# Suprachoroidal Delivery of Investigational ABBV-RGX-314 for Diabetic Retinopathy: The Phase II ALTITUDE® Study Dose Levels 1 and 2: One Year Results

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AAO

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# Disclosures

AbbVie Inc: C
Adverum Biotech: C, R
Alcon: C
Alimera: C
Allegro: C
Allergan: C
AmerisourceBergen: C
Annexon Biosciences: C, R
Apellis: BC
Arctic Vision: C
Bausch and Lomb: C
Biogen: C
CalciMedica: C, R
Clearside Biomedical: C, R
Coherus Biosciences: C
EyePoint Pharma: C, R
Gemini Therapeutics: R
Genentech: B, C, R
Gyroscope Therapeutics: R
Iveric Bio: B, C
Kodiak Sciences: C, R
Novartis: B, C, R
NeuBase: E
Neurotech: C
Ocular Therapeutix: C, R
Oculis: R
Opthea: C, R
Outlook Therapeutics: C
Oxular: R
Oxurion: E, R
Palatin Technologies: C
Regeneron: B
REGENXBIO: C, R
ReNeuron: R
RevOpsis Therapeutics: C, E
Ribomic: R
Roche: C
Stealth Biotherapeutics: C, R
Unity Biotechnology: R

B – Speakers' Bureau | C – Consultant | E – Equity | R – Grants/Research Support

# Diabetic Retinopathy is a Global Public Health Problem

**20M**

Is the expected DR patient population in US,EU,JP in the next 5 years[1]

**<1%**

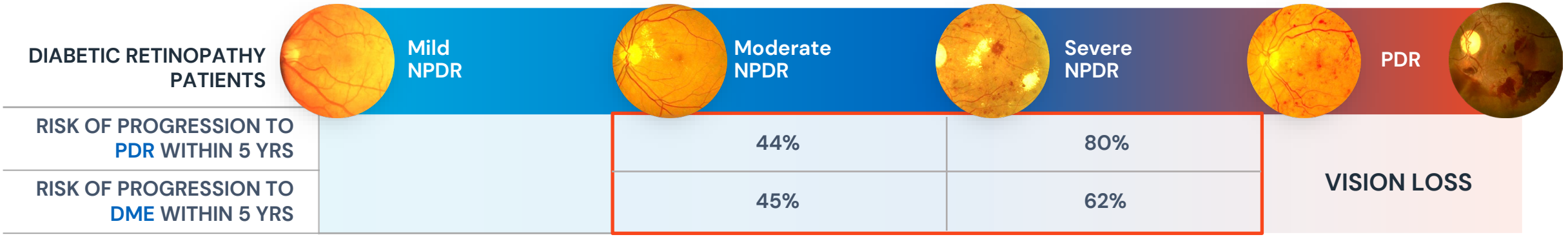
Of patients with early DR are treated due to high treatment burden[3]

**45–50 YRS**

Median age of disease onset

Early treatment with longer lasting therapy can potentially modify and prevent disease progression

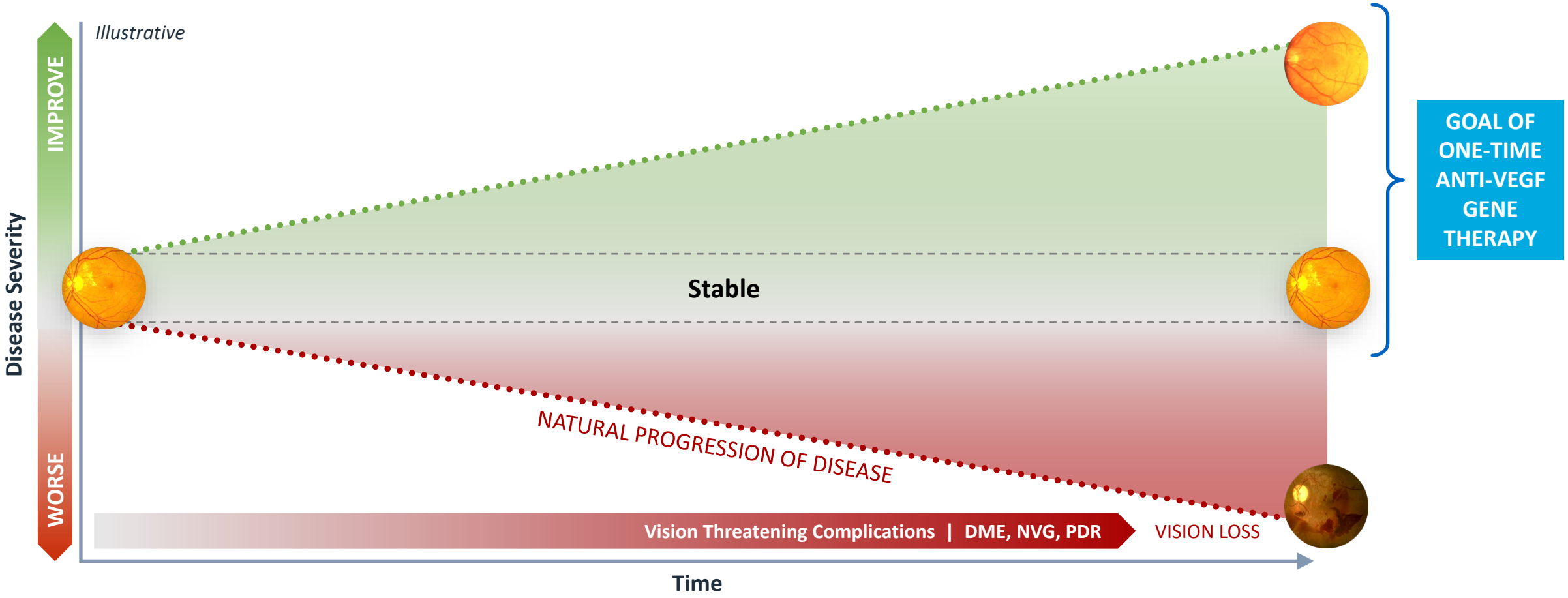

▸ INCREASING RISK OF DEVELOPING VISION THREATENING COMPLICATIONS[4,5] ▸




REGENXBIO

1.DR Market, Reports and Data 2022; 2. Market Scope 2022 Retinal Pharmaceuticals; 3. Market Scope Q4-2022 Retina Quarterly Summary Report; 4. ETDRS Trial Report 12, 1991; 5. Moshfeghi, 2020
DR = diabetic retinopathy; NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; DME = diabetic macular edema

# One time, in-office injection of gene therapy could potentially 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.

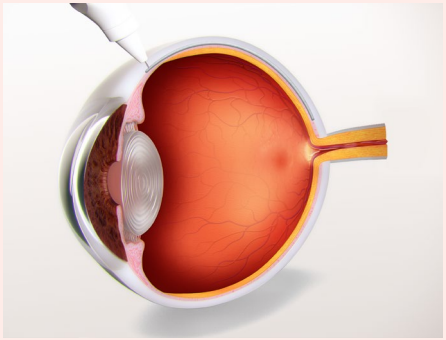
# Investigational In-office ABBV-RGX-314 for the Treatment of Diabetic Retinopathy (DR)

## ABBV-RGX-314 PRODUCT CANDIDATE

**Vector:** AAV8 | **Gene:** anti-VEGF fab

**Route of administration:**

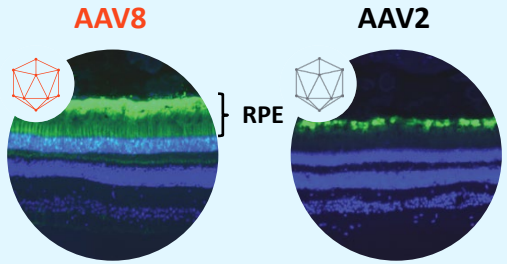
**Suprachoroidal**



**Mechanism of action:**

Reducing leaky blood vessel formation by giving ocular cells the ability to produce an anti-VEGF fab

Improved AAV vector technology




**More efficient gene delivery to the RPE[a]**

+

Leveraging current standard of care in transgene

- FDA-approved mAbs and mAb fragments that inhibit VEGF are used for the prevention of DR complications
- **ABBV-RGX-314 gene encodes an anti-VEGF mAb fragment (fab)**

=

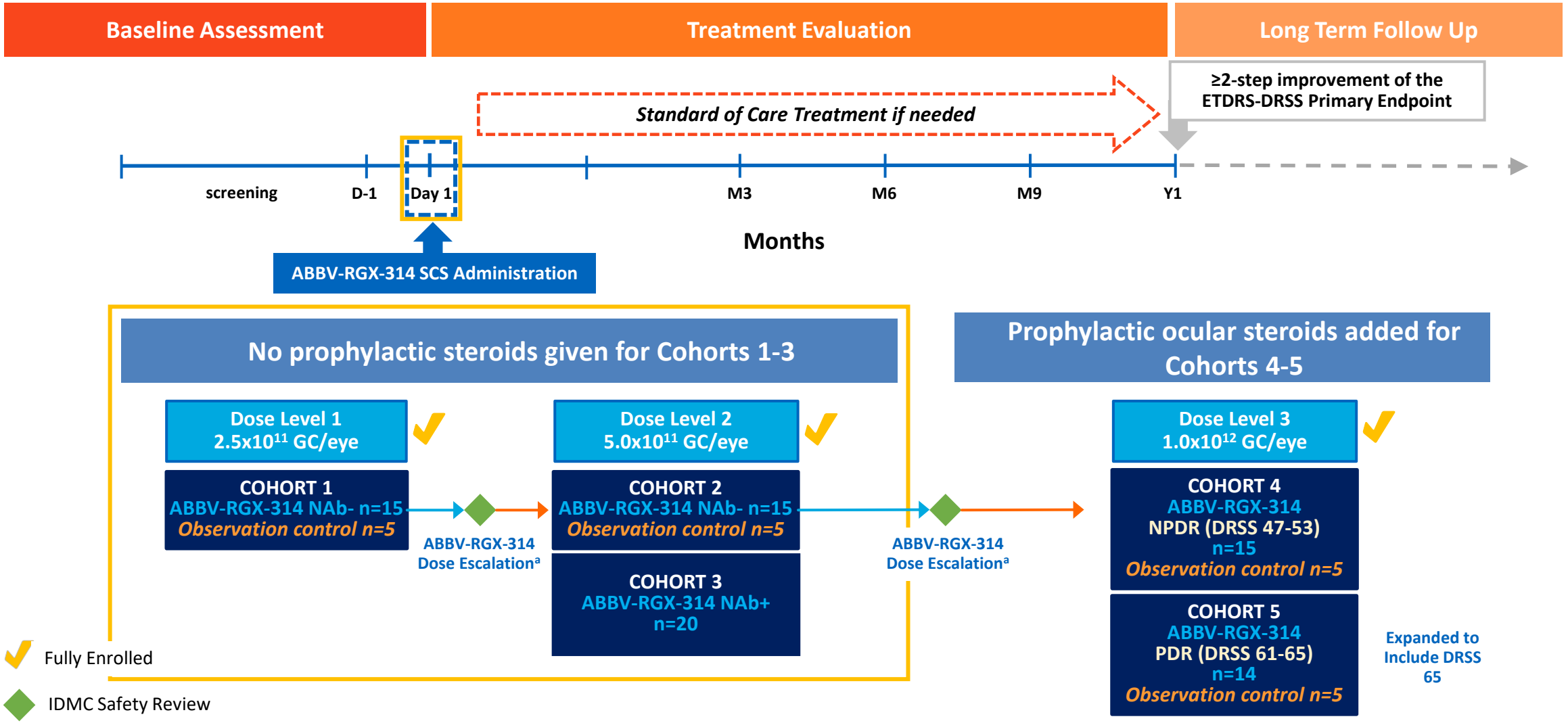
**ABBV-RGX–314**: AAV8 encoding anti–VEGF fab

