The DAVIO Trial: A Phase 1, Open-label, Dose-Escalation Study of a Single Injection of EYP-1901 (Vorolanib in Durasert® Platform) Demonstrating Reduced Treatment Burden in Wet Age-related Macular Degeneration

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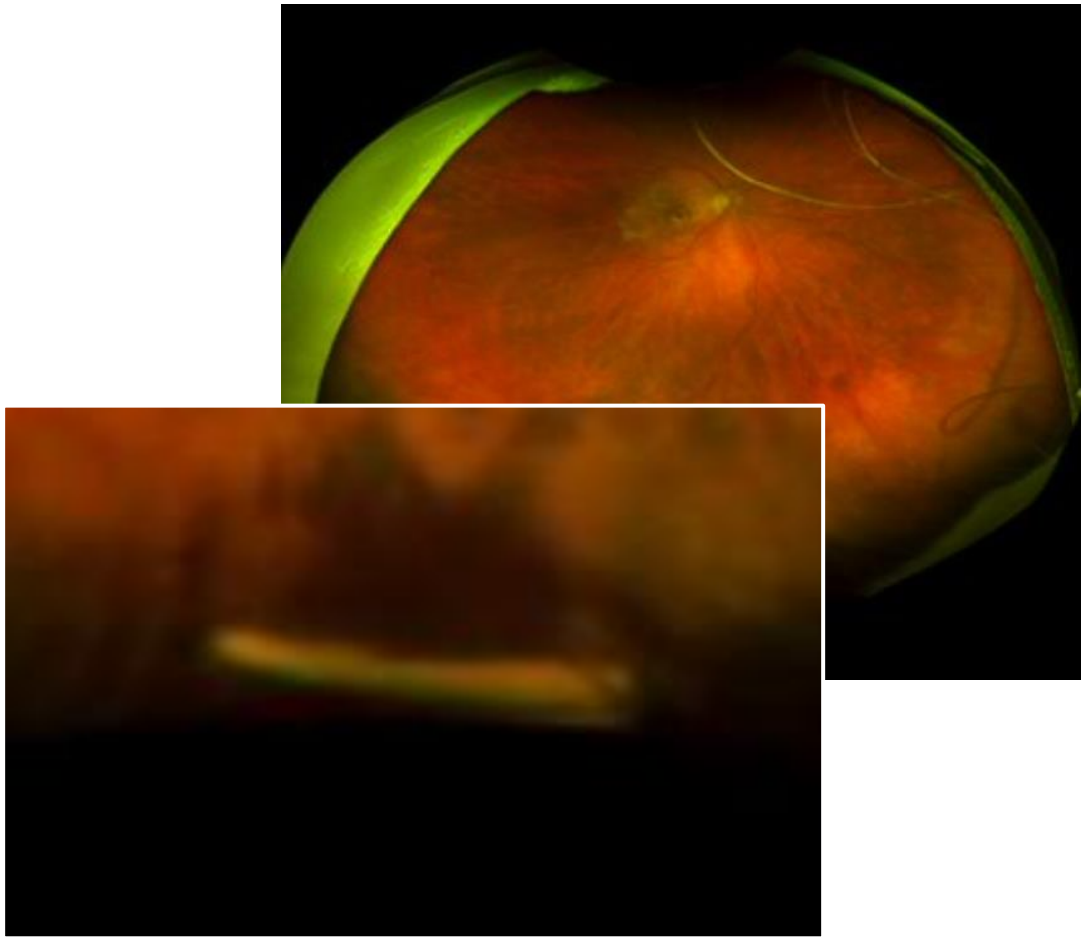
ARVO 2023

EYP-1901
Sustained Delivery of Vorolanib for wAMD

- In the real world, under treatment with anti-VEGF has increased the need for extended durability and new MOA[1,2]
- EYP-1901 is a novel intravitreal injection therapy consisting of, **Vorolanib,** a small molecule pan-VEGF receptor blocker, in a bio-erodible drug release system (**Durasert®**)
- The safety and preliminary efficacy of EYP-1901 as maintenance therapy in patients with previously treated neovascular AMD were investigated in the phase 1 DAVIO trial



EYP-1901 insert at month 5 post injection

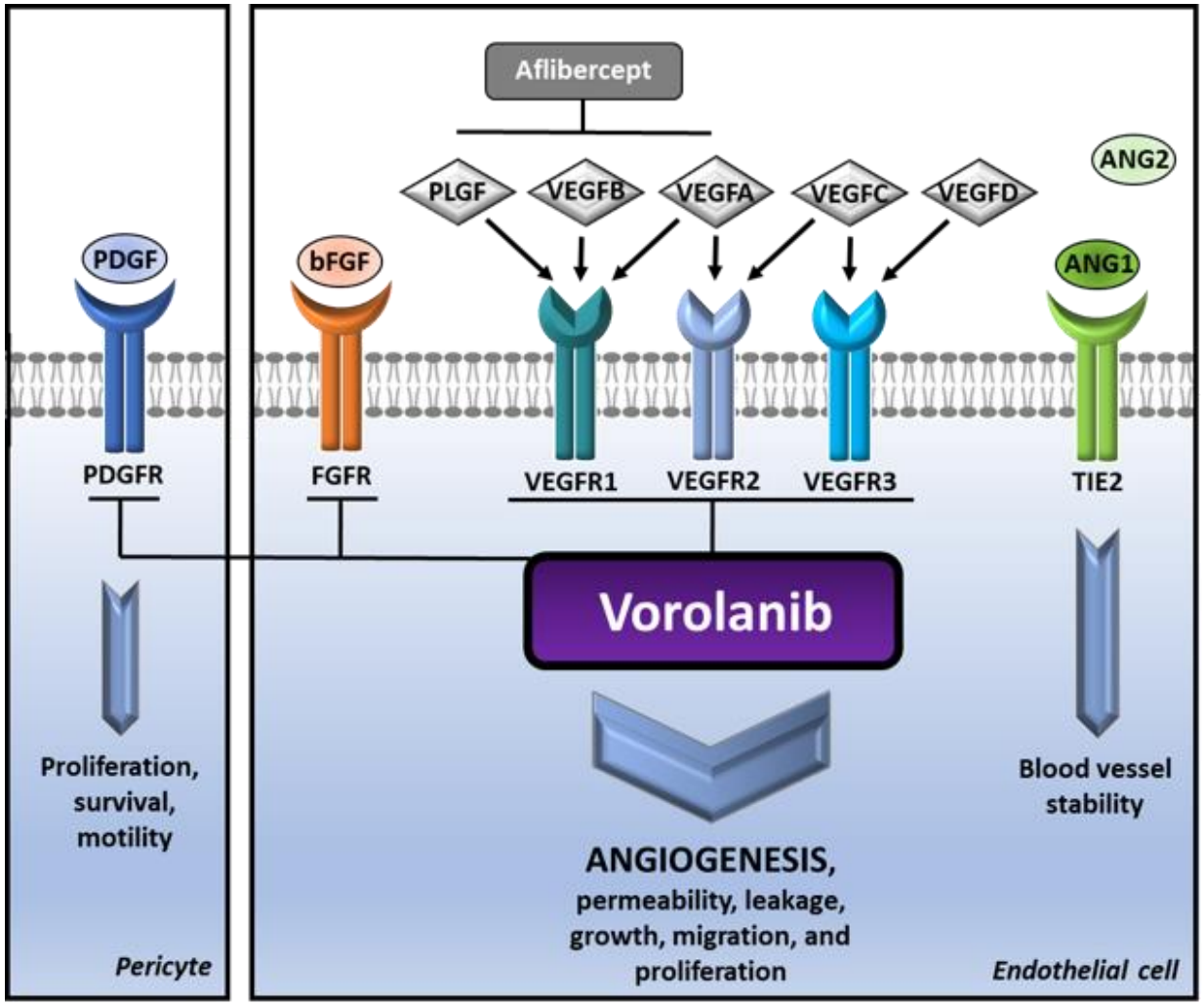
1. Sobolewska et al. *Clin Ophthalmol.* 2021;15:4317-4326. 2. Monés et al. *Ophthalmologica.* 2020;243(1):1-8.

