What Happens to Diabetic Retinopathy Severity Scores With Less Aggressive Treatment?

A Post Hoc Analysis of the RISE/RIDE Open-Label Extension Study Examining Instability of DRSS with Intermittent VEGF Suppression

Roger A. Goldberg, MD[1];
Lauren Hill, MS[2]; Anna Abolian, OD[2]; Ivaylo Stoilov, MD[2]

[1] Bay Area Retina Associates, Walnut Creek, CA;
[2] Genentech, Inc., South San Francisco, CA

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

Disclosures

- Financial Disclosures
  - RAG: Consultant: Alimera, Allergen, Genentech, Inc., Regeneron;
    Lecture Fees: Allergan, Carl Zeiss Meditec, Genentech, Inc., Novartis, Santen;
    Grant Support: Carl Zeiss Meditec, Genentech, Inc., Novartis, Santen
  - LH: Consultant: Aerpio, Alimera, Genentech, Inc., InFocus, PolyPhotonix, Recens Medical
  - AA, IS: Employee: Genentech, Inc.

- Study Disclosures
  - This study includes research conducted on human subjects
  - Institutional Review Board approval was obtained prior to study initiation
  - Funding was provided by Genentech, Inc., a member of the Roche Group, for the study and third-party writing assistance by Nibedita Gupta, PhD, of Envision Pharma Group

Summary

- Post-hoc analysis of changes in DRSS scores in patients from the 12-month RISE and RIDE open-label extension (OLE) who received 0.5 mg ranibizumab PRN

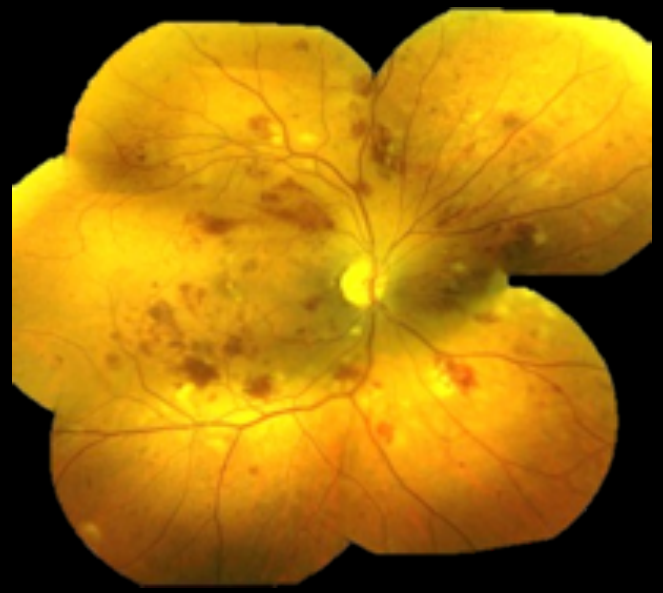
- Patients whose DRSS level improved to ≤ 43 (mild or moderate NPDR) with regular treatment were more prone to worsening when treated intermittently than those who had native DRSS level ≤ 43

- More severe diabetic retinopathy at baseline may indicate more unstable DRSS changes with intermittent dosing
  - This was most pronounced in patients who progressed to PDR – they were the cohort most likely to have the largest swings in DRSS

RISE: NCT00473330; RIDE: NCT00473382.
DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PRN, pro re nata.

VEGF Inhibition Can Improve DR Severity

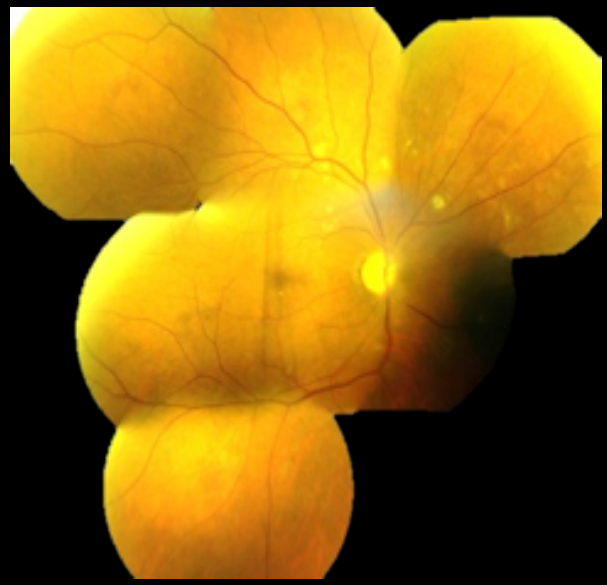
BL



High-risk PDR
DR Severity Level 71

Ranibizumab 0.3 mg Q4W

M36



Mild NPDR
DR Severity Level 35

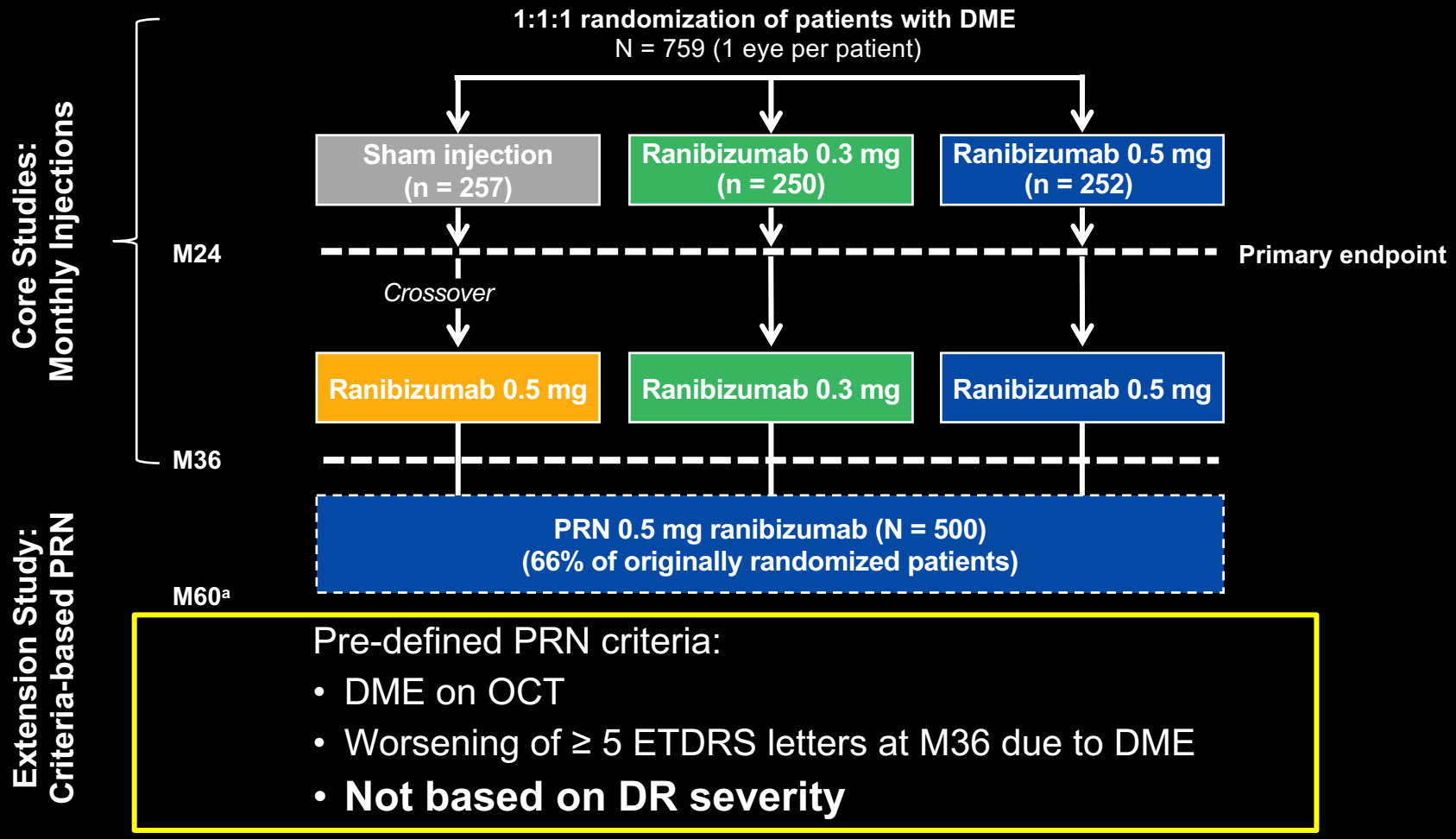
BL, baseline; DR, diabetic retinopathy; M, month; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; Q4W, every 4 weeks; VEGF, vascular endothelial growth factor.

