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Has the Time Come to Re-evaluate the Treatment Paradigm for Diabetic Retinopathy?

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Purpose:
To examine whether current evidence support a paradigm shift towards earlier intervention in patients with diabetic retinopathy (DR).

Methods:
We reviewed clinical trials and real-world studies that assessed disease progression and/or anti-vascular endothelial growth factor (VEGF) treatment in patients with DR, including RIDE/RISE, PANORAMA, Protocol I, and American Academy of Ophthalmology IRIS® Registry analyses.

Results:
Among 53,535 patients with DR in US clinical practice, IRIS Registry analyses found that patients diagnosed with moderate nonproliferative DR (NPDR), severe NPDR, and proliferative DR (PDR) were 2.6, 3.6, and 4.0 times more likely to develop sustained blindness within 2 years, respectively, than those with mild NPDR. In RIDE/RISE, rates of ≥ 2-step DR worsening from baseline at month (M) 24 were highest among untreated fellow eyes with moderately severe or severe NPDR (DR Severity Scale [DRSS] 47–53) and lowest in ranibizumab-treated eyes with DRSS 47–53 (29% and 2%, respectively). High rates of ≥ 2-step DR improvement were reported in anti-VEGF-treated eyes with DRSS 47–53 at baseline: 78–81% among ranibizumab-treated eyes at M24 of RIDE/RISE (vs. sham, 12%), and 65–80% among aflibercept-treated eyes at M12 of PANORAMA (vs. sham, 15%). In Protocol I, rates of DR improvement over 5 years were consistently higher among ranibizumab-treated eyes with DRSS 47–53 at baseline, versus those with mild or moderate NPDR (DRSS 35–43) and PDR (DRSS > 60). Greater DR improvement was associated with greater mean vision gains in RIDE/RISE: mean change in best-corrected visual acuity from baseline at M24 was +5.0 letters in ranibizumab-treated eyes with any DR worsening at M24, increasing to +15.1 letters in those with ≥ 3-step DR improvement.

Conclusions:
Analyses of real-world data have associated PDR with the development of sustained blindness in clinical practice. Meanwhile, landmark trials showed that patients with moderately severe or severe NPDR were vulnerable to DR progression without treatment, and more likely to achieve DR improvement with anti-VEGF therapy. Given the trend towards greater mean vision gains with greater DR improvement in RIDE/RISE, these data collectively suggest that the time has come to consider earlier intervention to delay progression towards PDR.