Interim 24-week Cohort 1 data from the OPTIC trial – Intravitreal gene therapy with ADVM-022 (AAV.7m8-aflibercept) for neovascular age-related macular degeneration

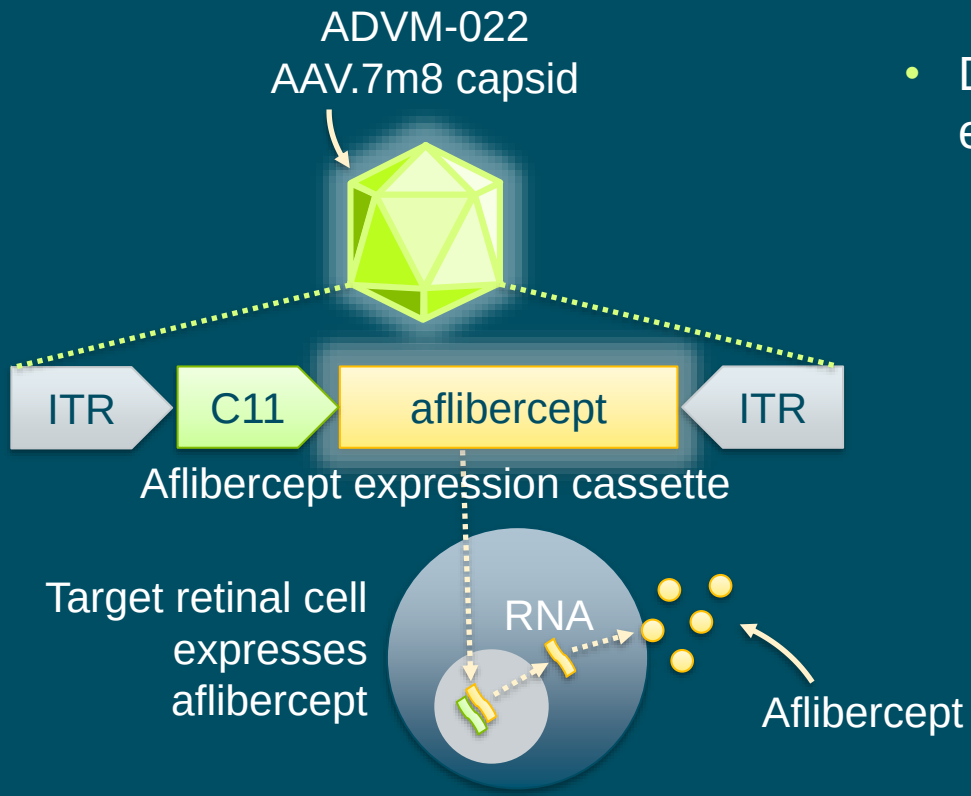
Szilárd Kiss MD
Director of Clinical Research, Associate Professor of Ophthalmology
Weill Cornell Medical College
– On behalf of the OPTIC investigators –

OPTIC
Gene Therapy in nAMD

Disclosures

- Adverum Biotechnologies – Consultant/Advisor, Equity
- Regenxbio - Consultant/Advisor, Equity
- Genentech/Roche – Consultant/Advisor
- Fortress Bio – Consultant/Advisor, Equity
- Optos – Consultant/Advisor, Research grant support
- Novartis – Consultant/Advisor
- Intellectual Property related to gene and cellular therapy – assigned to Weill Cornell/Cornell University

ADVM-022 is specifically designed for long-term intraocular VEGF suppression with a single intravitreal injection



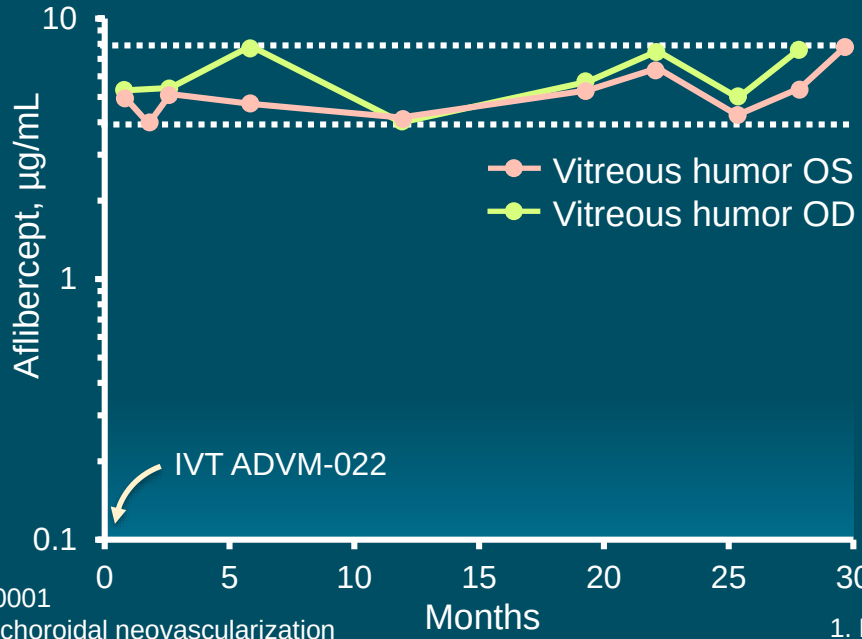
- Developed using directed evolution to:
  - Enable efficient intravitreal delivery
  - Increase transduction of retinal cells
  - Increase protein expression