AMD, age-related macular degeneration; VEGF, vascular endothelial growth factor.

Vorolanib Provides pan-VEGF Receptor Inhibition

- Vorolanib inhibits multiple pathways that play key roles in the regulation of angiogenesis:
  - Inhibits all **VEGF receptors**
  - Inhibits **PDGF receptors**
  - Inhibits **FGF receptors**

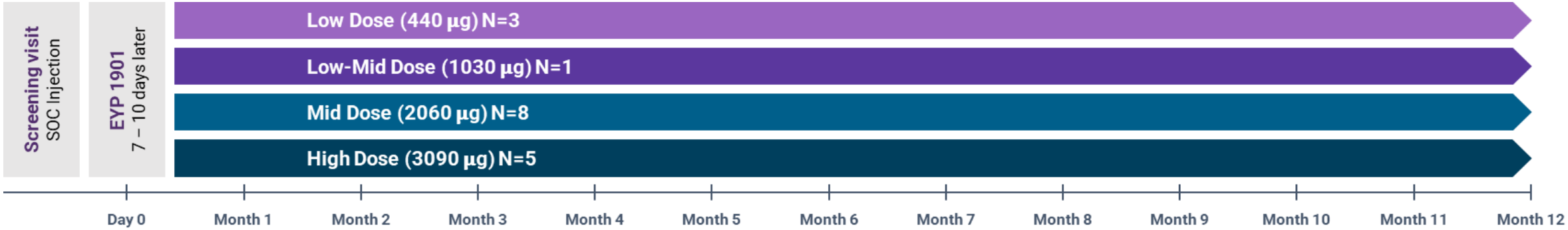
- **Highly selective**
  - Does not inhibit TIE2 receptor
  - Binds intracellularly



FGFR, fibroblast growth factor receptor; PDGFR, platelet-derived growth factor receptor; TIE2, tyrosine phosphorylated in normal adult endothelium tissues; VEGFR, vascular endothelial growth factor receptor. ANG, angiopoietin; bFGF, basic fibroblast growth factor; PDGF, platelet-derived growth factor; PLGF, placental growth factor; VEGF, vascular endothelial growth factor.

DAVIO Phase 1 Study Methods

DAVIO was a phase 1, single-injection, multicenter, open-label, dose-escalation trial



Methodology:

- Enrolled all comers, previously treated nAMD
- Minimum 3 anti-VEGF injections in previous 6 months
- Single intravitreal aflibercept followed by EYP-1901 injection

Criteria for supplemental anti-VEGF therapy:

- New or worsening vision-threatening hemorrhage
- Increase in CST of > 75 µm from baseline
- Loss of ≥ 10 ETDRS letters from baseline with intraretinal/ subretinal fluid and/or hemorrhage judged to be the cause of BCVA loss

Primary end point: safety

- Ocular and non-ocular treatment-emergent AEs through month 12

Secondary end points:

- Change in BCVA and CST
- Use of supplemental anti-VEGF therapy

DAVIO Participants

Screening Characteristics (N = 17)	
Mean age, y (range)	77.4 (67-94)
Female, %	76%
Mean BCVA, ETDRS letters (range)	69 (38-85)
Mean CST, µm (range)	299 (204-441)
Median length of time for wet AMD diagnosis prior to enrollment, mo (range)	17 (4-74)
Mean number of injections in the 12 months prior to enrollment (range)*	8.6 (3-10)

*Normalized.

AMD, age-related macular degeneration; BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; VEGF, vascular endothelial growth factor.

Primary End Point Results: Safety

Key findings:

- No ocular SAEs
- No drug-related systemic SAEs
- No evidence of vorolanib-related ocular or systemic toxicity
- No Durasert-related toxicity or tolerance issues
- No dose limiting toxicity

Ocular AEs of particular interest:

- No vitreous floaters
- No endophthalmitis
- No retinal detachment
- No insert migration in the anterior chamber
- No retinal vasculitis
- No posterior segment inflammation
- No occlusive events

Safety data reported as of June 2022.

AE, adverse event; SAE, serious adverse event.

