Clinical Trial Versus Real-world Outcomes With Anti-vascular Endothelial Growth Factor Therapy for Central Retinal Vein Occlusion

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Purpose:
To assess the impact of monitoring and anti–vascular endothelial growth factor (VEGF) injection frequency on vision outcomes in patients with central retinal vein occlusion (CRVO).

Methods:
We performed a cross-trial comparison between controlled clinical trials, long-term extension (LTE) studies, and real-world studies that assessed intravitreal anti-VEGF therapy in patients with macular edema due to CRVO. Published data were used to compare average injection frequencies and best-corrected visual acuity (BCVA) outcomes achieved with as-needed (PRN) anti-VEGF treatment regimens over 12 months. In a post hoc analysis of the HORIZON LTE trial (NCT00379795), we additionally assessed 12-month injection frequencies and BCVA outcomes among ranibizumab-treated patients with CRVO, stratified by PRN injection frequency during CRUISE (NCT00485836).

Results:
Our cross-trial comparison included 5 controlled clinical trials (most with monthly monitoring), 4 LTE studies (most with less-than-monthly monitoring), and 2 real-world studies (monitored per investigator discretion). On average, clinical trial subgroups received 7.8–11.8 injections over 12 months, compared with 3.3–4.5 and 1.5–5.1 injections in LTE and real-world studies, respectively. With frequent injections and close monitoring, estimated mean BCVA gains over 12 months ranged between 10.7–21.9 letters across clinical trial subgroups; however, these gains were not maintained in subsequent LTE studies (mean BCVA change over 12 months, −7.6 to 1.5 letters), nor achieved in real-world studies (4.1–7.1 letters). Moreover, our post hoc analyses found that greater need for injections during CRUISE (with monthly monitoring) was associated with greater vision loss during HORIZON (with less-than-monthly monitoring). On average, patients with CRVO who received 0, 1–3, 4–5, and 6 PRN injections in CRUISE (n = 177) went on to receive 0.0, 2.4, 3.7, and 4.3 PRN injections over 12 months in HORIZON, respectively, and experienced BCVA losses of 4.3, 2.7, 4.5, and 6.6 letters over this period.

Conclusions:
In real-world and LTE studies, patients with CRVO had less frequent visits, received fewer anti-VEGF injections, and did not achieve or maintain vision gains observed in clinical trials. These data highlight the need for new strategies that extend the durability of treatment for macular edema in CRVO, reduce treatment burden, and improve real-world vision outcomes.