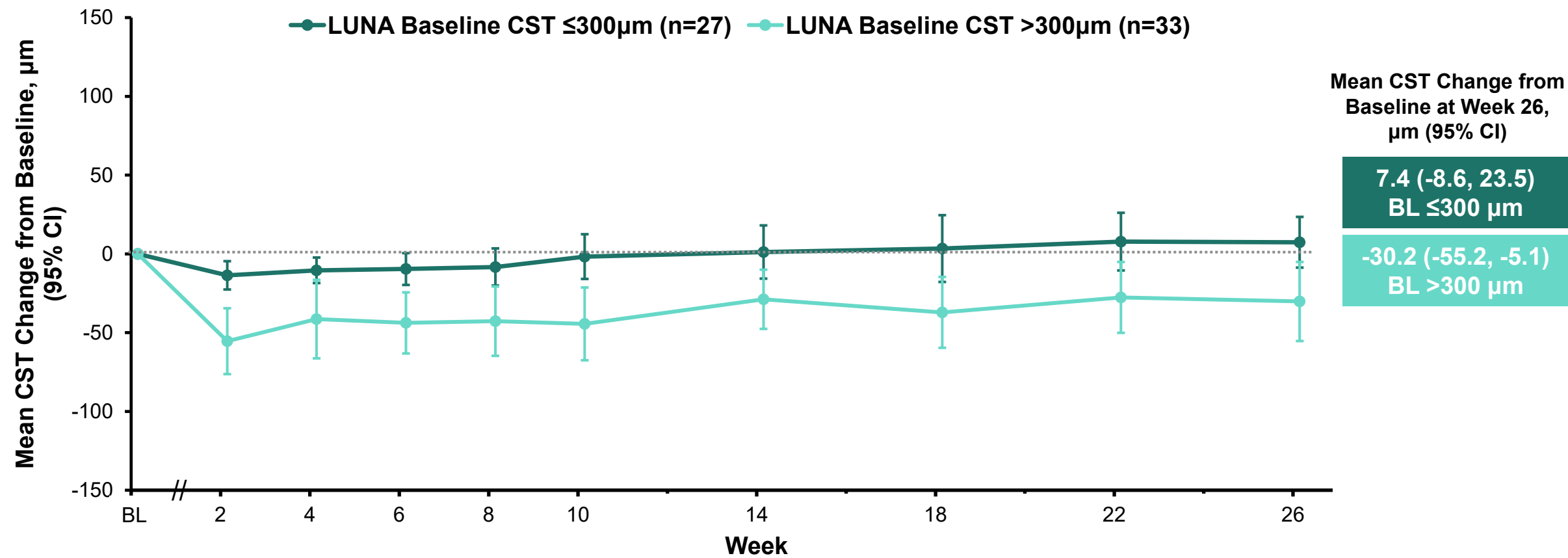
Mean Change in BCVA Over Time in Supplemental Injection Free Participants, by Dose



Mean Change in CST Over Time in Supplemental Injection Free Participants, by Dose

