Outcomes in Diabetic Macular Edema (DME) in Patients Who Used Systemic Dipeptidyl Peptidase-4 (DPP-4) Inhibitors in the VISTA and VIVID trials

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On behalf of the VIVID and VISTA study investigators
Ehsan Rahimy was a paid consultant for Allergan through the Fostering Innovative Retina Stars (FIRST) program at the time of this study.
Randomized, multicenter, double-masked trials in patients with clinically significant DME with central involvement and ETDRS BCVA 20/40 to 20/320
Randomized and Treated N=404 (VIVID) N=461 (VISTA®)

**Intravitreal Aflibercept injection (IAI)**
- 2 mg q4 wks

**IVT Aflibercept 2 mg q8 wks**
- Laser Control

**Primary endpoint:**
- Mean change in BCVA

**Key Secondary endpoints:**
- Change in DRSS
- Change in OCT

**Primary Endpoint:**
- Week 52
- Week 100

Rescue available beginning at week 24 (IAI for control group, laser for IAI groups)

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The VISTA and VIVID studies were funded by Regeneron Pharmaceuticals, Inc., Tarrytown, NY, and Bayer Healthcare, Berlin, Germany VISTA; Following 5 initial monthly doses

- IAI given q4 weeks or q8 weeks (following 5 monthly doses) significantly improved visual and anatomic outcomes over laser at week 52. These improvements were sustained through week 100 with both IAI regimens.

- In an integrated safety analysis, the most frequent serious ocular adverse event at week 100 was cataract (2.4%, 1.0%, and 0.3% for 2q4, 2q8, and control).

BCVA, best-corrected visual acuity; DME, diabetic macular edema; DRSS, Diabetic Retinopathy Severity Score; ETDRS, Early Treatment Diabetic Retinopathy Study; IAI, intravitreal aflibercept injection; OCT, optical coherence tomography; q4 wks, every 4 weeks; q8 wks, every 8 weeks
Recent evidence suggests that systemic DPP-4 inhibitor use in diabetics may be protective against the progression of DR\(^1\)

This post-hoc analysis examined whether DME patients taking systemic DPP-4 inhibitors differed in baseline characteristics and/or treatment outcomes in the VISTA and VIVID studies


DME; diabetic macular edema; DPP-4, dipeptidyl peptidase-4; DR, diabetic retinopathy
• Post-hoc analysis of integrated data from VISTA and VIVID
• Patients were categorized into two groups according to reported concomitant medication use at baseline:
  – Patients taking a DPP-4 inhibitor (+ DPP-4 inhibitor group)
  – Patients NOT taking a DPP-4 inhibitor (- DPP-4 inhibitor group)
• Analyses of baseline characteristics and treatment outcomes were conducted within each treatment group (laser, IAI 2q4, IAI 2q8)
• In patients receiving rescue treatment, data were censored from the time rescue treatment was given
**Methods**

**DPP-4 inhibitors included in this analysis**

1. Januvia (sitagliptin)
2. Onglyza (saxagliptin)
3. Tradjenta (linagliptin)
4. Nesina (alogliptin)
5. Janumet (combination of sitagliptin and metformin)
6. Jentadueto (combination of linagliptin and metformin)
7. Kazano (combination of alogliptin and metformin)
8. Komboglyze (combination of saxagliptin and metformin)
9. Oseni (combination of alogliptin and pioglitazone)
10. Juvisync (combination of sitagliptin and simvastatin)
Proportion of Patients by Baseline Concomitant Medication Class

(+) DPP-4

(-) DPP-4

DPP-4, dipeptidyl peptidase-4; IAI, intravitreal aflibercept; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks
### Baseline Characteristics

**BCVA, ETDRS Letters, mean (SD)**
- **(+)** DPP-4:
  - Laser: 62.3 (9.6)
  - IAI 2q4: 59.5 (10.9)
  - IAI 2q8: 62.0 (8.4)
- **(-)** DPP-4:
  - Laser: 60.0 (10.9)
  - IAI 2q4: 59.8 (10.8)
  - IAI 2q8: 58.6 (11.4)

**CRT, µm, mean (SD)**
- **(+)** DPP-4:
  - Laser: 502.5 (117.9)
  - IAI 2q4: 507.8 (146.7)
  - IAI 2q8: 476.6 (117.8)
- **(-)** DPP-4:
  - Laser: 510.7 (159.7)
  - IAI 2q4: 491.6 (151.2)
  - IAI 2q8: 501.4 (157.2)

**DRSS Score, n (%)**
- **(+)** DPP-4:
  - Low Risk (DRSS ≤ 43): 11 (31.4)
  - Moderate Risk (DRSS = 47): 5 (14.3)
  - High Risk (DRSS ≥ 53): 19 (54.3)
- **(-)** DPP-4:
  - Low Risk (DRSS ≤ 43): 97 (38.6)
  - Moderate Risk (DRSS = 47): 45 (17.9)
  - High Risk (DRSS ≥ 53): 109 (43.4)

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Integrated VISTA & VIVID. BCVA, best-corrected visual acuity; CRT: central retinal thickness; DPP-4, dipeptidyl peptidase-4; DRSS, Diabetic Retinopathy Severity Score; ETDRS, Early Treatment Diabetic Retinopathy Study; IAI, intravitreal aflibercept; SD, standard deviation; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks.
Mean BCVA Change

BCVA, best-corrected visual acuity; DPP-4, dipeptidyl peptidase-4; ETDRS, Early Treatment Diabetic Retinopathy Study; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks
Difference (-DPP4 vs +DPP4) in BCVA Change

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<th>Week 52</th>
<th>P-value</th>
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BCVA, best-corrected visual acuity; CI, confidence interval; DPP-4, dipeptidyl peptidase-4; IAI, intravitreal aflibercept; LS, least square; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks
Mean CRT Change

(+) DPP-4

Week

-81.2

-195.1

(-) DPP-4

Laser (n=35) 2q4 (n= 28) 2q8 (n= 44)

CRT, central retinal thickness; DPP-4, dipeptidyl peptidase-4; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks
Difference (-DPP4 vs +DPP4) in CRT Change

Treatment

Week 52
- Laser
- IAI 2q4
- IAI 2q8

Week 100
- Laser
- IAI 2q4
- IAI 2q8

P-value
- 0.3521
- 0.7396
- 0.4012
- 0.9410
- 0.9165
- 0.2560

CI, confidence interval; CRT, central retinal thickness; DPP-4, dipeptidyl peptidase-4; IAI, intravitreal aflibercept; LS, least square; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks
≥ 2-Step DRSS Score Improvement

DPP-4, dipeptidyl peptidase-4; DRSS, Diabetic Retinopathy Severity Score
Odds Ratio (-DPP4 vs +DPP4) for ≥ 2-Step DRSS Score Improvement

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CI, confidence interval; DPP-4, dipeptidyl peptidase-4; DRSS, Diabetic Retinopathy Severity Score; IAI, intravitreal aflibercept; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks
Conclusions

- At baseline, 12.2%, 9.7%, and 15.4% of patients in laser, IAI 2q4, and IAI 2q8 groups were on DPP-4 inhibitors.

- Baseline characteristics and BCVA, CRT, and DRSS outcomes in the baseline (+) DPP-4 inhibitor group do not appear to differ significantly from those patients not on DPP-4 inhibitors.

BCVA, best-corrected visual acuity; CRT, central retinal thickness; DPP-4, dipeptidyl peptidase-4; DRSS, Diabetic Retinopathy Severity Score; IAI, Intravitreal aflibercept; 2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks.