Interrelationships Between Macular Neovascularization Lesion Type, Retinal Fluid Location, and Visual Outcomes in the HARBOR Trial

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Disclosures

Financial Disclosures

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Study Disclosures

- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
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Key Takeaways

- This post hoc analysis of HARBOR represents the first application of CONAN Study Group criteria to a major nAMD dataset
- We aimed to evaluate the relationship between baseline MNV lesion type, retinal fluid location, and vision outcomes among eyes receiving ranibizumab therapy for nAMD
- Vision outcomes over 24 months were associated with MNV lesion type at baseline, and the location/presence of retinal fluid over time
- Anatomic classification of MNV lesion type and a nuanced assessment of retinal fluid should be considered in the management of nAMD

CONAN, Consensus on Neovascular Age-Related Macular Degeneration Nomenclature; MNV, macular neovascularization; nAMD, neovascular age-related macular degeneration.

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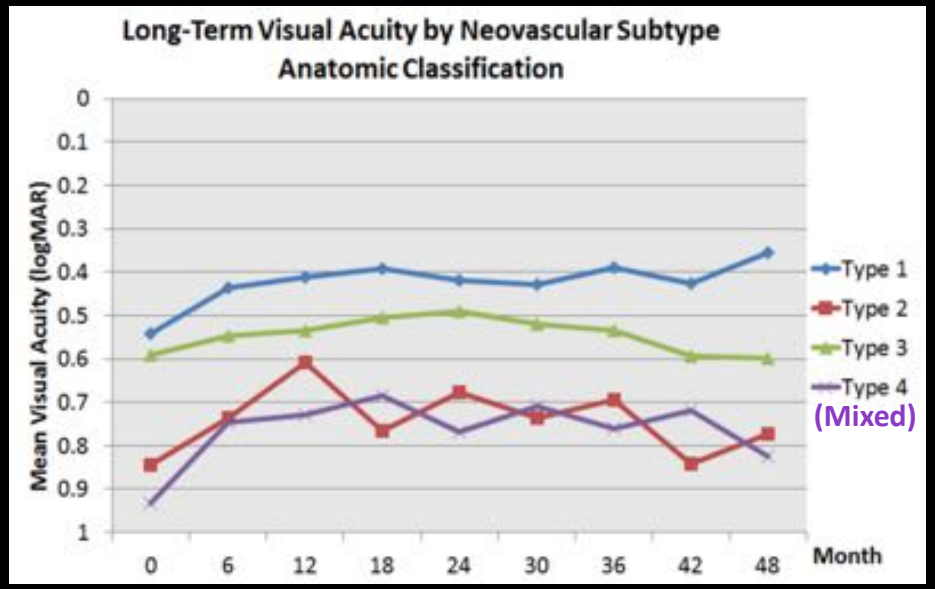
Editorial

Do We Need a New Classification for Choroidal Neovascularization in Age-Related Macular Degeneration?

RETINA
30(9):1333-49.

- In 2010, we proposed a classification for macular neovascularization (MNV) based on anatomic localization ascertained by multimodal imaging
- In 2015, we reported *"Long-term Visual Outcomes for a Treat-and-Extend Anti-VEGF Regimen in Eyes With nAMD"*[1]

- 210 treatment-naïve eyes
- Mean follow-up of 3.5 years
- Anatomic classification was an independent predictor of visual acuity at 6 months and years 1, 2, 3, and 4
- Eyes with Type 1 MNV lesions had better visual outcomes



From Mrejen S et al, 2015.[1]

1. Mrejen S et al. *J Clin Med*. 2015;4(7):1380-1402.

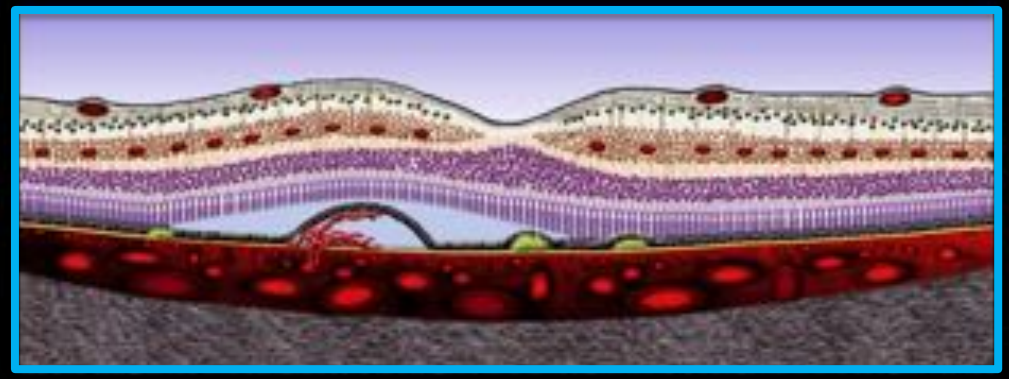
logMAR, logarithm of the minimum angle of resolution; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

CONAN Study Group Definitions

AMERICAN ACADEMY OF OPHTHALMOLOGY
Consensus Nomenclature for Reporting Neovascular Age-Related Macular Degeneration Data
Consensus on Neovascular Age-Related Macular Degeneration Nomenclature Study Group

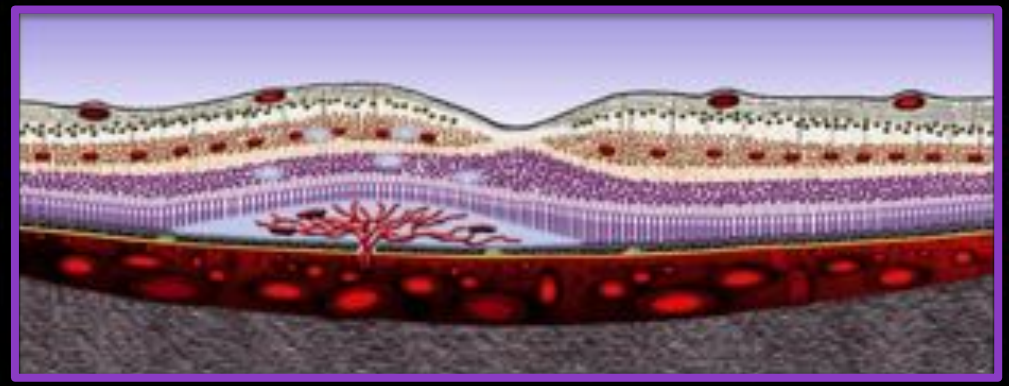
Type 1 MNV

Neovascularization located between the RPE and Bruch's membrane



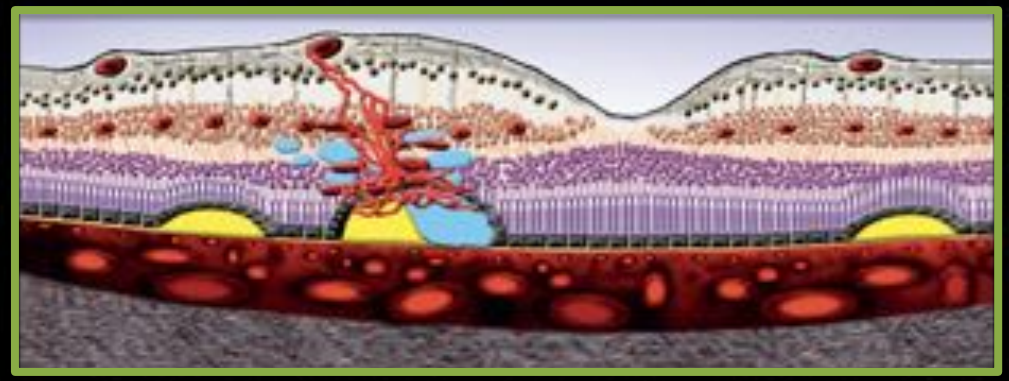
Type 2 MNV

Neovascularization in the subretinal space above the RPE



Type 3 MNV

Intraretinal neovascularization originating from the deep vascular complex



Spaide RF et al. *Ophthalmology*. 2020;127(5):616-636.

CONAN, Consensus on Neovascular Age-Related Macular Degeneration Nomenclature; MNV, macular neovascularization; RPE, retinal pigment epithelium.

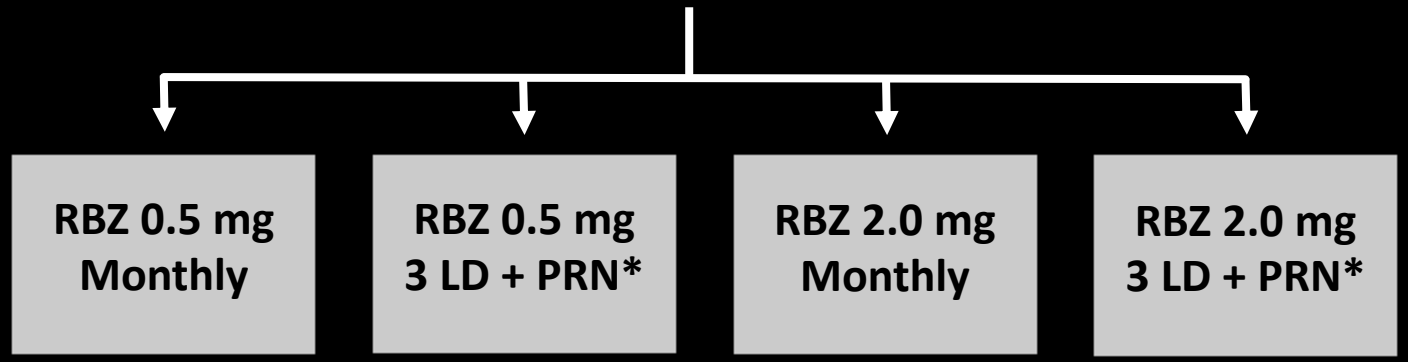
Objective

To evaluate the relationship between baseline MNV lesion type, retinal fluid location, and vision outcomes among eyes receiving ranibizumab for nAMD in HARBOR

MNV, macular neovascularization; nAMD, neovascular age-related macular degeneration.

HARBOR Compared Monthly and PRN Ranibizumab Therapy for nAMD Over 24 Months

Treatment-naïve patients with nAMD and active subfoveal MNV (N = 1097)



Current Analysis (n = 700)

Post hoc analysis of pooled data from study eyes with:

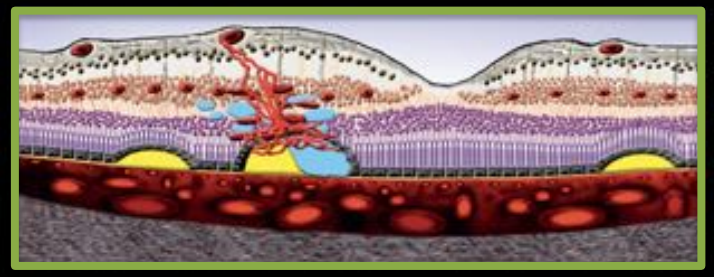
- Multimodal assessment of baseline MNV (SD-OCT, FA, CFP)
- Retinal fluid (SRF and/or IRF) at baseline, screening, or week 1
- SD-OCT follow-up over 24 months

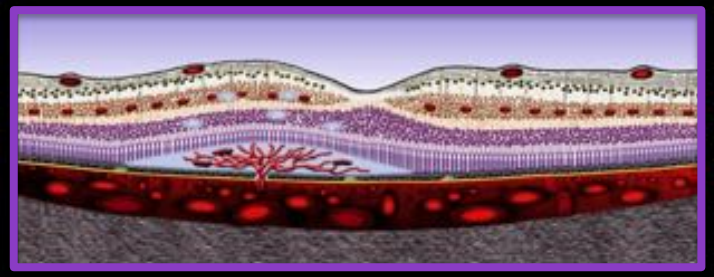
Outcomes of Interest:

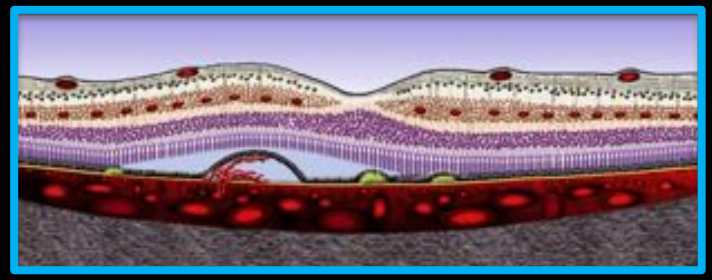
1. Baseline MNV lesion type
   - Classified using CONAN Study Group criteria[1]
     - Type 1
     - Type 2/Mixed Type 1 and 2 (Type 2/M)
     - Any Type 3
2. SRF and/or IRF over 24 months
   - Identified by SD-OCT
   - Location (central/noncentral) classified using a modified ETDRS grid
3. BCVA outcomes over 24 months
   - Assessed using standard ETDRS protocols

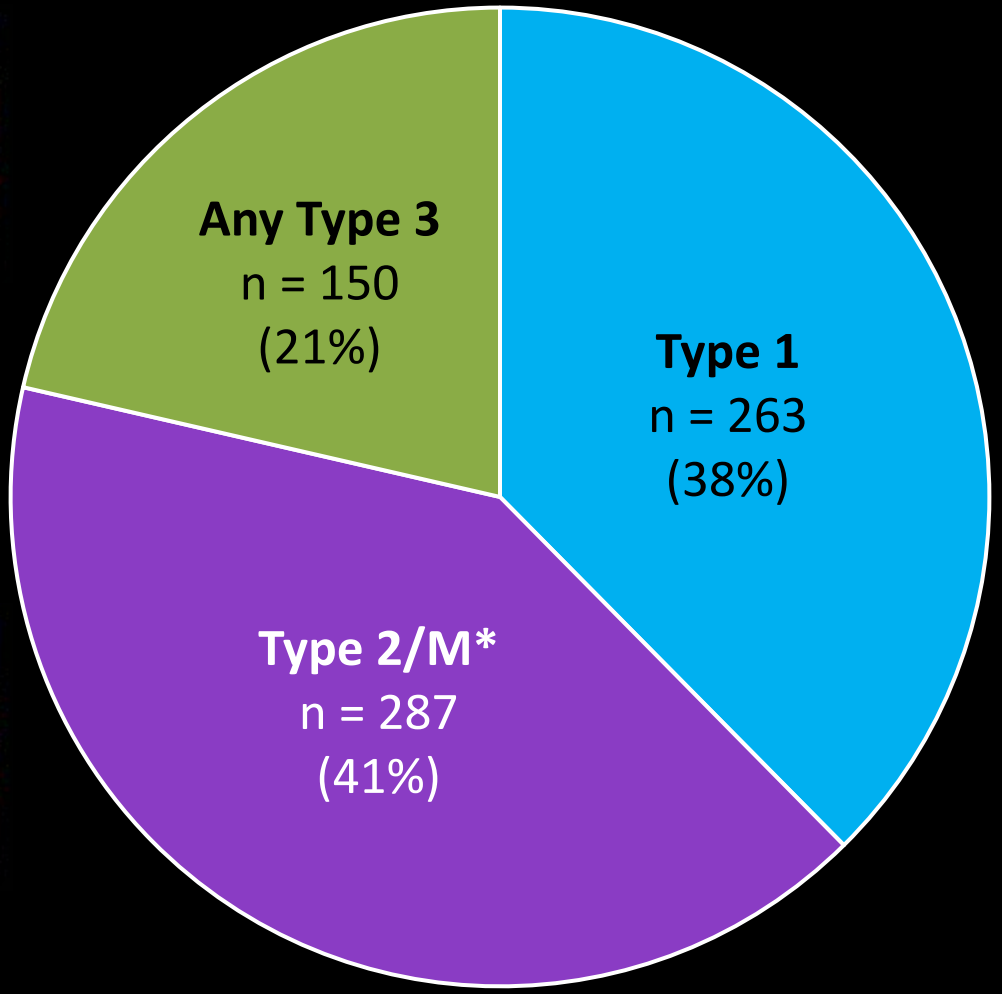
NCT00891735. *Re-treatment criteria for PRN arms: ≥ 5-letter decrease in BCVA from previous visit, or any evidence of disease activity on SD-OCT (SRF, IRF, or subretinal pigment epiretinal fluid). 1. Spaide RF et al. *Ophthalmology*. 2020;127(5):616-636. BCVA, best-corrected visual acuity; CFP, color fundus photography; CONAN, Consensus on Neovascular Age-Related Macular Degeneration Nomenclature; ETDRS, Early Treatment Diabetic Retinopathy Study; FA, fluorescein angiography; IRF, intraretinal fluid; LD, loading dose; MNV, macular neovascularization; nAMD, neovascular age-related macular degeneration; PRN, as-needed; RBZ, ranibizumab; SD-OCT, spectral-domain optical coherence tomography; SRF, subretinal fluid.