ITR, inverted terminal repeat

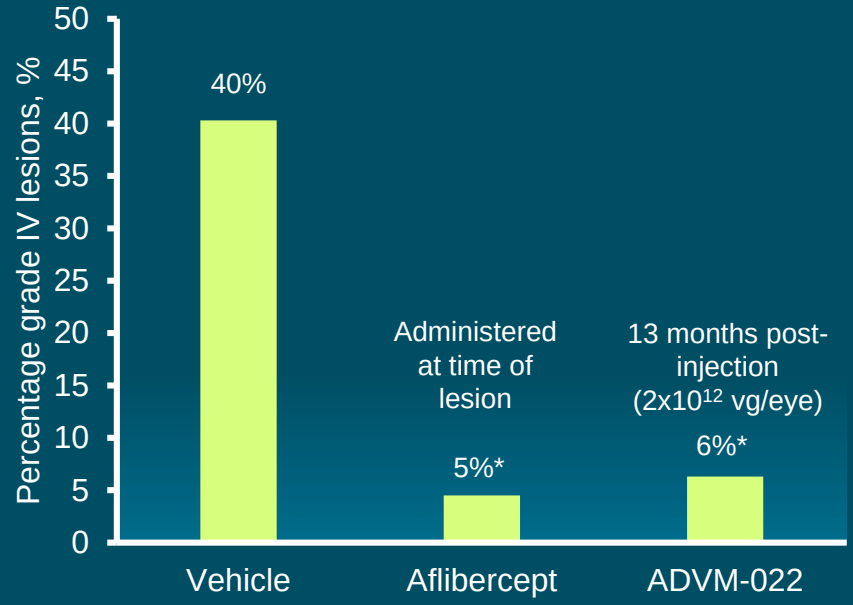
Grishanin, R. et al. Mol. Ther. 2019;27:118–29

Preclinical data demonstrates the potential for long-term efficacy with a single intravitreal injection of ADVM-022

Sustained aflibercept protein expression at pharmacologically relevant levels through 30 months[1]



ADVM-022 given 13 months prior to laser CNV is as effective as aflibercept at the time of laser[2]

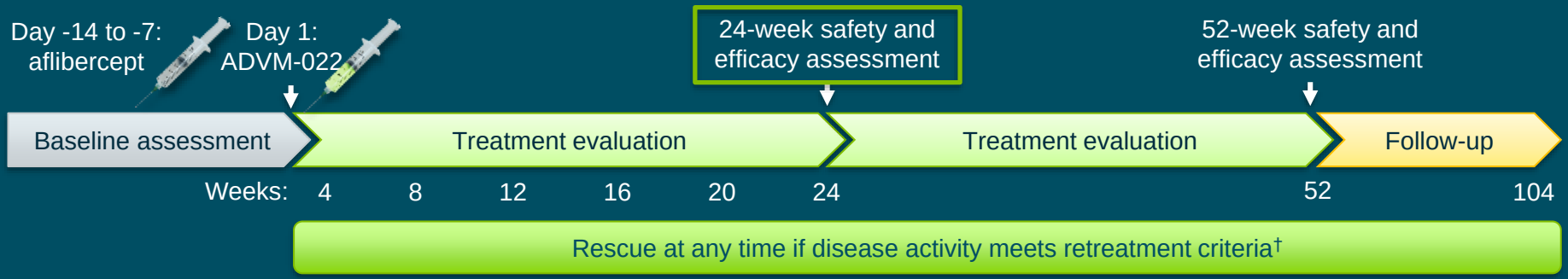


*p<0.0001
CNV, choroidal neovascularization
IVT, intravitreal therapy OD, right eye; OS, left eye

1. Kiss, S. Ann Meeting of the Am. Soc. Gene Cell Ther.; May 2019; Washington, DC
2. Grishanin, R. et al. Mol. Ther. 2019;27:118–29

OPTIC: Phase 1, Two-year multicenter study of ADVM-022 in neovascular AMD

- Primary objective
  - Assess the safety and tolerability of a single IVT injection of ADVM-022
- Secondary objectives
  - Evaluate the effect of ADVM-022 on vision (BCVA)
  - Evaluate the effect of ADVM-022 on anatomy (SD-OCT)
  - Assess the need for rescue therapy



†Patients receive rescue aflibercept (2mg IVT) if **any** of the following criteria are met: 1. Loss of ≥10 letters in BCVA from baseline due to intraretinal or subretinal fluid observed by SD-OCT; 2. Increase in central subfield thickness >75µm from baseline as assessed by SD-OCT; 3. Presence of vision-threatening hemorrhage due to macular degeneration

NCT03748784

Baseline patient characteristics

Characteristic	Value
Mean age, years	79
Mean time since nAMD diagnosis, years	3.3
Mean number anti-VEGF injections since initial diagnosis (range)	35.3 (7–109)
Mean number anti-VEGF injections in 8 months prior to screening	6.2
Average annualized injection frequency	9.3
Mean BCVA study eye, mean ETDRS letters Approximate Snellen equivalent	65.8 20/50
Mean CST study eye, mean µm	369

