Association Between Central Subfield Thickness Fluctuation and Visual Acuity Outcomes in Patients with Neovascular Age - Related Macular Degeneration: A Retrospective Analysis of the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight)

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Disclosures

Presenter Disclosures

- *Consulting Fees:* 4DMT, Astellas, Apellis, AbbVie, Boehringer Ingelheim, Bausch and Lomb, EyePoint, Genentech, Ocular Therapeutix, ONL Therapeutics, Regeneron, Verana Health
- *Speaker:* Astellas, Genentech

Study Disclosures

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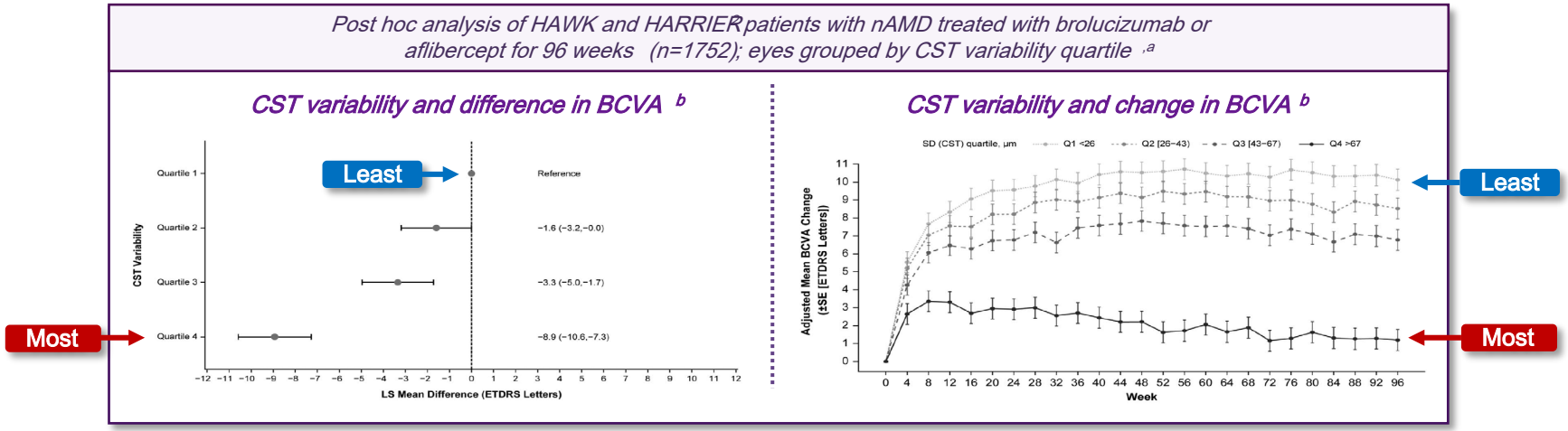
CST Fluctuations May Impact Visual Outcomes in Patients with nAMD

- In post hoc clinical trial analyses, fluid instability has been linked to worse long-term visual outcomes in patients with nAMD[1,2]
- Large-scale real-world evidence on the relationship between CST variability and visual outcomes is limited

Post hoc analysis of HAWK and HARRIER patients with nAMD treated with brolucizumab or aflibercept for 96 weeks (n=1752); eyes grouped by CST variability quartile [a]



Reproduced from Figures 1 and 2 from Dugel PU, et al. *Retina*. 2022; 1;42(3):511-5 [CC BY]. [a] Patients were categorized into quartiles (n=438 each) of increasing CST variability (Q1 [lowest] to Q4 [highest]). The quartiles ranged from minimal variability in CST post-loading phase in Q1 to marked variability in CST post-loading phase in Q4. [b] Association between CST variability and BCVA from baseline to Week 96 (pooled brolucizumab and aflibercept treatment arms). LS mean and SE estimates were calculated using a MMRM model with baseline BCVA, SD (CST) quartile, study, and age (<75, ≥75) as fixed effects. **1.** Evans RN, et al. *JAMA Ophthalmol*. 2020;138(10):1043-51. **2.** Dugel PU, et al. *Retina*. 2022; 1;42(3):511-5. **(BC)VA,** (best-corrected) visual acuity; **CST,** central subfield thickness; **ETDRS,** Early Treatment Diabetic Retinopathy Study; **LS,** least squares; **MMRM,** mixed model repeated measures; **nAMD,** neovascular age-related macular degeneration; **Q,** quartile; **VEGF,** vascular endothelial growth factor.

