Panretinal Photocoagulation Versus Ranibizumab for Proliferative Diabetic Retinopathy: Patient-Centered Outcomes in a Randomized Clinical Trial

- Calvin E. Mein, MD

OBJECTIVE Compare patient-centered outcomes from vision-related quality of life questionnaires and driving-related outcomes in eyes treated with ranibizumab vs PRP for proliferative diabetic retinopathy (PDR).

PURPOSE To compare questionnaire responses (NEI VFQ-25, UAB-LLQ, WPAIQ) and driving-related outcomes for eyes treated with ranibizumab vs PRP for PDR. Two-year vision outcomes were non-inferior with ranibizumab and several secondary outcomes favored ranibizumab (e.g., frequency of vitrectomy, development of central-involved DME). Patient-centered outcomes may influence treatment choice.

METHODS Pre-specified secondary outcomes and post-hoc analyses of a randomized clinical trial conducted at 55 US sites among 305 adults (394 eyes) with PDR assigned to ranibizumab or PRP (mean age 52 years; 44% women; 52% white). Analyses were conducted for the 216 participants with one study eye. Participants were at least 18 years old and had type 1 or type 2 diabetes mellitus. The National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25), University of Alabama Low Luminance Questionnaire (UAB-LLQ) and Workplace Productivity and Activity Impairment

Questionnaire (WPAIQ) were evaluated at baseline, 1, and 2 years (the primary endpoint of the trial).

RESULTS At 2-years the adjusted treatment group differences (ranibizumab-PRP) in change from baseline questionnaire score (99% CI) were +2.1 (-3.6, +7.9) for the NEI VFQ-25 composite, +2.1 (-4.7, +8.9) for the UAB-LLQ composite, and -4.3% (-14.5, +5.9) for the WPAIQ work productivity loss score. There were no statistically significant differences between the ranibizumab and PRP groups at 1 or 2 years for any of the subscales. Results were similar for the subgroup of participants where the study eye was the better-seeing eye at baseline. No differences were found in the NEI VFQ-25 or UAB-LLQ peripheral vision subscales, despite significant differences in Humphrey visual fields testing. In the ranibizumab group 96% of participants had at least one eye seeing 20/40 or better at the 2 year visit (the lower legal limit for driving in most states) compared with 88% in the PRP group (P=0.006).

CONCLUSION Patient-centered outcomes through 2 years provide further support to consider anti-VEGF for PDR as an alternative to PRP. There were no confident differences identified in questionnaire scores, while driving outcomes tended to favor the ranibizumab group. Questionnaire scores mirrored differences in visual acuity, which were more strongly in favor of ranibizumab at year 1 than year 2.

TAKE HOME MESSAGE Patient-centered outcomes through 2 years provide further support to consider anti-VEGF for PDR as an alternative to PRP.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Randomized Trial of PRP vs Intravitreal Ranibizumab Plus Deferred PRP for Proliferative Diabetic Retinopathy: Treatment Algorithm and Outcomes

- Andrew N. Antoszyk, MD

OBJECTIVE Review of treatment algorithm from a randomized clinical trial for eyes with proliferative diabetic retinopathy treated with intravitreous ranibizumab or panretinal photocoagulation (PRP).

PURPOSE To evaluate treatment course from a randomized clinical trial comparing intravitreous ranibizumab (ITV-R) with panretinal photocoagulation (PRP) for proliferative diabetic retinopathy (PDR).

METHODS Adults with PDR were randomly assigned to prompt PRP (N=203) or 0.5-mg ITV-R (N=191) with deferred PRP per protocol. First 6 months, most eyes received monthly ITV-R, with treatment deferral at months 4 and 5, only if neovascularization (NV) had resolved. Injections continued unless NV had stabilized for 3 consecutive visits or resolved. PRP was allowed if NV worsened despite anti-VEGF therapy. In both treatment groups, eyes with diabetic macular edema (DME) and vision impairment at baseline had to receive ITV-R and could receive ITV-R for treatment of DME that developed during follow-up at investigator discretion, with a DRCR.net DME treatment algorithm provided as a guideline.