Cohort of subjects requiring frequent injections to maintain vision

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

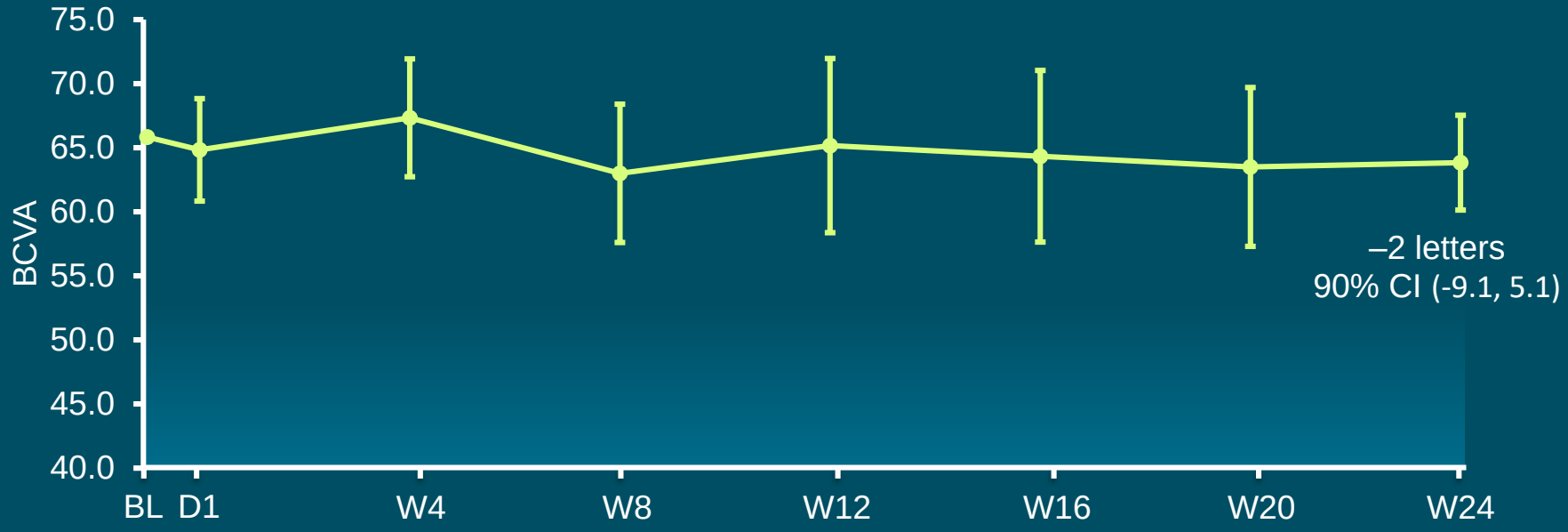
Primary endpoint: Cohort 1 safety results through Week 24

- No serious adverse events (SAEs)
- No adverse events (AEs) met criteria for dose-limiting toxicity (DLT)
- No drug-related non-ocular adverse events

- 19 ocular AEs potentially related to ADVM-022:
  - Inflammation observed in all patients
  - 14 Mild* AEs
  - 5 Moderate* AEs
    - Anterior chamber cells x2
    - Intermediate uveitis x2
    - Vitreous cells

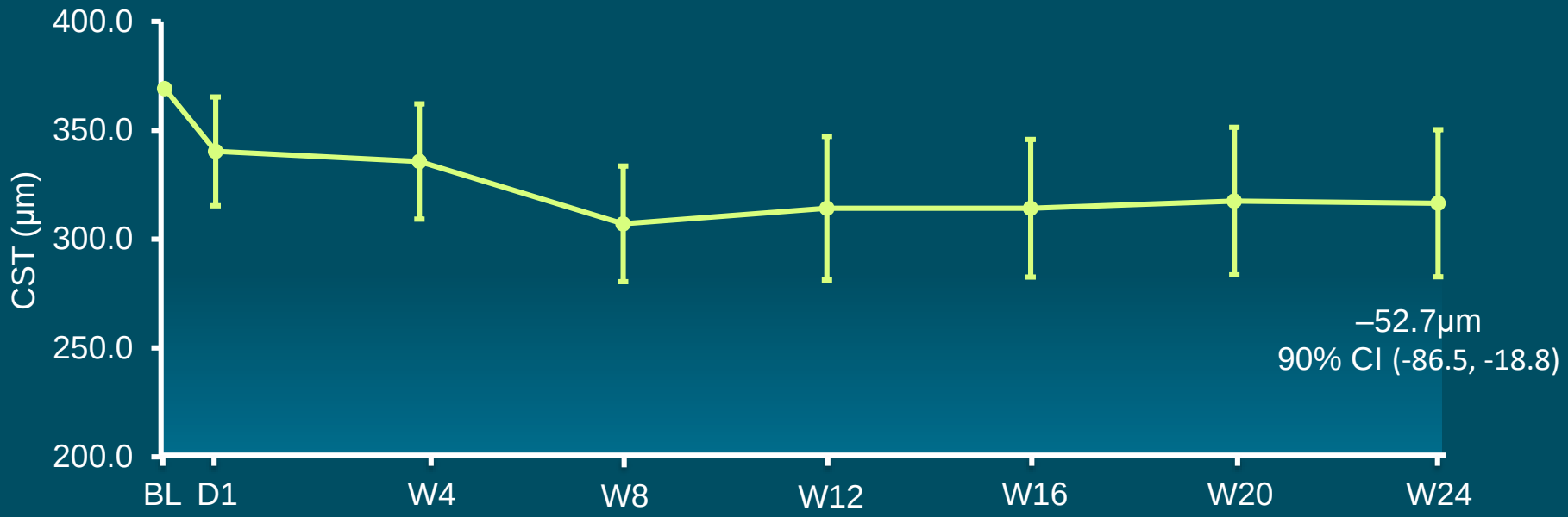
*CTCAE v5.0 AE severity grading system, general guidelines