But…How Do These Patients Behave After Monthly “Induction” Therapy Ends and Less Aggressive Treatment is Started?”

- How do these eyes behave compared with untreated eyes with the same DR severity?
- Which eyes are more prone to DRSS instability with intermittent dosing?

DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score.

RISE/RIDE: OLE Study



[a] The study finished early (as prespecified) when ranibizumab was approved by the US Food and Drug Administration for DME; most patients did not have follow-up through M60.
BL, baseline; DME, diabetic macular edema; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; ETDRS, Early Treatment Diabetic Retinopathy Study; M, month; OCT, optical coherence tomography; OLE, open-label extension; PRN, pro re nata.

RISE/RIDE: OLE Study

- 367/500 patients from RISE/RIDE OLE with evaluable DRSS data at both M36 and M48
- BL (M0) and M36 ocular characteristics were compared with DRSS response and injection frequency from M36 to M48
  - **Maintained**: At M48, DRSS improved or maintained from M36 DRSS
  - **Returned to BL**: At M48, DRSS worsened but not beyond BL DRSS
  - **Worsened**: At M48, DRSS worsened beyond BL DRSS

Extension Study: Criteria-based PRN

Pre-defined PRN criteria:

- DME on OCT
- Worsening of ≥ 5 ETDRS letters at M36 due to DME
- **Not based on DR severity**

[a] The study finished early (as prespecified) when ranibizumab was approved by the US Food and Drug Administration for DME; most patients did not have follow-up through M60.

BL, baseline; DME, diabetic macular edema; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; ETDRS, Early Treatment Diabetic Retinopathy Study; M, month; OCT, optical coherence tomography; OLE, open-label extension; PRN, pro re nata.

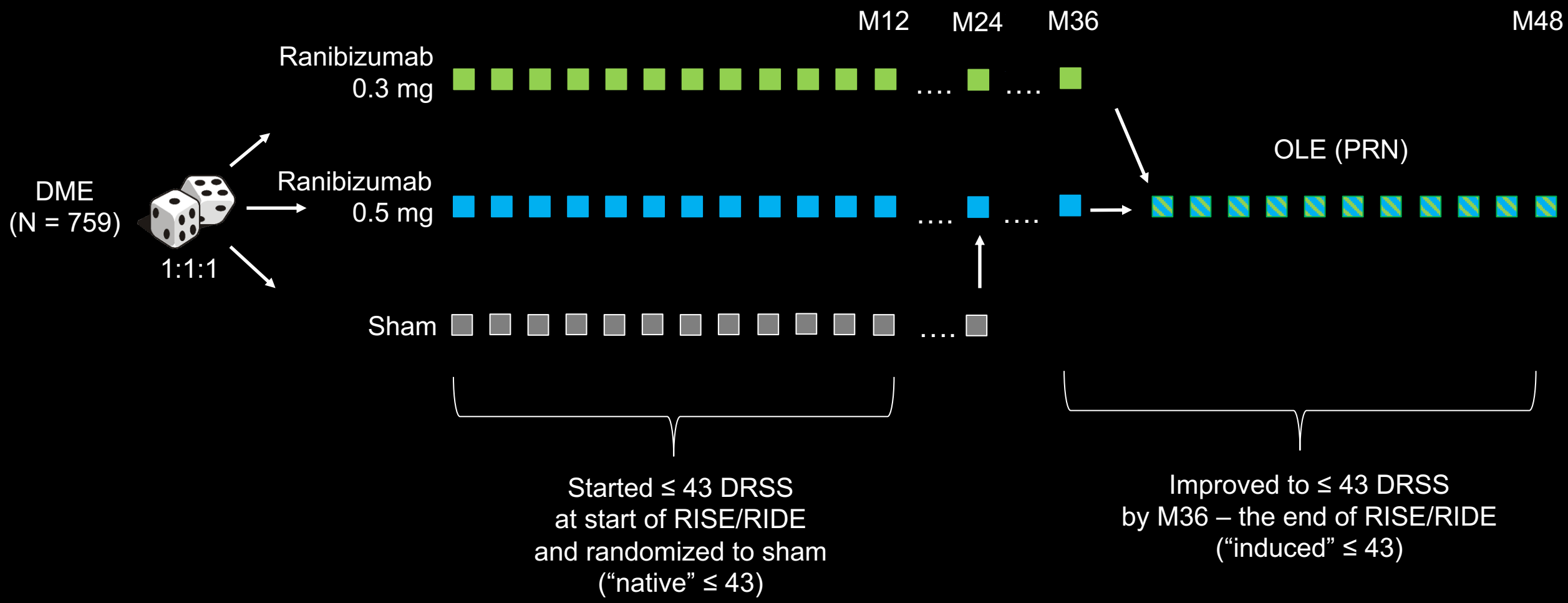
Do Patients With Improved Retinopathy Behave Similar to Patients With “Native” Retinopathy?

Improved to ≤ 43 DRSS
by end of RISE/RIDE
(“induced” ≤ 43)

Started RISE/RIDE
≤ 43 DRSS
and randomized to sham
(“native” ≤ 43)

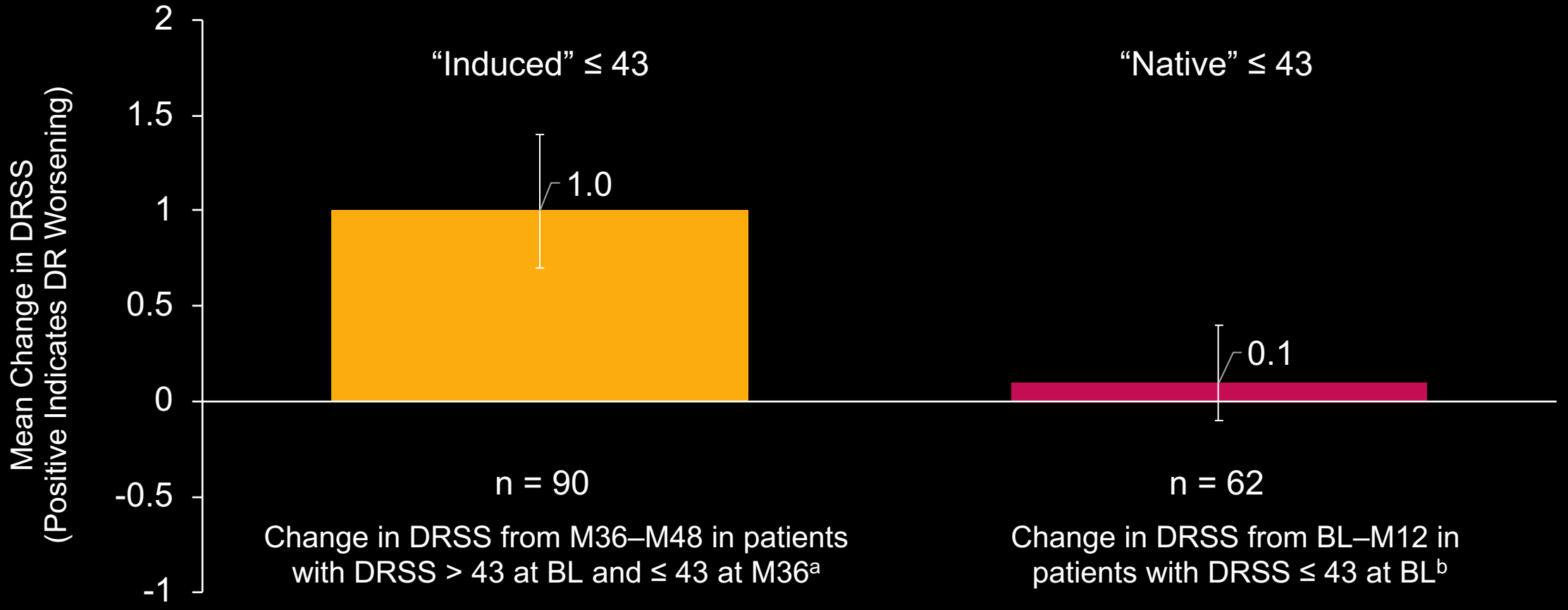
DRSS, Diabetic Retinopathy Severity Score.

Compare the Course of DR Over 12 Months for 2 Groups of Patients With Mild/Moderate NPDR



DME, diabetic macular edema; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; M, month, NPDR, nonproliferative diabetic retinopathy; OLE, open-label extension..

Patients With “Induced” DRSS ≤ 43 More Likely to Worsen Over 1 Year Than Control Patients With “Native” DRSS ≤ 43 at BL



Positive change in DRSS indicates DR worsening; negative change in DRSS indicates DR improvement.

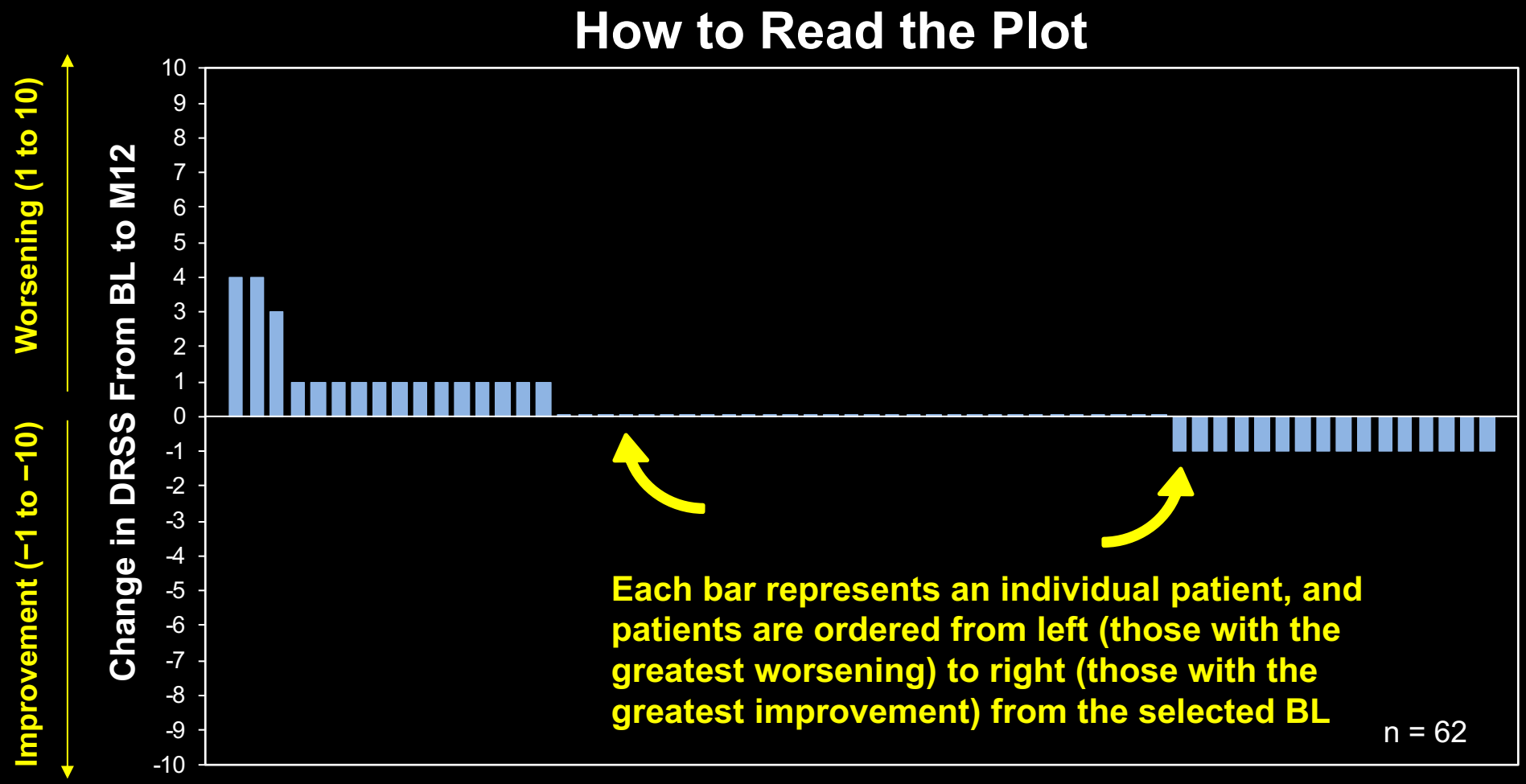
[a] Limited to patients with DR data at extension baseline (M36) and M48. [b] All sham treated eyes enrolled in RISE/RIDE with DR data at BL and M12.

BL, baseline; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; M, month

What Can We Learn From Individual Outcomes During OLE by Comparing Patients with “Native” Versus Those With “Induced” NPDR?

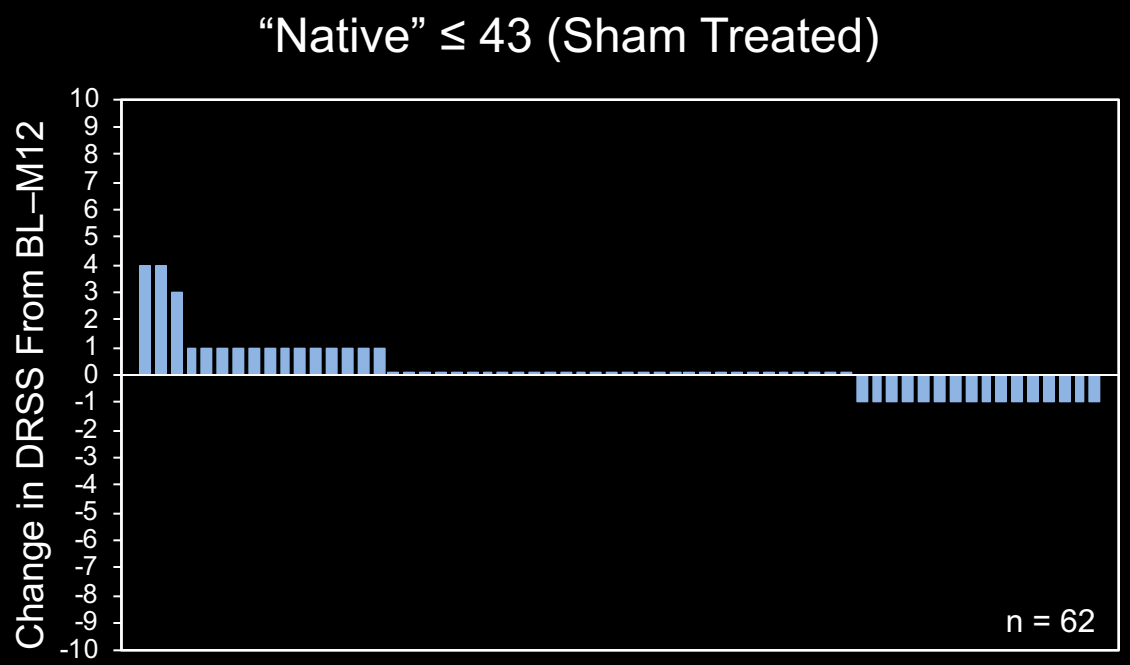
NPDR, nonproliferative diabetic retinopathy; OLE, open-label extension.