RESULTS The primary results of the study identified that among eyes with PDR, treatment with ranibizumab resulted in a mean visual acuity change (+2.8 letters) that was non-inferior to (not worse than) PRP treatment at two years (+0.2 letters). In the ranibizumab group that completed their 2-year visit, the median (25^{th}, 75^{th} percentile) number of injections through 2 years in eyes with (N=33) and without (N=126) baseline DME were 14 (10, 17) and 10 (6, 13), respectively. Ninety-seven percent of protocol-required injections for NV were given and were based on clinician assessment of NV status. In the ranibizumab group, 12 eyes (6%) received PRP including 8 during vitrectomy before 2 years. In the PRP group (N=203), all eyes received PRP at baseline and 92 (45%) received additional PRP with the median time to application of 7 months. In the prompt PRP group, 108 (53%) eyes received ranibizumab for DME; 72 (35%) at baseline and an additional 36 (18%) during follow-up.

CONCLUSION The results of the Protocol S were obtained with a DRCR.net treatment algorithm using 0.5 mg ranibizumab for PDR that led to non-inferior visual acuity outcomes at 2 years compared with PRP and the rare need for PRP for failure of ranibizumab to control the PDR NIDDK, NIH, DHHS EY14231, EY23207, EY18817. Genentech provided the ranibizumab for the study and funds to offset site costs.

TAKE HOME MESSAGE Treatment of PDR with 0.5 mg ranibizumab according to the DRCR.net treatment algorithm led to the rare need for PRP for failure while resulting in non-inferior vision compared with PRP treatment.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Cost Utility Comparsion Between Panretinal Photocoagulation vs Intravitreal Ranibizumab for Proliferative Diabetic Retinopathy

- Jonathan S. Chang, MD
- James Lin, MD
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OBJECTIVE Compare the cost-utility of panretinal photocoagulation (PRP) and intravitreal ranibizumab (IVL) according to the results of the Diabetic Retinopathy Clinical Research Network (DRCR) Protocol S.

PURPOSE The DRCR Protocol S recently demonstrated the effectiveness of anti-VEGF agents in management of proliferative diabetic retinopathy (PDR). A model of cost-utility was created that mirrored Protocol S, comparing PRP and IVL in primary management of PDR.

METHODS A cost-utility analysis utilizing Markov-style modeling was designed based on results from DRCR Protocol S. Two groups were modeled, one based on the group of patients initially treated with PRP and a second based on the group treated with IVL. Patients costs were based on the Center for Medicare and Medicaid Services Relative Value Units and included laser treatment, intravitreal injections, optical coherence tomography, photography, office visits and vitrectomy. Quality-adjusted life-year (QALY) data were adapted and an estimate of 8 lines of vision saved were used to determine cost per QALY. Calculations were performed for both facility and non-facility billing in the Manhattan, NY area.

RESULTS In cases with PRP as primary treatment the total imputed cost with facility billing with hospital surgery for 2 years of treatment was $9,854. The cost per line of vision saved was $1,232, and the cost per line-year saved was $41. The cost per QALY

was $1357. In the non-facility setting, the total cost for the same length of treatment was $7,119. The cost per line of vision saved was $890. The cost per line-year saved was $29, while the cost per QALY was $980. For patients receiving IVL as initial treatment with facility billing, the total imputed cost was $21,631. The cost per line saved was $2,704, the cost per line-year saved was $92, and the cost per QALY was $3,073. In the non-facility setting, the total imputed cost for PDR treated initially with IVL was $17006. The cost per line was $2126, the cost per line-year saved was $72, and the cost per QALY was $2416.

CONCLUSION Both PRP and IVL fall within the cost/QALY range of $50,000-100,000 that is generally considered acceptable. Clinicians can feel secure that treatment, even with combination therapy, is effective and provides value. These costs fall in line with previously outlined studies of cost-utility for other retinal conditions.

TAKE HOME MESSAGE When panretinal photocoagulation or intravitreal injection of ranibizumab are used as initial treatment for proliferative diabetic retinopathy, it is cost-effective.