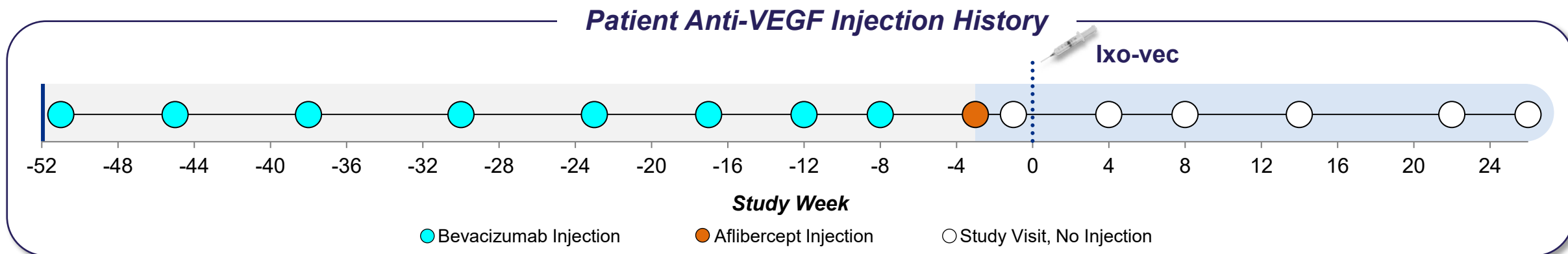


# Ixo-vec Maintains Anatomic Control with Greater CST Reduction Among Participants with Baseline CST >300 μm



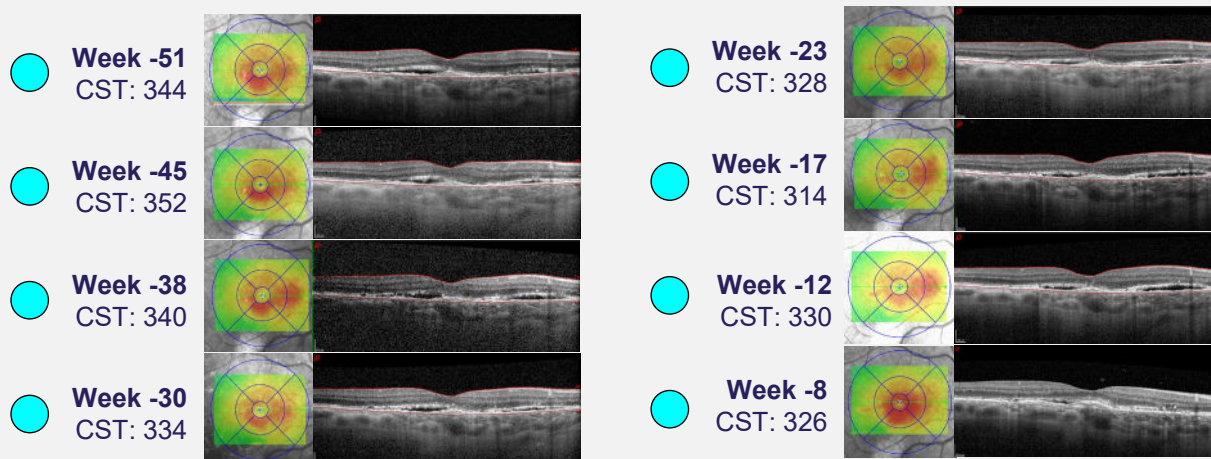
Baseline Characteristic for Subgroup	CST ≤300 μm	CST >300 μm
Mean CST, μm (SD)	269.9 (18.7)	416.6 (119.1)

# 6x10<sup>10</sup> vg/eye Patient Case Study: Anti-VEGF Injection History



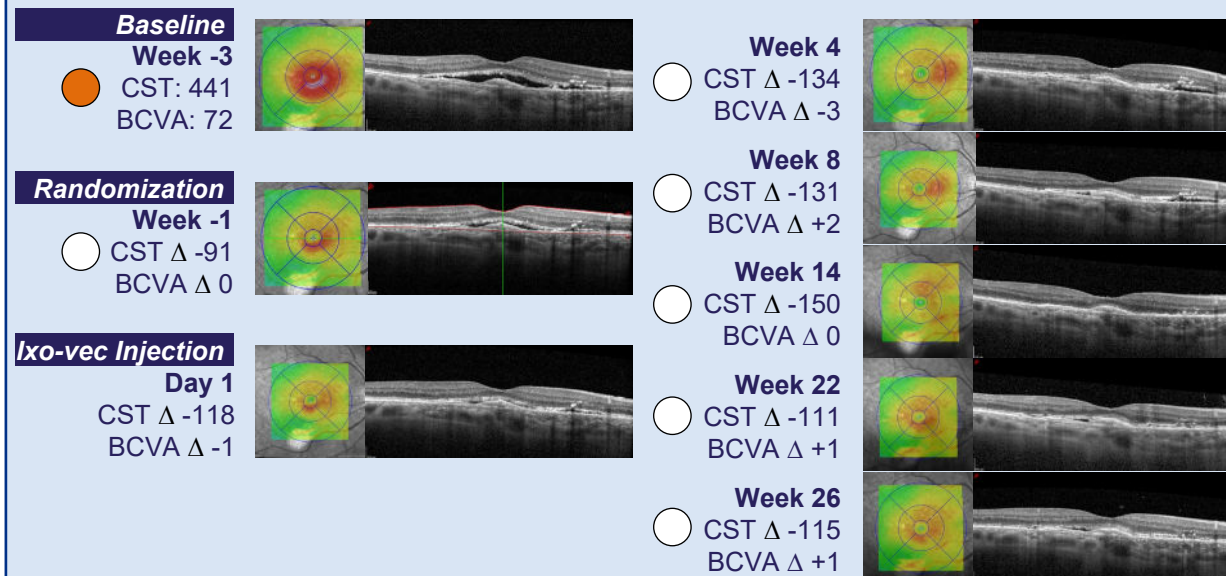
## Prior To LUNA

Patient Received Bevacizumab Anti-VEGF Injections Every 4-8 Weeks



## LUNA

BCVA & CST Levels Maintained With No Additional Anti-VEGF Injections Through 26 Weeks