Study Population & Objectives

Retrospective cohort study of patients with nAMD using American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) data

Key Eligibility Criteria:

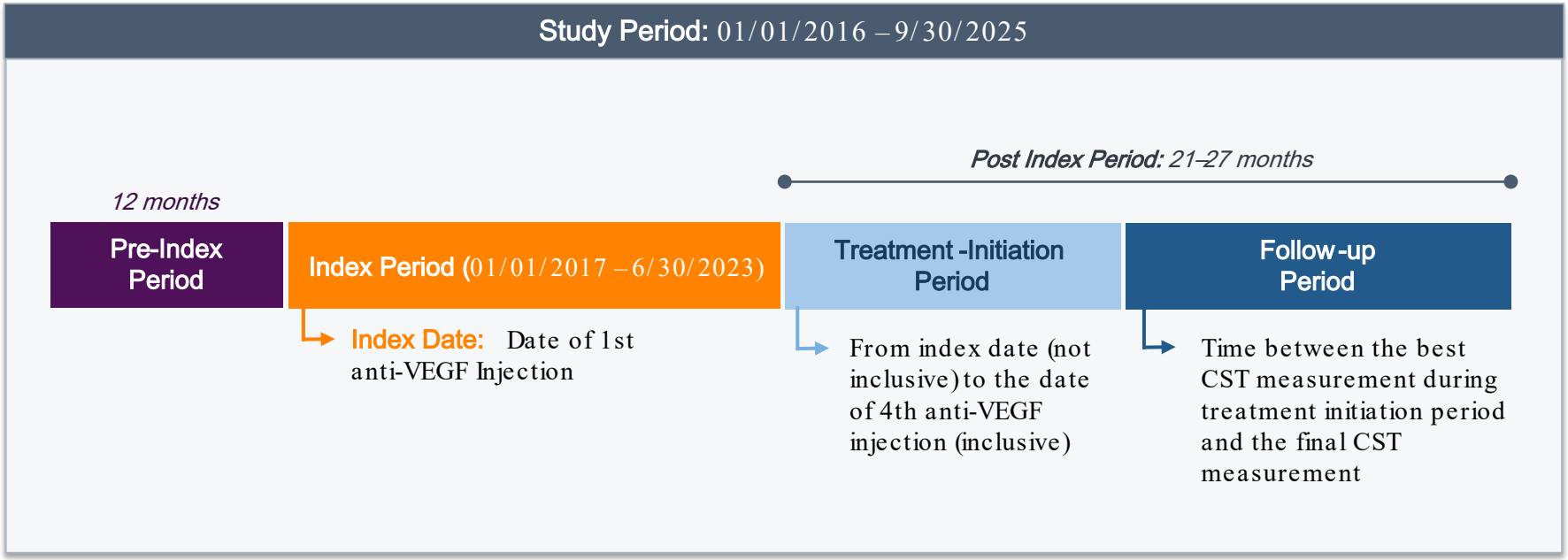
- Diagnosis of nAMD
- Initiation of anti-VEGF treatment between 01/01/2017—06/30/2023
- ≥4 anti-VEGF injections
- ≥6 CST measurements within 2 years of index date

Primary Study Objective	Secondary Study Objectives
• **Characterize CST variability and its association with VA outcomes** in treatment-naïve patients with nAMD initiating anti-VEGF therapy	• Assess anti-VEGF treatment patterns • Describe baseline demographics and clinical characteristics

CST, central subfield thickness; **IRIS,** Intelligent Research in Sight; **nAMD,** neovascular age-related macular degeneration; **VA,** visual acuity; **VEGF,** vascular endothelial growth factor.

