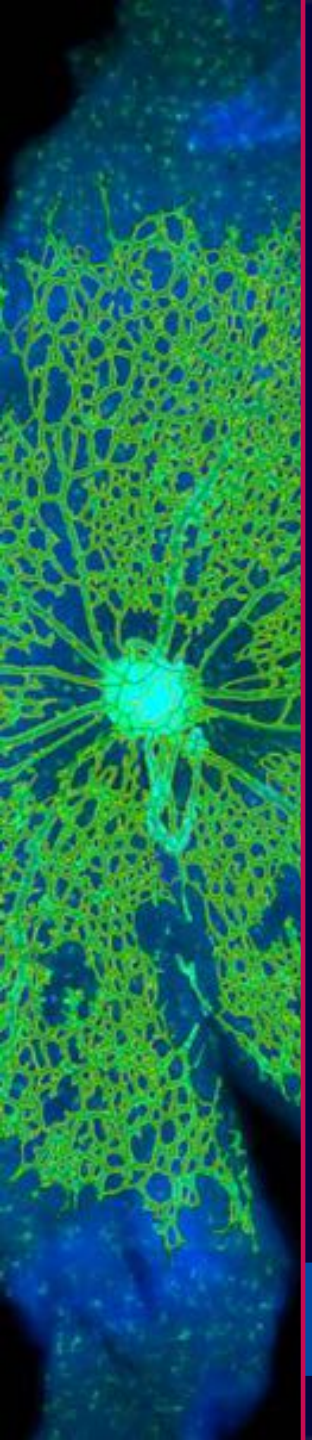


Is Residual Subretinal Fluid (SRF) Associated With Improved Vision Outcomes? Evaluation of Fluorescein Angiography (FA) Patterns From the HARBOR trial

Michael Singer, MD[1]
Lauren Hill, MS[2]
Miranda Hemphill, PhD[2]

[1] Medical Center Ophthalmology Associates, San Antonio, TX

[2] Genentech, Inc, South San Francisco, CA

Presented at Retina Society 2020 VR – 53rd Annual Scientific Meeting | September 21–22, 2020

Disclosures

- Financial disclosures
  - MS: consultant /speaker/ research support for Aerpio, Allegro, Allergan, Alimera, Appellis, Clearside, Eyepoint, Genentech, Inc, Guidepoint, Ionis, Kodiak, Mallinckrodt, Notal Vision, Novartis, Opthea, Optos, Regeneron, Roche, Santen, and Spark, Senju.
  - MH: employment by Genentech, Inc
  - LH: contract consultancy with Genentech, Inc, Alimera Sciences, PolyPhotonix, Aerpio, and Recens Medical.

- Study disclosures
  - This study includes research conducted on human subjects
  - Institutional Review Board approval was obtained prior to study initiation
  - Funding for this study was provided by Genentech, Inc, a member of the Roche Group
  - Third-party writing assistance, provided by Ray D Beck, Jr, PhD, of Envision Pharma Group, was funded by Genentech, Inc

Summary

- This *post hoc* analysis of data from HARBOR[1] (NCT00891735) evaluated the potential relationship of SRF thickness with VA over 2 years of monthly or PRN ranibizumab 0.5 mg or 2 mg treatment in patients with nAMD stratified by good (20/40 or better) or bad vision (worse than 20/40)
- In univariate analyses, numerous staining, fibrosis, and atrophy variables differed between patients with good or bad vision
- In multivariable analyses, characteristics predictive of the odds of good vision included:
  - At month 12
    - Absence of Subfoveal fibrosis with PRN ranibizumab
  - At month 24
    - Presence of a window defect
    - Absence of Subfoveal atrophy
- SRF was associated with lower rates of MA (all patients) and fibrosis (bad vision only), but higher rates of PED (all patients)

*mean±SE

1. Sharma et al. *Ophthalmology*. 2016; 123:865–875

MA, macular atrophy; nAMD, neovascular age-related macular degeneration; PRN, *pro re nata* (as needed); SRF, subretinal field; VA, visual acuity; VEGF, vascular endothelial growth factor

Background and Objective

- In CATT, after 2 years of monthly or PRN anti-VEGF therapy including ranibizumab for AMD, patients with foveal SRF demonstrated significantly better VA that those with extrafoveal SRF or without SRF (*P* = 0.0005)
  - Foveal SRF – 72.8±1.5* letters
  - Extrafoveal SRF – 69.6±1.2* letters
  - Without SRF – 66.6±0.7* letters
- **Objective**: To evaluate the relationship between SRF thickness at screening or week 1 with vision outcomes in patients with nAMD treated with intravitreal injections of ranibizumab