**Potential for long-term therapeutic anti-VEGF expression**

a. Vandenberghe et al. 2011 *Science Translational Medicine.*
AAV: Adeno-Associated Virus.

# ABBV-RGX-314 ALTITUDE® Study Design

## Moderately Severe NPDR, Severe NPDR, or Mild PDR Patients without active CI-DME




a. Dose escalation safety review to occur two weeks after final subject in each cohort has been dosed.
SCS: Suprachoroidal Space; NAb+ = AAV8 neutralizing antibody positive; NAb- = AAV8 neutralizing antibody negative/low; Y1 = 48 weeks; NPDR: Non-proliferative Diabetic Retinopathy; PDR: Proliferative Diabetic Retinopathy

# ALTITUDE® Baseline Characteristics (Dose Levels 1 and 2)

| | Variable | Observational Control (N=10) | Dose Level 1 Cohort 1 (N=15) | Dose Level 2 Cohort 2 (N=15) | Dose Level 2 Cohort 3 (N=20) | Total (N=60) |
|---|---|---|---|---|---|---|
| BASELINE[a] | **Mean Age** (Years) | 52.5 | 50.7 | 58.1 | 60.1 | 56.0 |
| | **Gender – Female** | 1(10.0%) | 9 (60.0%) | 7 (46.7%) | 8 (40.0%) | 25 (41.7%) |
| | **Hemoglobin A1c** | 7.7 | 8.2 | 8.5 | 8.2 | 8.2 |
| | **DR Category at Baseline** | | | | | |
| | DRSS 47 (Moderately Severe NPDR) | 8 (80.0%) | 4 (26.7%)[b] | 9 (60.0%) | 12 (60.0%) | 33 (55.0%) |
| | DRSS 53 (Severe NPDR) | 0 | 2 (13.3%) | 1 (6.7%) | 2 (10.0%) | 5 (8.3%) |
| | DRSS 61 (Mild PDR) | 2 (20.0%) | 8 (53.3%)[c] | 5 (33.3%) | 6 (30.0%) | 21 (35.0%) |
| | DRSS 65 (Moderate PDR) | 0 | 1 (6.7%)[d] | 0 | 0 | 1 (1.7%) |
| | **Screening BCVA** (Snellen equivalents) | 84.5 | 78.1 | 82.1 | 81.3 | 81.3 |
| | **Screening OCT CRT** (µm) | 271.6 | 259.5 | 272.4 | 274.4 | 270.4 |
| | **Lens Status – Phakic n** (%) | 9 (90.0%) | 13 (86.7%) | 10 (66.7%) | 13 (65.0%) | 45 (75.0%) |
| DISEASE HISTORY | **Study Eye with anti-VEGF Injections in the Past 36-months n** (%) | 1(10.0%) | 5 (33.3%) | 0 | 0 | 6 (10.0%) |
| | **Months Since DR Diagnosis[e] – Mean** | 23.7 | 27.8 | 26.0 | 22.5[f] | 24.9 |

a. Ocular variables refer to study eye only.
b. One patient had a missing HbA1c measurement at baseline.
c. During an interim central reading center masked adjudication, 1 patient had baseline DRSS updated from Grade 47 to Grade 61 since prior interim data release.
d. After randomization, central reading center DRSS was scored as Grade 65 on masked adjudication.
e. Calculation based on randomization date.
f. One patient is missing date of DR diagnosis and not included.