Mean change in BCVA of six subjects in Cohort 1 through Week 24



BCVA, best corrected visual acuity; BL, baseline; D, day; W, week
Day 1 visit is 7–15 days after baseline visit

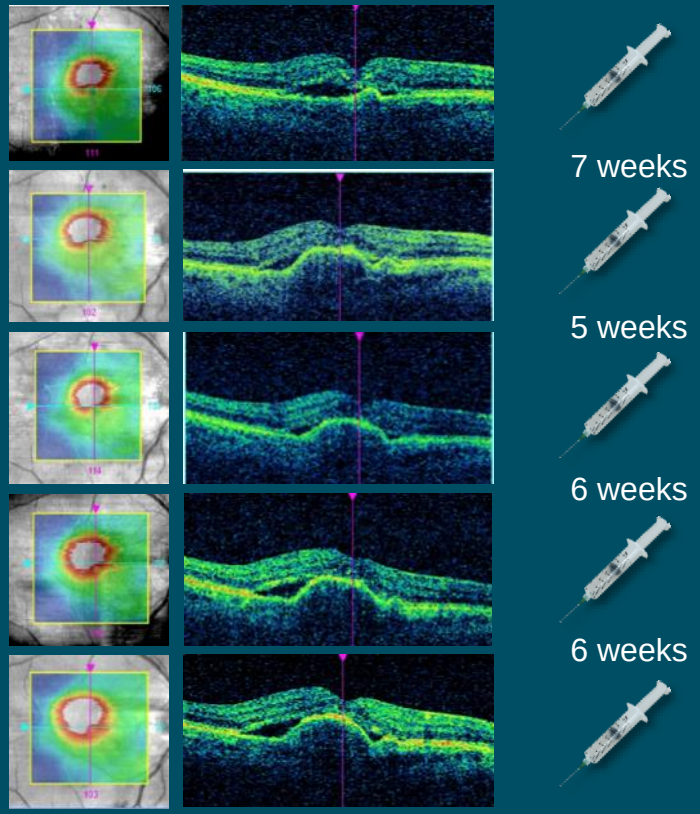
Mean change in CST of six subjects in Cohort 1 through Week 24



CST, central subfield thickness; BL, baseline; D, day; W, week
Day 1 visit is 7–15 days after baseline visit

Subject 1 – Prior nAMD treatment experience

76 year old male	
Previous IVT, n	18
IVT in last 8 months, n	5



Optical coherence tomography (OCT) scans and treatment intervals from most recent 5 anti-VEGF injections visits prior to OPTIC

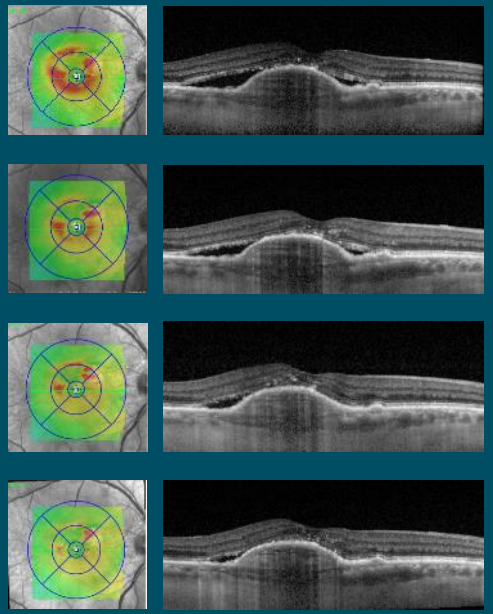
Subject 1 – OCT images in OPTIC by visit

