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Risk of RVO in Type 2 Diabetes: GLP-1 Receptor Agonists Versus DPP-4 Inhibitors

Dr. Mimi Maeusli:
You're listening to *Eye on Ocular Health* on ReachMD, and this is an *AudioAbstract*. I'm Dr. Mimi Maeusli, and today, we'll be discussing the impacts of different glucose-lowering agents on the risk of retinal vein occlusion, or RVO.

For context, RVO is the second most common retinal vascular disease after diabetic retinopathy. It's also a major cause of irreversible vision loss worldwide. Patients with type 2 diabetes are particularly vulnerable because of their high burden of vascular disease, which raises an important therapeutic question: can glucose-lowering agents influence the risk of RVO?

To answer this question, a multinational retrospective cohort study published in *Ophthalmology Science* in 2025 compared glucagon-like peptide-1 receptor agonists, or GLP-1 receptor agonists, with dipeptidyl peptidase-4 inhibitors, or DPP-4 inhibitors. Using the TriNetX global database, the investigators analyzed electronic health records from more than 200 million patients across 21 countries. After propensity score matching, the final study population included nearly 80,000 patients with type 2 diabetes—half prescribed a GLP-1 receptor agonist and half a DPP-4 inhibitor.

Now looking at the results, GLP-1 receptor agonist use was associated with a significantly lower risk of RVO compared with DPP-4 inhibitors over a five-year follow-up. The hazard ratio for any RVO was 0.73, and for branch RVO it was 0.62. No significant difference was found for central RVO.

The protective association was actually strongest in certain high-risk groups: patients over age fifty, women, Black and Asian patients, those with hemoglobin A1c above eight percent, body mass index of thirty or higher, and diabetes duration of three years or more. In these groups, GLP-1 receptor agonist therapy was consistently linked with lower risk of both RVO overall and particularly branch RVO.

To test the robustness of these findings, the authors performed multiple sensitivity analyses, including adjustment for diabetic retinopathy and restriction to patients with ophthalmology visits. And across all scenarios, the results held steady.

So, why does this matter? GLP-1 receptor agonists are already known to reduce cardiovascular events in type 2 diabetes, while DPP-4 inhibitors have shown neutral or less favorable vascular effects. This study suggests that the benefits of GLP-1 receptor agonists extend to the microvasculature of the eye, lowering the risk of RVO—especially branch occlusion, which is more closely tied to atherosclerotic changes.

That said, there are some limitations. This was an observational study, so causality can't be proven. Diagnoses were based on coded electronic health records, which raises the risk of misclassification. And treatment dosing or adherence couldn't be assessed. Still, the large, multinational dataset and consistent findings across sensitivity analyses strengthen the conclusions.

So the takeaway for clinicians is that in patients with type 2 diabetes, GLP-1 receptor agonists appear to offer protection against RVO compared with DPP-4 inhibitors. When choosing second-line therapy, these findings add to the argument for GLP-1 receptor agonists, particularly in patients at elevated risk of ocular vascular complications.

This has been an *AudioAbstract* for *Eye on Ocular Health,* and I'm Dr. Mimi Maeusli. To access this and other episodes in our series, visit ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

Reference:
Pan SY, Weng CH, Tsai SF, et al. Risk of retinal vein occlusion between glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes: a retrospective cohort study. *Ophthalmol Sci.* 2025;5(4):100734.

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