# ALTITUDE® Interim Safety Summary: Dose Levels 1 and 2 Through 1 Year

**ABBV-RGX-314 has been well-tolerated in Dose Levels 1 and 2 (n=50)**

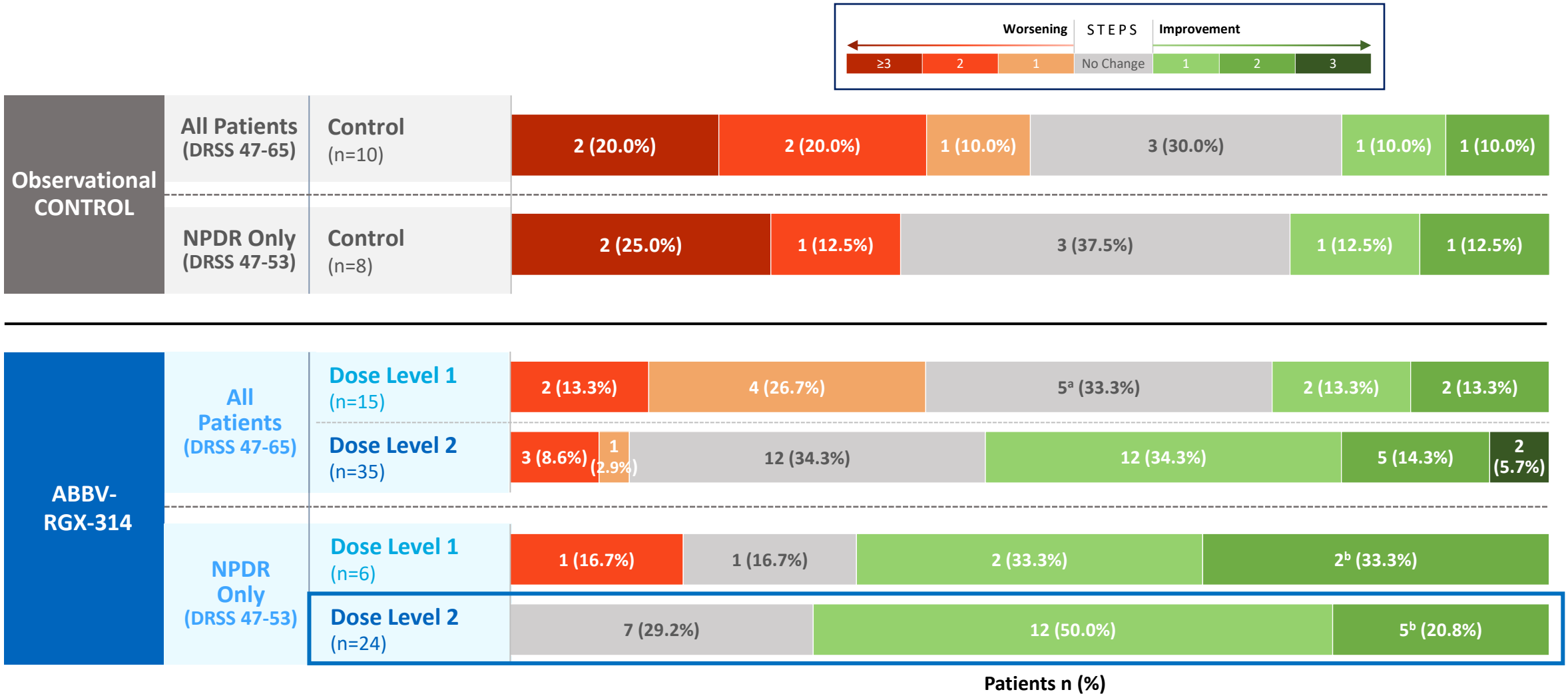
- 7 SAEs: none considered drug-related
- No cases of chorioretinitis, vasculitis, occlusion, or hypotony

| Dose Levels 1 and 2: Common Ocular TEAEs[a] in the Study Eye through 1 Year | No prophylactic steroids | | |
|---|---|---|---|
| | Dose Level 1 $2.5x10^{11}$ (C1) (N=15) | Dose Level 2 $5x10^{11}$ (C2/C3) (N=35) | Total N=50 |
| Conjunctival hyperemia | 4 (26.7%) | 11 (31.4%) | 15 (30.0%) |
| Conjunctival hemorrhage | 3 (20.0%) | 4 (11.4%) | 7 (14.0%) |
| Episcleritis[b] | 1 (6.7%) | 5 (14.3%) | 6 (12.0%) |
| IOP Increase | 1 (6.7%) | 3 (8.6%) | 4 (8.0%) |
| Intraocular Inflammation [c] | 0 (0.0%) | 3 (8.6%) | 3 (6.0%) |

