Impact of Exposure to Residual Intraretinal Fluid and Fluctuations of Central Subfield Thickness on Visual Outcomes in Eyes With Macular Edema Following Central Retinal Vein Occlusion: A 1-Year Post Hoc Analysis of the COPERNICUS and GALILEO Trials

Michael Ip, MD, PhD, on behalf of the COPERNICUS and GALILEO study investigators
Doheny Eye Center, UCLA, Pasadena, California
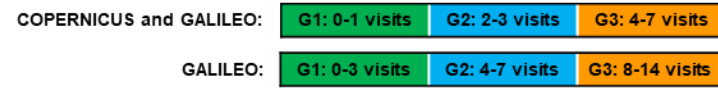
BACKGROUND & PURPOSE

- In the SCORE2 trial, greater central subfield thickness (CST) fluctuations were associated with worse visual outcomes in eyes with macular edema following central retinal vein occlusion (CRVO) receiving anti-vascular endothelial growth factor (VEGF) treatment[1]
- In the LEAVO trial, persistent or recurrent intraretinal fluid (IRF) was associated with worse visual outcomes in eyes with macular edema following CRVO receiving anti-VEGF treatment[2]
- The purpose of this post hoc analysis was to assess CST fluctuations and the impact of exposure to residual IRF on visual outcomes and vision-related quality of life in patients with macular edema following CRVO treated with intravitreal aflibercept injection (IAI) in the COPERNICUS[3] (NCT00943072) and GALILEO[4] (NCT01012973) trials

METHODS

- Analyses were conducted in eyes treated with IAI using the integrated COPERNICUS and GALILEO dataset through Week 24, and the GALILEO dataset alone through Week 52, as CST was not measured every 4 weeks after Week 24 in COPERNICUS
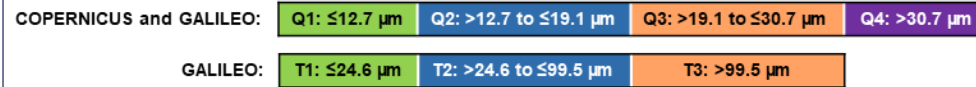
Impact of Exposure to Residual IRF

- Impact of exposure to residual IRF was assessed in groups (G) based on the number of visits with IRF from baseline to Week 24 or 52:

| COPERNICUS and GALILEO: | G1: 0-1 visits | G2: 2-3 visits | G3: 4-7 visits |
| GALILEO: | G1: 0-3 visits | G2: 4-7 visits | G3: 8-14 visits |

- Patients with ≥3 missing IRF assessments from baseline through Week 24 (n=13) or 52 (n=15) were excluded from the analysis

Impact of CST Fluctuation

- Impact of CST fluctuation was evaluated in quartiles (Q) or tertiles (T) of the standard deviation (SD) of CST of each eye from Weeks 4-24 and Weeks 4-52:

| COPERNICUS and GALILEO: | Q1: ≤12.7 µm | Q2: >12.7 to ≤19.1 µm | Q3: >19.1 to ≤30.7 µm | Q4: >30.7 µm |
| GALILEO: | T1: ≤24.6 µm | T2: >24.6 to ≤99.5 µm | T3: >99.5 µm |

- Patients with <3 CST observations from baseline through Week 24 (n=10) or 52 (n=6) were excluded from the analysis
- Vision-related quality of life (Visual Function Questionnaire-25 [VFQ-25] scores) was evaluated by exposure to residual IRF and CST fluctuation subgroups[5]

REFERENCES

1. Scott IU et al. Graefes Arch Clin Exp Ophthalmol. 2022;260(5):1491–1500.
2. Gurudas S et al. JAMA Ophthalmol. 2022;140(2):143–150.
3. Brown DM et al. Am J Ophthalmol. 2013;155(3):429–437.
4. Korobelnik JF et al. Ophthalmology. 2014;121(1):202–208.
5. Scott IU et al. Am J Ophthalmol. 2017;184:147–156.
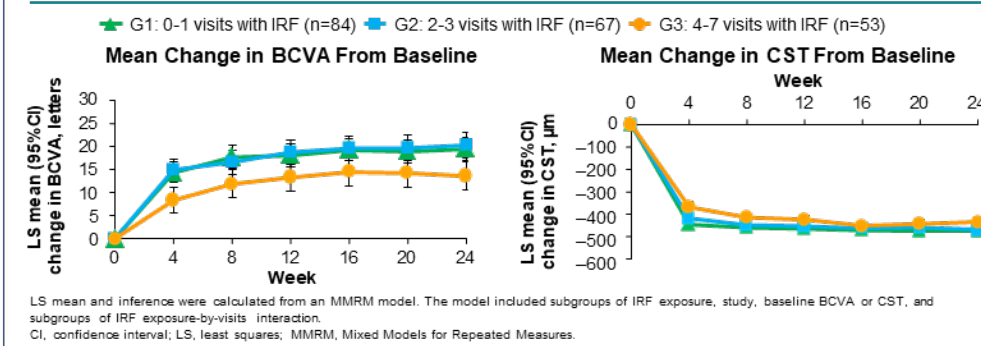
ACKNOWLEDGMENTS & DISCLOSURES

