



Clinical Significance of Diabetic Retinopathy Improvement: A Meta-Analysis of Vision and Anatomic Outcomes in Five Clinical Trials Evaluating Intravitreal Ranibizumab

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Disclosures

- Financial disclosures:

- SJB: consultant for Adverum, Alimera, Allergan, EyePoint, Kala, Genentech, Inc, Novartis, Roche
- SB, IS: employment by Genentech, Inc.
- LH: contract consultancy for 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
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Summary

- This meta-analysis assessed patients across 5 pivotal trials in which patients with DR and DME received monthly ranibizumab therapy
 - RIDE (NCT00473382); N = 382
 - RISE (NCT00473330); N = 377
 - Protocol I (NCT00444600); N = 854*
 - Protocol S (NCT01489189); N = 305
 - Protocol T (NCT01627249); N = 660
- Overall, trends were observed between greater improvements in DRSS and better vision outcomes and reductions in CST from BL through month 24

*N based on 854 eyes evaluated in 691 patients

BL, baseline; CST, central subfield thickness; DME, diabetic macular edema; DR, diabetic retinopathy; DRSS, diabetic retinopathy severity score

DR Improvement: Clinically Meaningful or Cosmetic Change of the Eye?

Baseline



Month 12

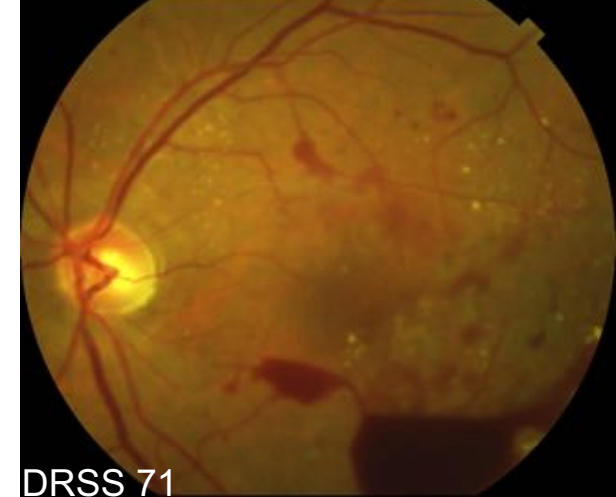


Month 24

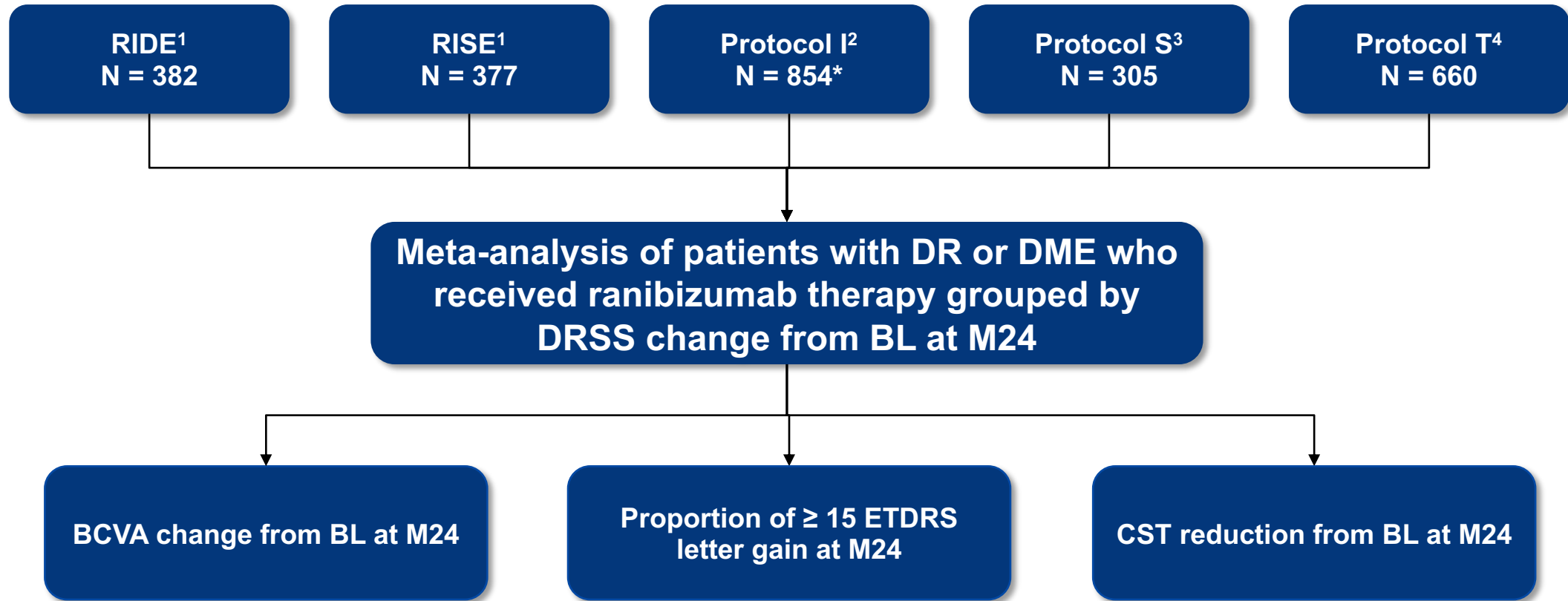


**DR Improvement
in Ranibizumab
(0.3 mg)-Treated Eye**

**DR Progression
in Untreated
Fellow Eye**



Methods



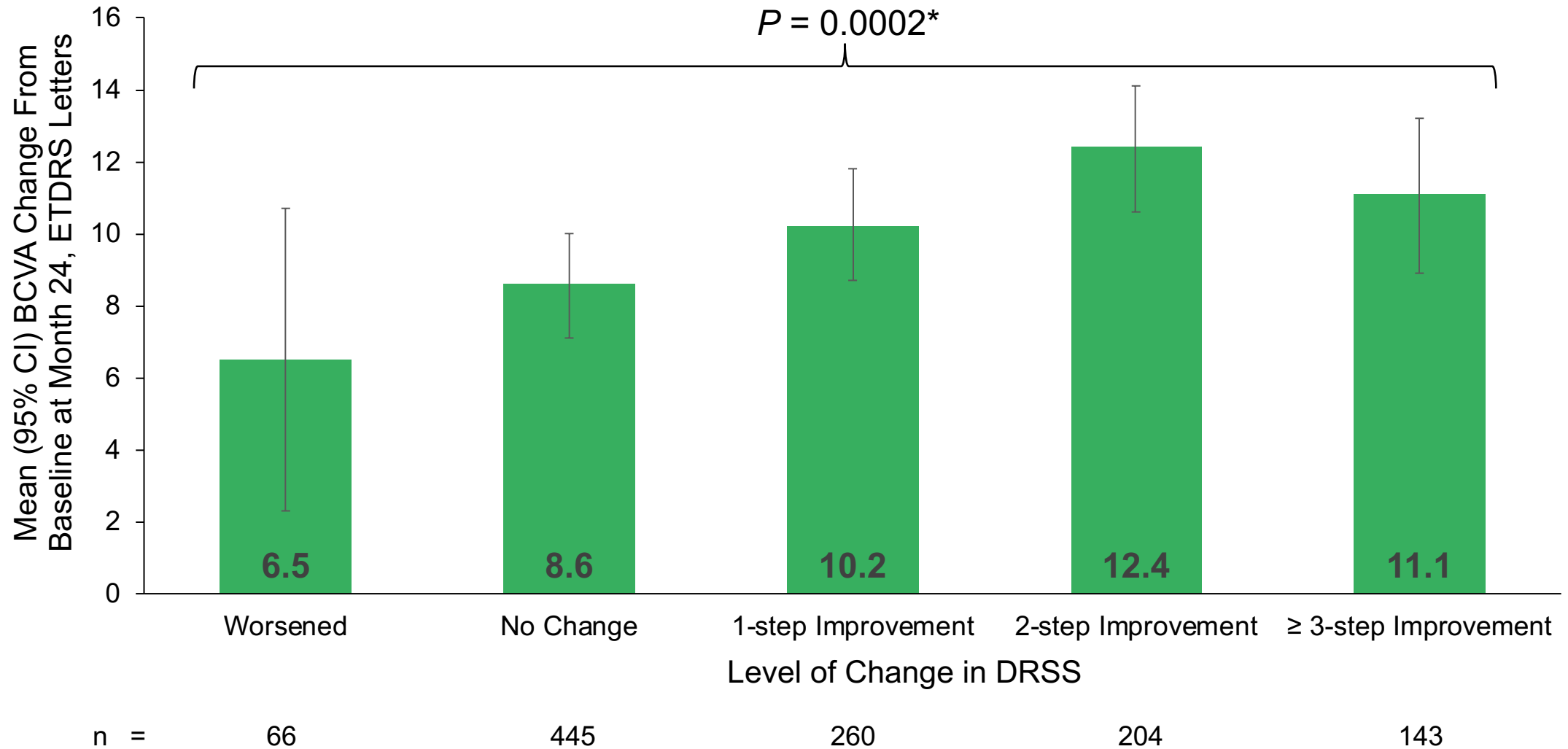
*N based on 854 eyes evaluated in 691 patients