Study Design

Retrospective cohort study of patients with nAMD using IRIS Registry data

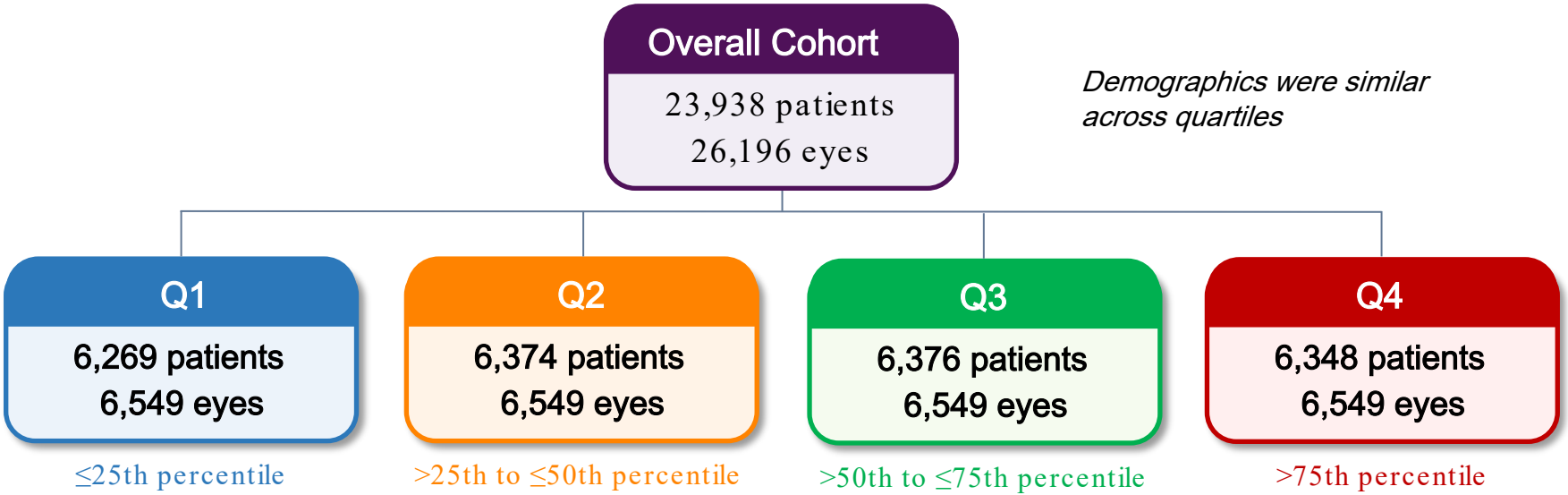


CST, central subfield thickness; **IRIS,** Intelligent Research in Sight; **nAMD,** neovascular age-related macular degeneration; **VEGF,** vascular endothelial growth factor.