- **Stable BCVA through One Year**

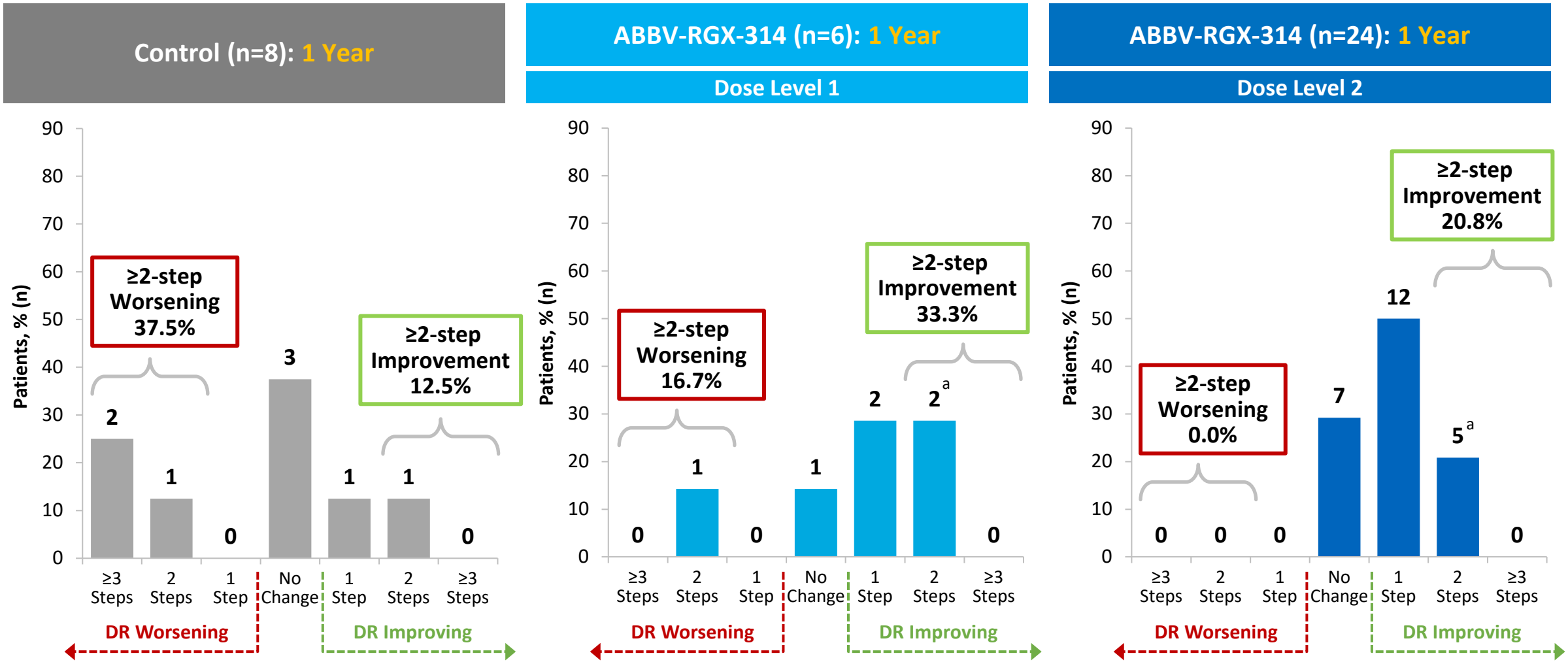
Data cut: September 25, 2023
a. Common TEAEs include AEs for total group ≥10%, as well as IOP increase and intraocular inflammation, with onset up to the 1 Year visit.
b. All cases were mild to moderate (grade 1 and grade 2) and have resolved on topical corticosteroids based on slit lamp examination.
c. 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.
SAE: Serious Adverse Event; TEAE: Treatment Emergent Adverse Event.

# Summary of DRSS Change With Dose Levels 1 and 2 Compared to Control at 1 Year




Data cut: September 25, 2023.
a. During an interim central reading center masked adjudication, 1 patient's DRSS grade at baseline was updated from Grade 47 to Grade 65.
b. One patient in each Dose Level missed their 1-Year visit, so their 6-month results were used.