# Safety Summary of the LUNA 26-week Interim Analysis

- Ixo-vec was well tolerated at both doses of  $6 \times 10^{10}$  and  $2 \times 10^{11}$  vg/eye
  - No Ixo-vec-related serious adverse events
  - No episcleritis, vasculitis, retinitis, choroiditis, vascular occlusion, or hypotony
  - All Ixo-vec-related AEs were either mild or moderate
    - Most common Ixo-vec-related AEs<sup>1</sup> were dose-dependent anterior inflammation responsive to local corticosteroids and anterior pigmentary changes with no impact on vision
- Improved inflammatory profile observed with enhanced corticosteroid prophylaxis in LUNA as compared to OPTIC<sup>2</sup>
  - Oral prednisone did not demonstrate incremental benefit
  - IVT dexamethasone without difluprednate did not provide adequate prophylaxis
  - Local corticosteroid prophylaxis<sup>3</sup> was effective in minimizing inflammation with 91% of participants having no or minimal inflammation (0 or trace/0.5+ AC cells) at any study visit through Week 26

1. Anterior chamber cell, anterior chamber pigmentation, iris transillumination defect, iritis

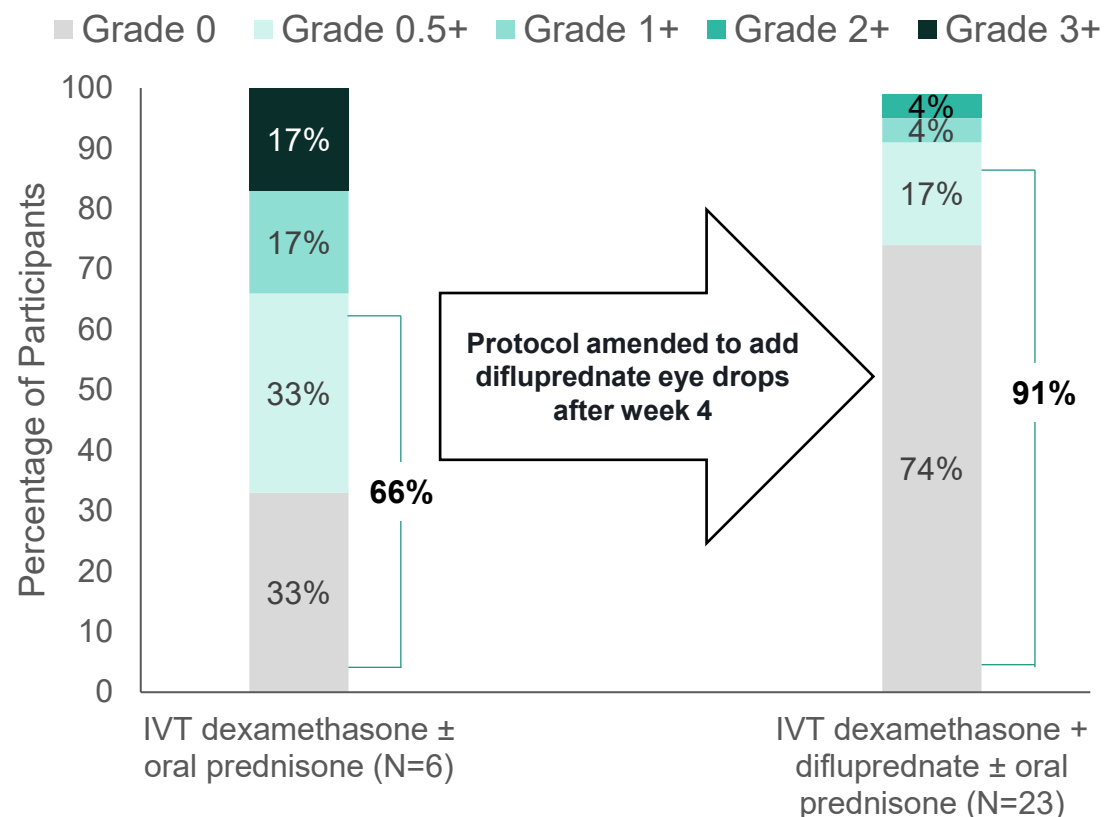
2. Khanani AM. Retina Society Annual Meeting Presentation 2021, Chicago, IL

