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

Sophie J. Bakri,\textsuperscript{1} MD
Lauren Hill, MS\textsuperscript{2}; Steve Blotner, MS\textsuperscript{2}; Ivaylo Stoilov, MD\textsuperscript{2}

\textsuperscript{1}Mayo Clinic, Rochester, Minnesota, USA
\textsuperscript{2}Genentech, Inc., South San Francisco, California, USA
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  - SB, IS: employment by Genentech, Inc.
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  - This study includes research conducted on human subjects
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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?

DR Improvement in Ranibizumab (0.3 mg)-Treated Eye

DR Progression in Untreated Fellow Eye

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DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale.
Methods

**Protocol S**
N = 305
**Protocol T**
N = 660

Meta-analysis of patients with DR or DME who received ranibizumab therapy grouped by DRSS change from BL at M24

- BCVA change from BL at M24
- Proportion of ≥ 15 ETDRS letter gain at M24
- CST reduction from BL at M24

*R 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.
Greater Vision Gains from Baseline With DRSS Improvements at Month 24

Mean (95% CI) BCVA Change From Baseline at Month 24, ETDRS Letters

- Worsened: 6.5
- No Change: 8.6
- 1-step Improvement: 10.2
- 2-step Improvement: 12.4
- ≥ 3-step Improvement: 11.1

Level of Change in DRSS

- n = 66
- n = 445
- n = 260
- n = 204
- n = 143

*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

OCT images from Wykoff et al. Presented at: American Society of Retina Specialist 2016 Annual Meeting; August 9-14, 2016; San Francisco, CA

BCVA, best-corrected visual acuity; DME, diabetic macular edema; DR, diabetic retinopathy; OCT, optical coherence tomography.
DR Improvements at Month 24 Were Associated with a Trend Towards Greater Reductions in CST from Baseline

**Mean (95% CI) Change in CST from BL at M24, μm**

- **Worsened**: -125.8 (-300 to 125.8)
- **No Change**: -141.1 (-250 to 11.9)
- **1-step Improvement**: -168.0 (-209.2 to -126.8)
- **2-step Improvement**: -209.2 (-223.3 to -195.1)
- **≥ 3-step Improvement**: -223.3 (-245.2 to -201.4)

**n =** 52, 374, 235, 183, 108

**Level of Change in DRSS**

*P < 0.0001* (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

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