*mean±SE

1. Sharma et al. *Ophthalmology*. 2016; 123:865–875

AMD, age-related macular degeneration; CATT, Comparison of Age-related Macular Degeneration Treatments Trials; nAMD, neovascular age-related macular degeneration; PRN, *pro re nata* (as needed); SRF, subretinal field; VA, visual acuity; VEGF, vascular endothelial growth factor

HARBOR Study Design

A large, prospective phase 3 trial (NCT00891735) that evaluated efficacy of 2 doses and 2 regimens of ranibizumab for nAMD over 2 years

Treatment-naïve patients (aged ≥50 years) with nAMD, active subfoveal CNV, and BCVA 20/40 to 20/320 (Snellen equivalent) using ETDRS (N = 1097)

Ranibizumab dose cohort

- **0.5 mg *Monthly*** (n = 275)
- **0.5 mg PRN *(with 3-mo LD)*** (n = 275)
- **2.0 mg *Monthly*** (n = 274)
- **2.0 mg PRN *(with 3-mo LD)*** (n = 273)

*PRN re-treatment criteria:
- ≥5-letter decrease in BCVA from previous visit
- Any evidence of disease activity on SD-OCT

1. Busbee et al. *Ophthalmology*. 2013; 120:1046-1056. 2. ClinicalTrials.gov NCT00891735.

BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; ETDRS, Early Treatment Diabetic Retinopathy Study; LD, monthly loading doses; mo, month; nAMD, neovascular age-related macular degeneration; PRN, *pro re nata* (as needed), SD-OCT, spectral-domain optical coherence tomography.

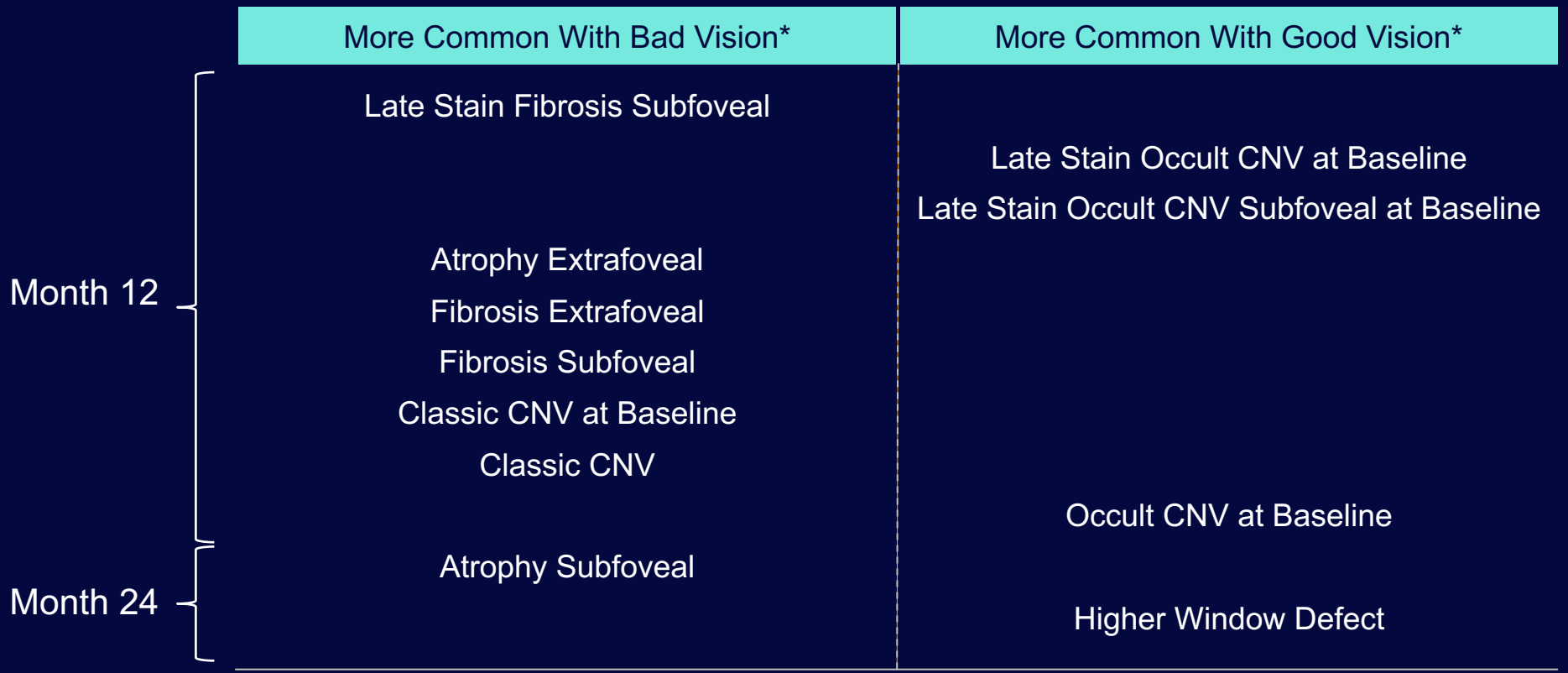
Endpoints and Sub-analyses

- Patients
  - HARBOR patients who had presence of SRF evaluated by OCT at screening, baseline or week 1 as well as months 12 and/or 24
  - Stratified by good (20/40 or better) and bad vision (worse than 20/40) at M12 and M24
  - Treatment arms pooled
- Endpoints and Analyses
  - Univariate analyses of staining, fibrosis, and atrophy characteristics at months 12 and 24 by good vs bad vision
  - Multivariable analyses of factors predictive of good vision at months 12 and 24
  - Rates of MA, fibrosis, and PED by fluid status evaluated at months 12 and 24
  - CNV area and leakage area at baseline and change from baseline by good vision vs bad vision at months 12 and 24

FA, fluorescein angiography; MA, macular atrophy; PED, pigment epithelial detachment

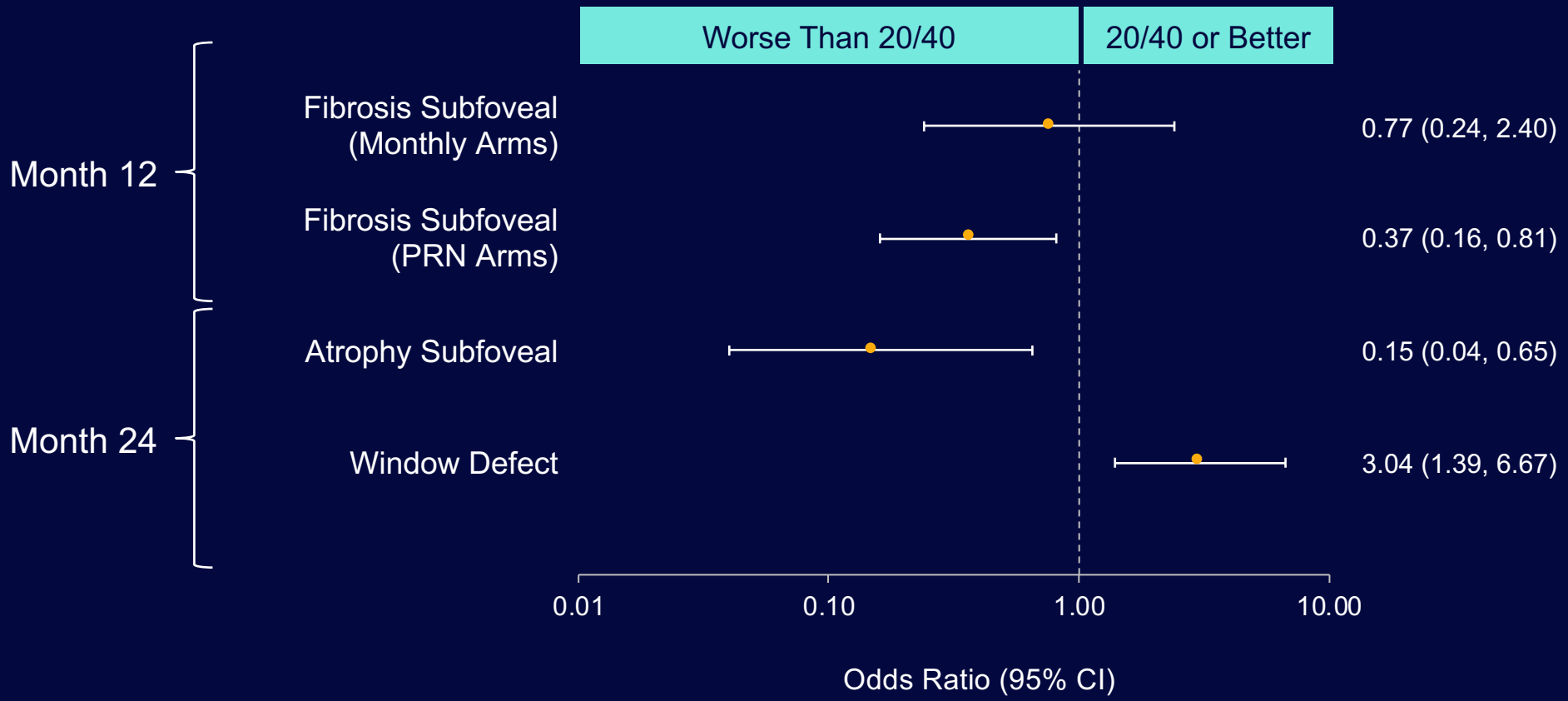
Statistically Significant Univariate Associations at Baseline and Months 12 or 24