3. Topical difluprednate with or without IVT dexamethasone (N=34)

# Benefit of Enhanced Local Corticosteroid Prophylaxis Highlighted in LUNA Interim Analysis

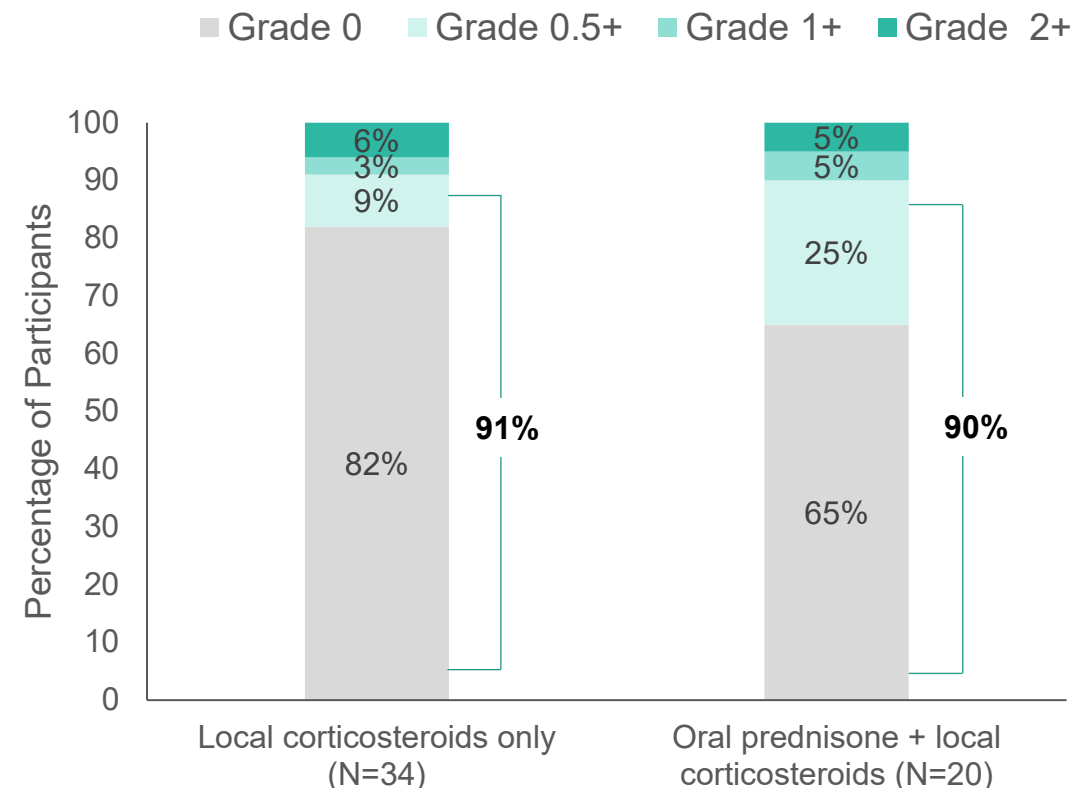
## Observed Benefit of Difluprednate Added to IVT Dexamethasone

