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Cost Evaluation of Laser versus Intravitreal Aflibercept for Proliferative Diabetic Retinopathy

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Diabetic retinopathy affects 8 million Americans with diabetes and proliferative diabetic retinopathy (PDR) is associated with severe vision loss. The Diabetic Retinopathy Study (DRS) established panretinal photocoagulation (PRP) as an effective treatment for PDR. Reports including randomized clinical trials^{1,2} have established intravitreal ranibizumab (TVR) as a noninferior treatment option for PDR. The Diabetic Retinopathy Clinical Research (DRCR) Protocol S showed that eyes treated with TVR had less macular edema, visual field loss, and need for pars plana vitrectomy compared with PRP.

Although patients with coexisting diabetic macular edema (DME) and PDR may derive concurrent benefit from intravitreal anti-vascular endothelial growth factor treatment, concern about the financial impact of chronic intravitreal injections and the burden of continuous follow-up visits has been expressed. Cost analyses based on Protocol S have shown that both TVR and, more so, PRP have acceptable cost per quality-adjusted life-year (QALY), but extrapolated over a lifetime, the cost differential grows.³

Intravitreal aflibercept (IVA) was approved for treating diabetic retinopathy with DME, like ranibizumab, in 2015. Moreover, whereas ranibizumab has also been approved for treating diabetic retinopathy (i.e., PDR), IVA has not been approved for use with PDR without DME. Only 1 prospective, multicenter, single-masked, randomized clinical trial has evaluated IVA for PDR, the CLARITY trial (Clinical efficacy of intravitreal aflibercept versus panretinal photocoagulation for best corrected visual acuity in patients with proliferative diabetic

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HUMAN SUBJECTS: This study does not include human subjects/tissues. No animal subjects were used in this study. The study was exempt from internal review board approval because no patient information was accessed.

retinopathy at 52 weeks).⁴ The 1-year results demonstrated IVA to be an acceptable alternative to PRP (noninferior) and reported a 4-letter superior visual outcome.

The purpose of this report is to provide a cost analysis of treatment of PDR with aflibercept versus PRP using the published CLARITY data.

This cost analysis used published data from the CLARITY trial.⁴ The study was exempt from internal review board approval because no patient information was accessed. Medicare fee data for 2017 in the Miami, Florida area were used to calculate the costs range from facility (hospital-based) to nonfacility (office-based) practice settings.

A decision analysis, modeled for each treatment scenario, included 1-year costs for IVA, office visits, imaging, PRP, and vitrectomy as encountered in the CLARITY trial and assumptions for years 2 and 3 and beyond assuming survival per Social Security Administration actuarial tables (Table S1, available at www.aaojournal.org). The utility values for PRP were calculated as previously published,⁴ based on DRS visual results, assuming second eye utility values as per previously published time tradeoff utility values for ocular diseases. CLARITY was designed for noninferiority, but reported 4-letter IVA benefit compared with PRP, so we modeled 2 separate scenarios: equal utility and 0.8-line IVA advantage.

The Current decision analysis study demonstrates that the 1-year IVA cost and cost/QALY to be 2.8 to 5.1 times less favorable than PRP and 10 times for lifetime estimates. PRP remains well below the \$50 000 to \$100 000/QALY range, whereas IVA measures substantially above it, even assuming 4-letter superiority.

A similar analysis using published 2-year DRCR Protocol S data concluded that IVR was less cost-effective than PRP; although both treatments were within acceptable levels of cost/QALY, the study assumed no further treatment costs and a durable lifetime treatment effect. The estimated cost differential enlarged when projecting lifetime costs. Another cost analysis of Protocol S data⁵ found PRP more cost effective than IVR at the 2-year study mark, but observed IVR might have more favorable cost utility for patients with baseline DME. Utilization and results beyond the 2-year mark were not estimated.

This study is a model and is based on extrapolation of group data; therefore, it has several limitations. CLARITY excluded eyes with DME, a weakness that has been cited. Had these types of patients been included, IVA may have yielded more favorable, subthreshold cost/QALY. Second, assumptions (rather than data) were used to project lifetime costs and utility. Extrapolated rates in our analysis might overestimate the exact magnitude of costs, but they are likely to be substantially higher with IVA than PRP. However tenuous, such assumptions are required because lifetime use is so pertinent to evaluating cost-utility given the chronic nature of PDR.

It is clear from CLARITY and Protocol S that anti-vascular endothelial growth factor therapy is a highly effective treatment for PDR and may deliver slightly better visual acuity results than PRP, especially in patients with concurrent DME. However, this study impugns the fiscal dismissiveness inherent in the scientifically valid clinical trial reports. However,

the possibly marginal benefit of the substantially higher cost options, and the impact of more extensive, prolonged treatment burden on patient compliance should not be discounted. The authors of this study strongly stipulate, however, that financial considerations inherent in the current study are no substitute for currently established practice and clinical judgment.

Decision analysis modeling for management of PDR (without DME) using results from the CLARITY trial concluded that treatment with PRP is less costly with a favorable cost-utility profile compared with IVA. Over a lifetime of therapy, the cost and cost-utility differential presumably widens.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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