Study Cohort Attrition

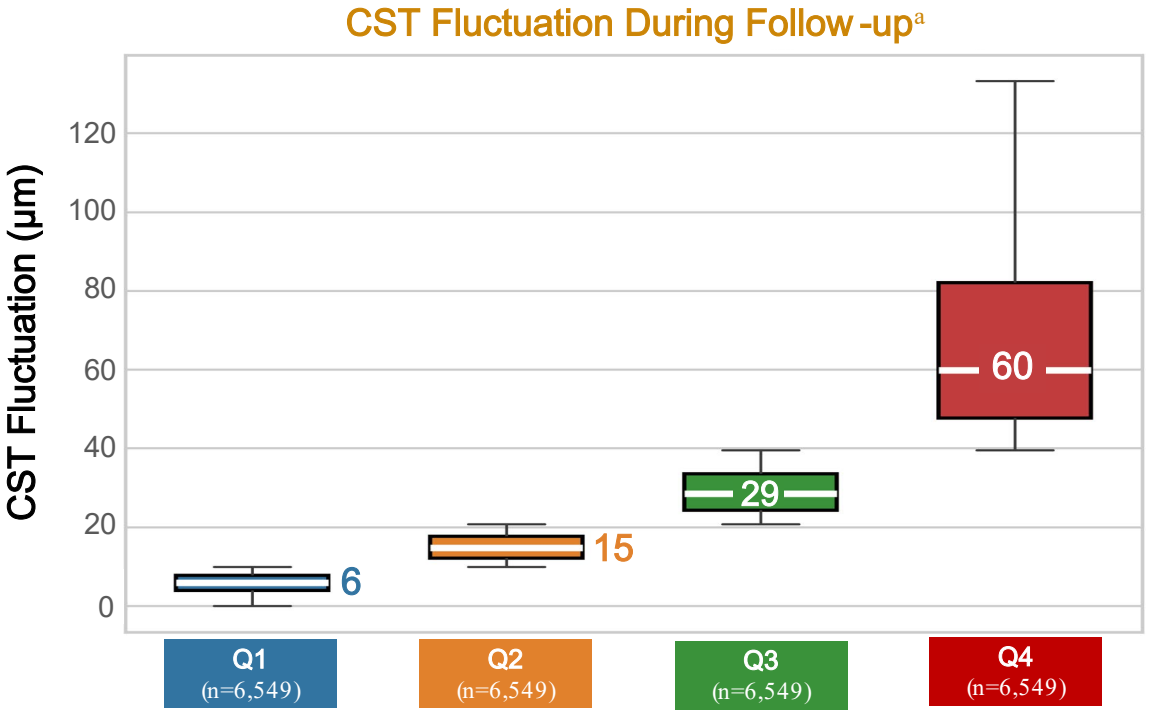
Patients were divided into CST fluctuation quartiles

- Defined by the standard deviation of all CST measurements from **best CST during the treatment initiation period** through **final CST measurement at 2 years post -index**



CST, central subfield thickness; **Q,** quartile.

CST Fluctuations Increased Across Quartiles

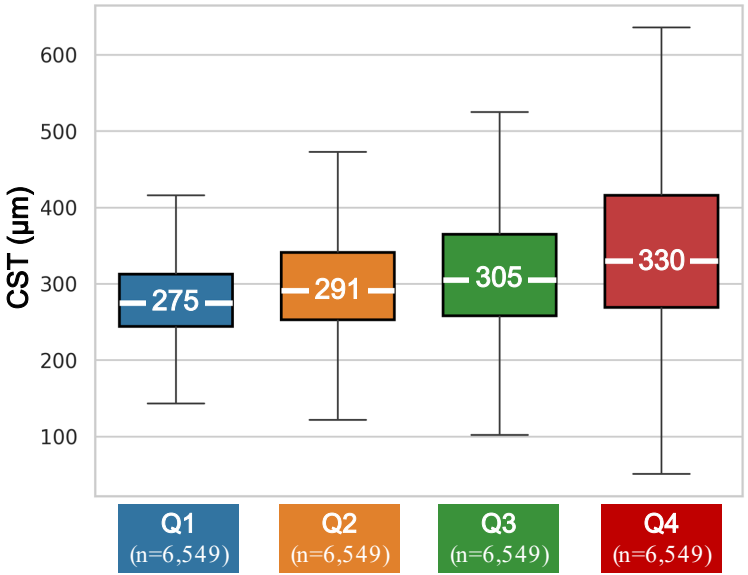


- CST fluctuation was defined by SD of all CST measurements taken during follow-up
- Median CST fluctuation ranged from 6 µm in Q1 to 60 µm in Q4

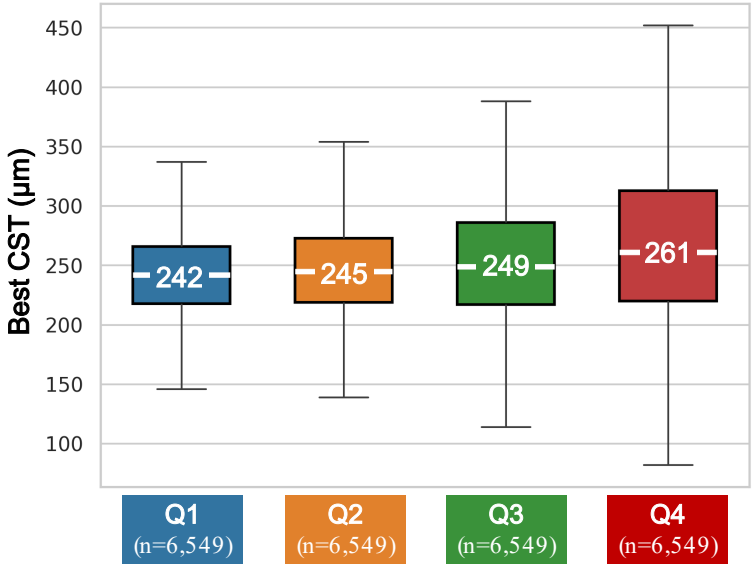
[a] Follow-up period is defined as the time between the best CST measurement during treatment initiation period and the final CST measurement.
CST, central subfield thickness; **Q,** quartile.