Good (20/40 or Better) vs Bad Vision (Worse Than 20/40)



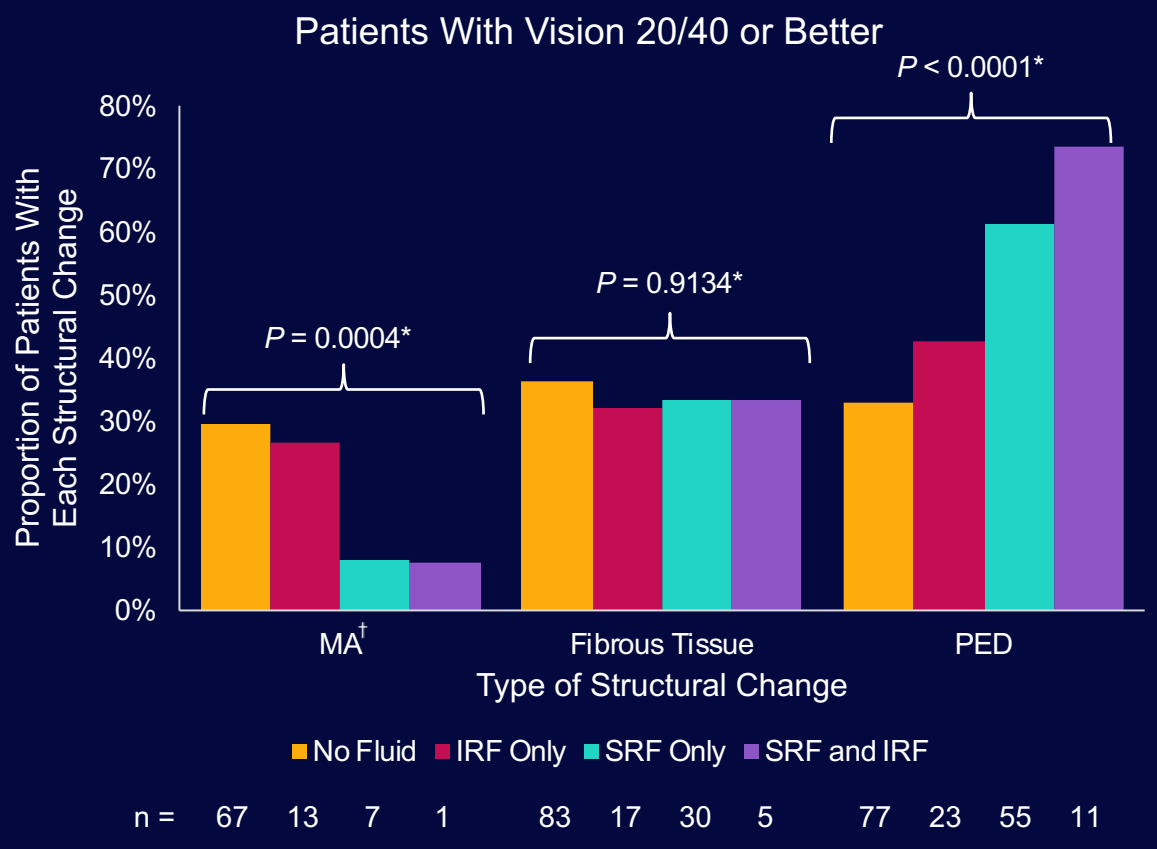
*All $P < 0.05$ in univariate analyses comparing proportion of patients with good vision vs bad vision.
CI, confidence interval; M12, month 12; M24, month 24; PRN, *pro re nata* (as needed), VA, visual acuity.