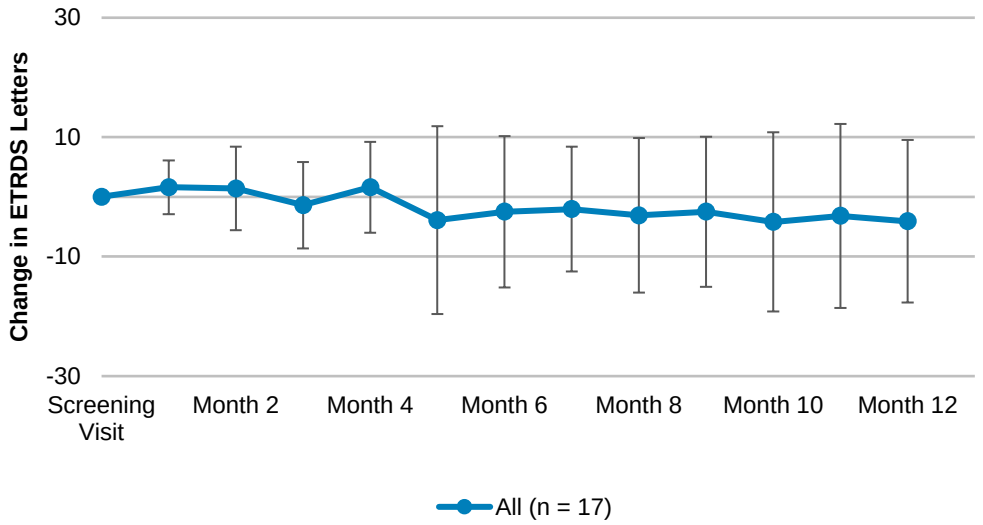
Secondary End Point Results:
Mean BCVA and CST at 12 Months

Mean Change From Screening Visit

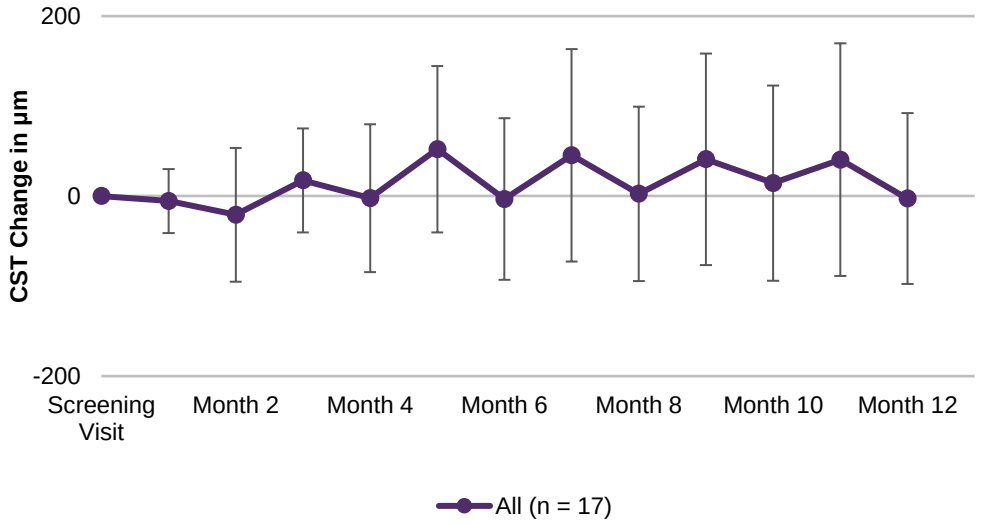
Parameter	6 Months	12 Months
BCVA	–2.5	–4.1
CST	–3.4	–2.8

BCVA units were ETDRS letters. CST units were µm.

Mean Change in BCVA From Screening Visit



Mean Change in CST From Screening Visit

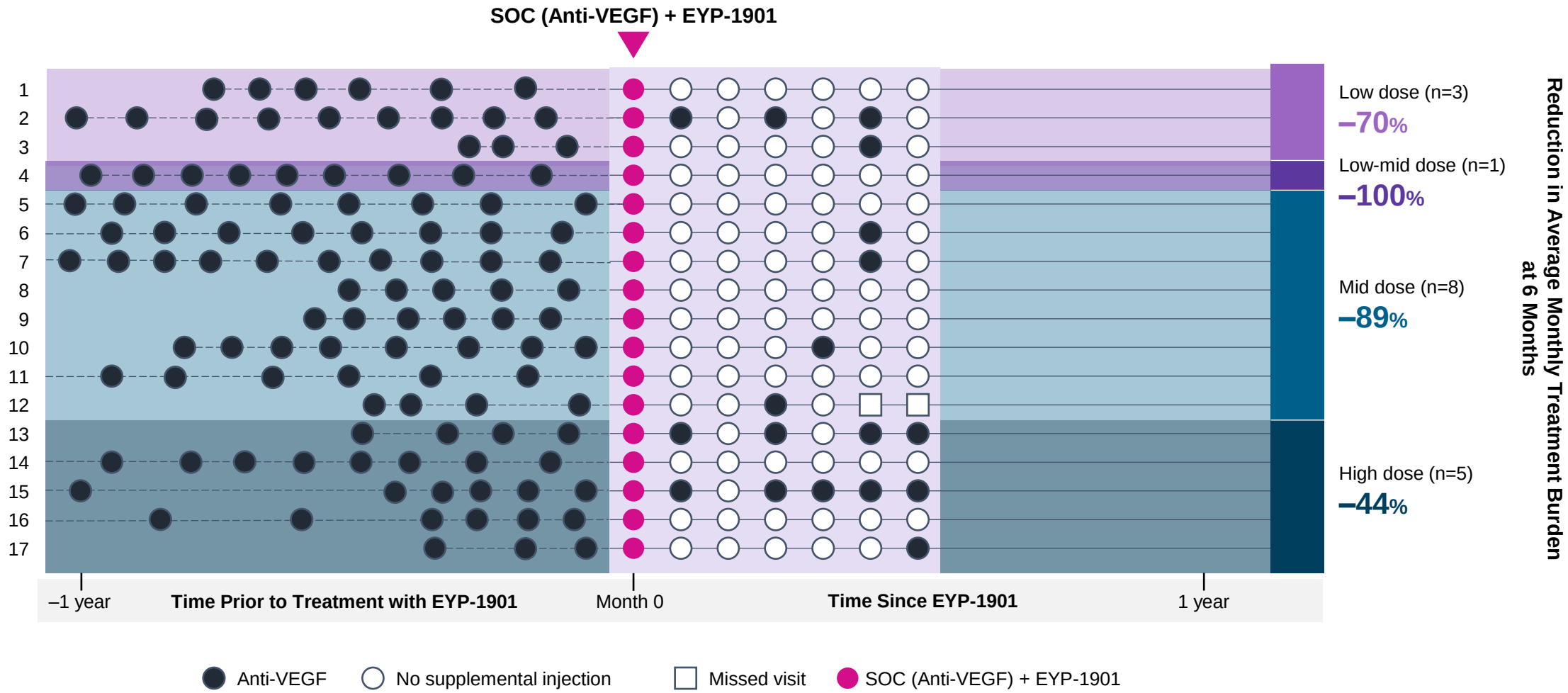


Error bars represent the standard deviation.

BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study.

Secondary End Point Results:
Reduction in Treatment Burden-75% at 6 Months

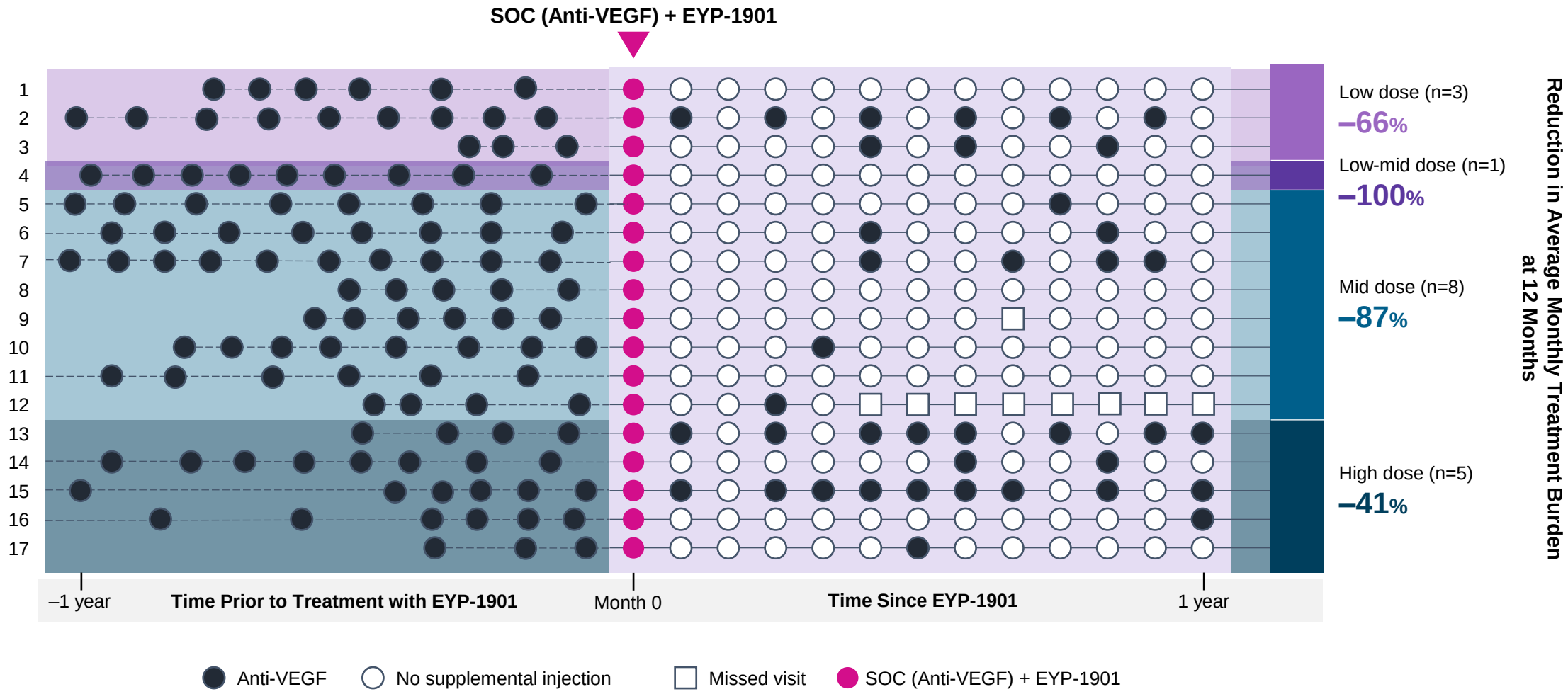
SOC Anti-VEGF Injections Before and After Treatment



BCVA, best-corrected visual acuity; CST, central subfield thickness; SOC, standard of care; VEGF, vascular endothelial growth factor.