CST Variability Associated with Progressively Higher CST at Treatment Initiation

CST on Index Date[a]



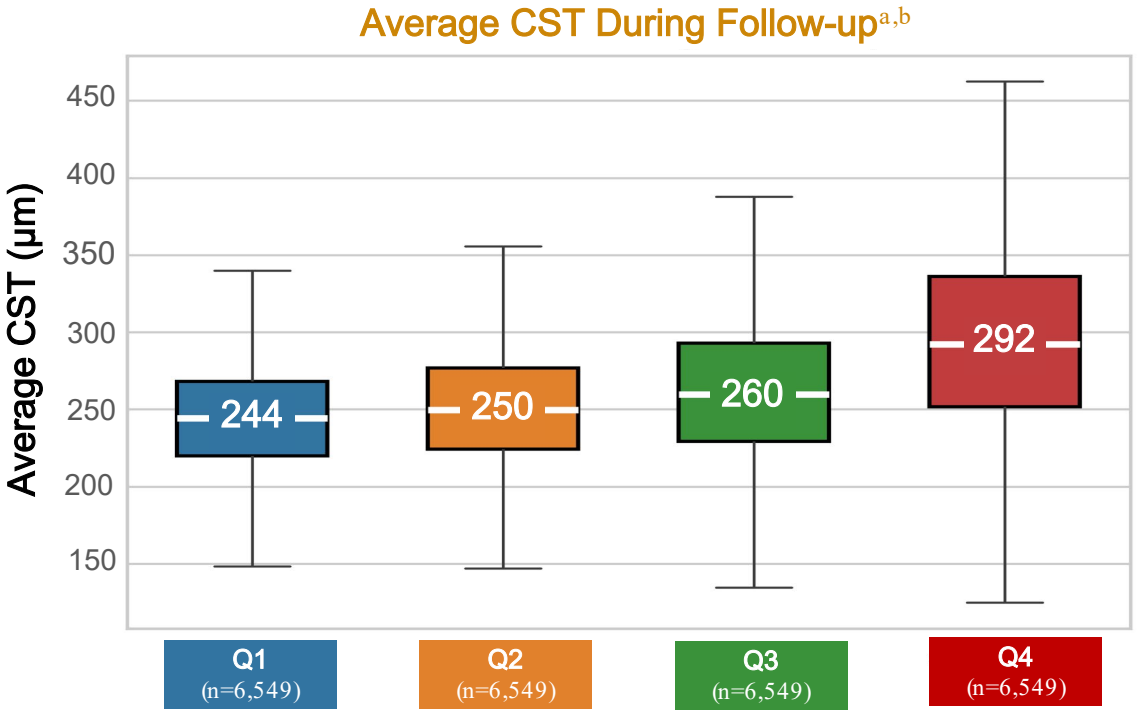
Best CST During Treatment Initiation Period[b]



CST was progressively higher across quartiles at index and during the treatment initiation period

[a] Index date is the date of the first anti-VEGF injection. [b] Treatment initiation period is defined by the index date (not inclusive) and the date of the 4th anti-VEGF injection (inclusive).
CST, central subfield thickness; **Q,** quartile; **VEGF,** vascular endothelial growth factor.