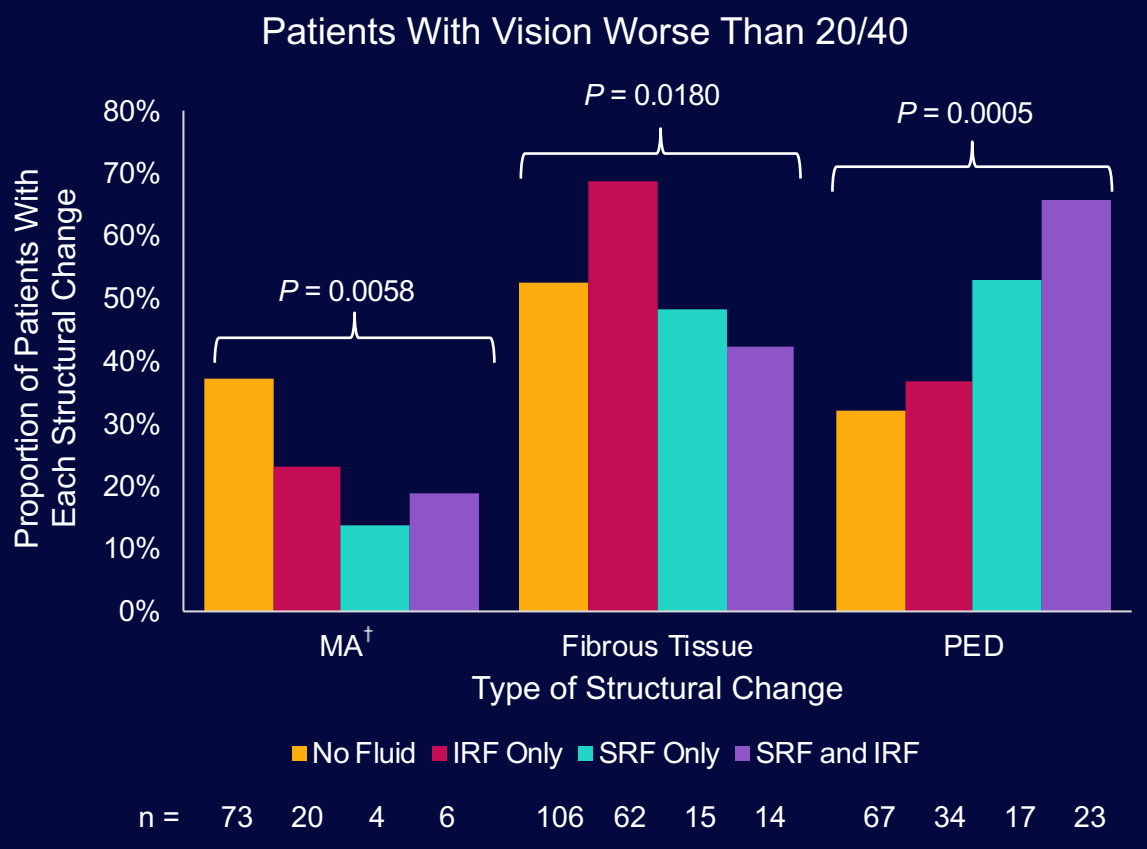
Multivariable Regression: Factors Associated With Vision at Months 12 or 24



CI, confidence interval; M12, month 12; M24, month 24; PRN, *pro re nata* (as needed), VA, visual acuity.