Aflibercept IVT

Day 1: ADVM-022

Week 4

Week 8

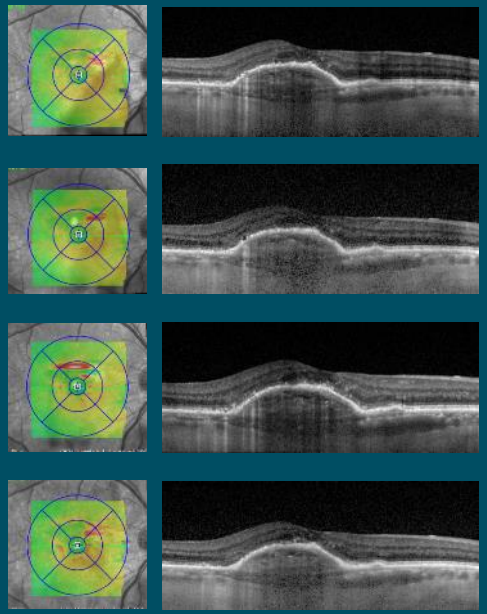


Week 12

Week 16

Week 20

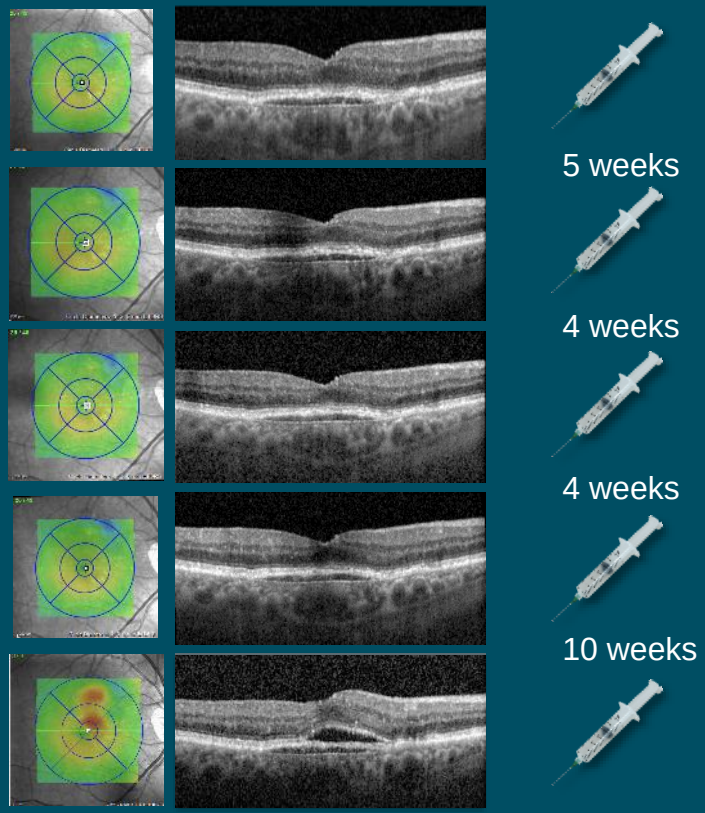
Week 24



No rescue injection received over 24 weeks

Subject 2 – Prior nAMD treatment experience

83 year old male	
Previous IVT, n	9
IVT in last 8 months, n	6



OCT scans and treatment intervals from most recent 5 anti-VEGF injections visits prior to OPTIC

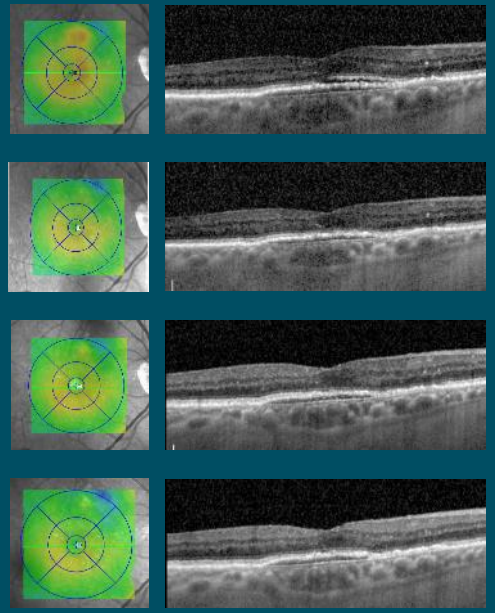
Subject 2 – OCT images in OPTIC by visit

