# Suprachoroidal Surabgene Lomparvovec (Sura-vec, ABBV-RGX-314*)

## *First Time 2-Year Results in NPDR*

Retina
Consultants
of Texas

**Charles C. Wykoff MD PhD**

*Sura-vec is an investigational product that has not been approved by any regulatory authority. No conclusions regarding the safety and efficacy of the product can be made.

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

## Study Related Disclosures

- Funding was provided by AbbVie/REGENXBIO Inc.
- This study includes research conducted on human subjects.
  Institutional Review Board approval was obtained prior to study initiation.
- This is an interim analysis performed by REGENXBIO for an ongoing trial.

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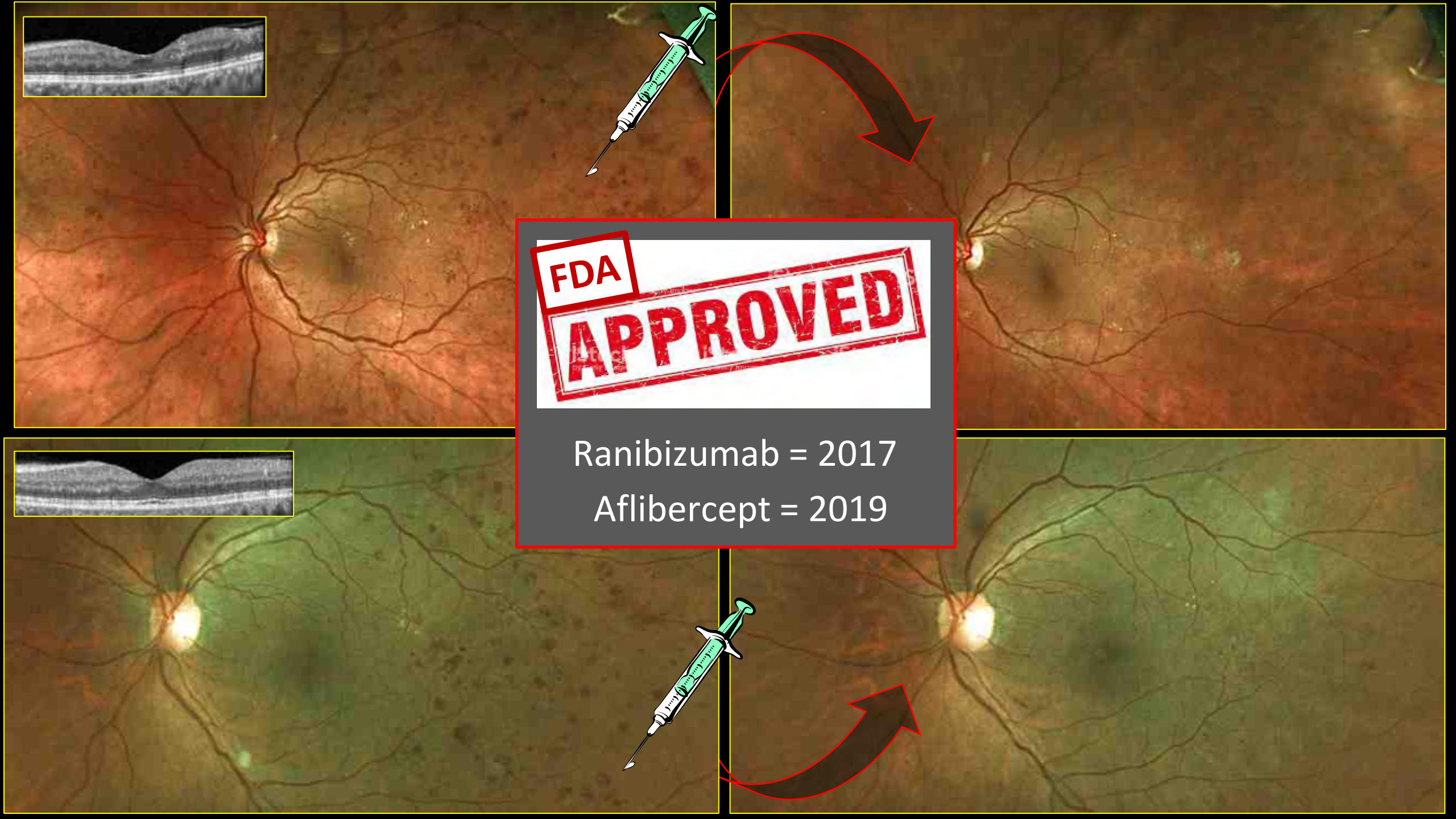
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APPROVED
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Aflibercept = 2019

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American Society of Retina Specialists

2025
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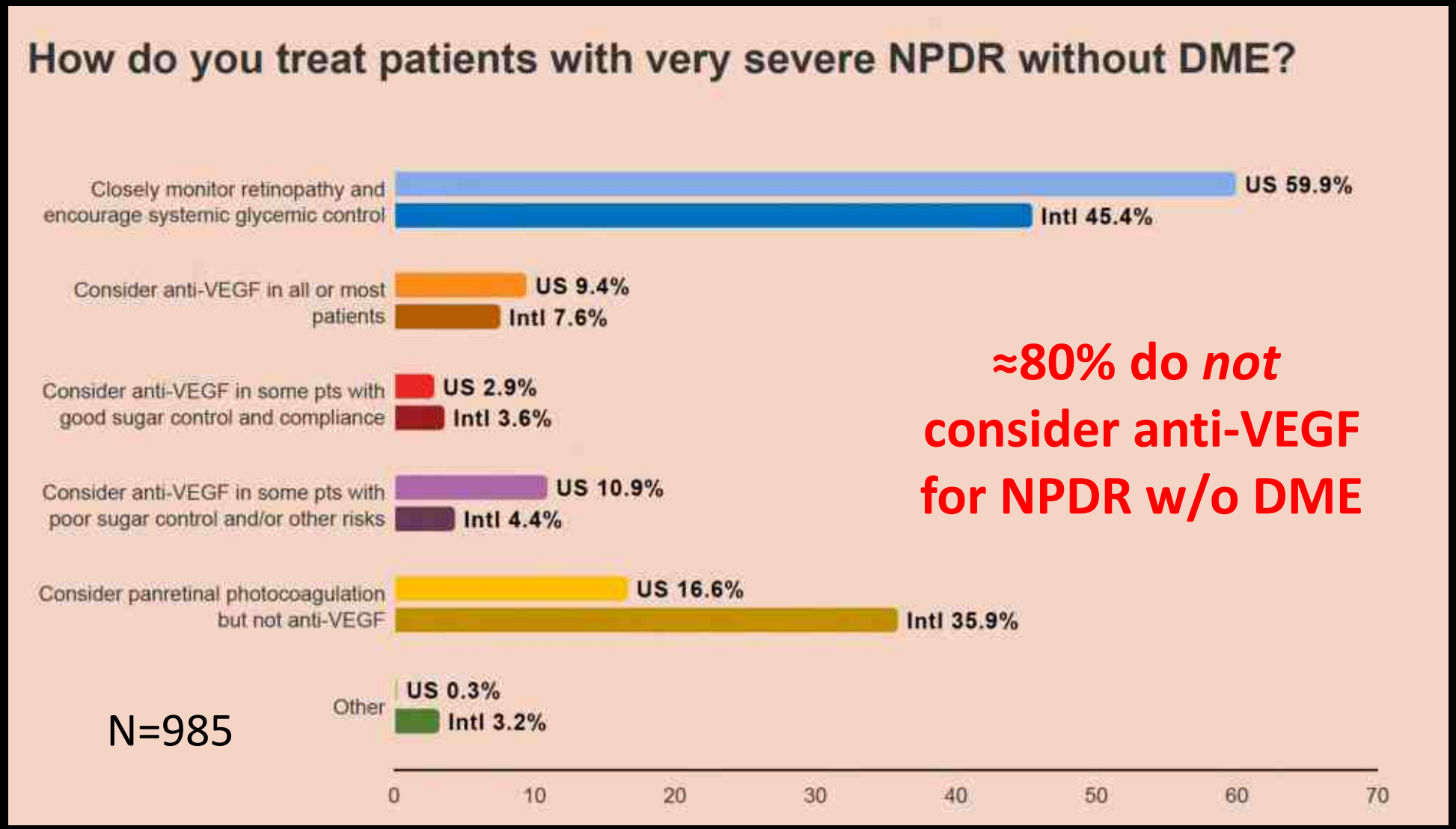