With Good (20/40 or Better) and Bad (Worse Than 20/40) Vision, MA and PED Were Significantly Associated With Fluid Status at Month 12

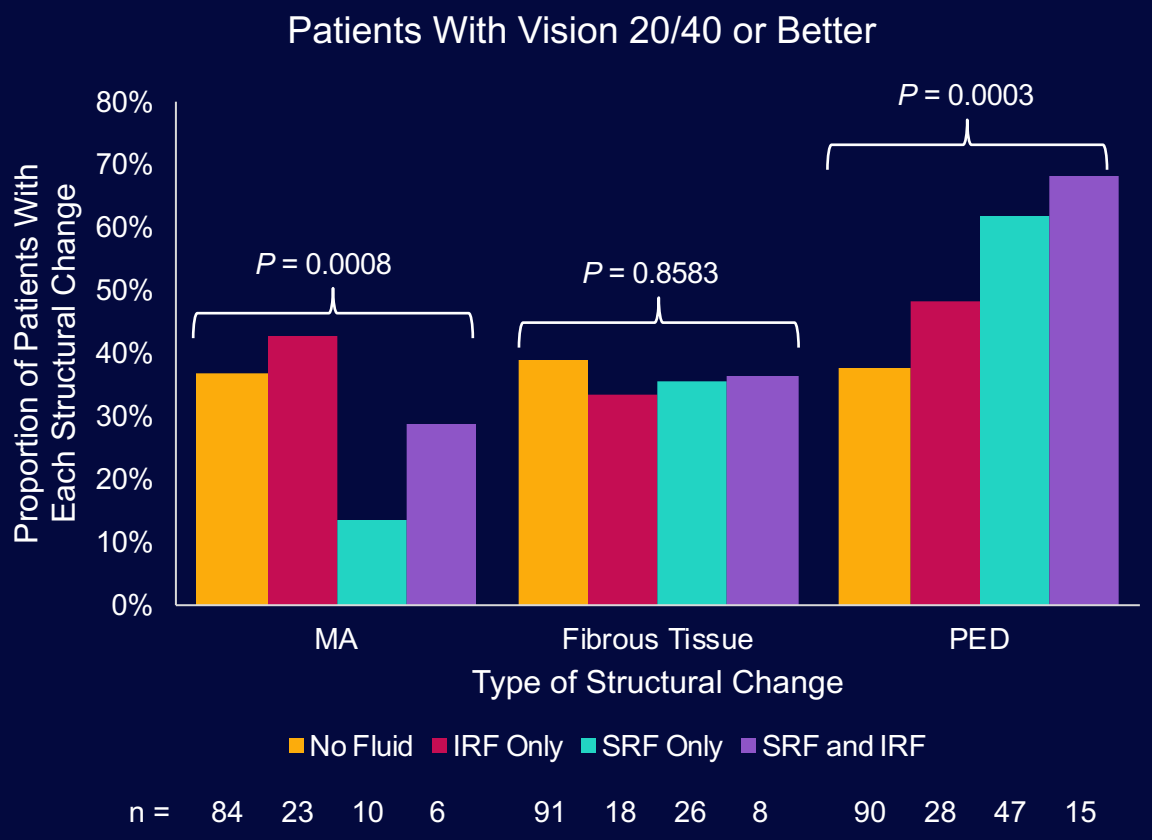


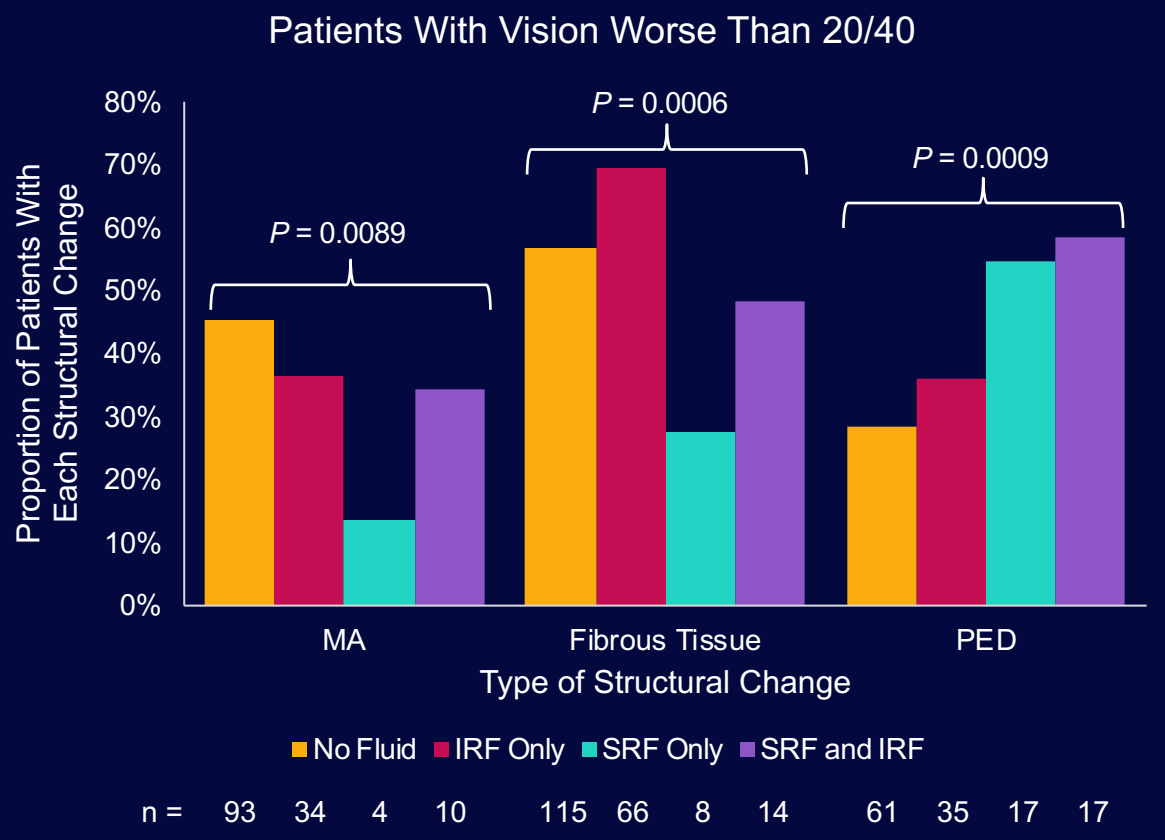


- SRF was associated with less atrophy and more PED than IRF or no fluid
- In patients with bad vision, fibrous tissue was higher with IRF than SRF

*P-values assess for any difference in each structural change across fluid groups; no pairwise comparisons were conducted to analyze differences between individual fluid subgroups
†MA includes patients with CD (Good Vision: no fluid 2.2%, IRF only 9.3%, SRF only 4.4%, SRF and IRF 13.3%. Bad Vision: no fluid 4.4%, IRF only 5.4%, SRF only 9.4%, SRF and IRF 5.9%)
IRF, intraretinal fluid; MA, macular atrophy; PED, pigment epithelial detachment; SRF, subretinal fluid

With Good (20/40 or Better) and Bad (Worse Than 20/40) Vision, MA and PED Were Significantly Associated With Fluid Status at Month 24





- A lower proportion of SRF (vs IRF or no fluid) patients had atrophy and more had PED
- In patients with bad vision, fibrous tissue was more common with IRF than SRF

*P-values assess for any difference in each structural change across fluid groups; no pairwise comparisons were conducted to analyze differences between individual fluid subgroups
†MA includes patients with CD (Good Vision: no fluid 3.8%, IRF only 6.9%, SRF only 2.6%, SRF and IRF 4.5%. Bad Vision: no fluid 4.2%, IRF only 3.1%, SRF only 6.5%)
