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

Sophie Bakri, MD
Rochester, MN
Lauren Hill, MS, Steven Blotner, MS, Ivaylo Stoilov, M.D.

Purpose:
There is a lot of interest in understanding the clinical significance of diabetic retinopathy (DR) improvement on the classic Early Treatment Diabetic Retinopathy Study (ETDRS) scale. We investigated if vision outcomes in patients with DR and diabetic macular edema treated with intravitreal ranibizumab (0.3 or 0.5 mg) are impacted by concomitant changes in DR severity.

Methods:
A meta-analysis was conducted evaluating study eyes treated with ranibizumab from RIDE/RISE (NCT00473382/NCT00473330), Protocol I (NCT00444600), Protocol T (NCT01627249), and Protocol S (NCT01489189). Analyses of this pooled patient population were stratified by change from baseline at month 24 in ETDRS DR Severity Scale (DRSS) score. Outcomes evaluated included change from baseline to month 24 in best-corrected visual acuity (BCVA), central subfield thickness (CST) over time, as well as frequency of ≥ 15 ETDRS letter gain/loss at month 24.

Results:
There were 1118 patients included from the meta-analysis. There was a trend towards greater BCVA gains as DRSS improved from baseline to month 24 (any DR worsening, 6.5 letters [95% CI, 2.3, 10.7]; no change, 8.6 letters [7.1, 10.0]; 1-step improvement, 10.2 letters [8.7, 11.8]; 2-step improvement, 12.4 letters [10.6, 14.1]; ≥ 3-step improvement, 11.1 letters [8.9, 13.2]). Approximately 44% of eyes with a 2-step DRSS improvement had an ≥ 15-letter gain (89/204), while 24.2% of eyes with any DRSS worsening had an ≥ 15-letter gain (16/66). There was a trend towards a greater CST reduction from baseline, with DRSS improvements at month 24 (any DRSS worsening, −125.8 µm [−165.9, −85.7]; no change, −141.1 µm [−155.6, −126.6]; 1-step improvement, −168.0 µm [−187.2, −148.8]; 2-step improvement, −209.2 µm [−230.2, −188.3]; ≥ 3-step DRSS improvement, −223.3 µm [−256.7, −190.0]).

Conclusions:
In a meta-analysis of patients with DR receiving monthly ranibizumab, there was a trend for better vision outcomes and reduction in CST in patients experiencing greater DR severity improvements.