BCVA, best-corrected visual acuity; BL, baseline; CST, central subfield thickness; DR, diabetic retinopathy; DME, diabetic macular edema; DRSS, diabetic retinopathy severity score; ETDRS, Early Treatment Diabetic Retinopathy Study; M24, month 24.

1. Nguyen QD, et al. *Ophthalmology*. 2012;119(4):789–801. 2. Diabetic Retinopathy Clinical Research Network, Elman MJ, Aiello LP, Beck RW, et al. *Ophthalmology*. 2010;117(6):1064–1077.e35.

3. Diabetic Retinopathy Clinical Research Network. *JAMA* 2015;314(20):2137–2146. 4. Diabetic Retinopathy Clinical Research Network, Wells JA, Glassman AR, Ayala AR, et al. *N Engl J Med* 2015;372(13):1193–1203.

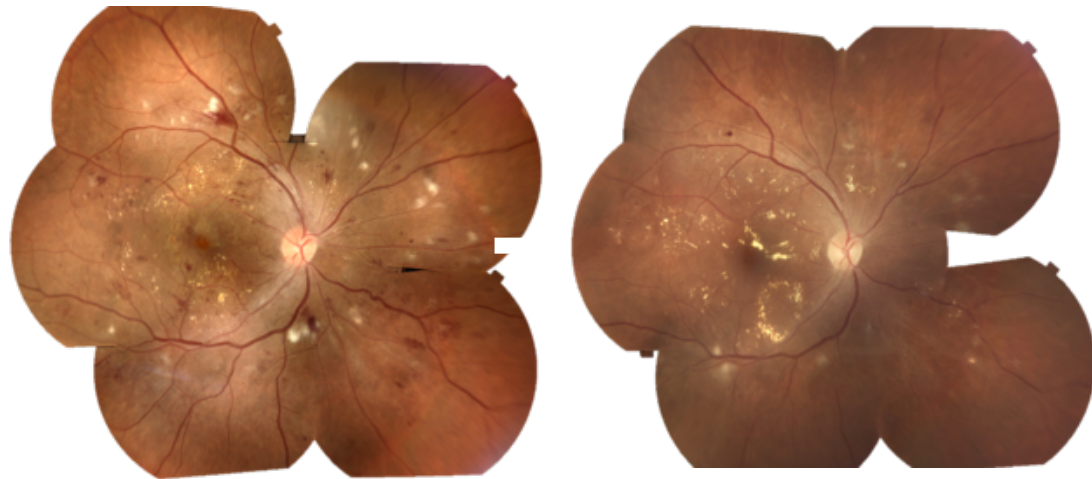
Greater Vision Gains from Baseline With DRSS Improvements at Month 24



*Trend P -value based on Jonckheere-Terpstra Test
BCVA, best-corrected visual acuity; DRSS, diabetic retinopathy severity score; ETDRS, Early Treatment Diabetic Retinopathy Study.