# Change in DRSS at 1 Year by Dose Level – NPDR Only (DRSS 47-53)

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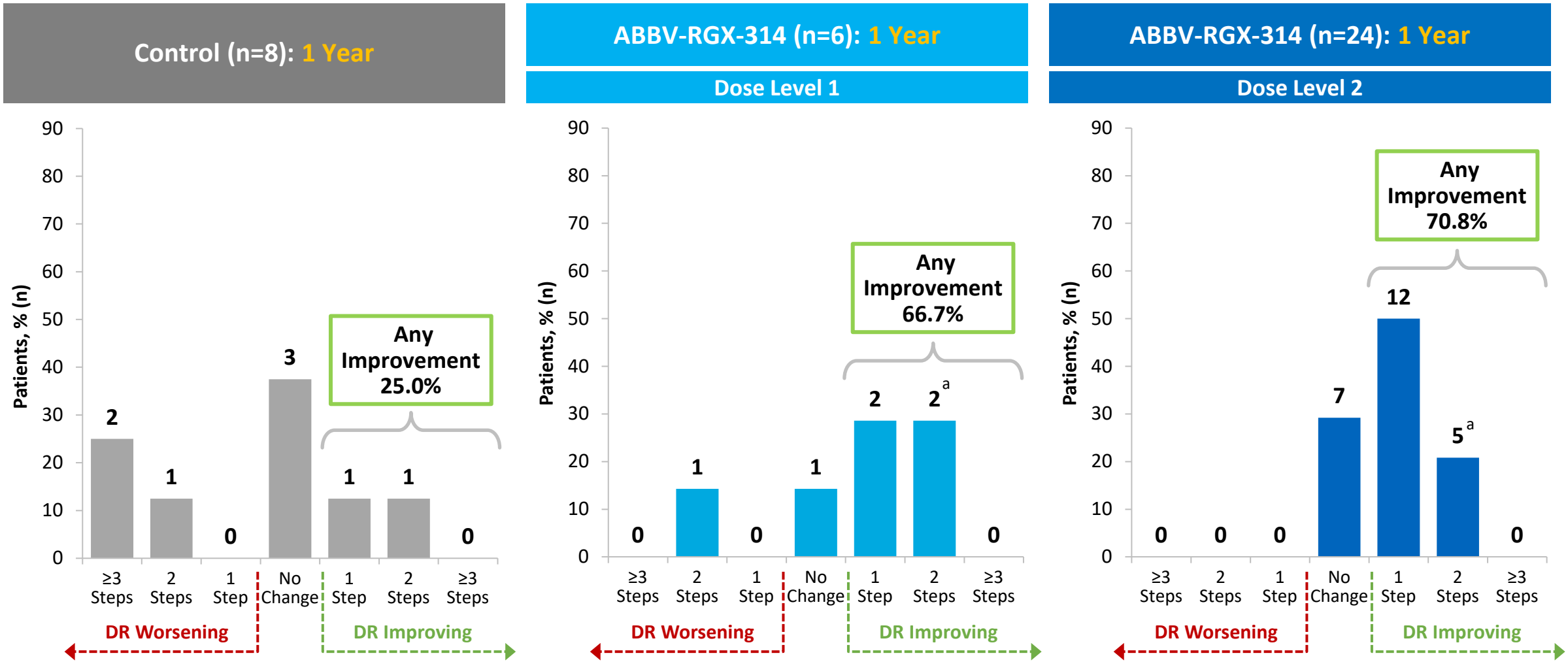
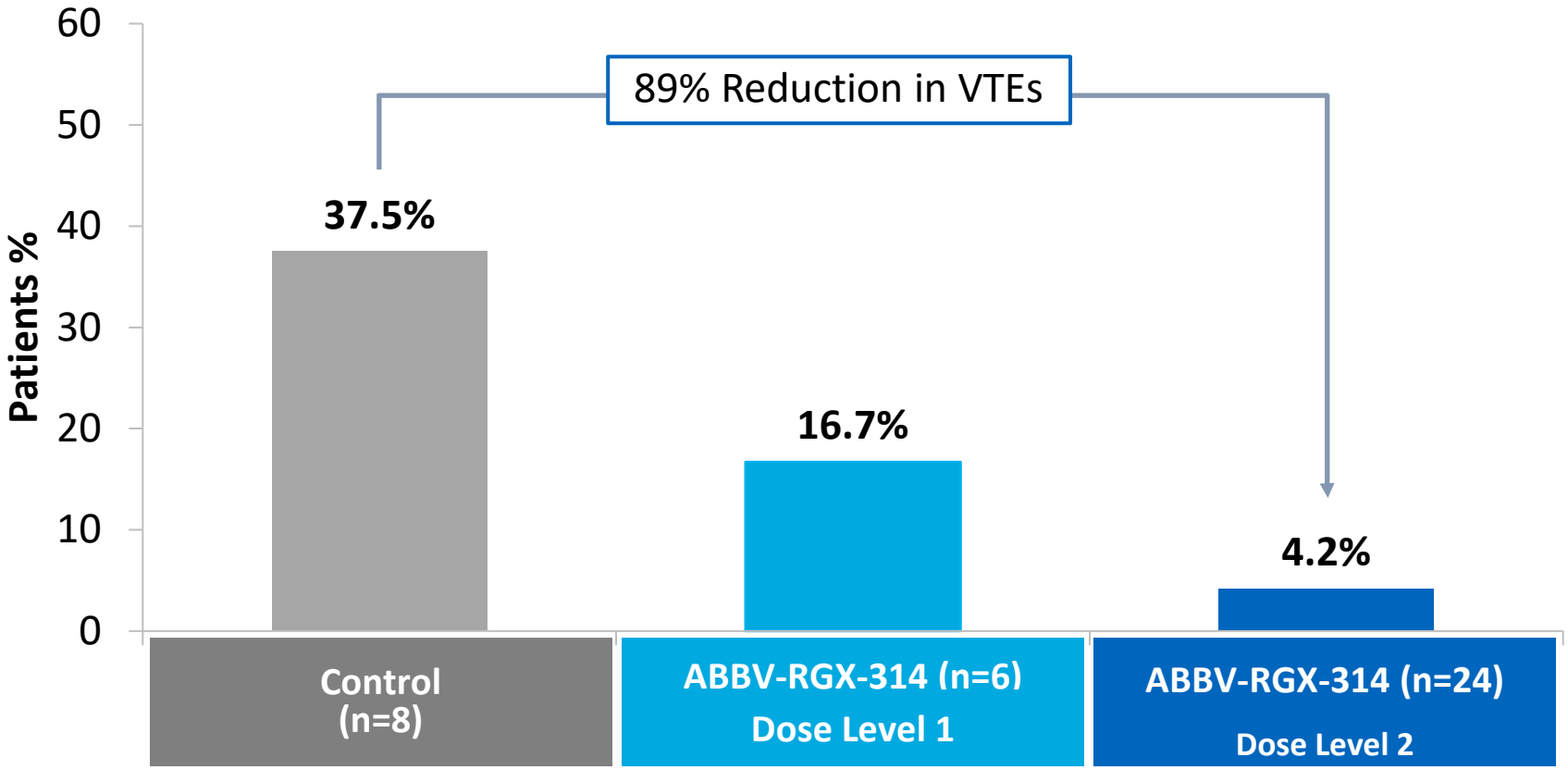
# Change in DRSS at 1 Year by Dose Level – NPDR Only (DRSS 47-53)




Data cut: September 25, 2023.
a. One patient in each Dose Level missed their 1-Year visit, so their 6-month results were used.