N=985

**≈80% do *not* consider anti-VEGF for NPDR w/o DME**

# Key Barriers to Clinical Adoption
## *of Intravitreal injections for NPDR w/o DME*

**Repeated Injections**

&

**ENDOPHTHALMITIS AFTER INTRAVITREAL INJECTION**

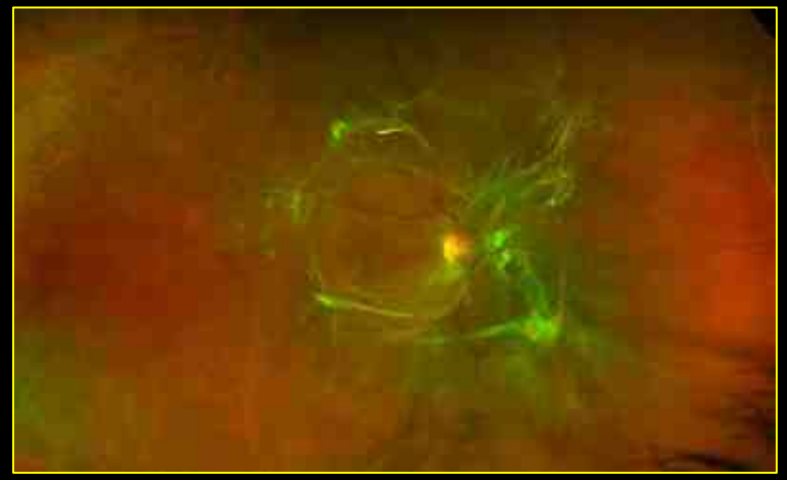
**Role of Prophylactic Topical Ophthalmic Antibiotics**

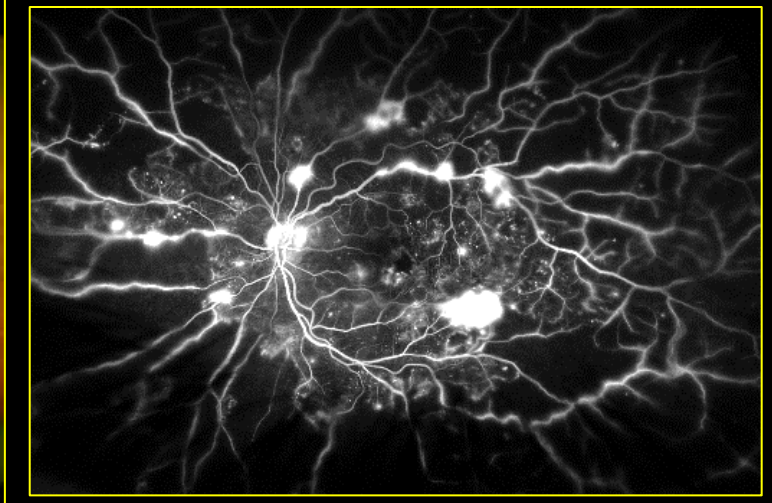
***Editorial***

**Endophthalmitis After Intravitreal Injection: Prevention and Management**

Prophylaxis for Endophthalmitis Following Intravitreal Injection: Antisepsis and Antibiotics

CHARLES C. WYKOFF, HARRY W. FLYNN JR, AND PHILIP J. ROSENFELD



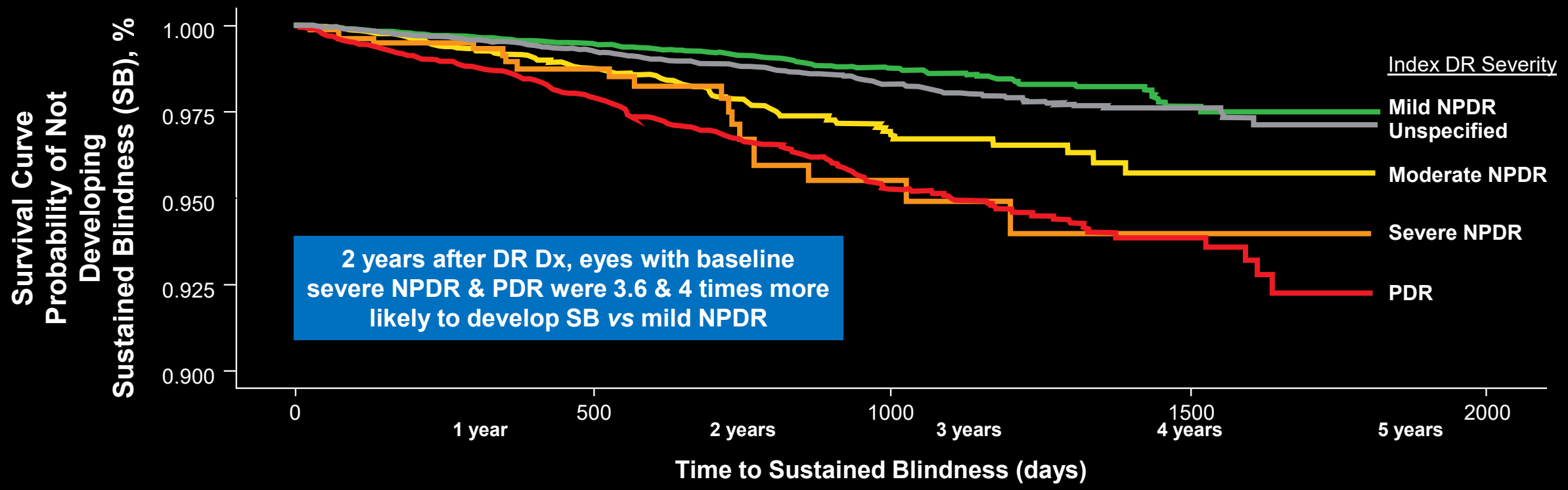


**Leading Cause of Vision Loss**

# More advanced DR is associated with greater probability of blindness

Risk of Blindness Among Patients With Diabetes and Newly Diagnosed Diabetic Retinopathy

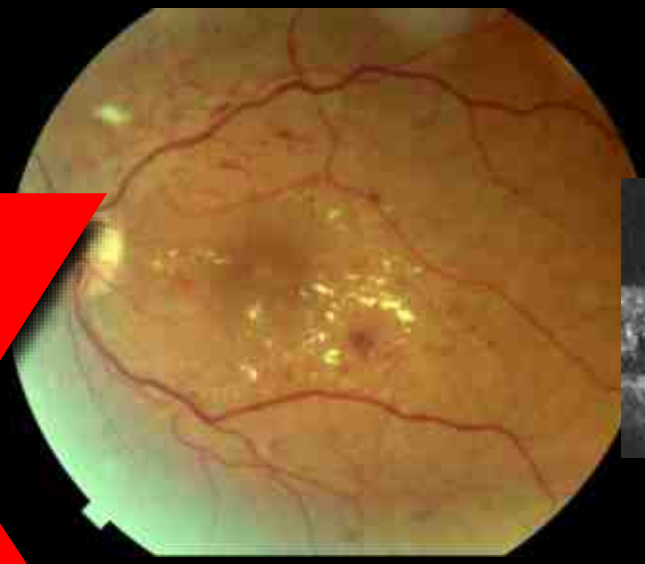
Diabetes Care 2021;44:748–756 | https://doi.org/10.2337/dc20-0413

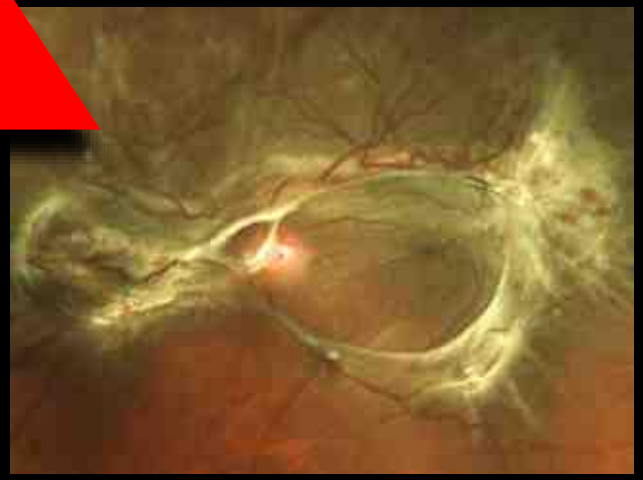



| Index DR Severity | | Cumulative number of events | | | |
|---|---|---|---|---|---|
| Mild NPDR | n = 26,306 | 113 | 163 | 181 | 182 |
| Moderate NPDR | n = 4870 | 46 | 74 | 79 | 79 |
| Severe NPDR | n = 813 | 8 | 17 | 19 | 19 |
| PDR | n = 5573 | 97 | 161 | 176 | 180 |
| Unspecified | n = 15,711 | 105 | 189 | 215 | 218 |

Log-rank $P < 0.0001$. Adjusted for baseline characteristics. N=53,273.

# Unmet need: better, more durable, safer therapies





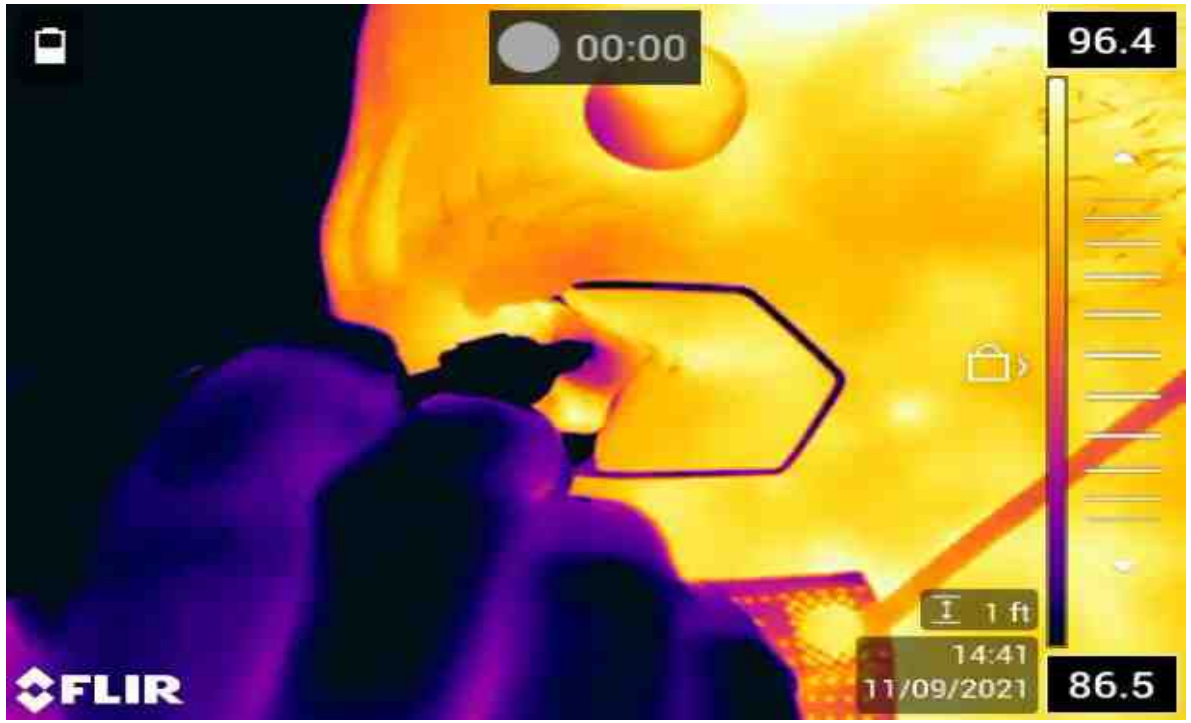
# Challenges & Failures

*Systemic or Non-Intravitreal Bolus Therapies to Slow DR Progression*

- **Oral Pills**
  - APX-3330
  - CU06-1004
  - ASP8232
  - OPL-0401
  - Vicasinabin (RG7774)
  - Runcaciguat
  - Ruboxistaurin
  - Vatalanib
  - Ripasudil
  - Pazopanib
- **Eye Drops**
  - Nesvategrast (OTT166 5%)

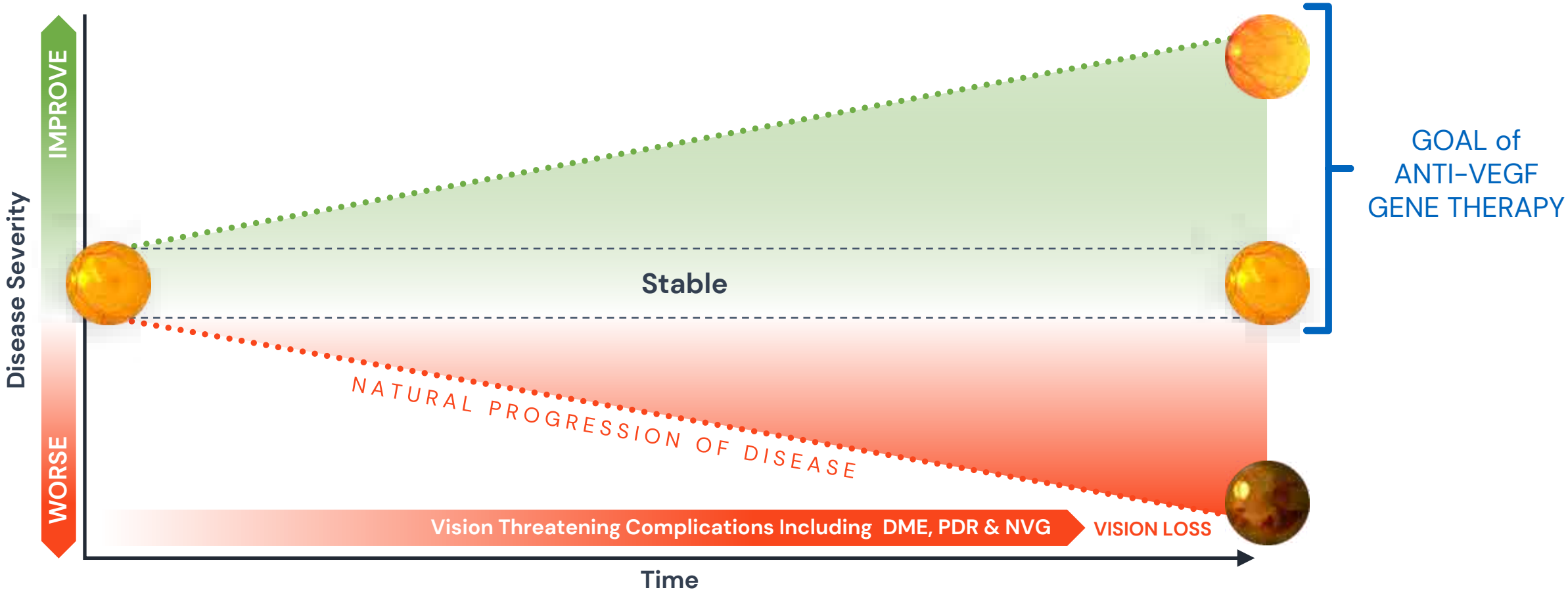
# Sura-vec: AAV8-based Investigational Gene Therapy Designed to Produce an Anti-VEGF Fab

Artistic View of Suprachoroidal Delivery




Thermal Imaging of in-office SCS delivery of sura-vec in ALTITUDE subject

# The goal of a one-time, in-office SCS-injection of gene therapy is to provide long-lasting improvement in DR severity and reduce risk of vision-threatening complications




DME = Diabetic Macular Edema.
NVG = Neovascular Glaucoma.
PDR = Proliferative Diabetic Retinopathy.