Case Examples of a 2-step and 3-step Improvement in DR With Ranibizumab Treatment

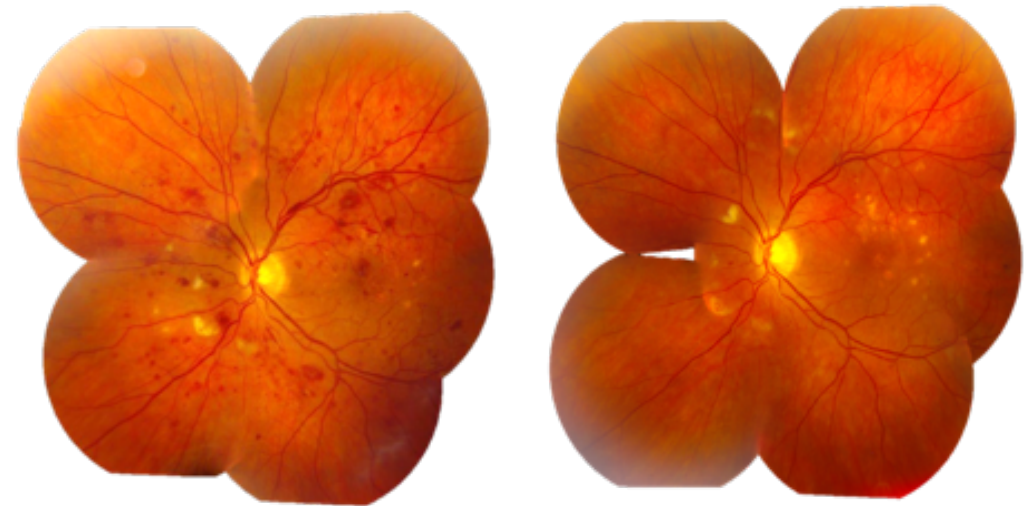
2-step improvement



Baseline:
Moderately severe
Nonproliferative DR
(DRSS 47)

Month 12:
Mild Nonproliferative DR
(DRSS 35)