Secondary End Point Results:
Reduction in Treatment Burden-73% at 12 Months

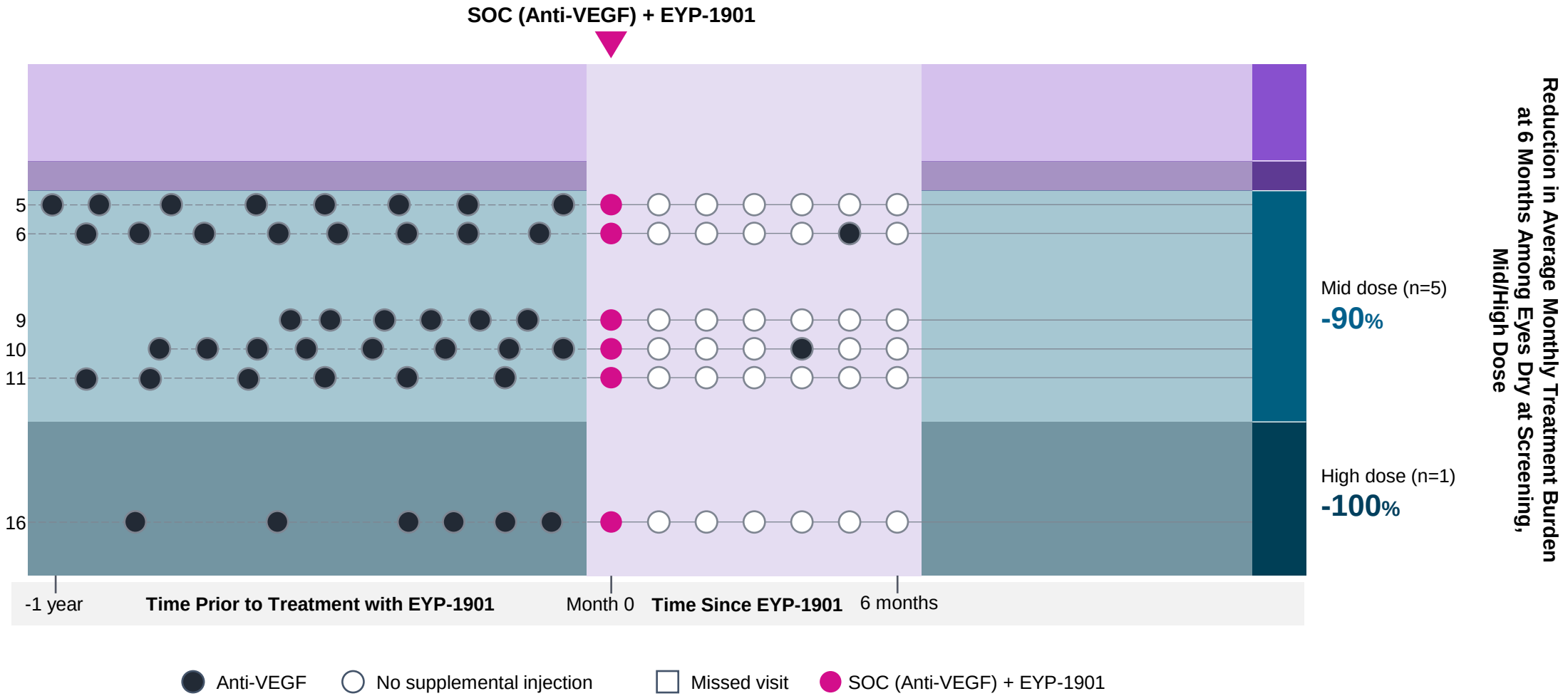
SOC Anti-VEGF Injections Before and After Treatment



BCVA, best-corrected visual acuity; CST, central subfield thickness; SOC, standard of care; VEGF, vascular endothelial growth factor.

Subgroup Analysis: Reduction in Treatment Burden - 92% at 6 Months Among Mid/High Dose Subjects with No Excess Fluid at Screening (n=6)

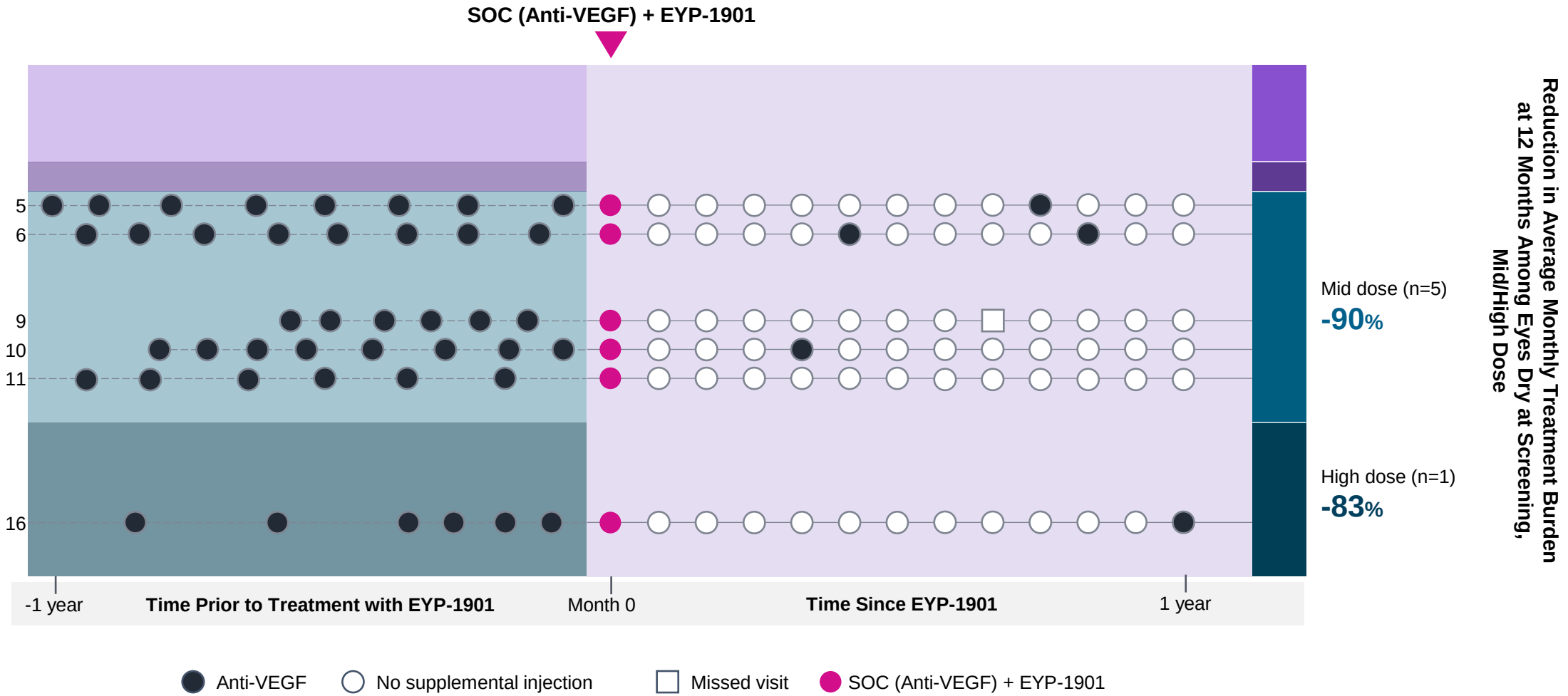
SOC Anti-VEGF Injections Before and After Treatment



BCVA, best-corrected visual acuity; CST, central subfield thickness; SOC, standard of care; VEGF, vascular endothelial growth factor.