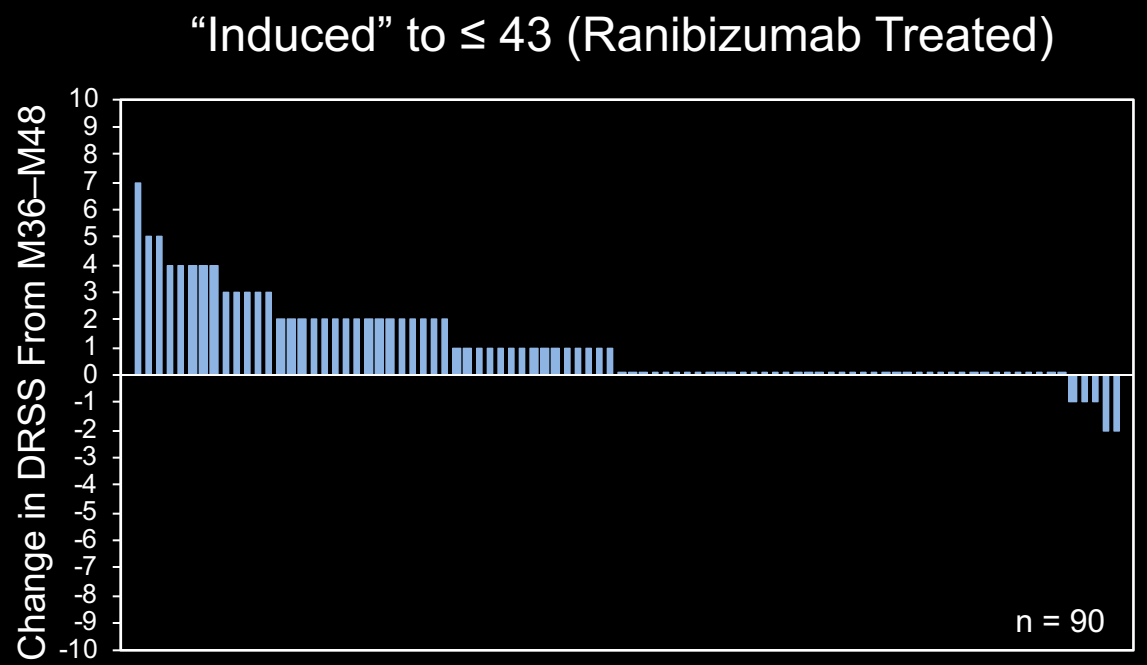
DRSS Changes in Patients Receiving Ranibizumab in RISE/RIDE and OLE



BL, baseline; DRSS, Diabetic Retinopathy Severity Score; M, month; OLE, open-label extension.

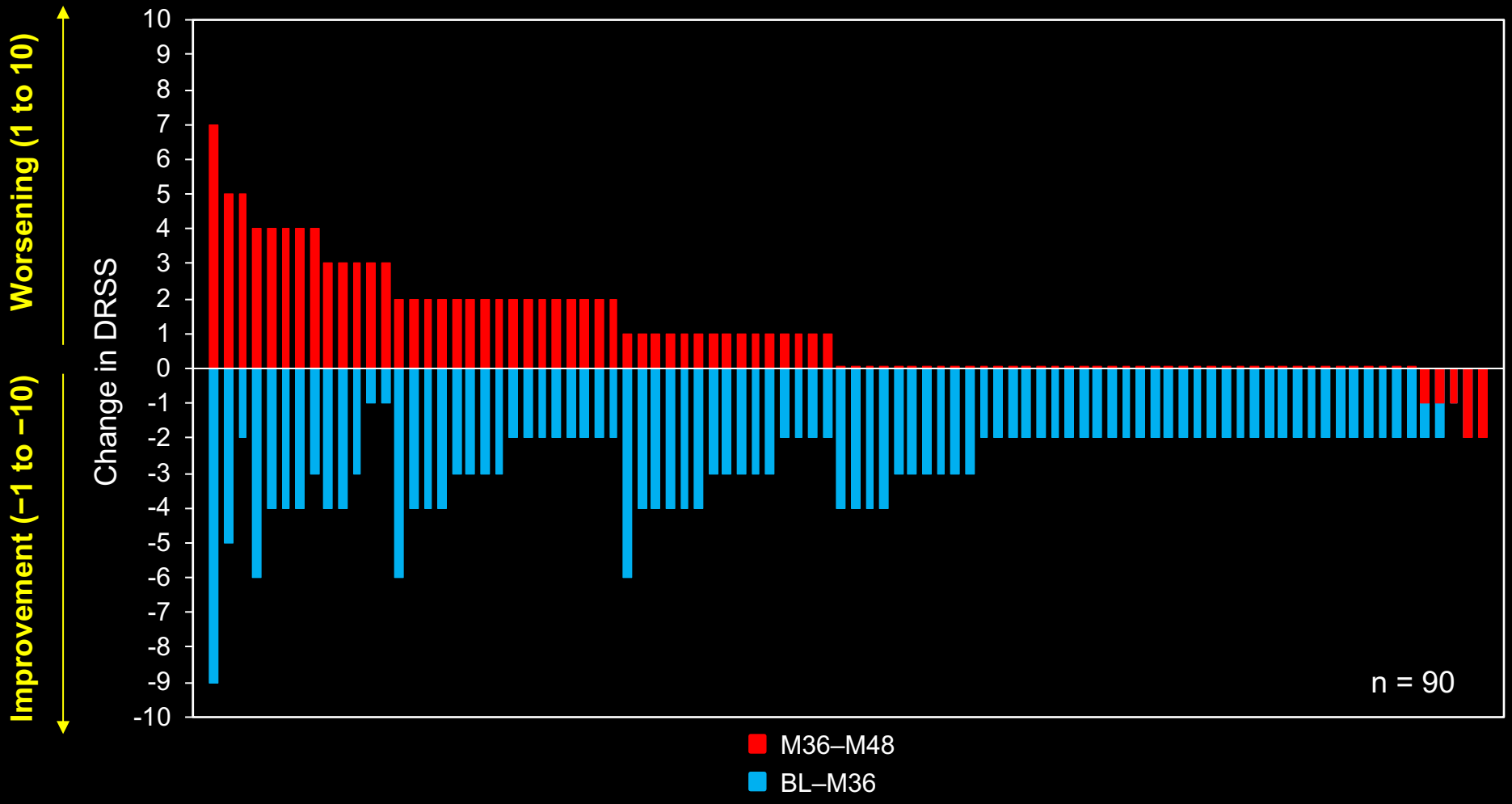
The “Native” Mild NPDR Appears to be More Stable Than the “Induced” NPDR





BL, baseline; DRSS, Diabetic Retinopathy Severity Score; M, month; NPDR, nonproliferative diabetic retinopathy.