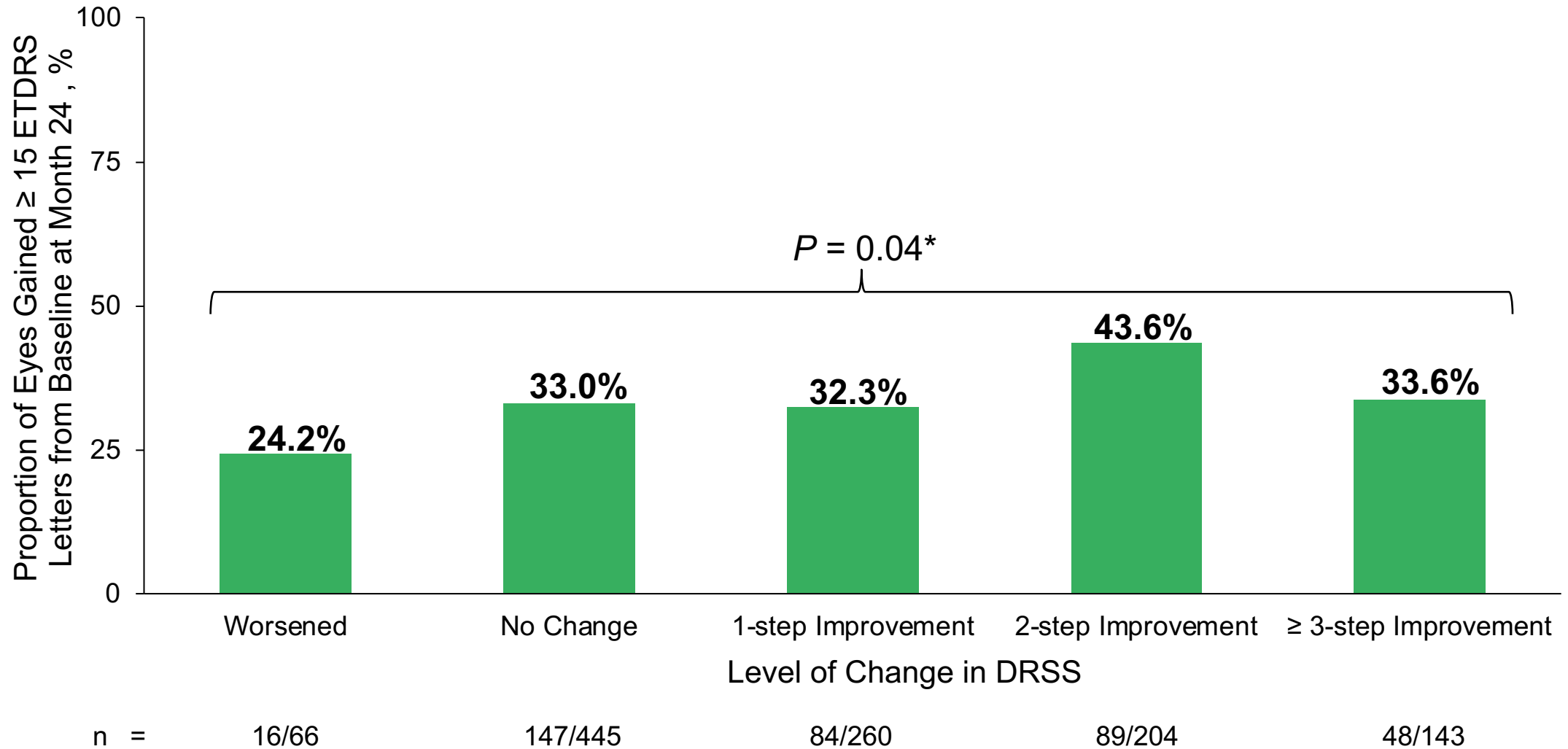
3-step improvement



Baseline:
Severe Nonproliferative DR
(DRSS 53)

Month 12:
Mild Nonproliferative DR
(DRSS 35)

Greater Proportion of Patients Gaining ≥ 15 ETDRS Letters from Baseline at Month 24 With DRSS Improvements

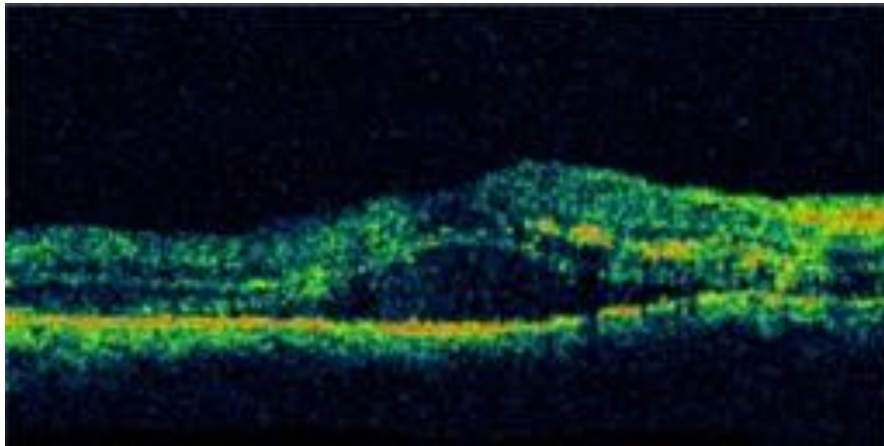


*Trend *P*-value for ≥ 15 letter gain based on Jonckheere-Terpstra Test

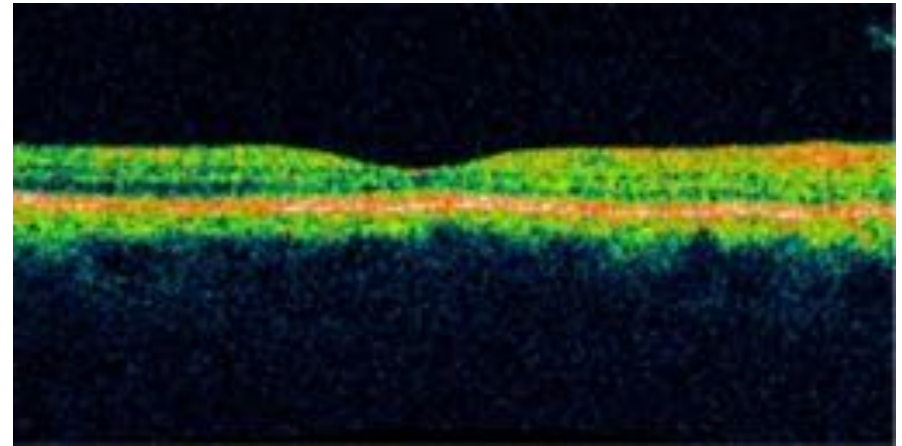
BCVA, best-corrected visual acuity; DRSS, diabetic retinopathy severity score; ETDRS, Early Treatment Diabetic Retinopathy Study.