Subgroup Analysis: Reduction in Treatment Burden - 89% at 12 Months Among Mid/High Dose Subjects with No Excess Fluid at Screening (n=6)

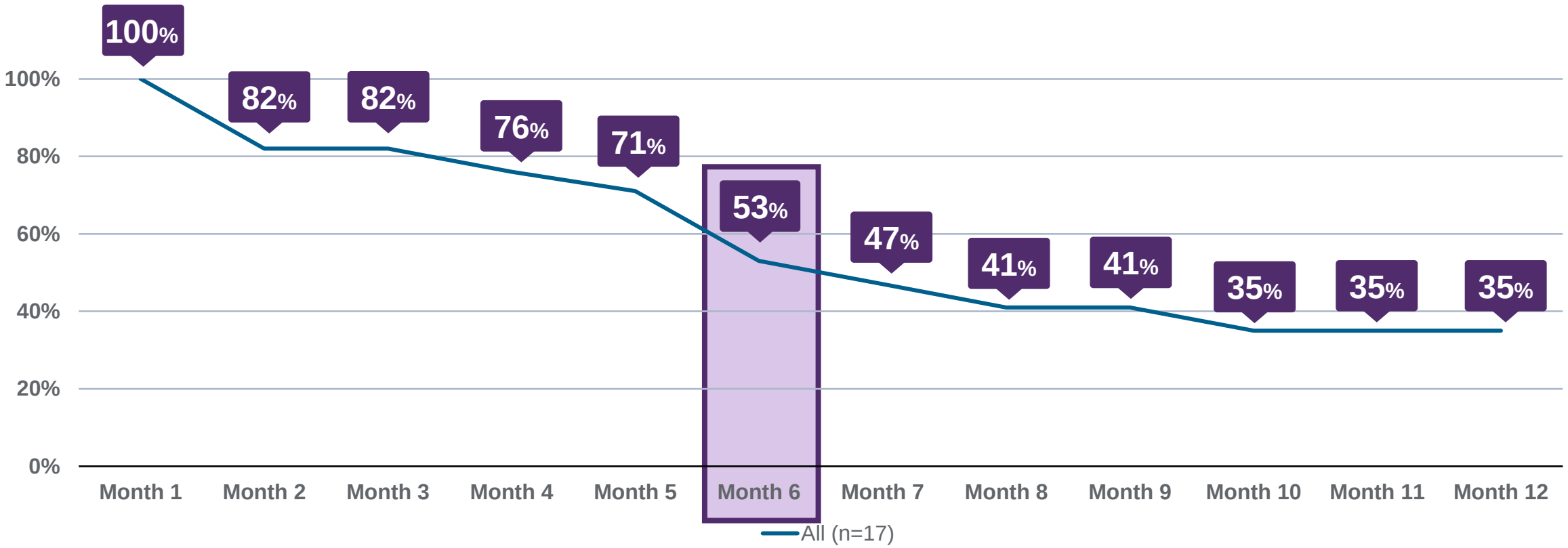
SOC Anti-VEGF Injections Before and After Treatment



BCVA, best-corrected visual acuity; CST, central subfield thickness; SOC, standard of care; VEGF, vascular endothelial growth factor.

Secondary End Point Results:
Supplemental Injection-Free Rates Up to Each Visit in All Subjects (n=17)

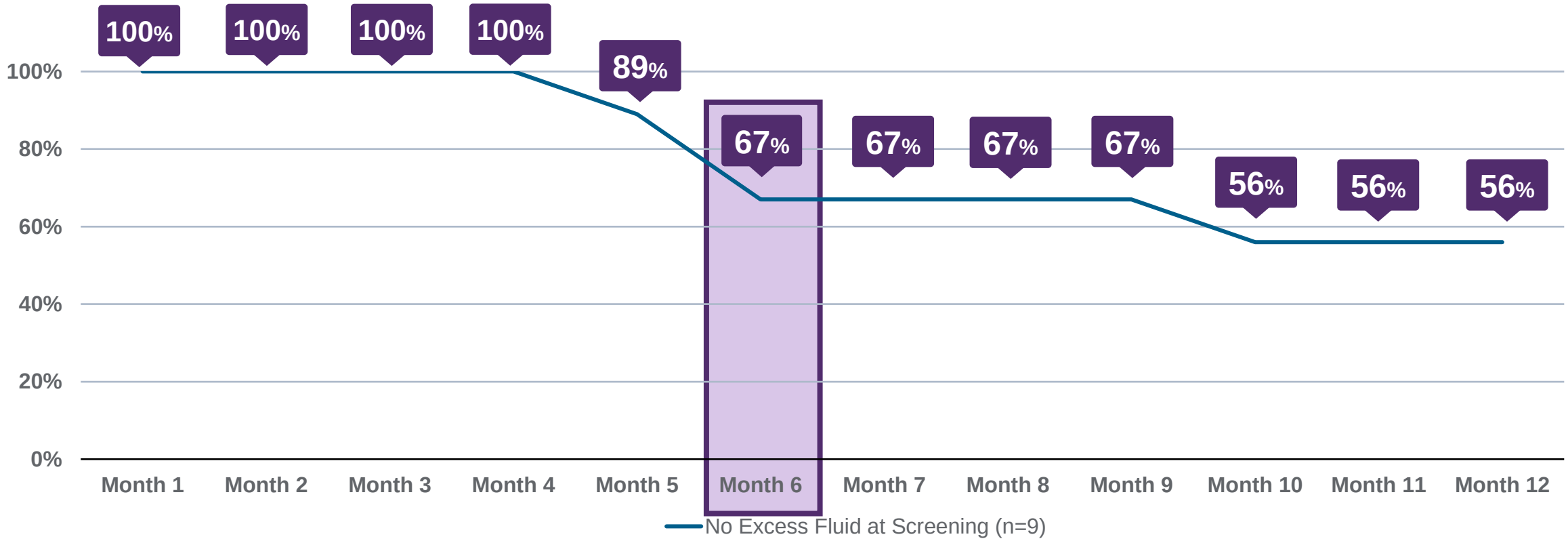
Median time to supplemental anti-VEGF: 6 months