### Highest Inflammatory AC Cell Grade through Week 26



## No Observed Benefit of Oral Prednisone

### Highest Inflammatory AC Cell Grade through Week 26



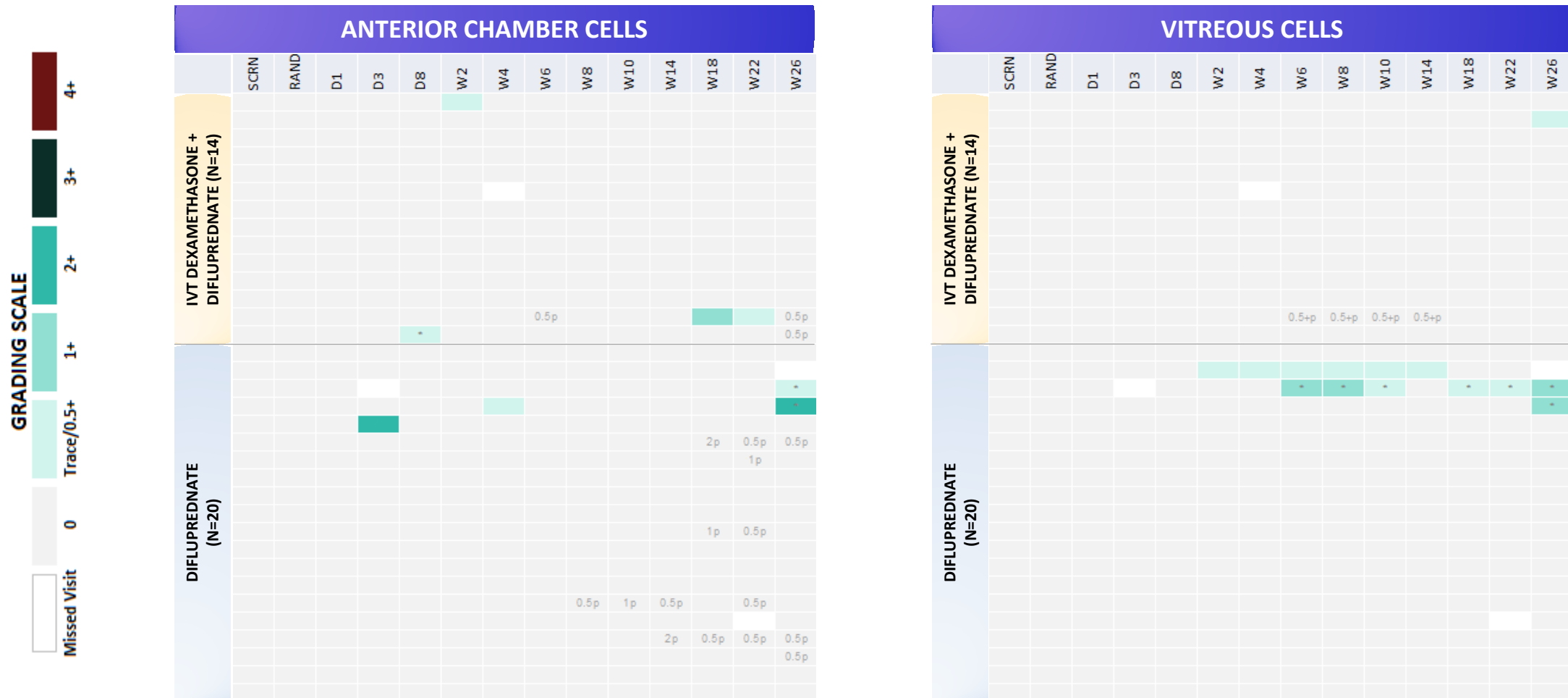
AC, anterior chamber. 100% pigmented cells excluded from analysis. Protocol amended early in study to include difluprednate after week 4 to match the taper in difluprednate regimens; if initiated after week 4 visit difluprednate may be adjusted at the discretion of investigator in consult with medical monitors (6 participants did not receive difluprednate topical as part of prophylaxis). 4+ AC cells due to Staph. epidermidis+ endophthalmitis post-AC tap (unrelated to Ixo-vec) in one participant excluded. Cell grades as assessed by slit lamp; grade categories are based on the Standardization of Uveitis Nomenclature (SUN) criteria for white blood cells.

Data cut: 14Feb2024



## Local Corticosteroid Prophylaxis Regimens were Effective in Minimizing Inflammation

**Interim LUNA data indicate that ocular inflammation is primarily located in anterior chamber and is responsive to local corticosteroids**