Distribution of Lesion Types at Baseline







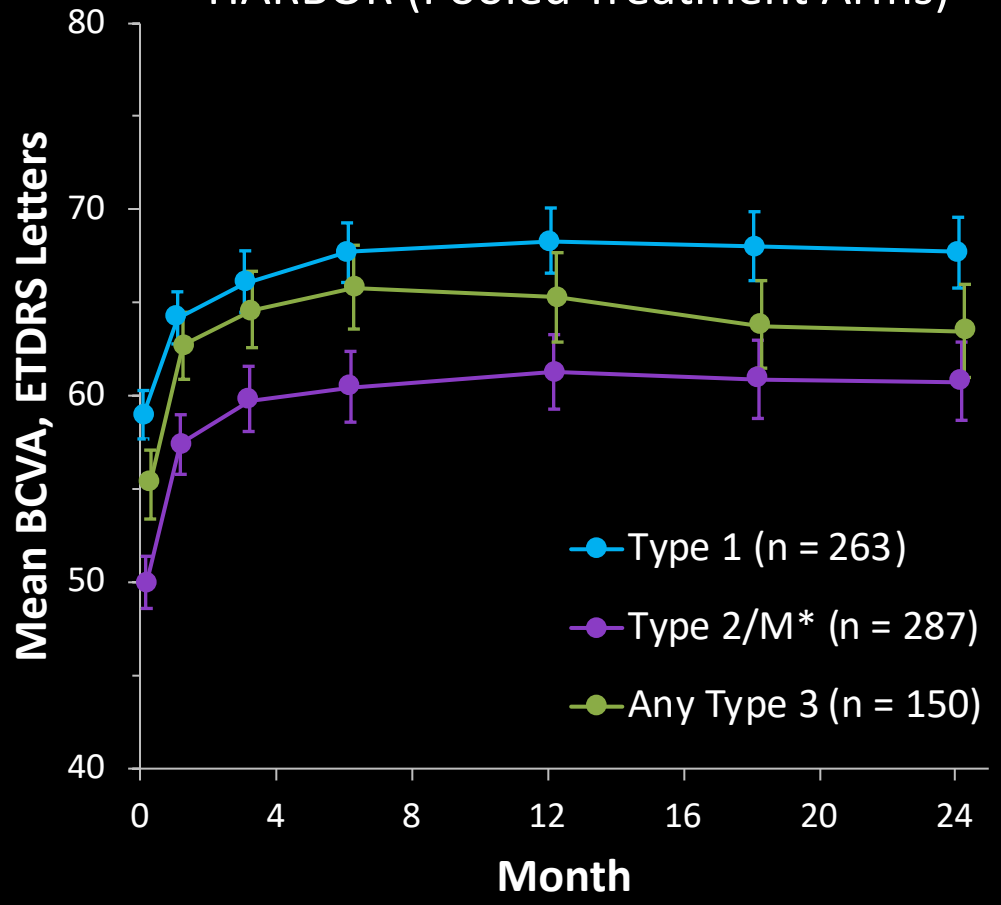


*Type 2/Mixed Type 1 and 2.

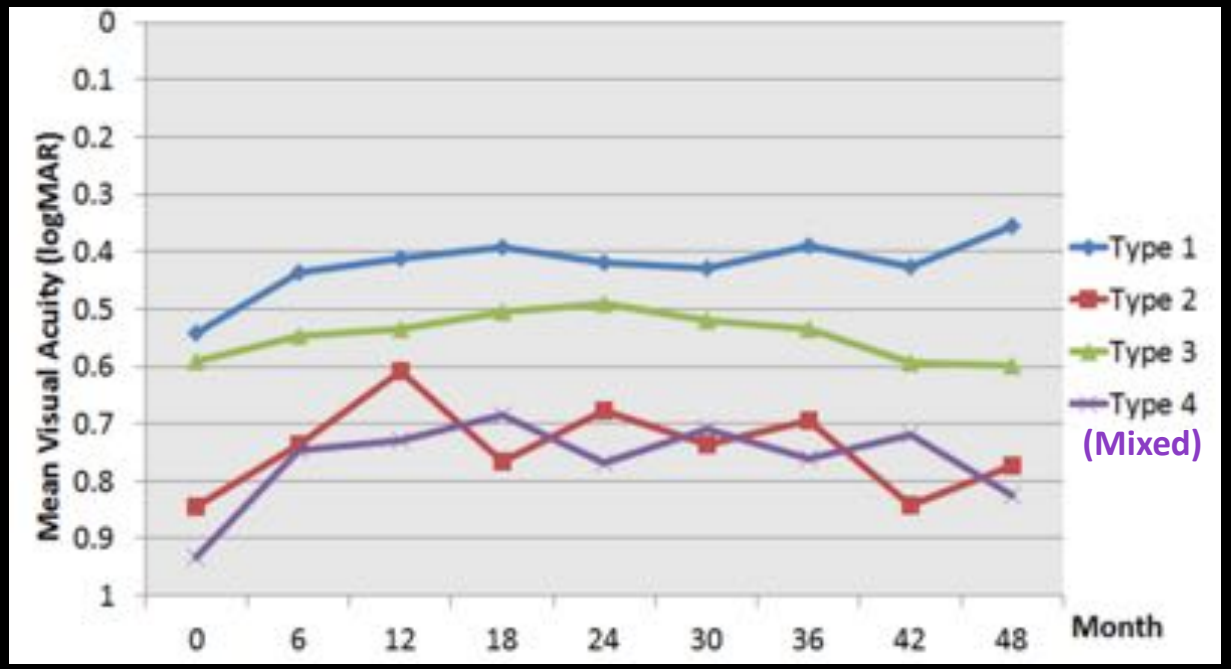
Type 1 Eyes Had the Best Mean BCVA Profile Over 24 Months, While Type 2/M* Eyes Had the Worst

BCVA Over Time by Baseline Lesion Type

HARBOR (Pooled Treatment Arms)



Mrejen et al, 2015[1]



*Type 2/Mixed Type 1 and 2. Error bars represent 95% CI.