DAVIO Final 12-Months Data

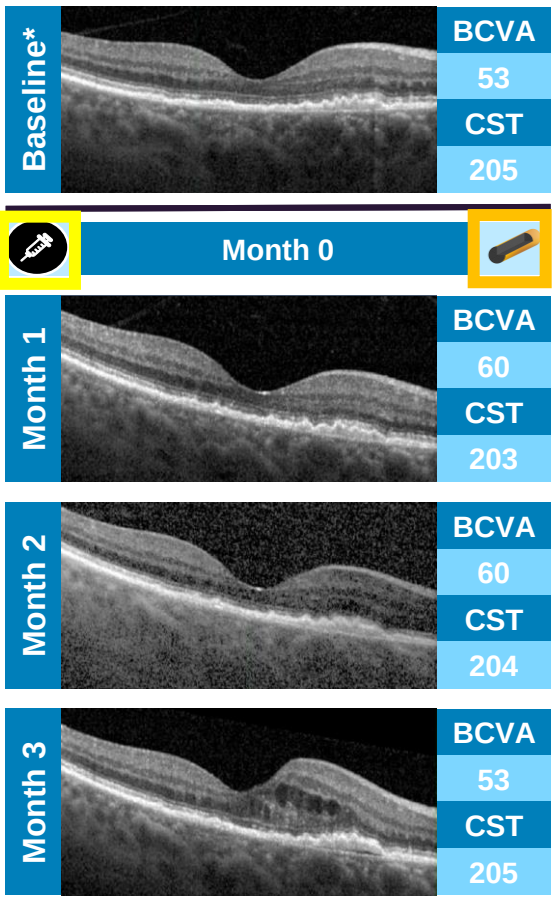
Subgroup Analysis: Supplemental Injection-Free Rates Up to Each Visit in Subjects with No Excess Fluid at Screening (n=9)

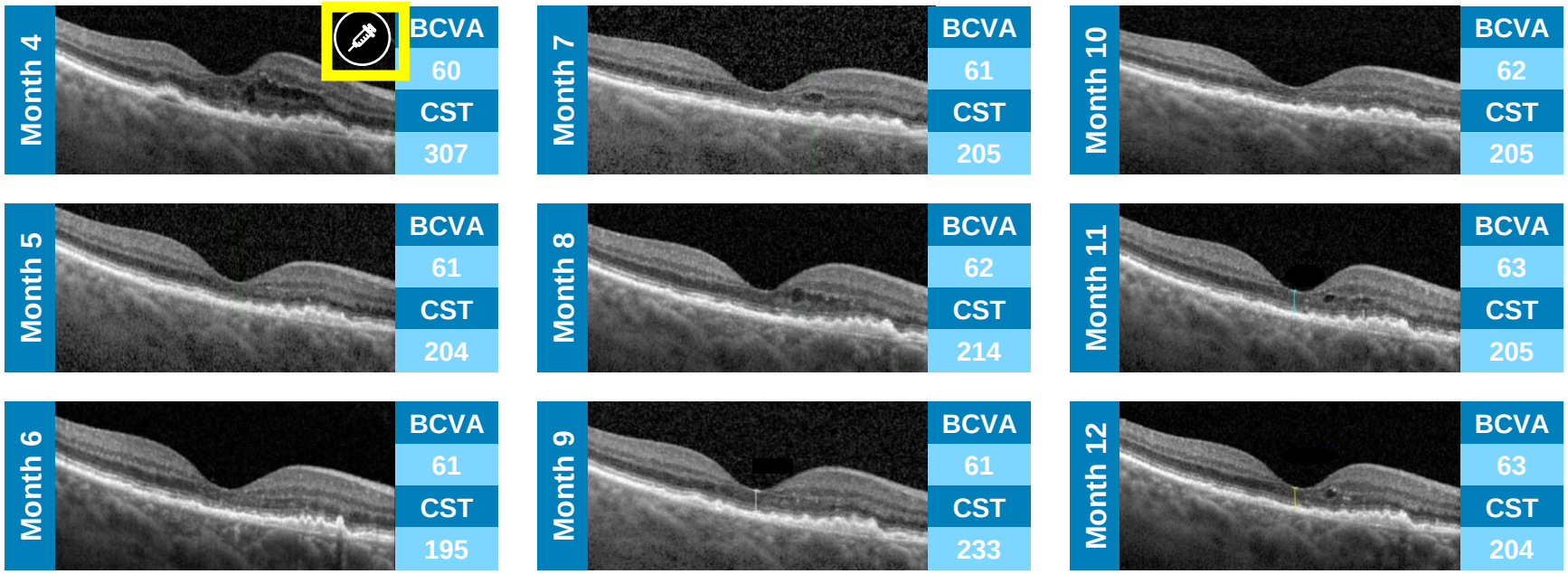
Median time to supplemental anti-VEGF: 12 months



Case 1: Mid-Dose Cohort

Remained Dry Without Additional Treatment After Single Supplemental Injection at 4 Months