CST Variability Persists with Anti - VEGF Treatment

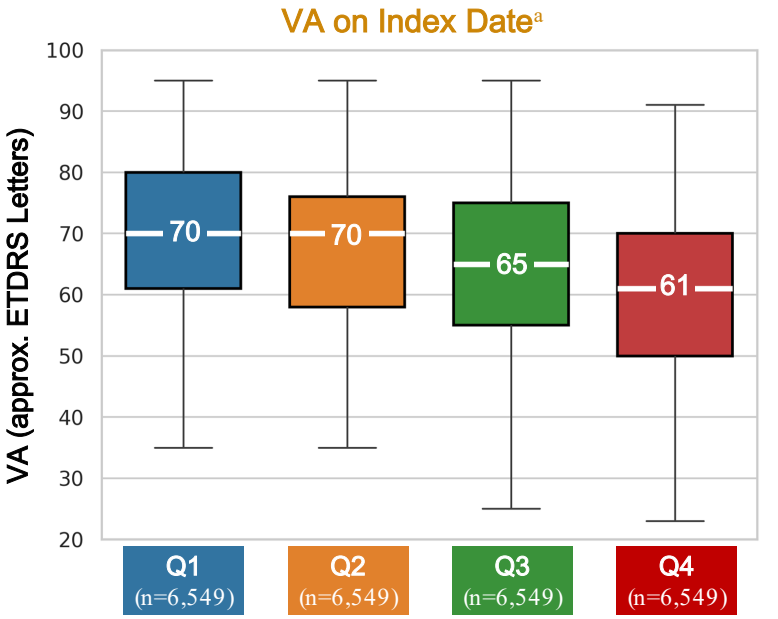


Eyes with greater CST variability maintained higher CST on average during follow-up

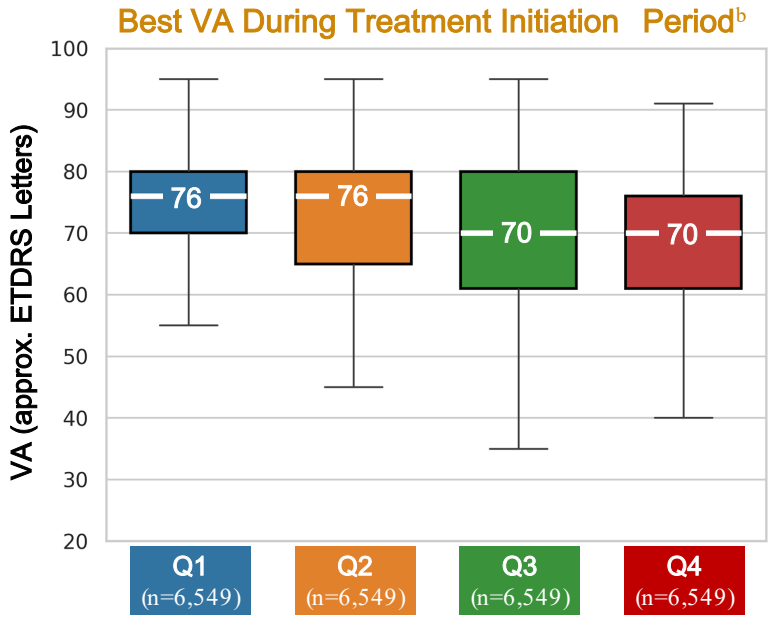
[a] Average CST is defined as the mean of all CST measurements (patient-eye level) during follow-up. [b] Follow-up period is defined as the time between the best CST measurement during treatment initiation period and the final CST measurement.

CST, central subfield thickness; **Q,** quartile; **VEGF,** vascular endothelial growth factor.