1. Mrejen S et al. *J Clin Med*. 2015;4(7):1380-1402.

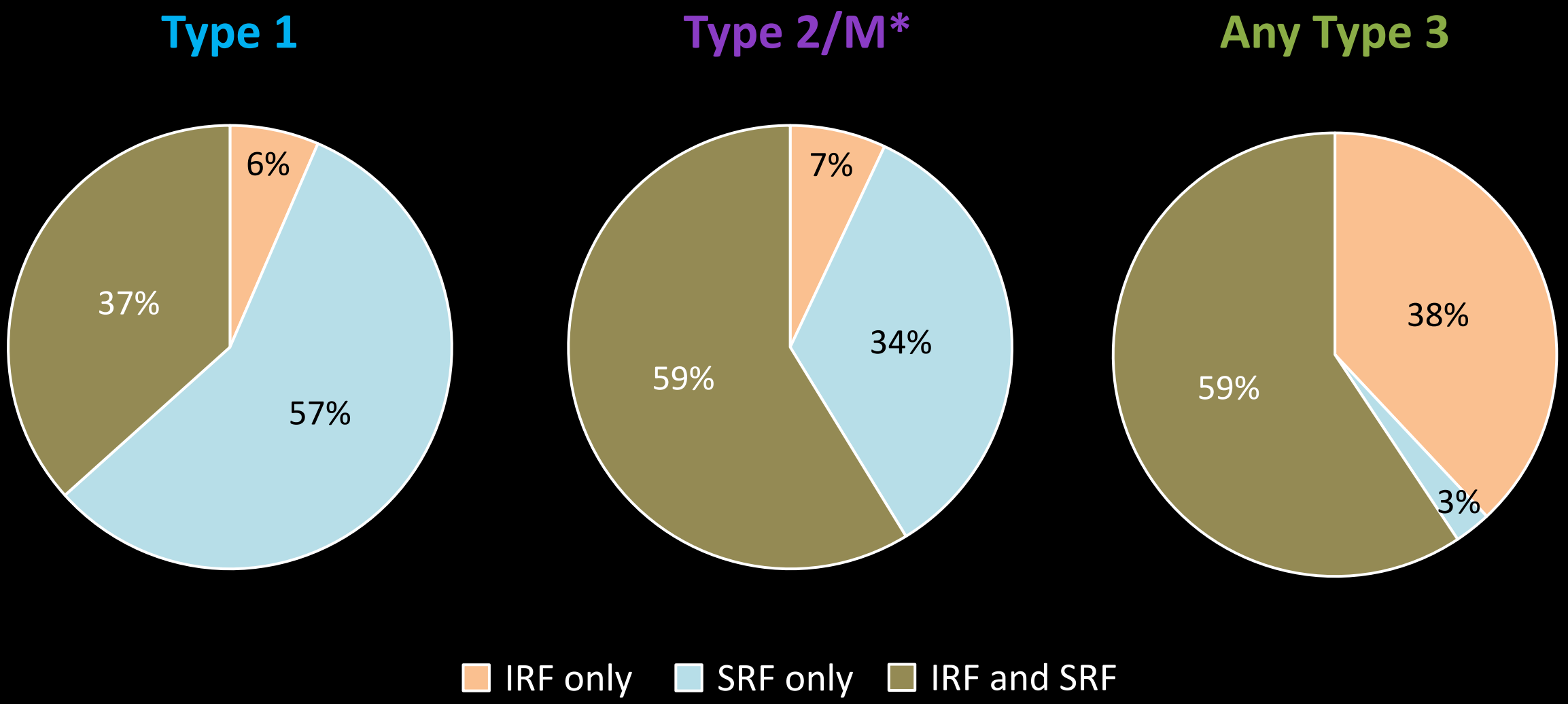
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; logMAR, logarithm of the minimum angle of resolution.

Mean Vision Gains Over 24 Months Were Numerically Greatest Among Monthly-Treated Type 2/M* Eyes

*Type 2/Mixed Type 1 and 2. Error bars represent 95% CI.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PRN, as-needed.

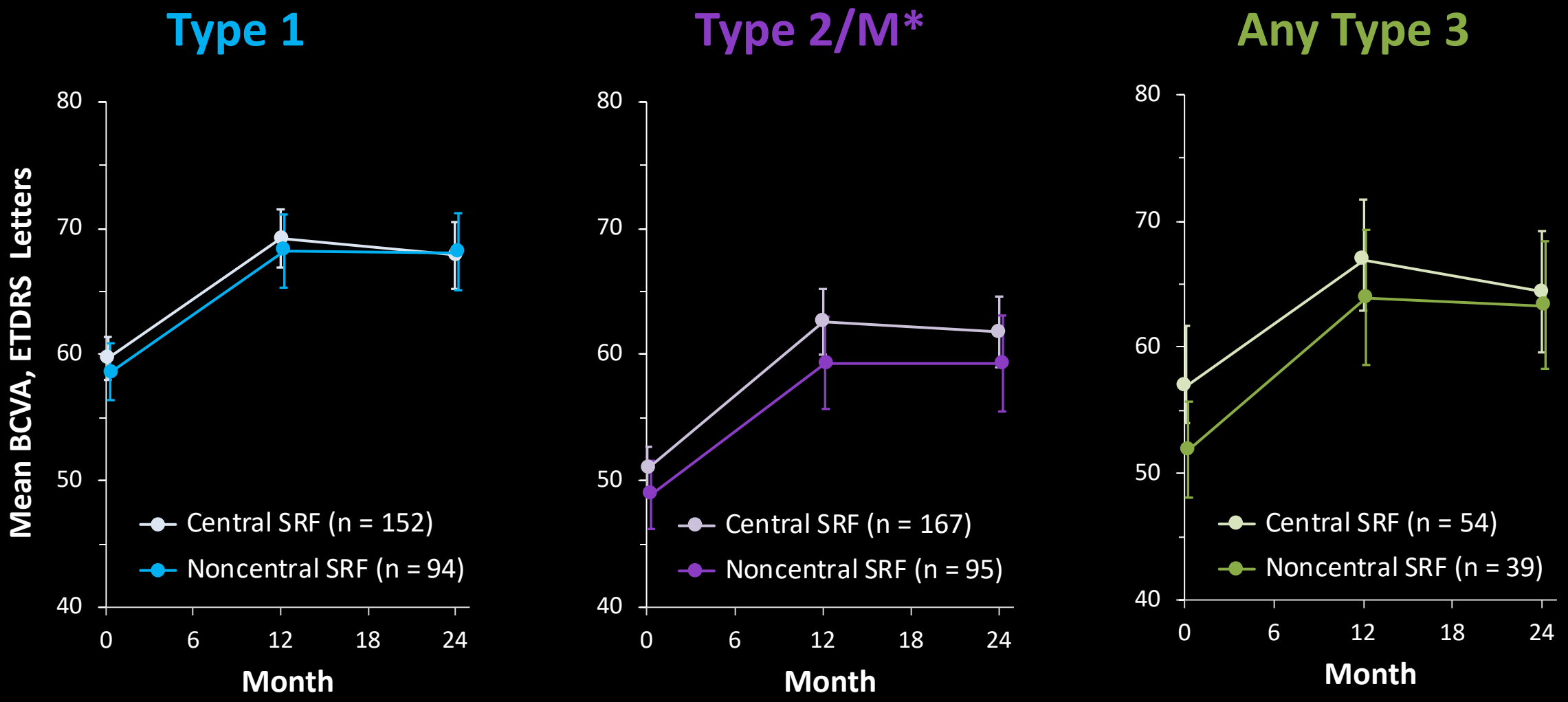
The Majority of Type 1 Eyes Had SRF Only at Baseline