# ALTITUDE®: A Phase II, Randomized, Dose-escalation, Observation-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of Investigational Sura-vec via Suprachoroidal Injection in DR

## Primary Objective

- Evaluate proportion of patients with ≥2 step improvement in severity on the Diabetic Retinopathy Severity Scale (DRSS) at one year

## Secondary Objectives

- Safety and tolerability of sura-vec
- Development of DR-related ocular complications
- Need for additional standard of care interventions

## Subjects: 99 patients enrolled in Cohorts 1-5

- 79 sura-vec; 20 observation control
- 21 study sites across the United States

## Route of Administration

- In-office SCS Microinjector™ delivers sura-vec to the **suprachoroidal space**

## Key Inclusion Criteria

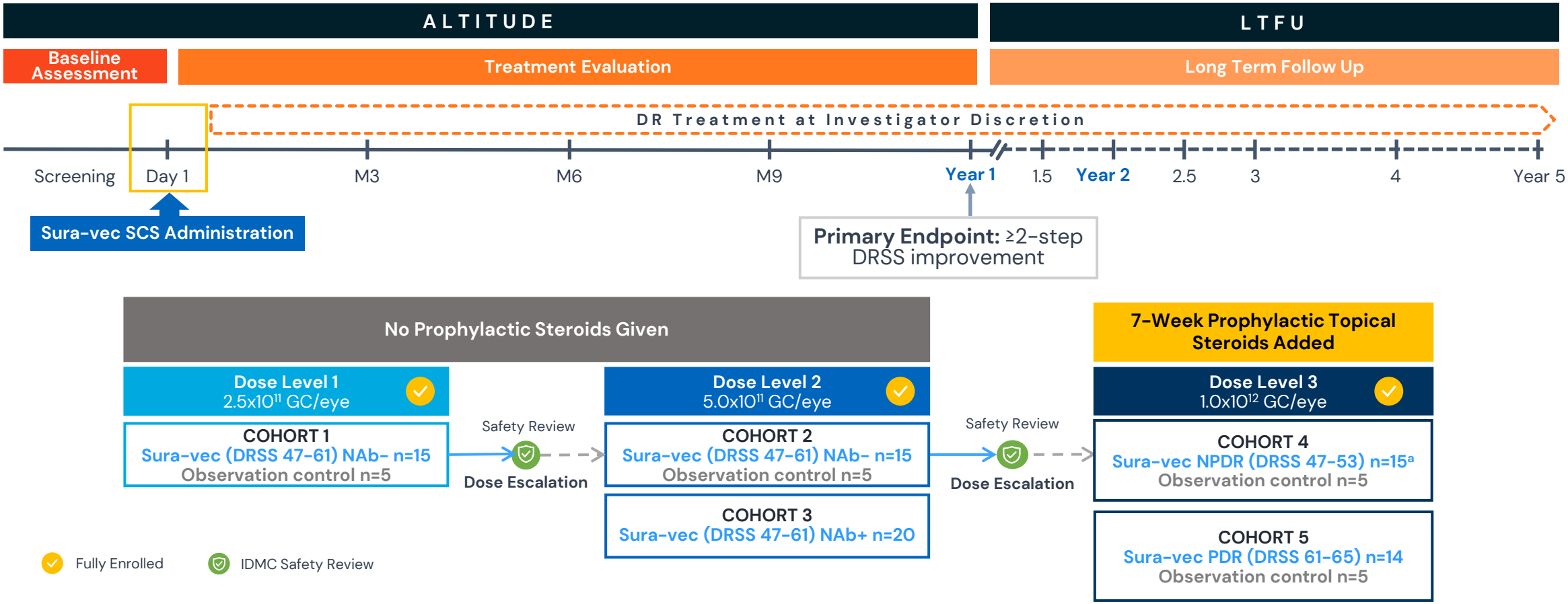
- Male or female ≥ 25 to 89 years of age with DR secondary to diabetes mellitus Type 1 or Type 2
- **Moderately Severe NPDR, Severe NPDR, or Mild PDR (DRSS levels 47-65)**
- No active CI-DME with CST ≥ 320 µm
- Vision of 20/40 or better (≥ 69 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) in the study eye
- No anti-VEGF injection(s) in prior 6 months



Adapted from: Wykoff, Retina Society 2024

# Phase II ALTITUDE® Study Design

## Sura-vec for the treatment of diabetic retinopathy




**Presentation will focus on 1 and 2 Year data in NPDR Population**

a. One subject in Dose Level 3 was randomized and dosed but was later found to have disease at baseline that confounded efficacy outcome assessment.
CI-DME: center-involved diabetic macular edema; DRSS: Diabetic Retinopathy Severity Scale; GC: genome copies; LTFU: long-term follow-up; NAb+: AAV8 neutralizing antibody positive; NAb-: AAV8 neutralizing antibody negative/low; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; SCS: suprachoroidal space; Year 1 = 48 weeks.

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# Baseline Characteristics

## NPDR (DRSS 47-53)

| | VARIABLE | Observational Control (N=12) | Dose Level 1 (N=6) | Dose Level 2 (N=24) | Dose Level 3 (N=14[b]) | Total (N=56) |
|---|---|---|---|---|---|---|
| BASELINE[a] | **Mean Age** (Years) | 54.9 | 57.2 | 60.1 | 54.4 | **57.2** |
| | **Gender – Female** | 3(25.0%) | 4 (66.7%) | 10 (41.7%) | 4 (28.6%) | **21 (37.5%)** |
| | **Hemoglobin A1c- Mean** | 7.7 | 7.9 | 7.8 | 7.7 | **7.7** |
| | **DR Category at Baseline** | | | | | |
| | DRSS 47 (Moderately Severe NPDR) | 12 (100.0%) | 4 (66.7%) | 21 (87.5%) | 10 (71.4%) | **47 (83.9%)** |
| | DRSS 53 (Severe NPDR) | 0 | 2 (33.3%) | 3 (12.5%) | 4 (28.6%) | **9 (16.1%)** |
| | **Screening BCVA** (ETDRS letters) | 85.3 | 74.7 | 83.0 | 80.1 | **81.9** |
| | **Screening OCT CRT** (µm) | 273.7 | 250.5 | 272.2 | 279.4 | **272.0** |
| | **Lens Status – Phakic n** (%) | 10 (83.3%) | 5 (83.3%) | 15 (62.5%) | 13 (92.9%) | **43 (76.8%)** |
| | **Subjects That Completed the Study (1Y)** | 12 | 6 | 24 | 14[b] | **56** |
| | **Subjects That Entered LTFU** | n/a | 6 | 20 | 12 | **38** |