Despite Similar Early VA Gains, CST Variability Associated with Lower VA at Treatment Initiation



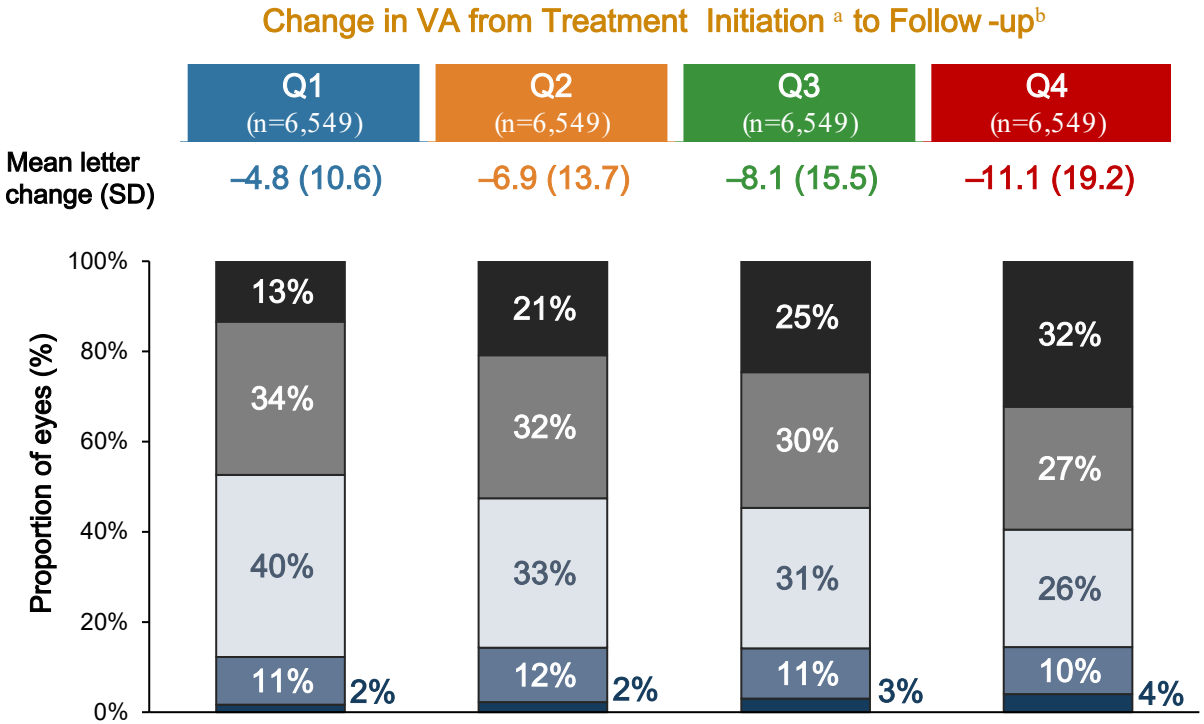
Median VA at index was higher among eyes with lower CST variability



Improvements in median VA ranging between 5–9 letters observed across quartiles

[a] Index date is the date of the first anti-VEGF injection. [b] Treatment initiation period is defined by the index date (not inclusive) and the date of the 4th anti-VEGF injection (inclusive).
CST, central subfield thickness; **Q,** quartile; **VA,** visual acuity; **VEGF,** vascular endothelial growth factor.

Greater CST Variability Associated with Greater VA Loss During Anti - VEGF Treatment