*Type 2/Mixed Type 1 and 2.

IRF, intraretinal fluid; SRF, subretinal fluid.

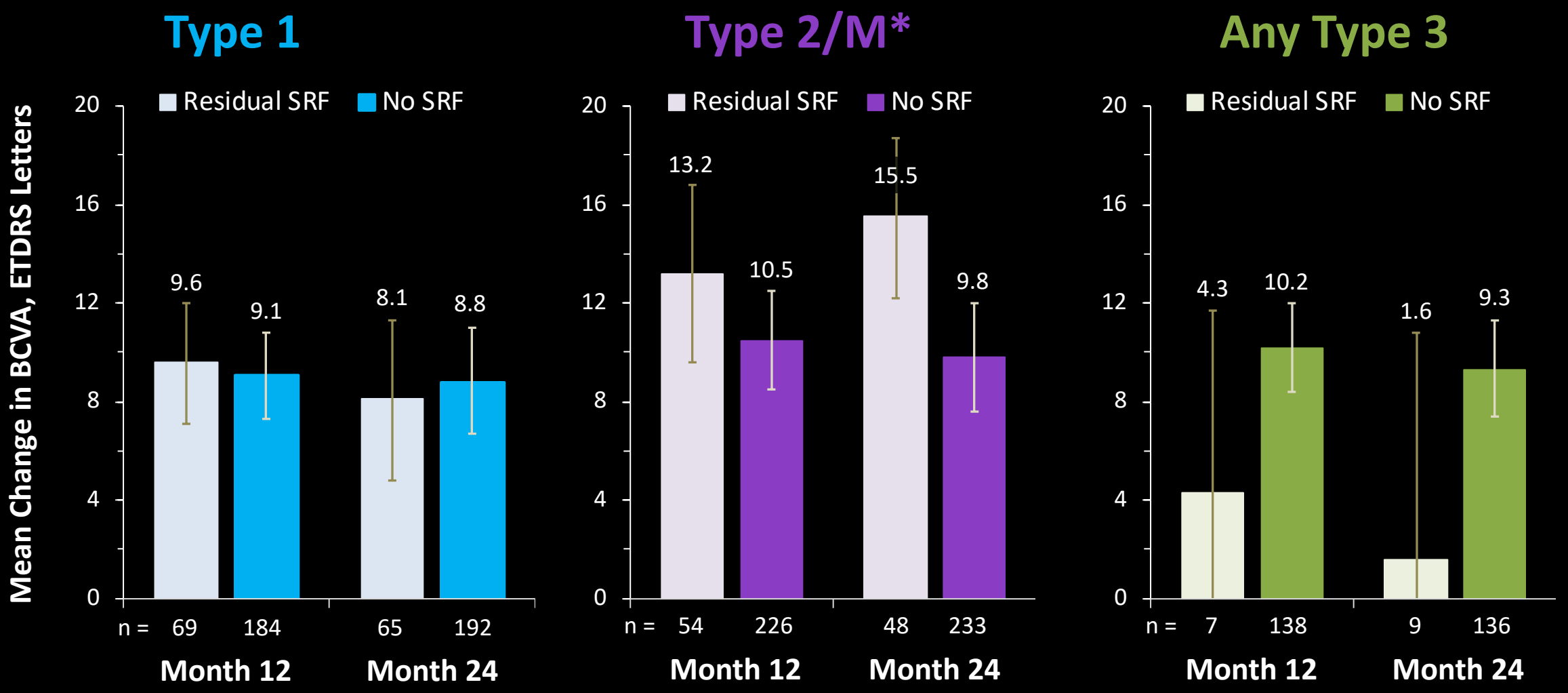
Across All Lesion Types, BCVA Outcomes Over 24 Months Were Similar Regardless of SRF Location at Baseline



*Type 2/Mixed Type 1 and 2. Error bars represent 95% CI.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SRF, subretinal fluid.