Aflibercept IVT

Day 1: ADVM-022

Week 4

Week 8

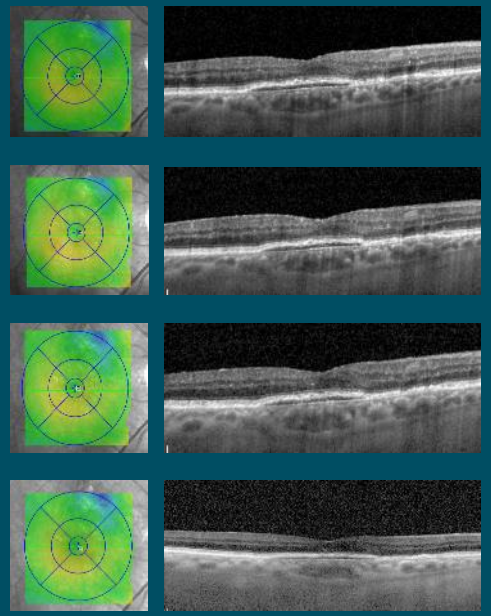


Week 12

Week 16

Week 20

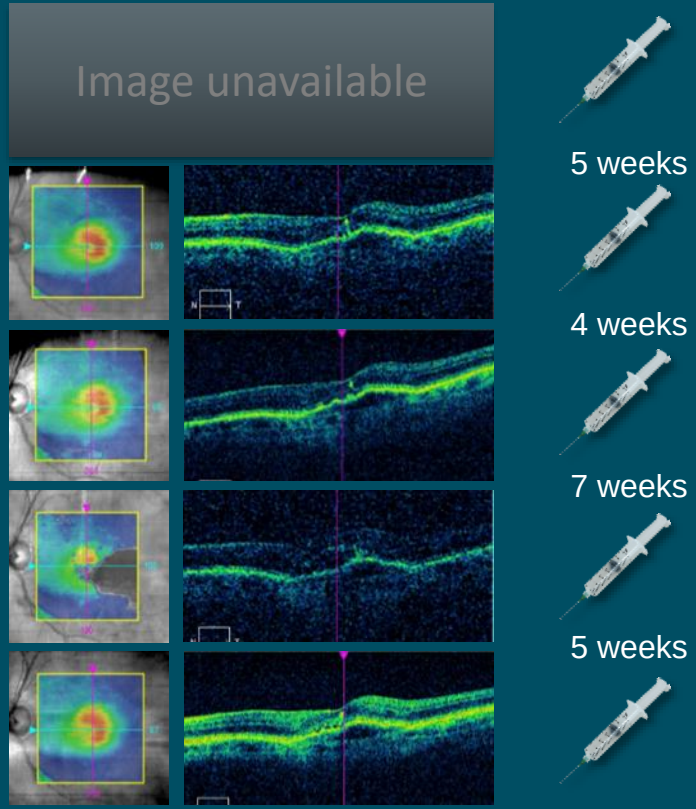
Week 24



No rescue injection received over 24 weeks

Subject 3 – Prior nAMD treatment experience

87 year old male	
Previous IVT, n	29
IVT in last 8 months, n	6



Available OCT scans and treatment intervals from most recent 5 anti-VEGF injections visits prior to OPTIC

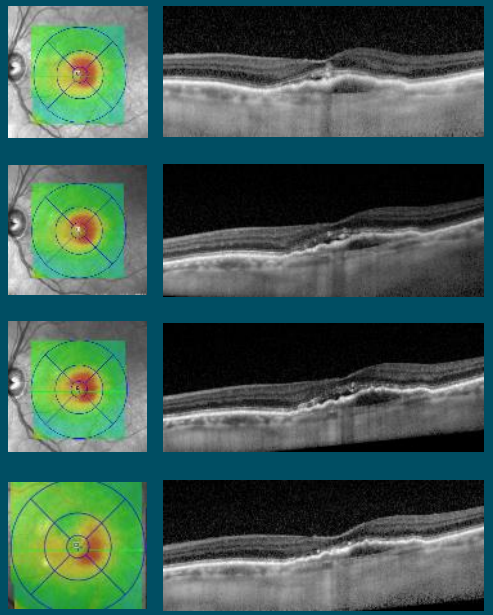
Subject 3 – OCT images in OPTIC by visit

Aflibercept IVT

Day 1: ADVM-022

Week 4

Week 8

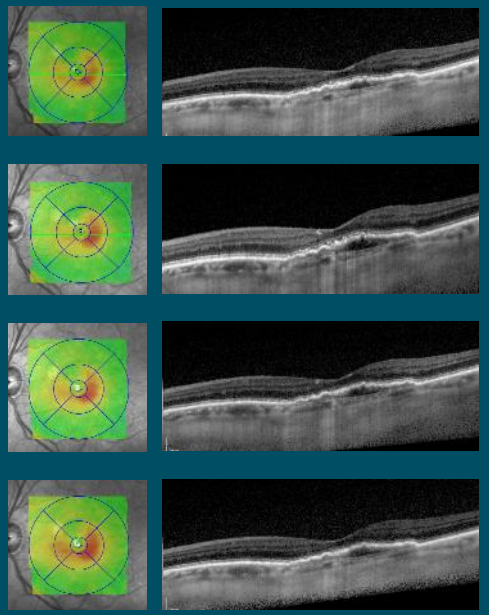


Week 12

Week 16

Week 20

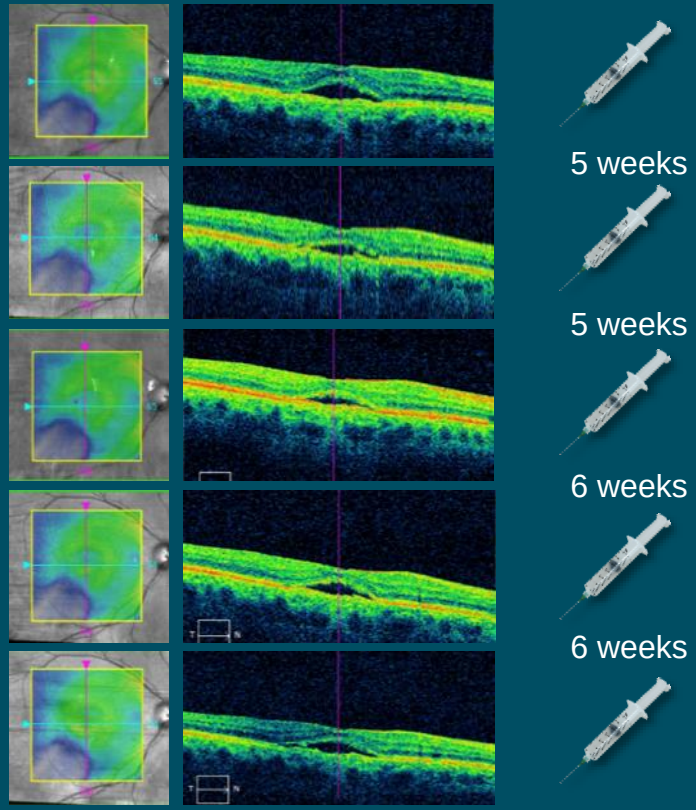
Week 24



No rescue injection received over 24 weeks

Subject 4 – Prior nAMD treatment experience

62 year old male	
Previous IVT, n	109
IVT in last 8 months, n	6



OCT scans and treatment intervals from most recent 5 anti-VEGF injections visits prior to OPTIC