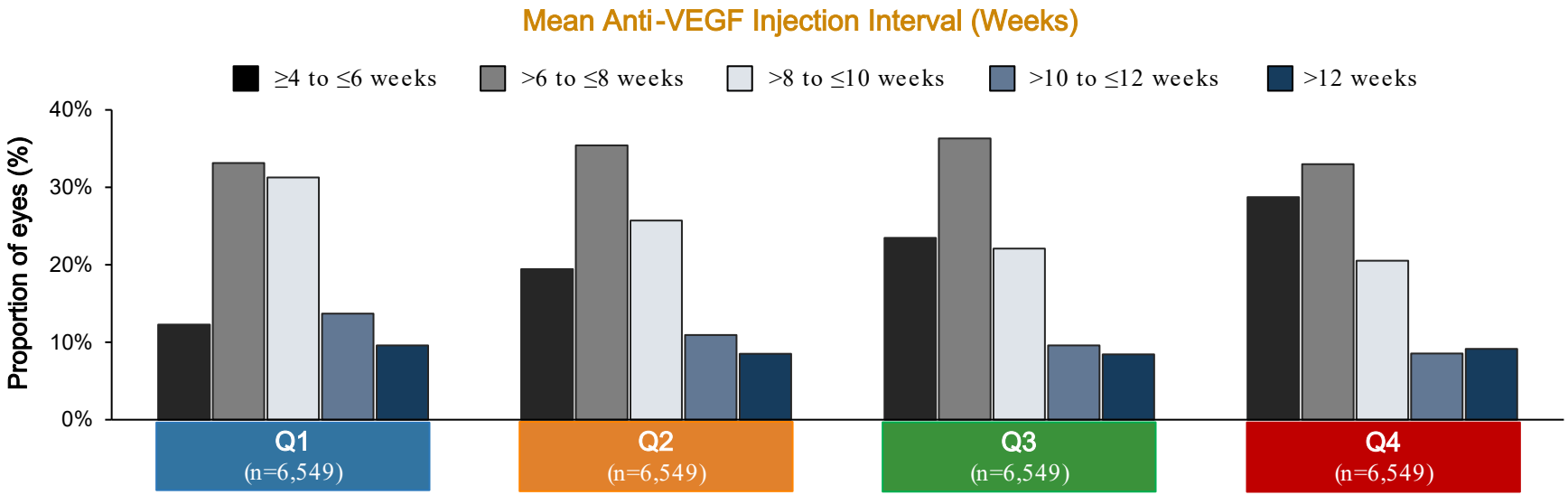


Eyes with greater CST variability experienced **greater mean letter loss** and had higher rates of significant VA loss of ⩾15 letters

- **Significant loss** (≥15 letters)
- **Mild loss** (5–<15 letters)
- **Stable** (<5-letter change)
- **Mild gain** (5–<15 letters)
- **Significant gain** (≥15 letters)

Change in VA from best VA during treatment initiation to VA nearest to last CST measurement. [a] Treatment initiation period is defined by the index date (not inclusive) and the date of the 4th anti-VEGF injection (inclusive). [b] Follow-up period is defined as the time between the best CST measurement during treatment initiation period and the final CST measurement.
CST, central subfield thickness; **Q,** quartile; **VA,** visual acuity; **VEGF,** vascular endothelial growth factor.

Treatment Patterns were Relatively Similar Across Quartiles



Results suggest that greater VA decline in Q4 was not driven by the number of anti-VEGF injections

There were almost no eyes with mean injection interval <4 weeks (0.04–0.09% across quartiles). [a] The number of injections received between index date and visit with VA measurement closest to the date of the final CST measurement from a visit at 2 years ± 3 months. [b] Injection treatment intervals computed up to the date of the final CST measurement from a visit at 2 years ± 3 months.
CST, central subfield thickness; **Q,** quartile; **VA,** visual acuity; **VEGF,** vascular endothelial growth factor.

Conclusions

Greater CST fluctuation was associated with greater VA decline in nAMD

In this study:

- CST variability persisted despite anti-VEGF treatment, with clinically meaningful fluctuation >50 µm[1] in Q4
- Eyes with greater CST variability experienced greater VA decline during treatment, despite Q4 having worse vision at initiation

Key Data Summary	Q1	Q4
Median CST fluctuation (µm)[a]	6	60
Mean VA change (letters)[b]	–4.8	–11.1
Mean injection interval (weeks)[c]	8.8	8.0
Mean number of injections[d]	15.9	18.3

There remains an unmet need for more durable therapies that minimize CST fluctuations and improve long - term visual outcomes in patients with nAMD

1. Sheth VS, et al. *Ophthalmol Retina*. 2025;9(4):330-342. [a] Fluctuation in CST is defined by SD of all CST measurements taken during follow-up (the time between the best CST measurement during treatment initiation period and the final CST measurement). [b] Change in VA from best VA during treatment initiation to VA nearest to last CST measurement. [c] Injection treatment intervals computed up to the date of the final CST measurement from a visit at 2 years ± 3 months. [d] The number of injections received between index date and visit with VA measurement closest to the date of the final CST measurement from a visit at 2 years ± 3 months. **CST**, central subfield thickness; **nAMD**, neovascular age-related macular degeneration; **Q**, quartile; **VA**, visual acuity; **VEGF**, vascular endothelial growth factor.