Patients With “Induced” Mild NPDR: DR Severity Changes Before and After M36



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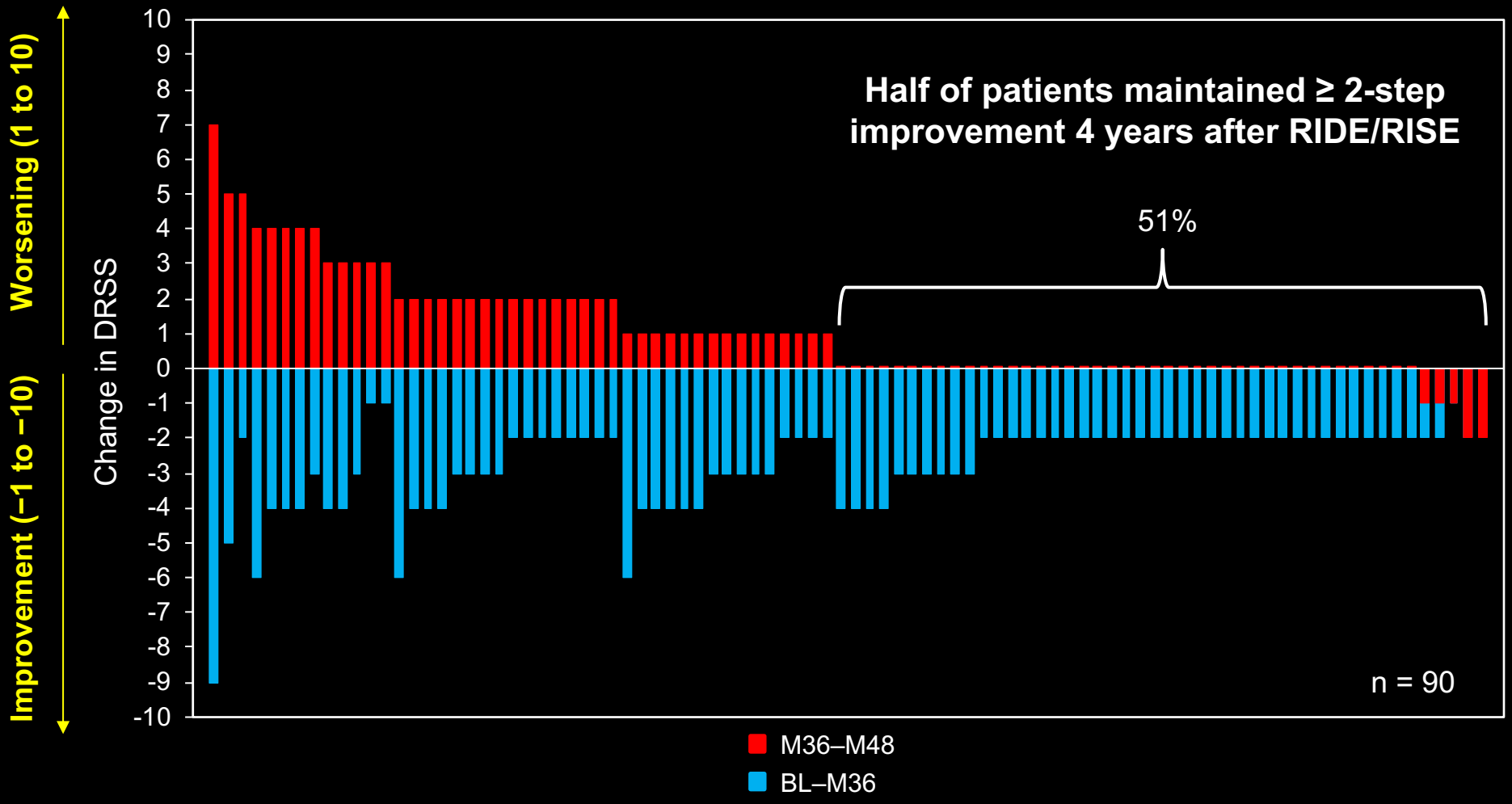
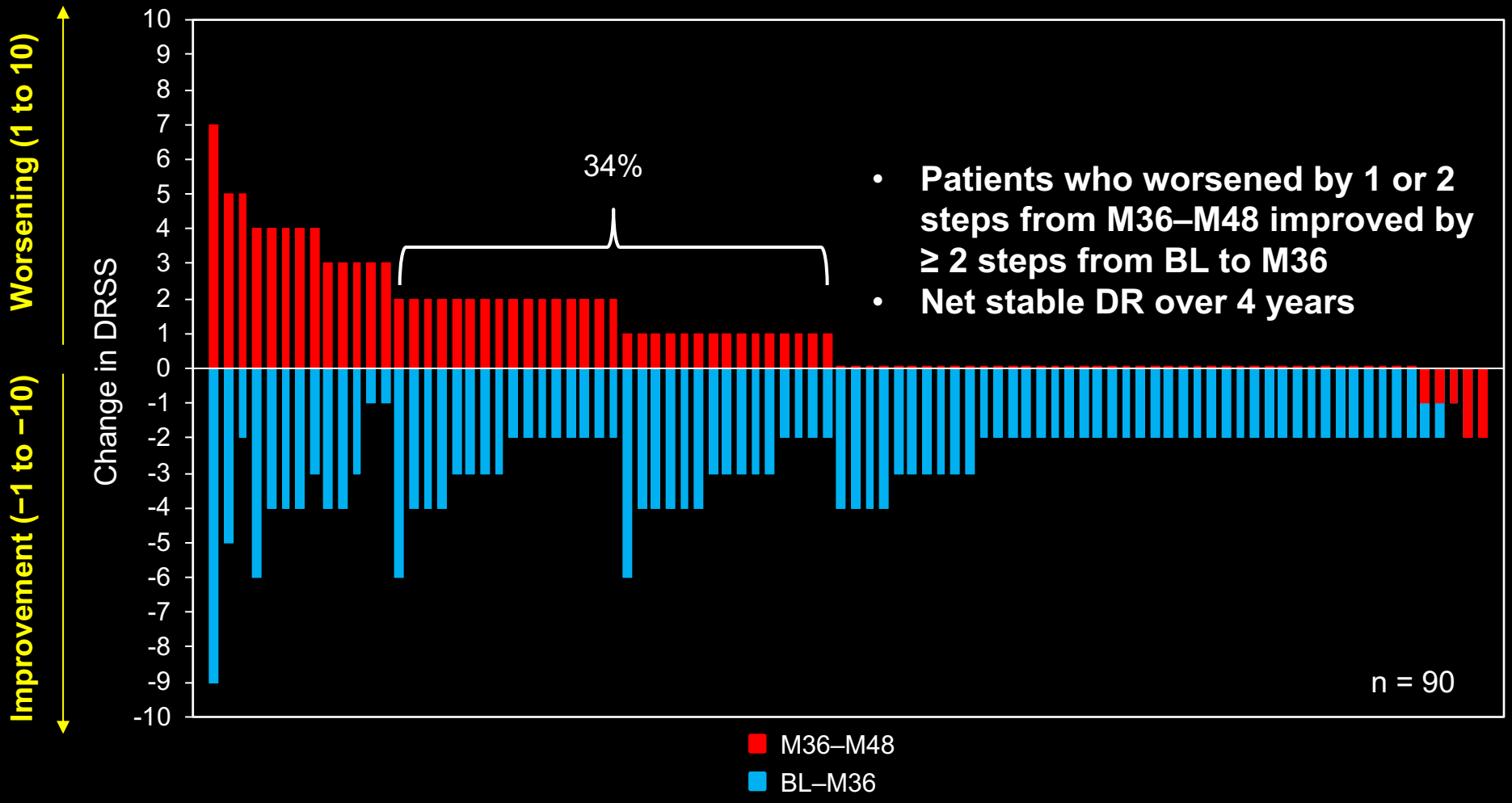
Patients With “Induced” Mild-to-Moderate NPDR: DR Severity Changes Before and After M36