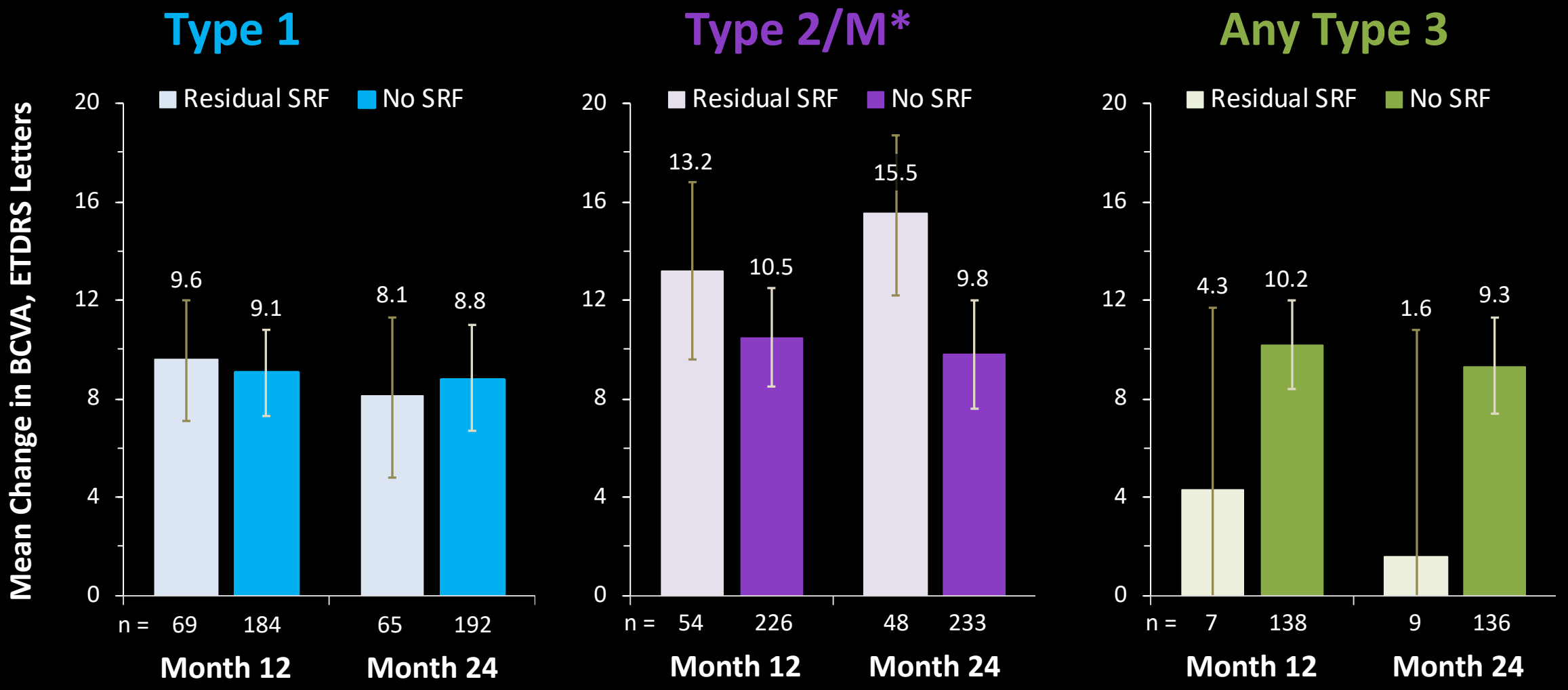
Mean Vision Gains Were Similar in Type 1 Eyes With and Without Residual SRF Over 24 Months



*Type 2/Mixed Type 1 and 2. Error bars represent 95% CI.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SRF, subretinal fluid.

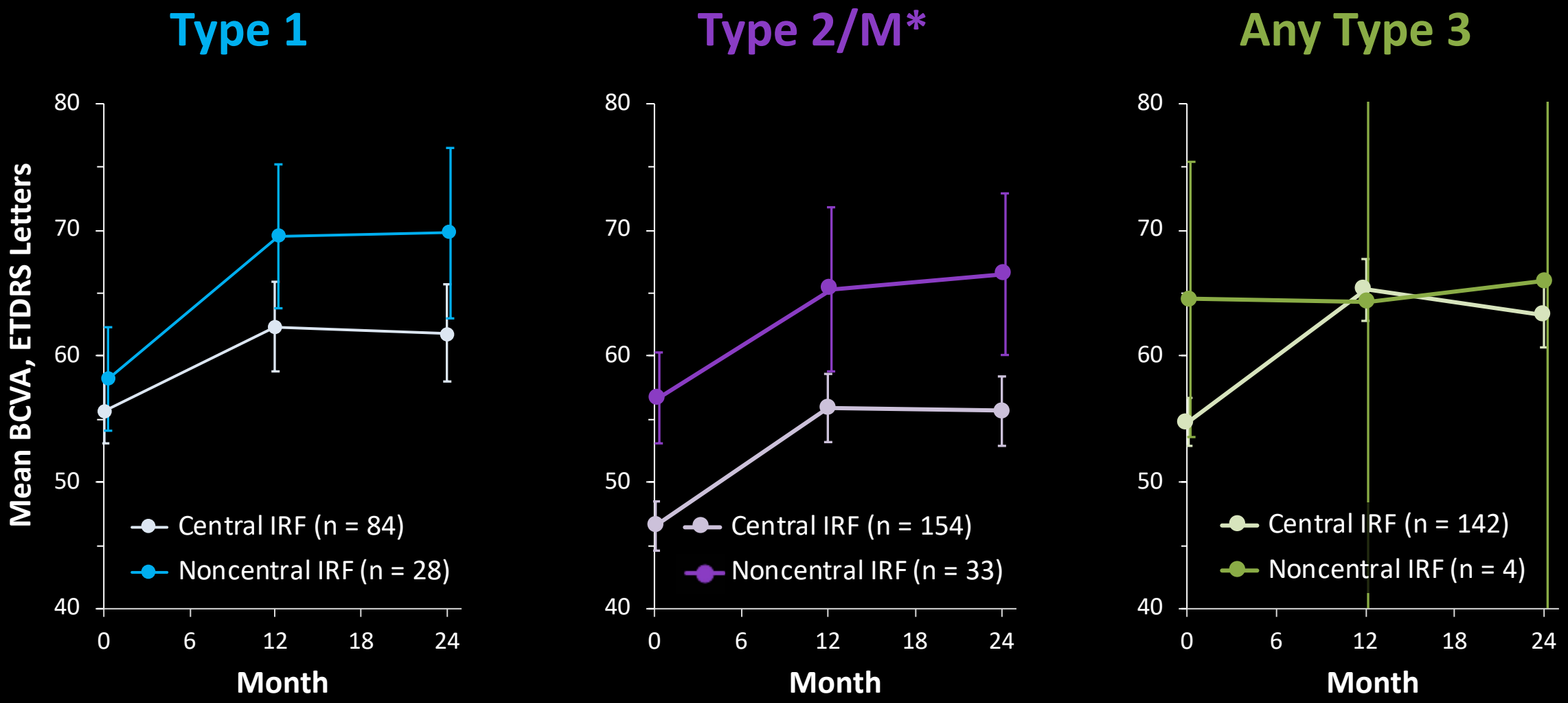
Mean Vision Gains Were Significantly Better in Type 2/M* Eyes With Residual SRF at Month 24



*Type 2/Mixed Type 1 and 2. Error bars represent 95% CI.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SRF, subretinal fluid.