# Vision-Threatening Events (VTEs) Through Year 1 by Dose Level – NPDR Only (DRSS 47-53)

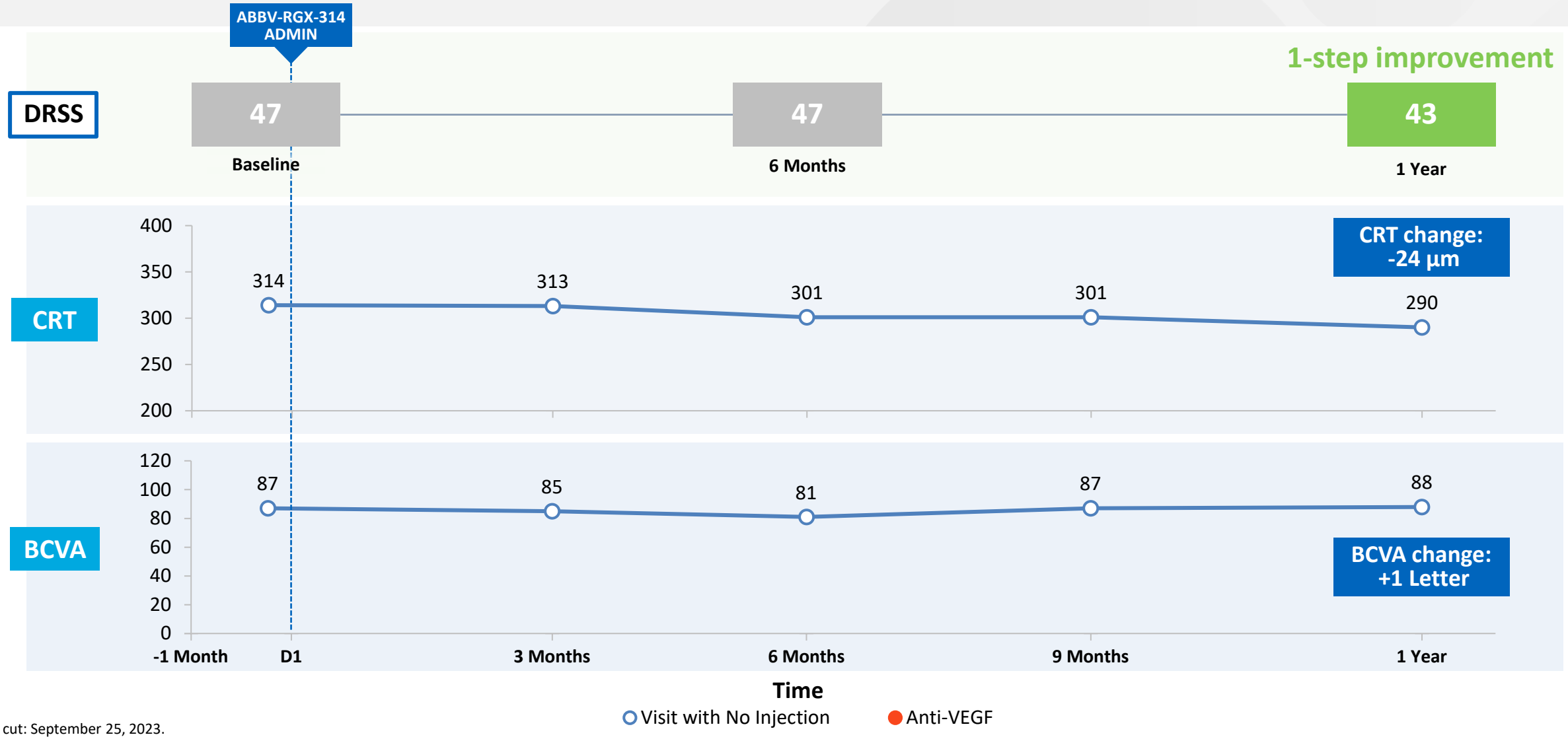
## ABBV-RGX-314 treatment reduced VTEs compared to Control Group through 1 Year




Data cut: September 25, 2023.
CI-DME: Center-Involved Diabetic Macular Edema; PDR: Proliferative Diabetic Retinopathy; ASNV: Anterior Segment Neovascularization; VTCs: Vision-Threatening Complications; VTEs: Vision-Threatening Events
VTEs = VTCs + CI-DME; VTCs could include PDR or ASNV. No cases of ASNV were reported.

# Patient A: 65yo Male that Received Dose Level 2 of ABBV-RGX-314

## DRSS, CRT, and BCVA Change Over Time




Data cut: September 25, 2023.