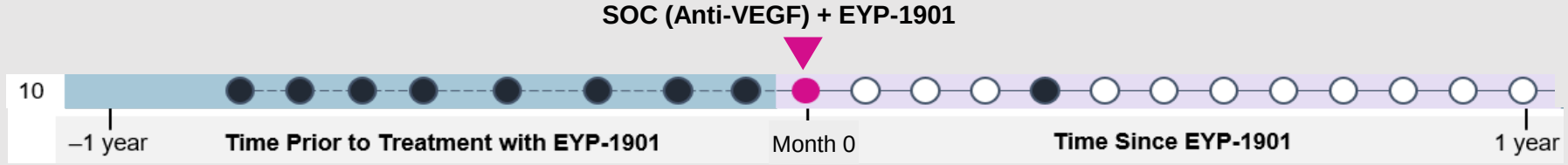




*Screening also serves as baseline image

= administration of anti-VEGF

= administration of EYP-1901

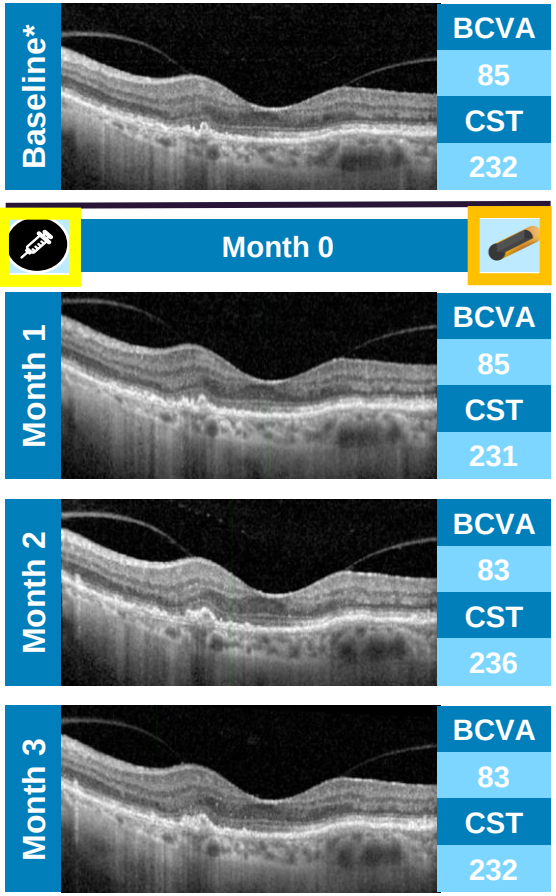


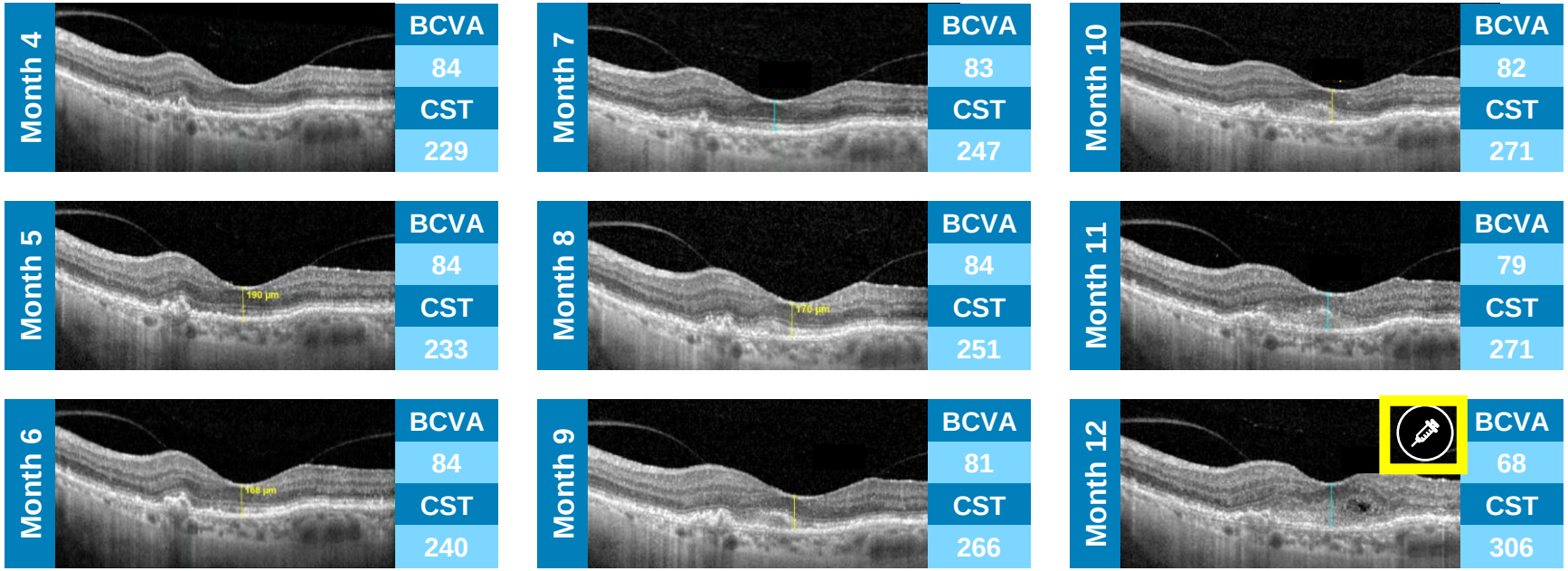
Case 1: SOC Anti-VEGF Injections Before and After Treatment

BCVA, best-corrected visual acuity; CST, central subfield thickness; M, month; SOC, standard of care; VEGF, vascular endothelial growth factor.

Case 2: High-Dose Cohort

Remained Dry Without Supplemental Injection Up To 12 Months After Single EYP-1901 Treatment

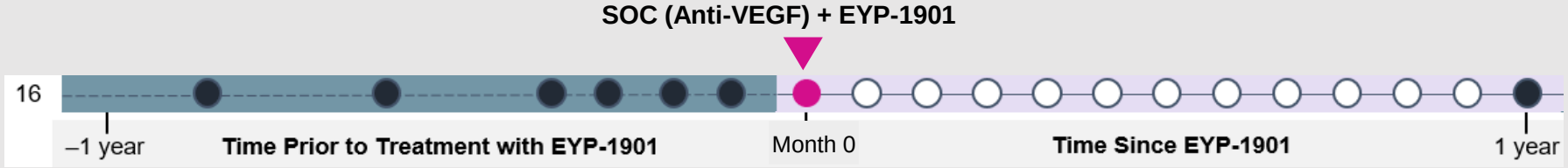




*Screening also serves as baseline image

= administration of anti-VEGF

= administration of EYP-1901



Case 2: SOC Anti-VEGF Injections Before and After Treatment

BCVA, best-corrected visual acuity; CST, central subfield thickness; M, month; SOC, standard of care; VEGF, vascular endothelial growth factor.

Conclusions: DAVIO Phase 1 Study EYP-1901 in nAMD

Primary end point: safety

- No ocular SAEs reported
- No drug-related systemic SAEs reported
- Majority of ocular AEs were mild and expected

Secondary end points: efficacy & durability single EYP-1901 injection

6 months
median time to supplemental anti-VEGF

35%
supplemental injection–free up to 12 months

73%
reduction in treatment burden at 12 months

- Phase 2 wet AMD trial DAVIO-2 enrollment completed; results Q4 2023
- Phase 2 NPDR trial PAVIA initiated
- Phase 2 DME trial planned

AE, adverse event; AMD, age-related macular degeneration; NPDR, nonproliferative diabetic retinopathy; SAE, serious adverse event; VEGF, vascular endothelial growth factor.