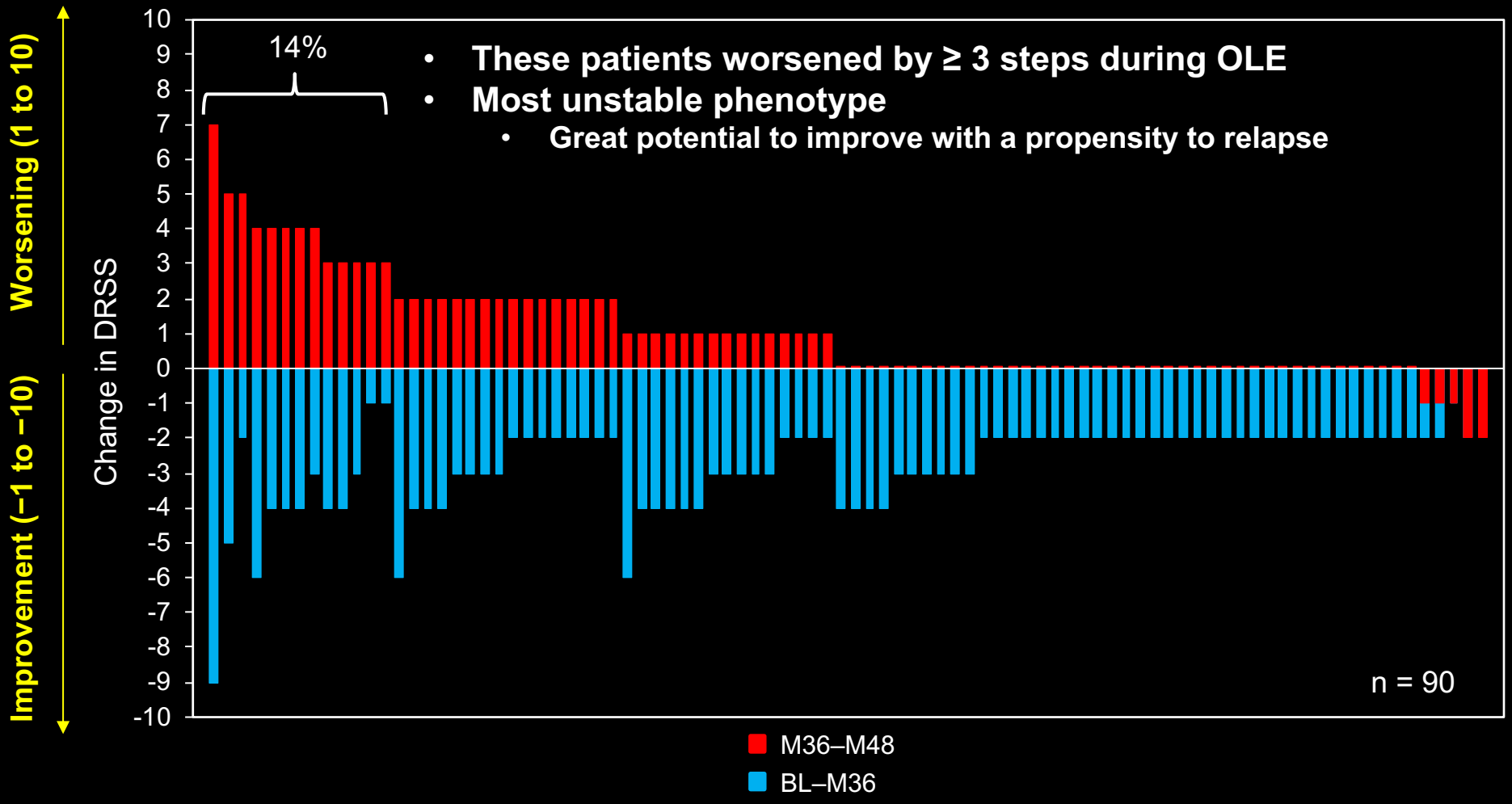
BL, baseline; DRSS, Diabetic Retinopathy Severity Score; M, month; NPDR, nonproliferative diabetic retinopathy.

Patients With “Induced” Mild-to-Moderate NPDR: DR Severity Changes Before and After M36



BL, baseline; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; M, month; NPDR, nonproliferative diabetic retinopathy.

Patients With “Induced” Mild-to-Moderate NPDR: DR Severity Changes Before and After M36



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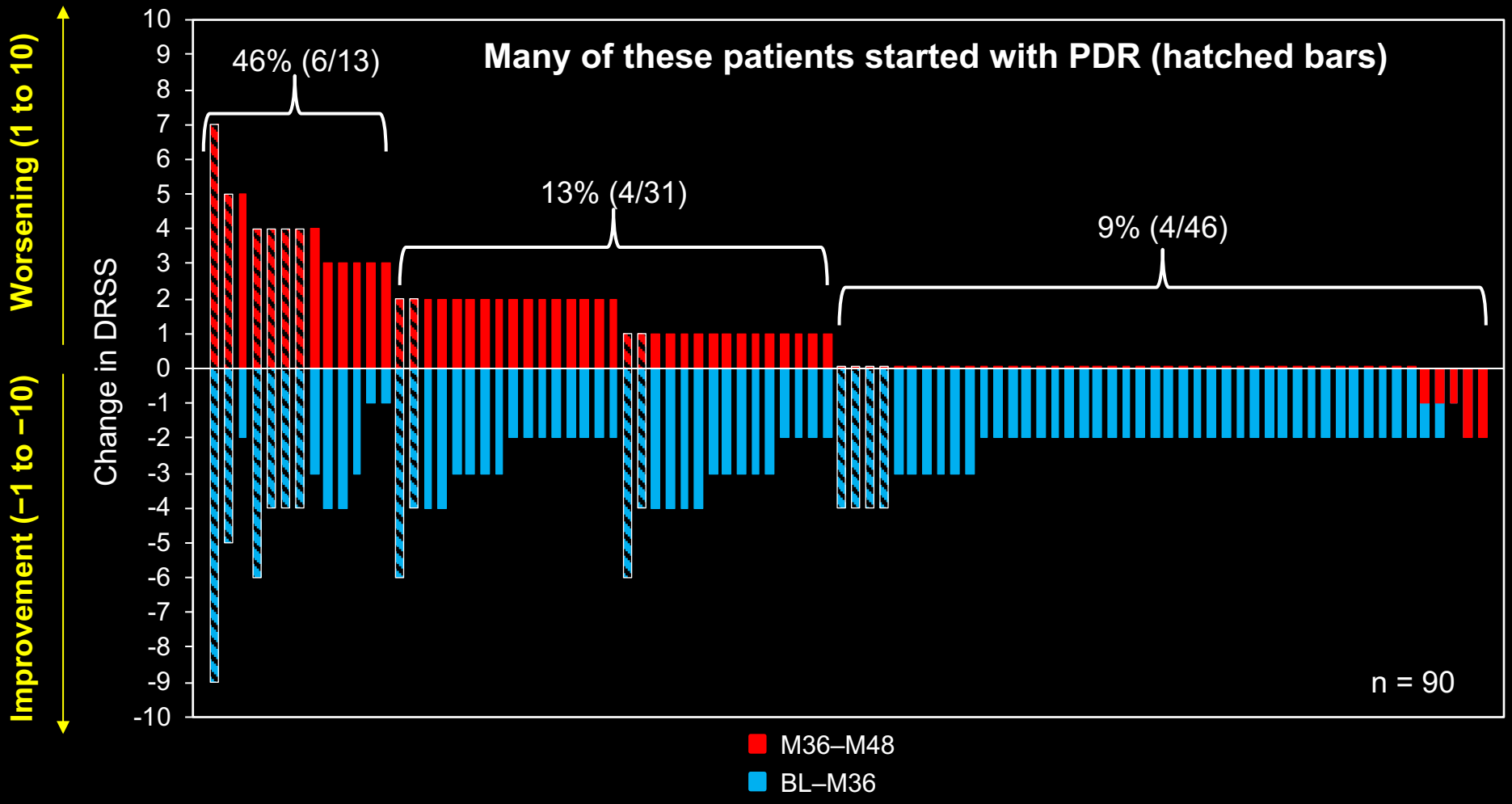
Patients With “Induced” Mild-to-Moderate NPDR: DR Severity Changes Before and After M36