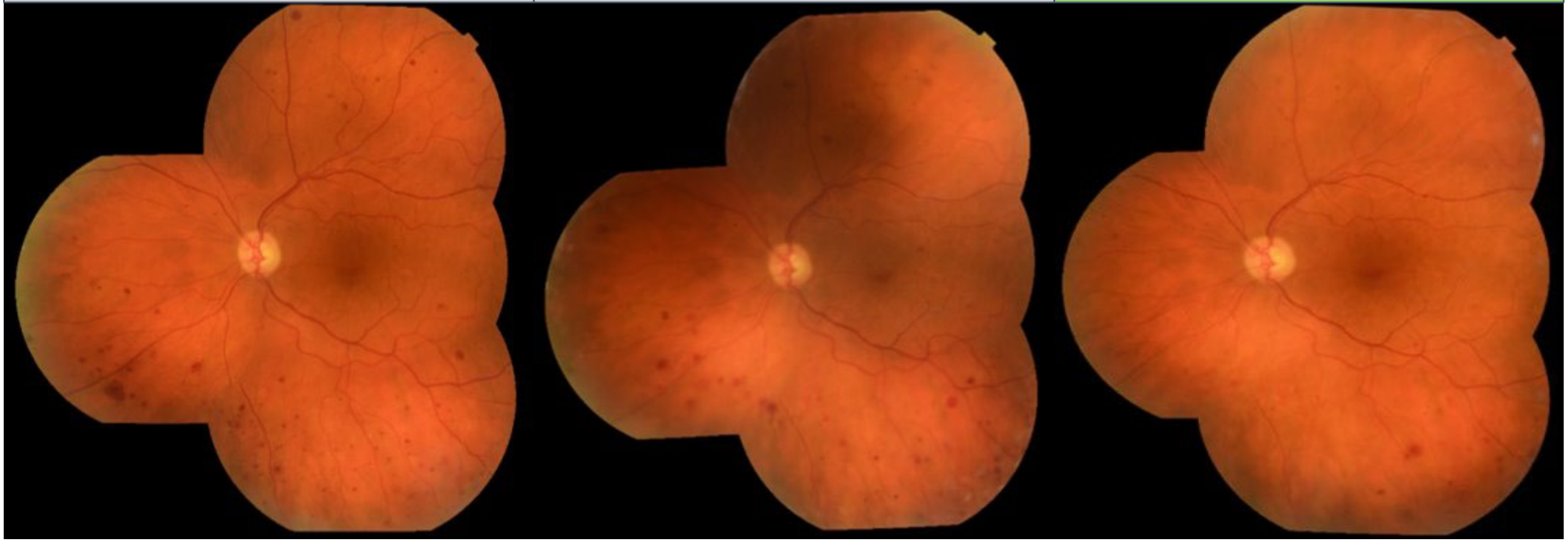
This slide presents results from an individual patient and is not indicative of outcomes experienced by all patients in this trial.

DRSS: Diabetic Retinopathy Severity Scale; CRT: Central Retinal Thickness; BCVA: Best Corrected Visual Acuity

# Patient A: 65yo Male that Received Dose Level 2 of ABBV-RGX-314

**DRSS 1-Step Improvement (47 to 43) at 1 Year**

| Baseline<br>**DRSS 47** | Month 6<br>**DRSS 47** | Year 1<br>**DRSS 43** |
|---|---|---|

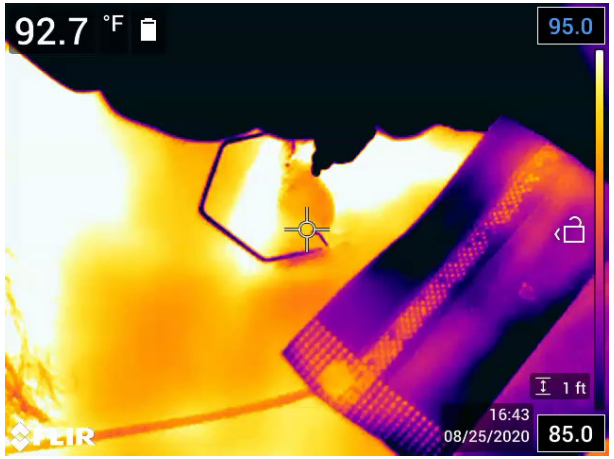


Data cut: September 25, 2023.

This slide presents results from an individual patient and is not indicative of outcomes experienced by all patients in this trial.

DRSS: Diabetic Retinopathy Severity Scale

# Summary of ABBV-RGX-314 1 Year Results from the Phase II ALTITUDE DR Study: Dose Level 1 and 2




Video: M. Barakat

- **Safety**
  - Suprachoroidal ABBV-RGX-314 continues to be **well-tolerated in Dose Levels 1 and 2 (n=50) through 1 Year**
  - No prophylactic corticosteroids administered in Dose Levels 1 and 2
  - A few cases of mild intraocular inflammation were observed; resolved with topical corticosteroids
- **Efficacy Endpoints**
  - **One-time in-office injection** of investigational ABBV-RGX-314 demonstrated clinically meaningful improvements in disease severity and reduction of VTEs in NPDR patients
  - **In Dose Level 2 patients with baseline NPDR (n=24):**
    - **100%** demonstrated stable to improved disease severity
      - 70.8% achieved any disease improvement vs. 25.0 % in Control
      - 0% worsened ≥2 steps vs. 37.5 % in Control
    - 4.2% developed VTEs vs. 37.5% in Control

**Dose Level 2 prevented disease progression in all NPDR patients and reduced Vision-Threatening Events by 89%**

Data cut: September 25, 2023.
VTEs: Vision-Threatening Events = VTCs + CI-DME