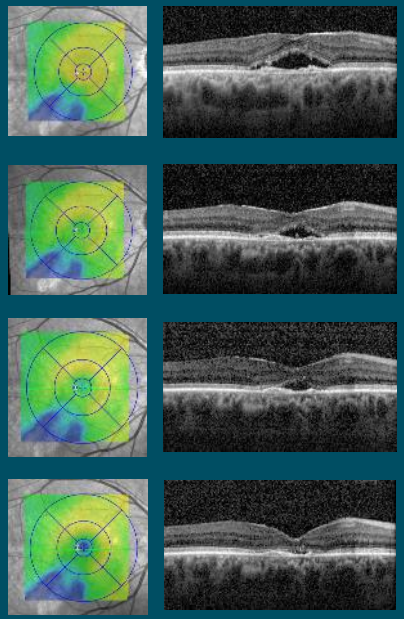
Subject 4 – OCT images in OPTIC by visit

Aflibercept IVT

Day 1: ADVM-022

Week 4

Week 8

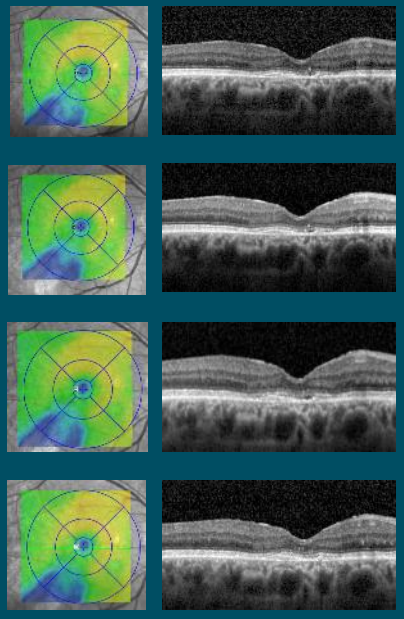


Week 12

Week 16

Week 20

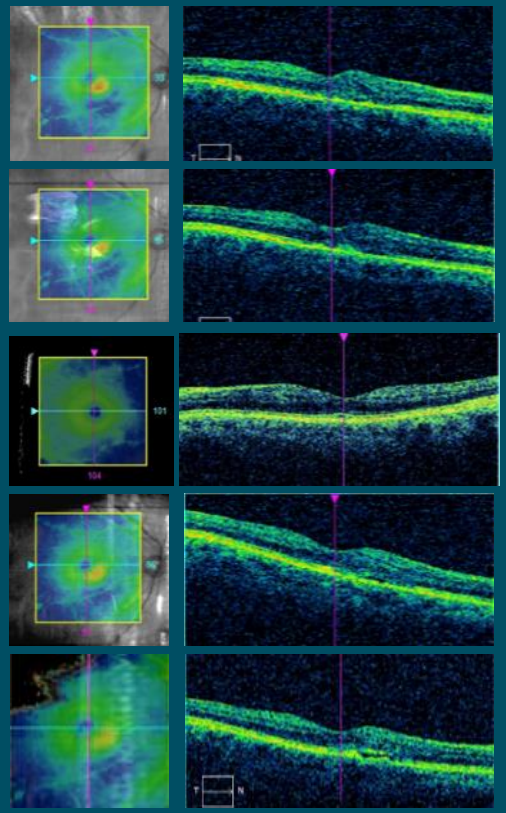
Week 24



No rescue injection received over 24 weeks

Subject 5 – Prior nAMD treatment experience

88 year old male	
Previous IVT, n	7
IVT in last 8 months, n	6



5 weeks

5 weeks

6 weeks

7 weeks

OCT scans and treatment intervals from most recent 5 anti-VEGF injections visits prior to OPTIC

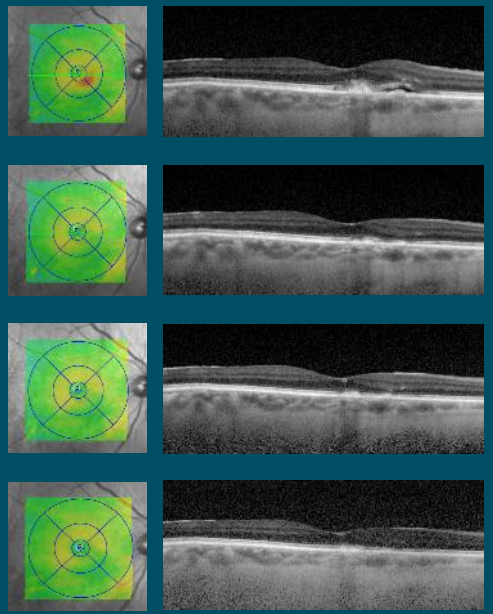
Subject 5 – OCT images in OPTIC by visit

Aflibercept IVT

Day 1: ADVM-022

Week 4

Week 8

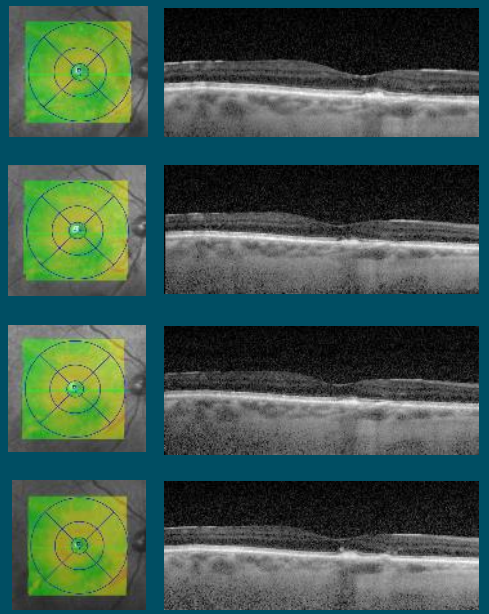


Week 12

Week 16

Week 20

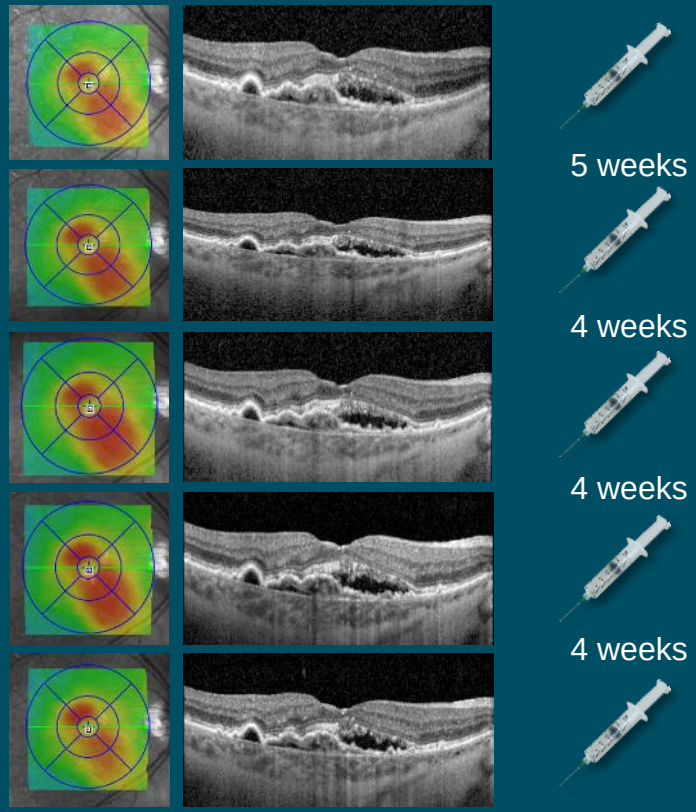
Week 24



No rescue injection received over 24 weeks

Subject 6 – Prior nAMD treatment experience

77 year old female	
Previous IVT, n	8
IVT in last 8 months, n	8



OCT scans and treatment intervals from most recent 5 anti-VEGF injections visits prior to OPTIC

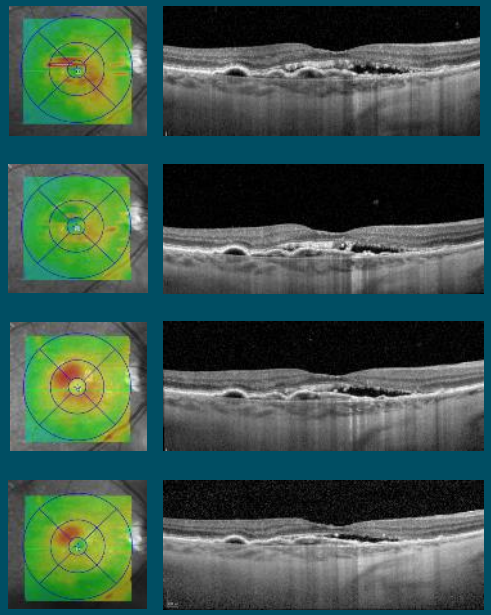
Subject 6 – OCT images in OPTIC by visit

Aflibercept IVT

Day 1: ADVM-022

Week 4

Week 8

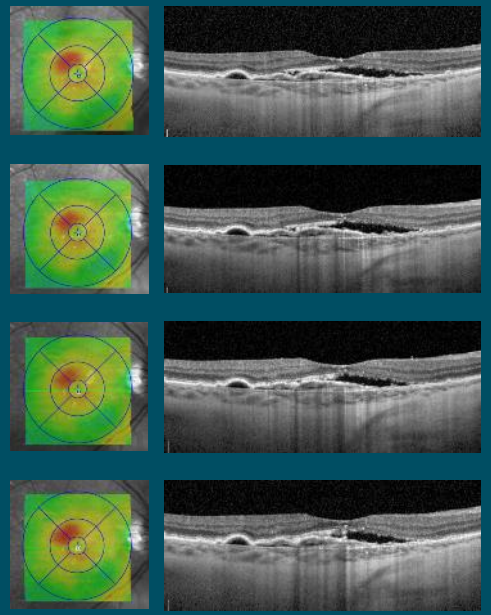


Week 12

Week 16

Week 20

Week 24



No rescue injection received over 24 weeks

OPTIC Cohort 1: 24-week conclusions

- Zero rescue injections required for any subject
- Consistent and sustained anatomical improvements on OCT
- BCVA stability maintained
- ADVM-022 was safe and well tolerated

ADVM-022 offers transformative potential to greatly reduce treatment burden and improve retinal anatomy with a single intravitreal injection in nAMD

BCVA, best-corrected visual acuity; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography

ADVM-022 Outlook

- Thank you to investigators, study teams and participants
  - CA, CO, NV, PA, TX, TN
- Cohort 2 has completed enrollment
- Cohort 1 52-week data H1 2020
- Cohort 2 24-week data H1 2020
- IND in Diabetic Retinopathy planned for submission H1 2020