Data cut: June 09, 2025.
a. Ocular variables refer to study eye only.
b. One subject in Dose Level 3 was randomized and dosed but was later found to have disease at baseline that confounded efficacy outcome assessment.
BCVA: best corrected visual acuity; CRT: central retinal thickness; DRSS: Diabetic Retinopathy Severity Scale: ETDRS: Early Treatment Diabetic Retinopathy Study; NPDR: non-proliferative diabetic retinopathy; OCT: optical coherence tomography; LTFU: long-term follow-up.
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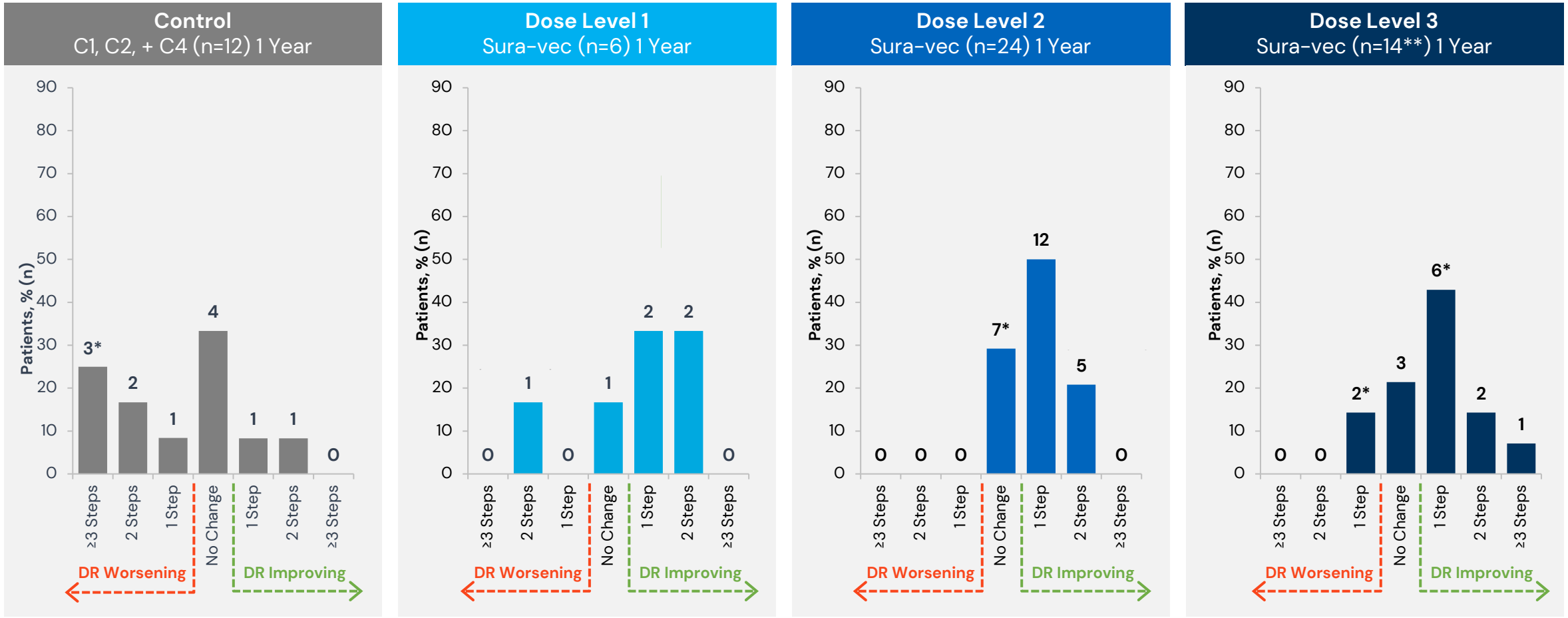
# Change in DRSS at 1 Year

## Dose Level 2 and 3 sura-vec treated subjects outperform control with similar outcomes at 1 yr




Data cut: June 09, 2025. LOCF (Last Observation Carried Forward) data.
*Includes one subject who received on-study anti-VEGF. **One subject in Dose Level 3 was found to have confounding disease at baseline and their data was excluded.
One subject each in Dose Levels 1 and 2 missed their 1-Year visit, so their 6-month results were used.
C: Cohort; DR: diabetic retinopathy; DRSS: Diabetic Retinopathy Severity Scale; VEGF: vascular endothelial growth factor.
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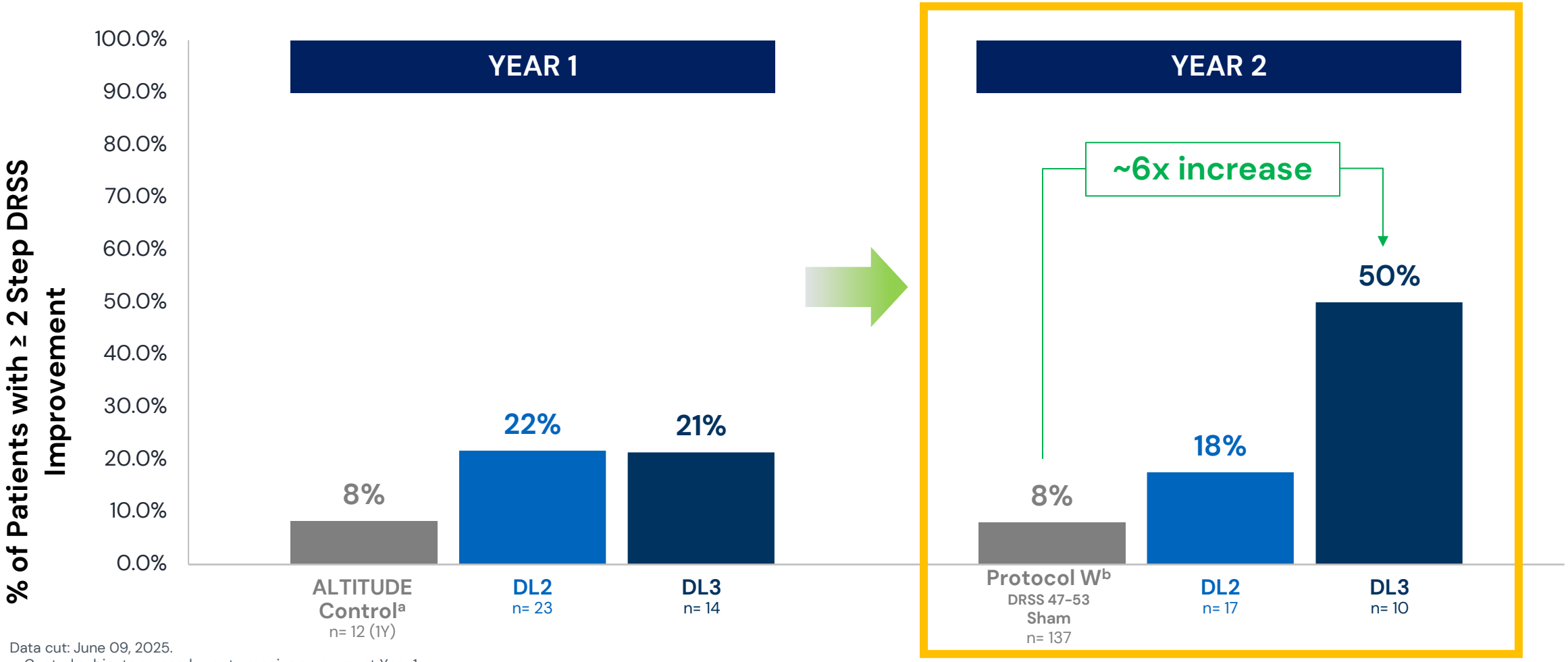
# ≥2-Step DRSS Improvement Without Additional DR Treatment Through Year 2