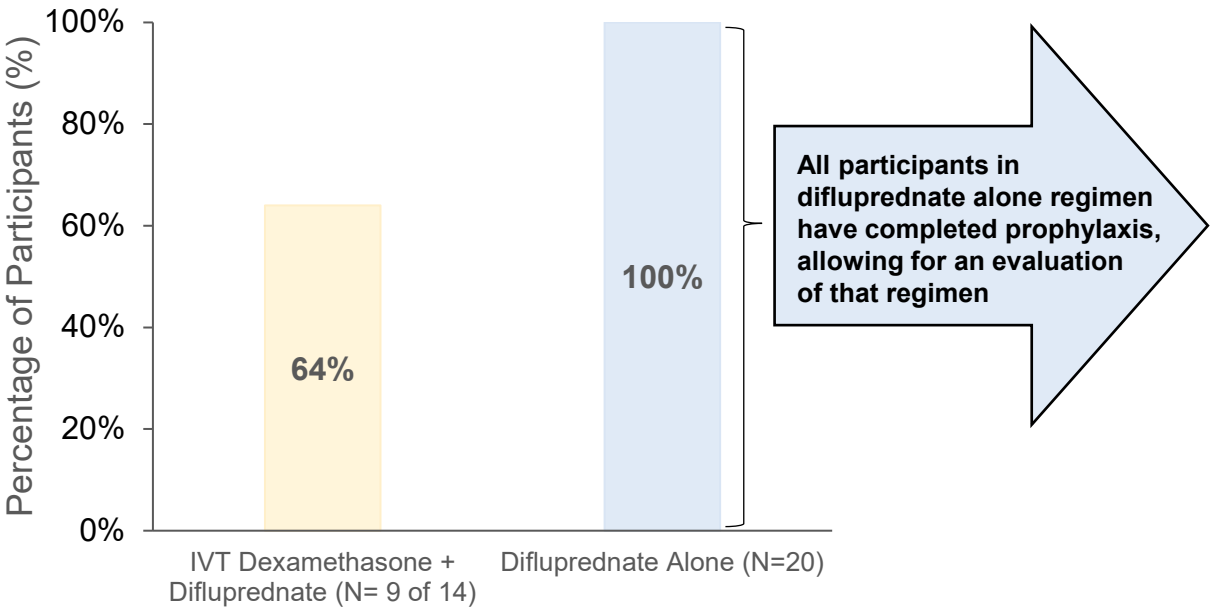


Doses pooled in heatmaps to preserve investigator masking in an ongoing double masked study. \*Mixed pigmented and non-pigmented cells are graded with the same color scheme and scale as non-pigmented cells. p, pigmented cell. Cell grades as assessed by slit lamp; grade categories are based on the Standardization of Uveitis Nomenclature (SUN) and National Eye Institute Scores for white blood cells. No participant in the displayed arms had more than 2+.

# In the Difluprednate Alone Regimen, Inflammation was Dose Dependent and Responsive to Topical Corticosteroids

## Local Corticosteroid Prophylaxis Arms (N=34)

### Proportion of Participants Who Completed Prespecified Prophylactic Regimen at Week 26



Not all participants had completed prophylaxis at week 26 due to amended protocol regimens starting prophylaxis after week 4

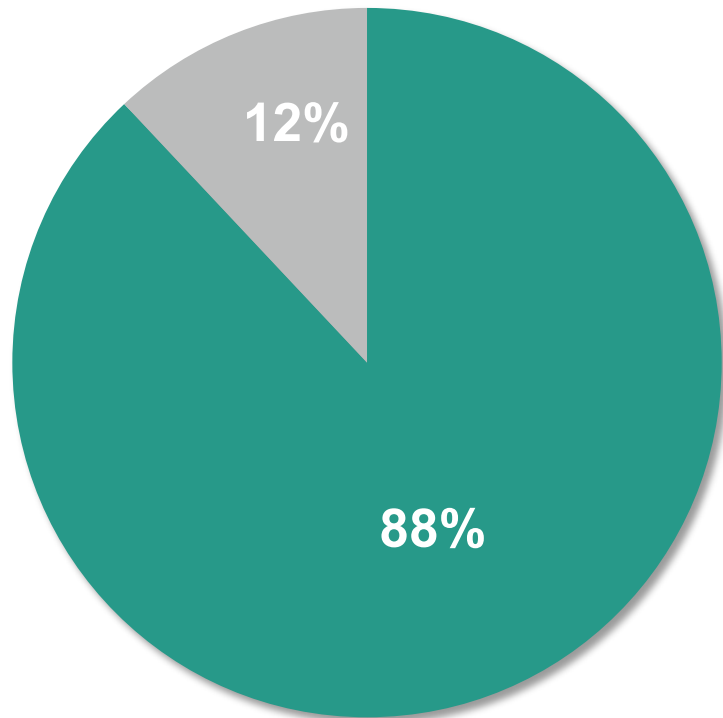
## Difluprednate Alone Prophylaxis Arms (N=20)