Case Example of a Patient With DR Treated With Ranibizumab, Who Had Improved BCVA at Month 24

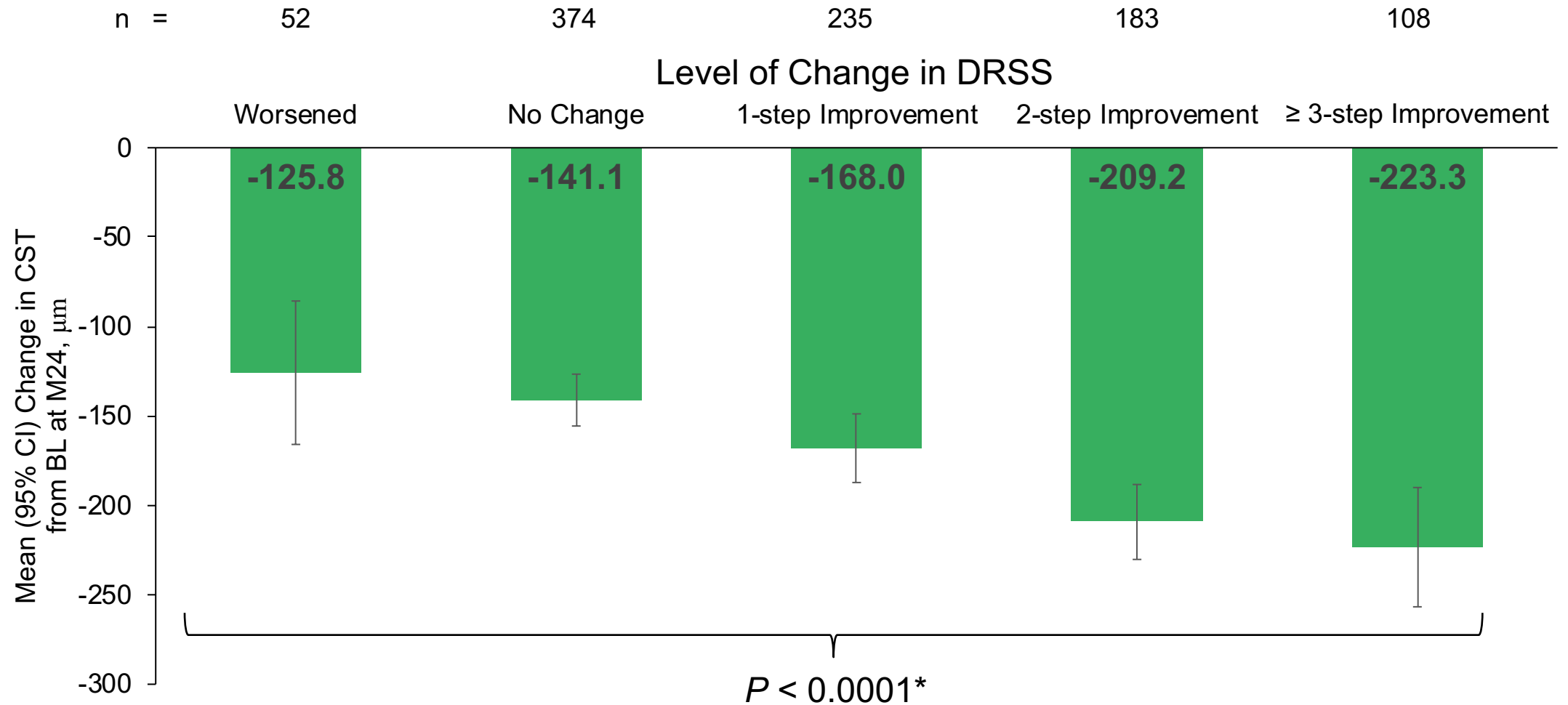
Baseline



Month 24



DR Improvements at Month 24 Were Associated with a Trend Towards Greater Reductions in CST from Baseline



*Trend *P*-value based on Jonckheere-Terpstra Test

BL, baseline; CST, central subfield thickness; DR, diabetic retinopathy; DRSS, diabetic retinopathy severity score; M24, month 24.

Conclusions

- Patients with DR or DME who received ranibizumab therapy demonstrated trends for improvements in DRSS being associated with:
 - Greater vision gains (change in BCVA from baseline) at Month 24
 - A greater proportion of eyes with 2-step DRSS improvement gained ≥ 15 ETDRS letters from BL at M24 compared with eyes with worsened DRSS
 - Larger reductions in CST from BL at M24