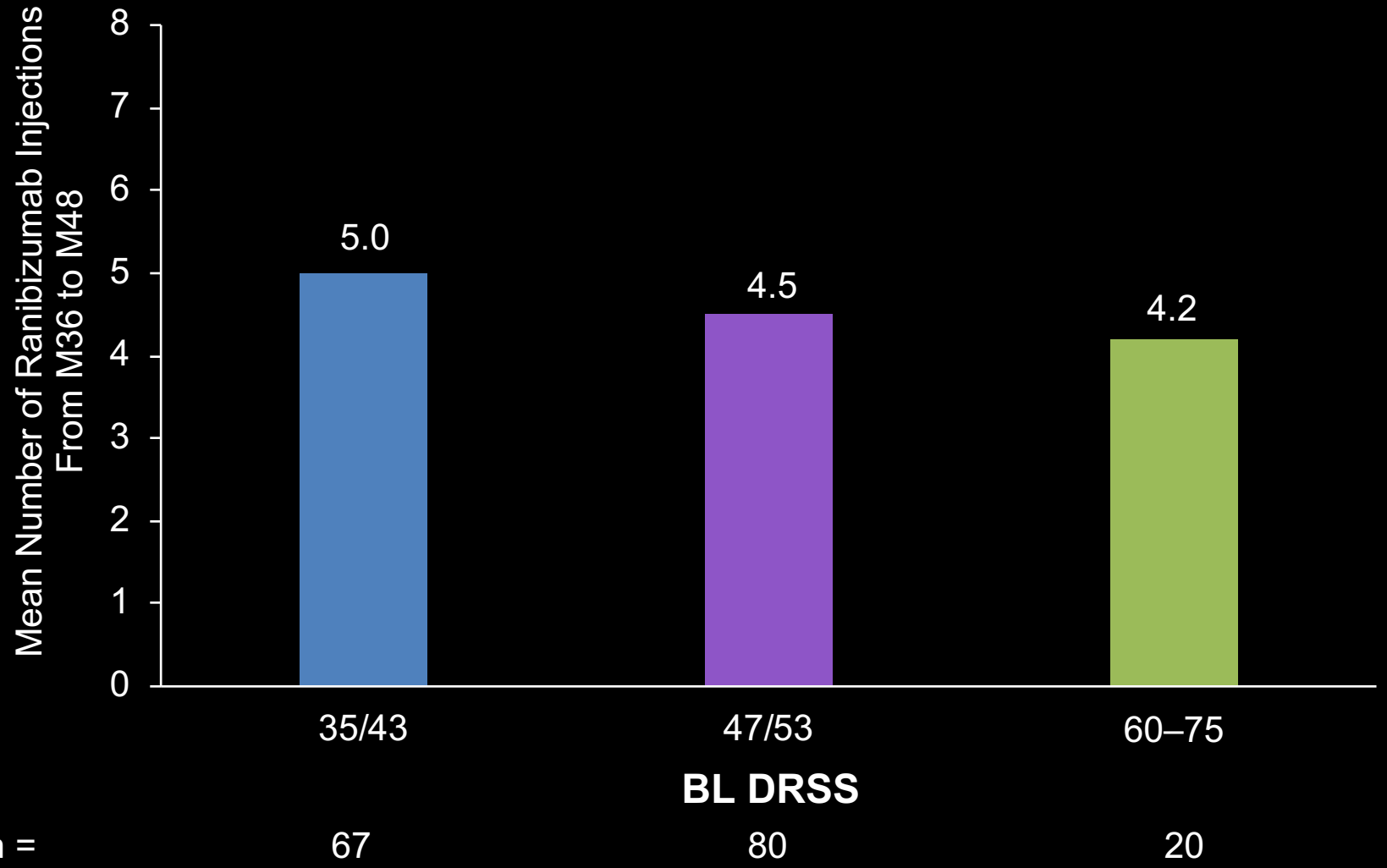
BL, baseline; DRSS, Diabetic Retinopathy Severity Score; M, month; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

What if we look at a broader patient population?

- Not just those eyes that improved to mild/moderate NPDR during RISE/RIDE
- How does BL DR severity impact changes in DRSS with regular treatment, followed by intermittent treatment?

BL, baseline; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; NPDR, nonproliferative diabetic retinopathy.

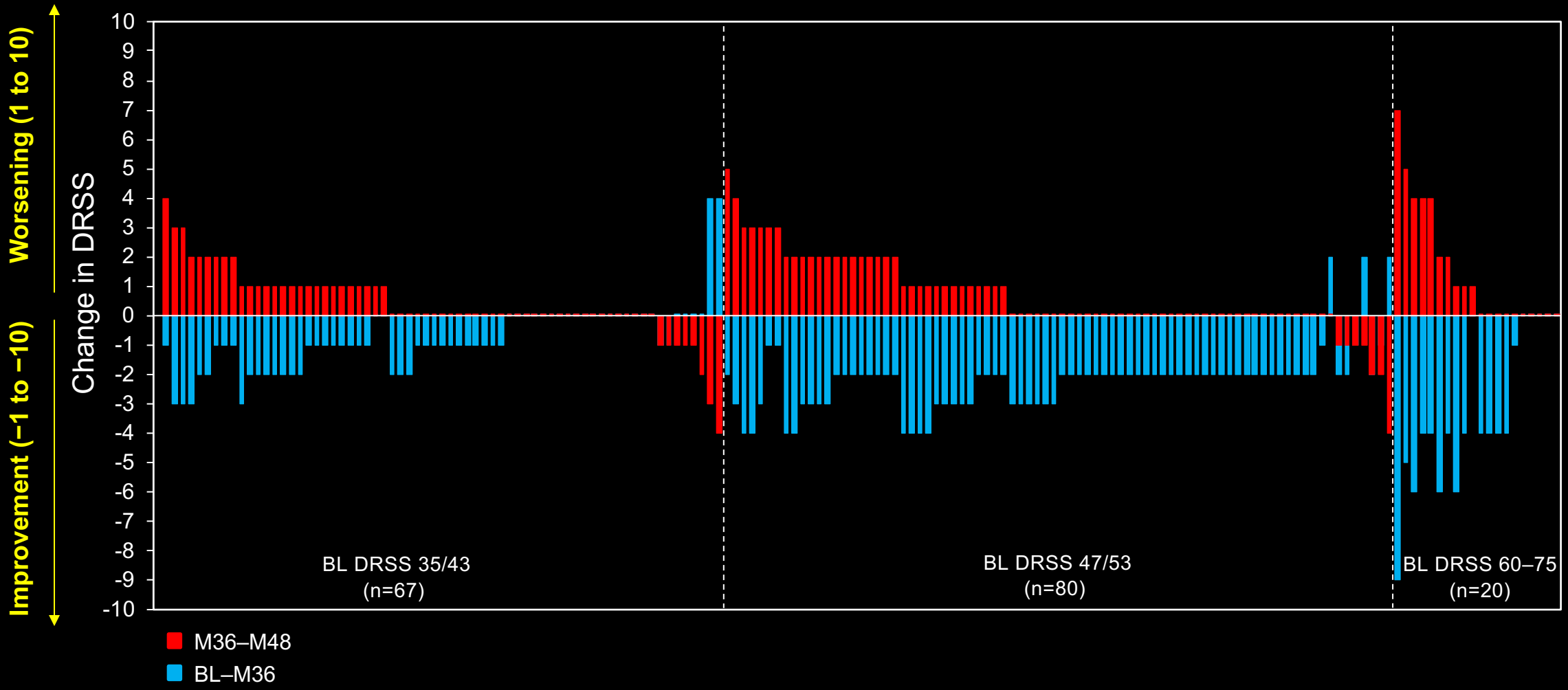
Patients Received an Average 4–5 Ranibizumab Injections During OLE, Regardless of BL DRSS



This analysis includes 167 patients from OLE who were randomized to ranibizumab treatment during RISE/RIDE, and who did not have DRSS better than 35, or the presence of PRP at baseline
BL, baseline; DRSS, Diabetic Retinopathy Severity Score; M, month; OLE, open-label extension.

Note: Slide is animated and best viewed in Presentation Mode

DRSS Changes in Patients Receiving Ranibizumab with Baseline PDR Were the Most Unstable Over RIDE/RISE and OLE



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BL, baseline; DRSS, Diabetic Retinopathy Severity Score; M, month; OLE, open-label extension.