	Ixo-vec 6x10 <sup>10</sup> vg/eye N = 10	Ixo-vec 2x10 <sup>11</sup> vg/eye N = 10
Participants, n		
AC Cell Grade at Week 26		
0.5+	1	0
1+	0	0
2+	0	1
Anterior pigment-related AEs through Week 26		
Mild	3	2
Moderate	1	3

- No participants in the 6x10<sup>10</sup> vg/eye dose cohort received corticosteroids for treatment of AC/V cells beyond the taper
- Topical difluprednate effectively managed AC/V cells when present in the 2x10<sup>11</sup> vg/eye dose cohort
- Pigment-related AEs have had no impact on vision

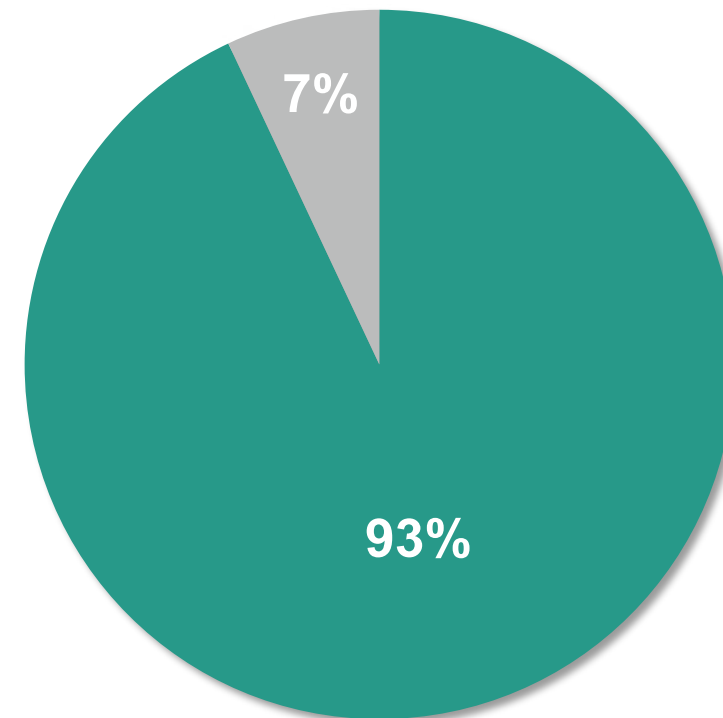
# 88-93% of LUNA Participants Prefer Ixo-vec in the Prespecified Patient Preference Survey

Would you prefer Ixo-vec therapy over the prior treatment(s) you received to treat your wet AMD?



N=57

Would you want to receive Ixo-vec therapy in your other eye if you had wet AMD in both eyes?



N=57

■ Yes ■ No

# LUNA 26-week Interim Analysis Key Takeaways

## Efficacy

- Visual and anatomic outcomes were maintained through 26 weeks at both Ixo-vec doses of  $6 \times 10^{10}$  and  $2 \times 10^{11}$  vg/eye
- Substantial treatment burden reduction observed in patients previously requiring  $\geq 10$  annualized anti-VEGF injections:
  - $\geq 90\%$  reduction in annualized anti-VEGF injections at both doses
  - 76% and 83% of patients remain free of injections at 6 months at the  $6 \times 10^{10}$  and  $2 \times 10^{11}$  doses, respectively

## Safety

- Ixo-vec was well tolerated at both doses,  $6 \times 10^{10}$  and  $2 \times 10^{11}$  vg/eye, with no Ixo-vec-related serious adverse events
- Local corticosteroid prophylaxis<sup>1</sup> was effective in minimizing inflammation, with  $>90\%$  of participants having no or minimal inflammation<sup>2</sup> through Week 26

## Patient Preference

- 88% of LUNA participants prefer Ixo-vec over the previous anti-VEGF therapy they received for treatment of nAMD

**LUNA is ongoing with analysis of the primary efficacy and safety endpoints to be performed at Week 52**

1. Topical difluprednate with or without IVT dexamethasone  
2. 0 or trace/0.5+ AC cells

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