IRF, intraretinal fluid; MA, macular atrophy; PED, pigment epithelial detachment; SRF, subretinal fluid

Trend for Eyes with Bad Vision (vs Good Vision) to Have a Larger Change From Baseline in CNV at Month 12

- No clinically significant differences between patients with good vision (20/40 or better) or bad vision (worse than 20/40) in change from baseline values of:
  - Total area of CNV (DA) at months 12 or 24
  - Total area of leak CNV at months 12 or 24
- In patients who had residual SRF, total area of CNV (DA) and CNV leakage were higher at baseline in eyes with bad vs good vision
- There was a trend for larger reductions in total area of CNV (DA) and CNV leakage in eyes with bad vs good vision at month 12

CNV, choroidal neovascular membranes; DA, disc area

Conclusions

- In univariate analyses of data from HARBOR, rates of staining, fibrosis, and atrophy differed between patients with good (20/40 or better) vs bad (worse than 20/40) vision in eyes with residual SRF
- In multivariable analyses, factors predictive of good vision in eyes with residual SRF at months 12 or 24 included:
  - Absence of subfoveal fibrosis at month 12 in the PRN arms
  - Absence of subfoveal atrophy at month 24
  - Presence of window defect at month 24
- Presence of residual SRF at months 12 and 24 was associated with:
  - Lower rates of MA
  - Higher rates of PED
  - Lower rates of fibrosis (in eyes with bad vision only)

MA, macular atrophy; PED, pigment epithelial detachment; SRF, subretinal field