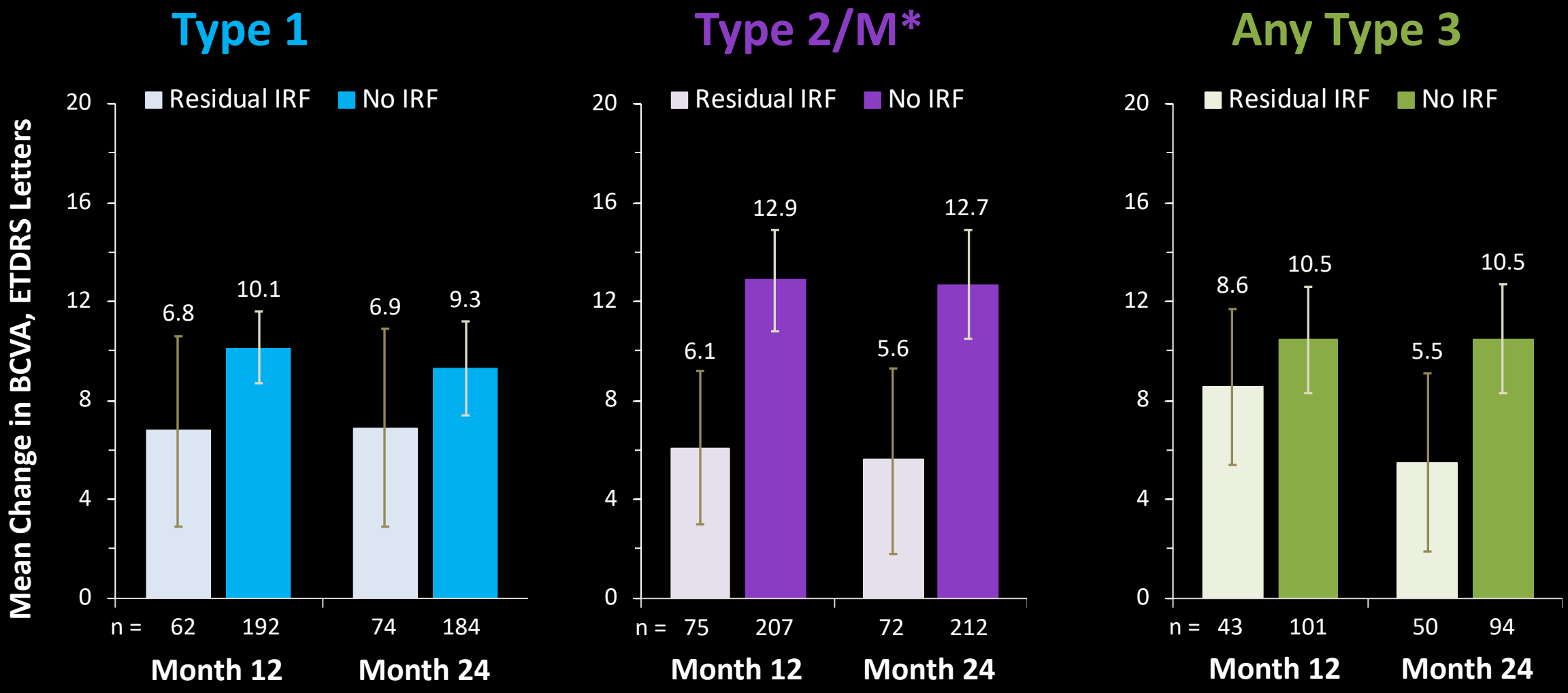
In Type 1 and Type 2/M* Eyes, BCVA Outcomes Over 24 Months Were Generally Worse When Central IRF Was Present at Baseline



*Type 2/Mixed Type 1 and 2. Error bars represent 95% CI.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid.

Mean Vision Gains Were Significantly Worse in Type 2/M* Eyes With Residual IRF at Months 12 and 24



*Type 2/Mixed Type 1 and 2. Error bars represent 95% CI.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid.

Conclusions

- In this first application of CONAN Study Group criteria to a major nAMD dataset, MNV lesion type correlated with visual and anatomic endpoints in HARBOR
- Regardless of regimen, eyes with **Type 1** lesions had the best BCVA profile over 24 months, while **Type 2/M** eyes had the worst
- Vision gains over 24 months were numerically greatest among monthly-treated **Type 2/M** eyes, and better in **Type 2/M** eyes with residual versus no SRF
- In eyes with **Type 1** lesions, vision outcomes over 24 months were similar regardless of concurrent residual SRF
- Central IRF at baseline and residual IRF at month 24 correlated with poor vision across MNV lesion types

Anatomic classification of MNV lesion type and a nuanced assessment of retinal fluid should be considered in the management of nAMD

BCVA, best-corrected visual acuity; CONAN, Consensus on Neovascular Age-Related Macular Degeneration Nomenclature; IRF, intraretinal fluid; MNV, macular neovascularization; nAMD, neovascular age-related macular degeneration; PRN, as-needed; SRF, subretinal fluid; Type 2/M, Type 2/Mixed Type 1 and 2.