Shifting Paradigms: Evaluating Risks of Retinopathy and Macular Edema with Insulin and Novel Oral Agents

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Background

- Diabetic retinopathy (DR) or macular edema (ME) are leading cause of vision impairment and blindness among working-age adults worldwide.
- Macular edema, the accumulation of fluid in the macula, can occur at any stage of DR and is a major cause of vision loss.
- In 2021 across all ages, an estimated 9.6 million people in the US were living with diabetic retinopathy.
- Of these, 1.84 million were living with vision-threatening diabetic retinopathy.
- Newer hypoglycemic drugs may offer additional protective benefits.

Objective

The aim of this study is to compare the impact of insulin versus newer oral agents in delaying retinopathy and macular edema in patients with Type 2 diabetes.

Methodology

- **Data Source**: Optum® Market Clarity Database
- **Patient identification**: ≥1 claim or EHR for insulin or GLP-1, SGLT-2, or DPP-4i treatment from Jan 1, 2009, through Dec 31, 2013.
- Patients aged over 50 years with both medical and pharmacy coverage and 10 years of continuous eligibility (CE) or clinical activity (CA) post-index period.
- No evidence of GLP-1, SGLT-2, or DPP-4i treatment during the 10-year follow-up period in patients taking insulin.
- No evidence of insulin treatment during the 10-year follow-up period in patients taking GLP-1, SGLT-2, or DPP-4i.
- **Index date**: The index date was the first medication date of insulin or GLP-1, SGLT-2, or DPP-4i.
- **Cohort :** Two intervention cohorts were determined: patients on SGLT2i, GLP1, or DPP-4i, and patients only on insulin, followed for 10 years.
- **Study Measures:** Patient demographics and diabetic retinopathy or macular edema outcomes during the follow-up period.
- **Statistical Methods:** Kaplan-Meier (KM) analysis to estimate the risk of developing diabetic retinopathy or macular edema, compared among the medication cohorts; all tests were two-sided at $\alpha=0.05*$.

Health Surveillance System | CDC References: 1. VEHSS Modeled Estimates: Prevalence of Diabetic Retinopathy (DR) | Vision and Eye
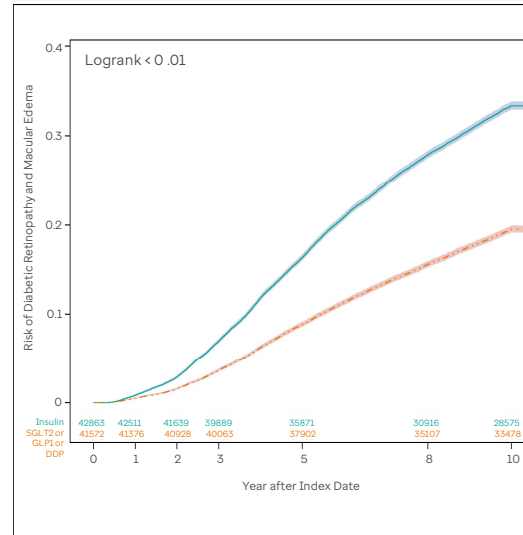
Results

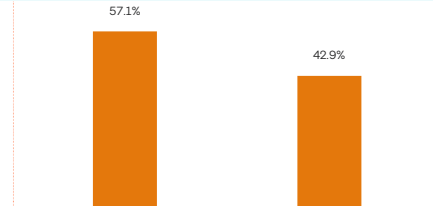Figure 1. KM Curve – Risk of DR or ME among Patients

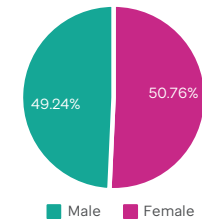Figure 2. Age distribution (in years) of DR or ME Patients

Figure 3. Gender distribution of DR or ME Patients

- A total of 41,572 patients treated with GLP-1, SGLT-2, or DPP-4i were identified (mean ± SD age: 62.81 ± 7.81 years; 50.80% females and 49.20% males; 84.56% Non-Hispanic Whites; and other ethnicities constituting the remaining 15.44%).
- A total of 42,863 patients treated with insulin were identified (mean ± SD age: 63.35 ± 7.91 years; 50.76% females and 49.24% males; 80.98% Non-Hispanic Whites; and other ethnicities constituting the remaining 19.02%).
- The 10-year cumulative incidence rate of diabetic retinopathy (DR) or macular edema (ME) in patients treated with insulin and SGLT2i, GLP1, or DPP-4i was 33.36% and 19.50%, respectively ($p<0.001$) (**Figure 1**). Newer drugs like SGLT2i, GLP1, or DPP-4i slow down the progression.

Conclusion

The data demonstrate that insulin remains the predominant treatment modality among patients with diabetic retinopathy or diabetic macular edema, while the use of SGLT2i, GLP1, or DPP-4i inhibitors as monotherapy potentially reduces the risk of diabetic retinopathy (DR) and macular edema (ME) compared to insulin.

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