## Dose Level 3 sura-vec treated subjects outperformed all other groups




Data cut: June 09, 2025.
a. Control subjects crossed over to receive sura-vec at Year 1.
b. Maturi RK, et al. *JAMA Ophthalmology*. 2021;139(7):701-712. Protocol W results based on subgroup analysis of subjects with Baseline DRSS 47 and 53.
One subject in Dose Level 2 missed their 1-Year visit. One subject in Dose Level 3 was found to have confounding disease at baseline and their data was excluded. One subject In Dose Level 3 without IVT missed their 2Y visit but had a 2-Step DRSS improvement at their 2.5Y visit.
DL: Dose Level; DRSS: Diabetic Retinopathy Severity Scale; IVT: intra-vitreal therapy.
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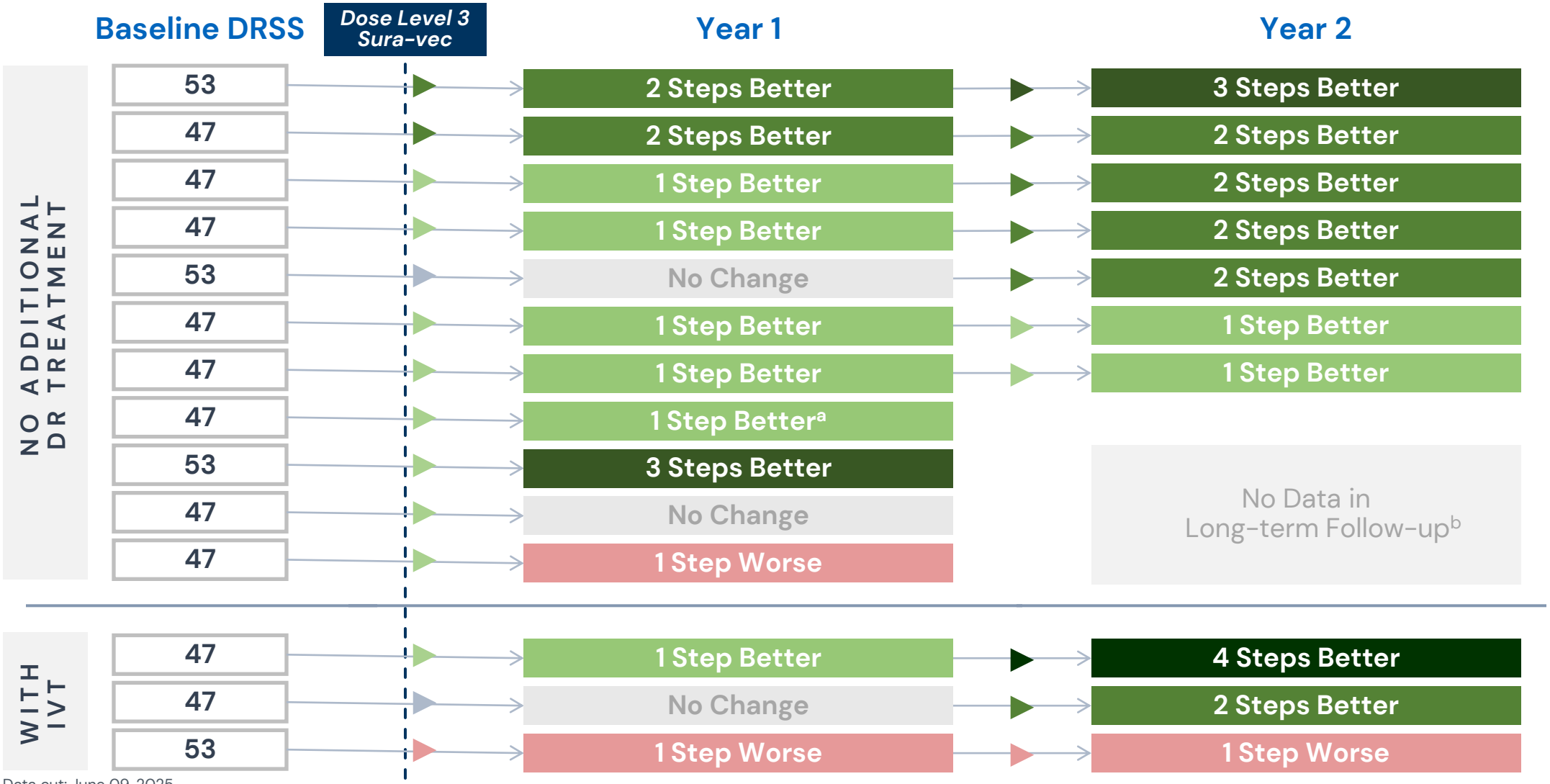
# DRSS Outcomes in Dose Level 3 Subjects over 2 Years

## Majority of subjects improved ≥ 2 steps with a single injection of sura-vec




Data cut: June 09, 2025.
a. One subject without IVT missed their 2Y visit but had a 2-Step DRSS improvement at their 2.5Y visit.
b. One subject enrolled in long-term follow-up and had no return visits. One subject in Dose Level 3 was found to have confounding disease at baseline and their data was excluded.
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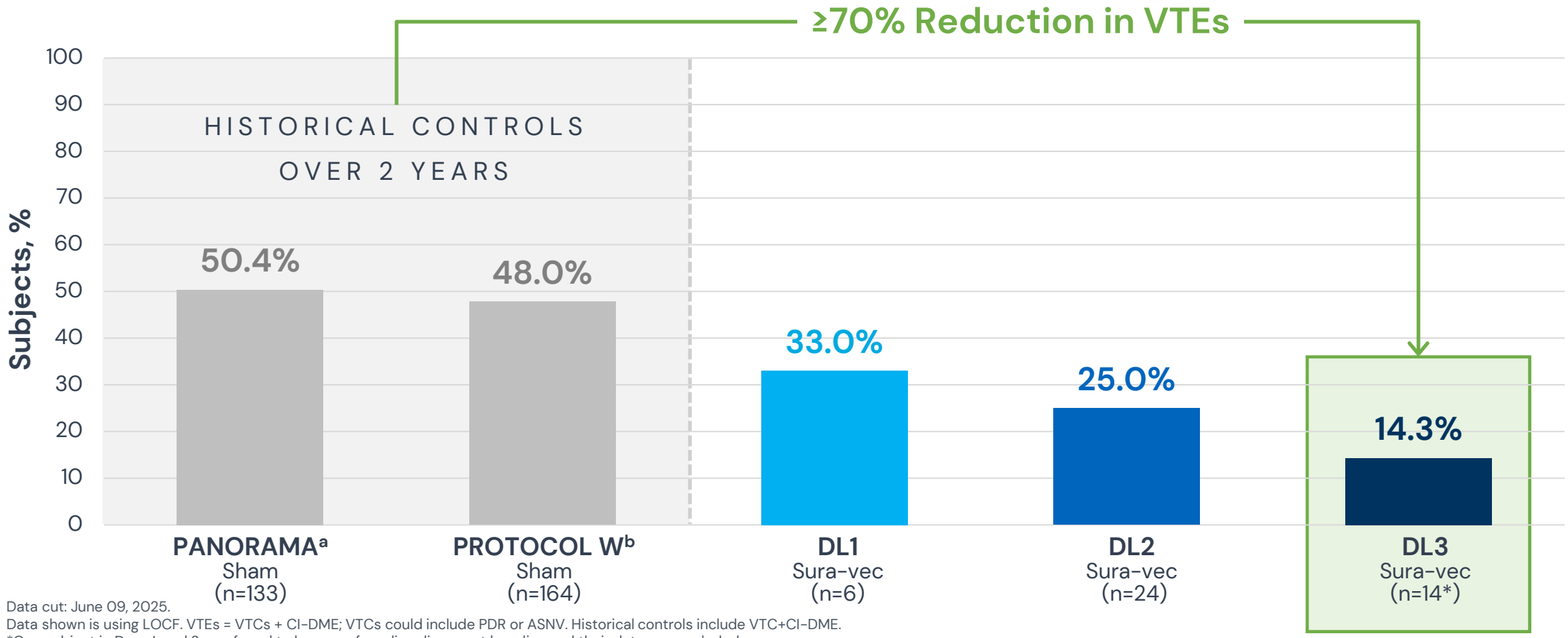
# Vision Threatening Events Over 2 Years

## ≥ 70% risk reduction in VTEs observed in DL3 subjects treated with a single dose




Data cut: June 09, 2025.
Data shown is using LOCF. VTEs = VTCs + CI-DME; VTCs could include PDR or ASNV. Historical controls include VTC+CI-DME.
*One subject in Dose Level 3 was found to have confounding disease at baseline and their data was excluded.
a. Brown DM, et al. *JAMA Ophthalmology*. 2021;139(9):946-955. b. Maturi RK, et al. *JAMA Ophthalmology*. 2021;139(7):701-712. Protocol W results are based on the 2-year cumulative probability for development of PDR and CI-DME applied to the sub-population with Baseline DRSS 47 and 53.
ASNV: anterior segment neovascularization; CI-DME: center-involved diabetic macular edema; DL: dose level; LOCF: Last Observation Carried Forward; PDR: proliferative diabetic retinopathy; VTCs: vision-threatening complications; VTEs: vision-threatening events.
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# Cumulative Safety Summary