Conclusions

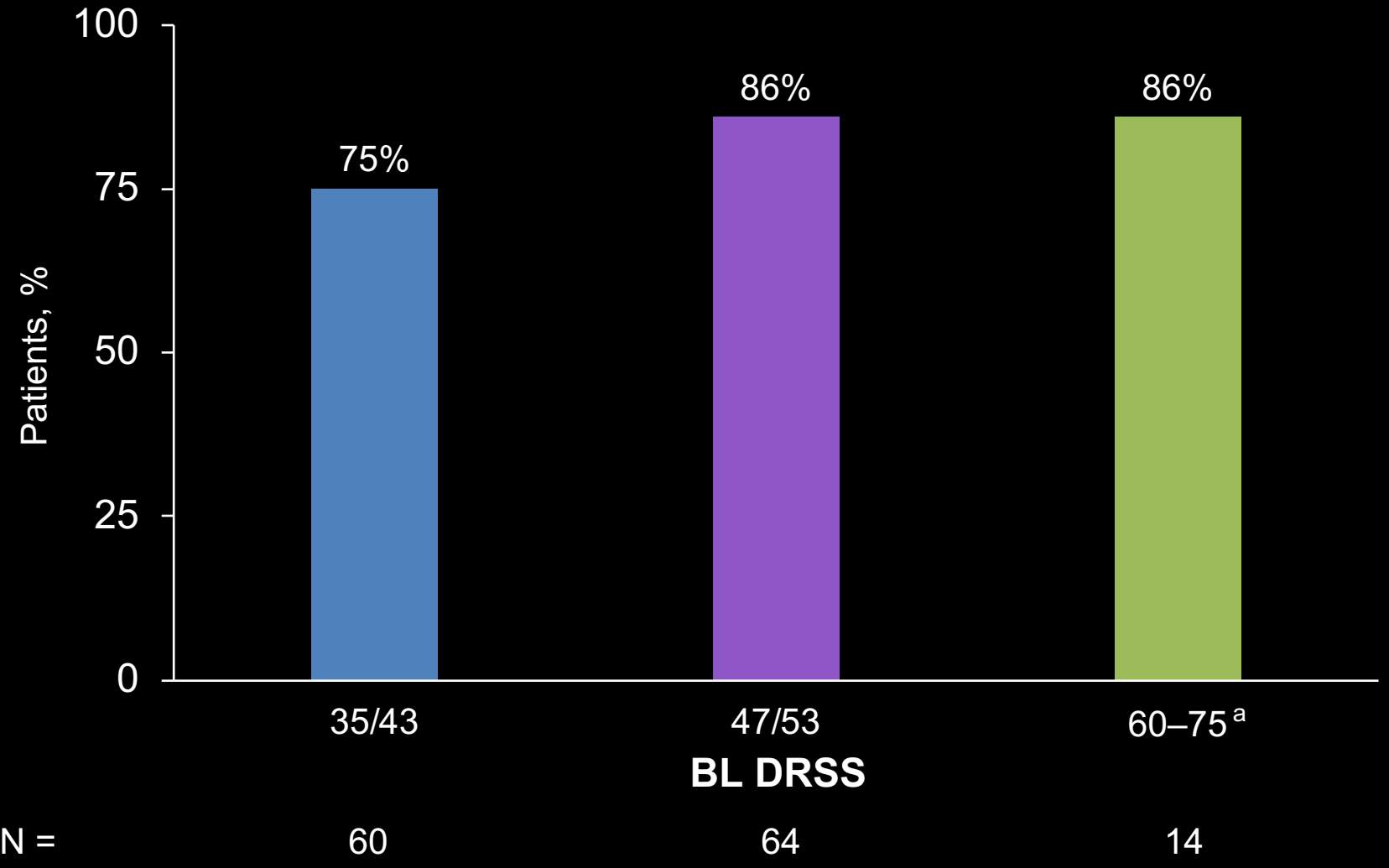
- The majority of ranibizumab-treated patients were able to improve or maintain their DRSS with less-than-monthly treatment
  - Some minimum treatment may be necessary to maintain DRSS improvement
- Regardless of BL DRSS, patients received an average of 4–5 injections during OLE
  - Continuous long-term monitoring and treatment may be necessary to maintain DRSS stability
- More severe DR at BL may be indicative of more unstable DRSS changes with intermittent dosing
- Small patient sample is an important limitation of this analysis

BL, baseline; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Score; OLE, open-label extension.

BACKUP

Instability in DRSS in Sham-Treated Patients

Majority Improved or Maintained BL DRSS Through M12

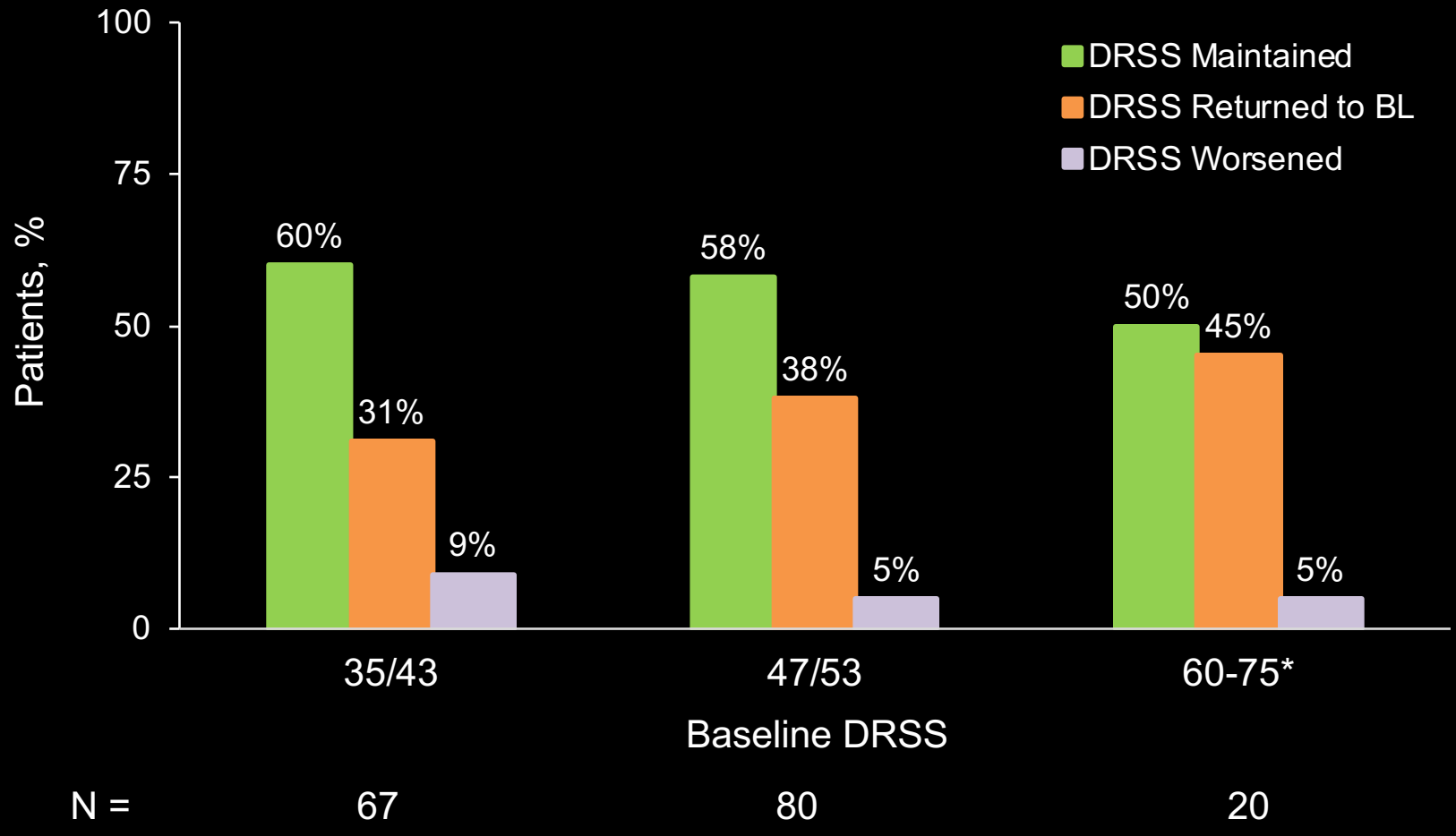


[a] Without prior panretinal photocoagulation.

BL, baseline; DRSS, Diabetic Retinopathy Severity Score; M, month.

Note: Slide is animated and best viewed in Presentation Mode

Majority of Patients Improved or Maintained Their DRSS From M36 to M48 on PRN Treatment



[a] Without prior panretinal photocoagulation.

DRSS response was defined as ≥ 0 step improvement from M36 to M48 (improved or maintained) or ≥ 1 step DRSS worsening from M36 to 48 (worsening).

DRSS, diabetic retinopathy severity score; M, month; OLE, open-label extension; PRP, panretinal photocoagulation.