## Dose Levels 1–3 Through 2 Years: NPDR (DRSS 47-53)

**Sura-vec has been well–tolerated in Dose Levels 1, 2 and 3 NPDR subjects (n=45)**

- **16 SAEs: none considered drug-related**
- **No cases of vasculitis, occlusion, hypotony, or chorioretinitis**
- **Zero IOI with short course of prophylactic topical steroids**

| | No prophylactic steroids | | Prophylactic 7-week topical steroids |
|---|---|---|---|
| **DOSE LEVELS 1–3:** *Common Ocular TEAEs[a] in the Study Eye through 2 Years* | Dose Level 1 $2.5 \times 10^{11}$ DRSS 47-53 (N=6) | Dose Level 2 $5 \times 10^{11}$ DRSS 47-53 (N=24) | Dose Level 3 $1 \times 10^{12}$ DRSS 47-53 (N=15) |
| **Conjunctival hyperemia** | 1 (16.7%) | 7 (29.2%) | 0 (0%) |
| **Conjunctival hemorrhage** | 1 (16.7%) | 3 (12.5%) | 3 (20.0%) |
| **Cataract** | 2 (33.3%) | 3 (12.5%) | 1 (6.7%) |
| **Episcleritis[b]** | 0 (0.0%) | 3 (12.5%) | 3 (20.0%) |
| **IOP increase[c]** | 0 (0.0%) | 2 (8.3%) | 3 (20.0%) |
| **Intraocular inflammation[d]** | 1 (16.7%) | 2 (8.3%) | 0 (0%) |

Data cut: June 09, 2025.
a. Common TEAEs include AEs for total group ≥10% + intraocular inflammation, with onset through the 2-year visit; includes 2 subjects who missed the 2-year visit but had data at 2.5 years.
b. All cases were mild to moderate (grade 1 - 2) and have resolved on topical corticosteroids based on slit lamp examination.
c. All cases were mild to moderate (grade 1 - 2) and resolved after steroid discontinuation and are off IOP lowering medications, except one case of bilateral Primary Angle Closure Glaucoma (grade 2) unrelated to drug which was treated with bilateral iridectomy.
d. All cases were mild (range +0.5 to +1) and most presented 2-6 weeks post injection, predominantly as anterior cells on slit lamp examination. Resolved on topical corticosteroids.
AE: adverse event; DRSS: Diabetic Retinopathy Severity Scale; IOI: intraocular inflammation; IOP: intraocular pressure; NPDR: non-proliferative diabetic retinopathy; SAE: serious adverse event; TEAE: treatment emergent adverse event.
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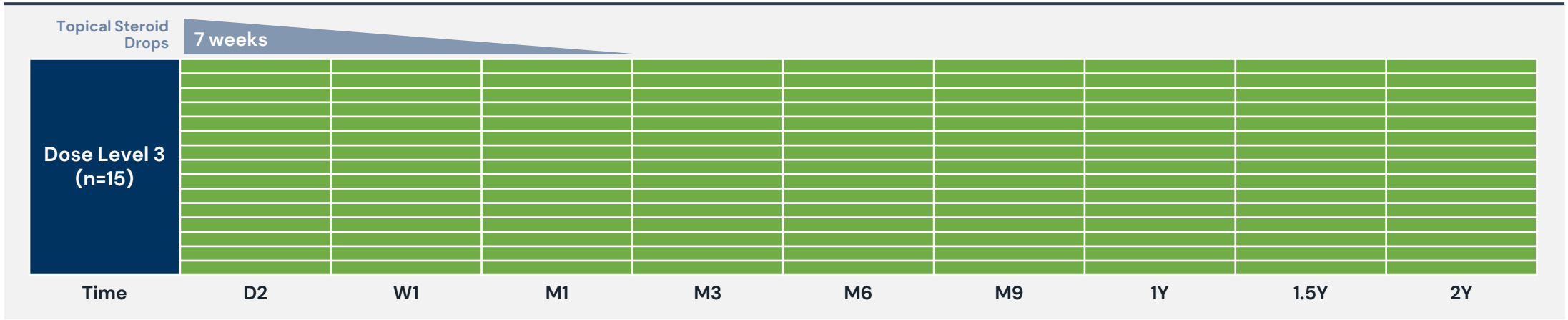
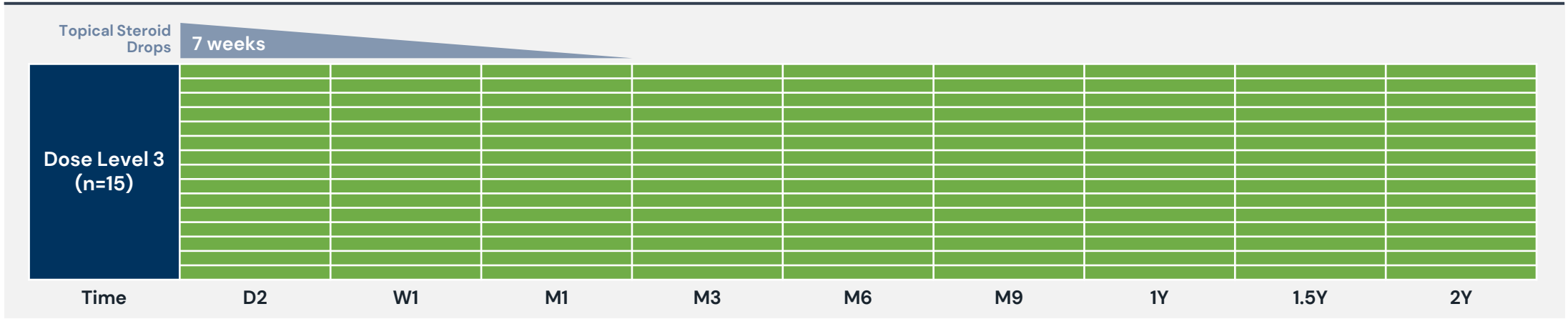
# No Intraocular Inflammation in Dose Level 3 NPDR Subjects at 2 Years with Short-course Prophylactic Topical Steroids

## ANTERIOR CHAMBER CELLS, FLARE, OR PIGMENTED CELLS




## VITREOUS CELLS, FLARE, OR PIGMENTED CELLS




Data cut: June 09, 2025.
Data shown is using LOCF (Last Observation Carried Forward) for missed visits.
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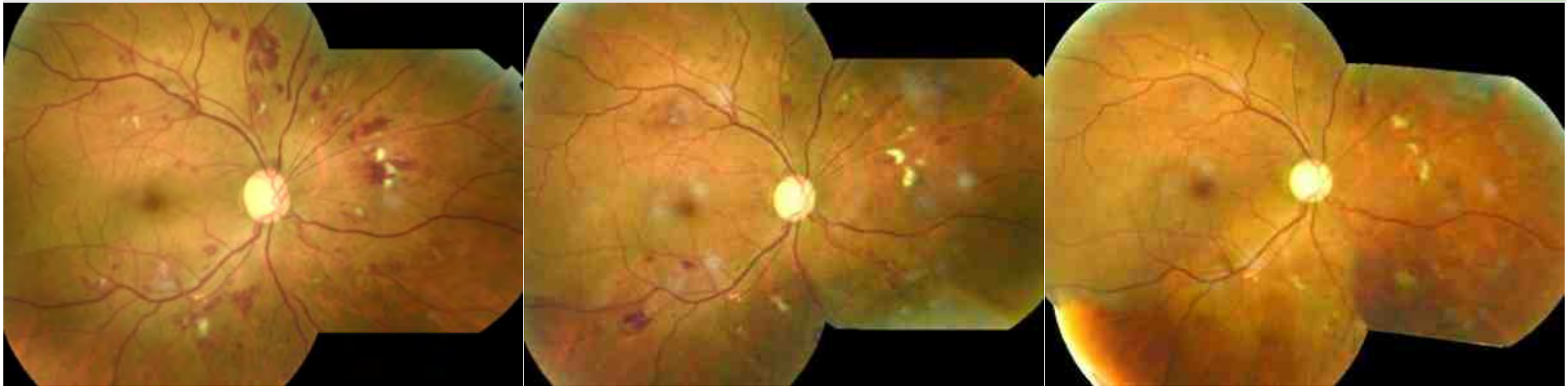
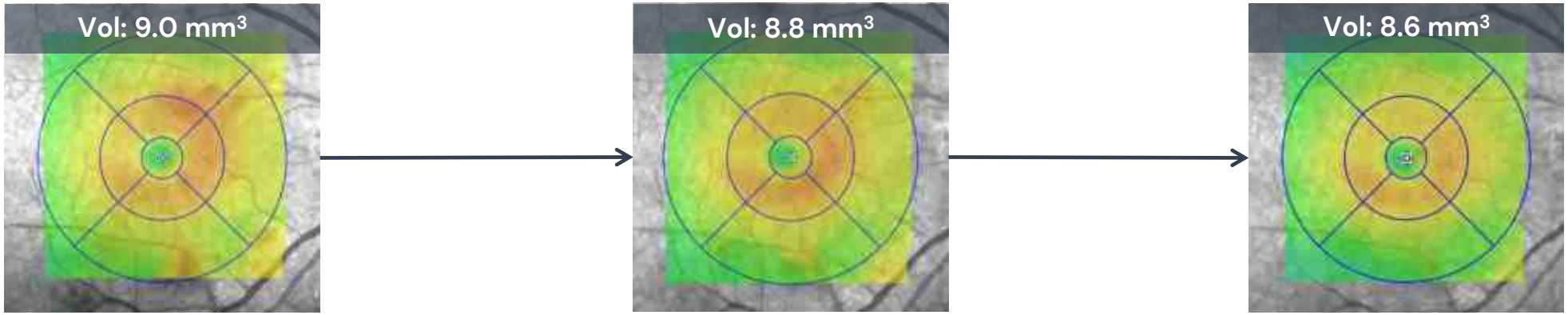
# Case #1: Dose Level 3

## Courtesy of Amr Dessouki, MD

**2-Step Improvement**

| Baseline | Year 1 | Year 2 |
|---|---|---|
| **DRSS 53** | **DRSS 53** | **DRSS 43** |






Data cut: June 09, 2025.
This slide presents results from individual participants and is not indicative of outcomes experienced by all participants in this trial.
DRSS: Diabetic Retinopathy Severity Scale; Vol: volume.
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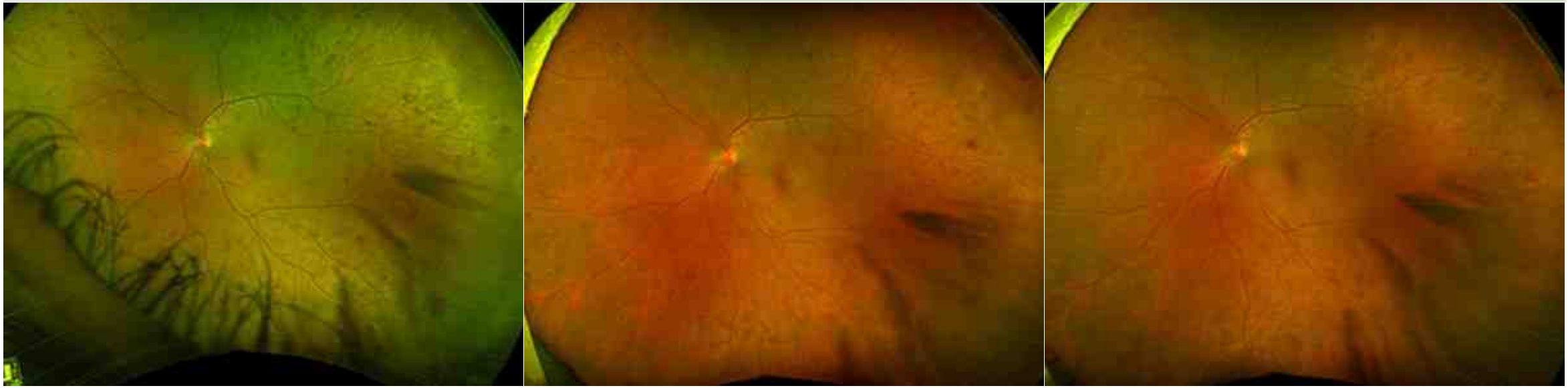
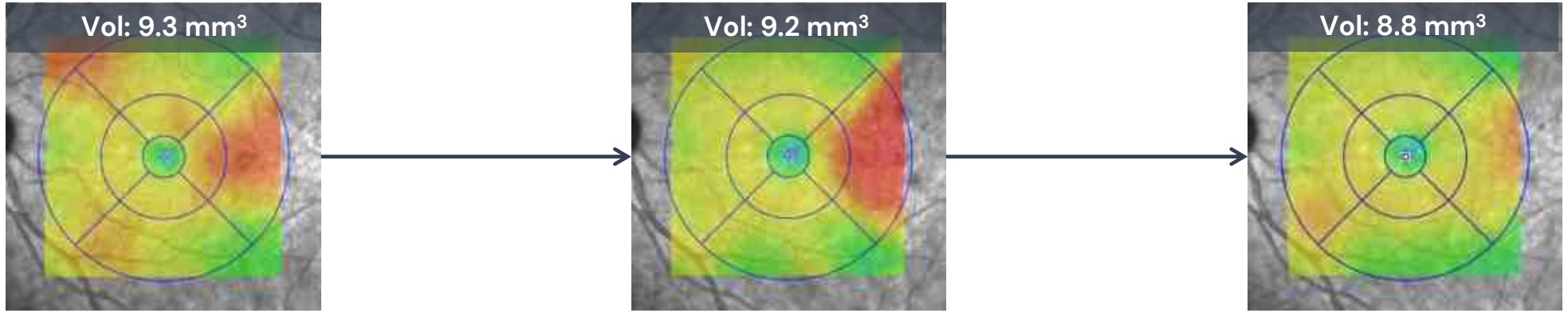
# Case #2: Dose Level 3

## Courtesy of Charles Wykoff, MD, PhD

| | 1-Step Improvement | 2-Step Improvement |
|---|---|---|
| Baseline<br>**DRSS 47** | Year 1<br>**DRSS 43** | Year 2<br>**DRSS 35** |






Data cut: June 09, 2025.
This slide presents results from individual participants and is not indicative of outcomes experienced by all participants in this trial.
DRSS: Diabetic Retinopathy Severity Scale; Vol: volume.
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# Sura-vec 2 Year Results in NPDR Subjects from the Phase II ALTITUDE® Study

## Single in-office suprachoroidal injection of sura-vec

### **Well-tolerated** at Dose Levels 1, 2, and 3

- **No IOI** in Dose Level 3 NPDR subjects with **short-course topical steroids**
- No drug-related serious adverse events.
- No cases of vasculitis, occlusion, hypotony or cases of chorioretinitis.

### Durable, long-term efficacy observed in Dose Level 3

- **Majority** of subjects achieved **DRSS improvement**
  - **50%** achieved **≥2-step** improvement **without additional DR treatment**
- **Reduced** the risk of **disease progression**
  - **≥ 70% risk reduction** in vision-threatening events compared to historical controls

**Pivotal Phase IIb/III trial in NPDR will be initiated**

Data cut: June 09, 2025.
VTEs = VTCs + CI-DME.
CI-DME: center-involved diabetic macular edema; DRSS: Diabetic Retinopathy Severity Scale: IOI: intraocular inflammation; NPDR: non-proliferative diabetic retinopathy; VEGF: vascular endothelial growth factor; VTCs: vision-threatening complications; VTEs: vision-threatening events.
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