RESULTS

Outcomes by Exposure to Residual IRF Through Week 24: COPERNICUS and GALILEO Integrated Analysis
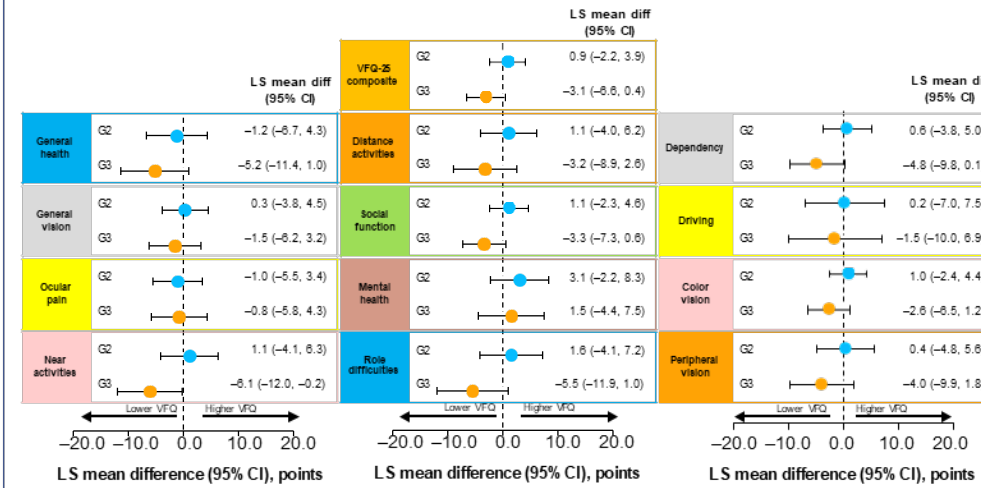
- Mean best-corrected visual acuity (BCVA) gain through Week 24 was lowest in eyes in G3 compared with G1 or G2
  - CST improvement was similar across all groups of exposure to residual IRF (**Figure 1**)

Figure 1. Outcomes Through Week 24 by Subgroups of IRF Exposure

G1: 0-1 visits with IRF (n=84)　G2: 2-3 visits with IRF (n=67)　G3: 4-7 visits with IRF (n=53)

LS mean and inference were calculated from an MMRM model. The model included subgroups of IRF exposure, study, baseline BCVA or CST, and subgroups of IRF exposure-by-visits interaction.
CI, confidence interval; LS, least squares; MMRM, Mixed Models for Repeated Measures.

- At Week 24, patients in G3 had a numerically lower general health, near activities, distance activities, social function, role difficulties, dependency, and peripheral vision subscale scores compared with those in G1 (**Figure 2**)
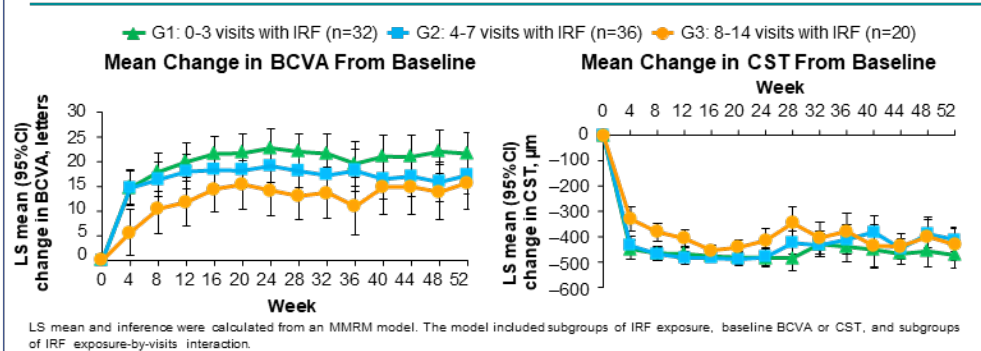
Figure 2. Difference in VFQ-25 Composite and Subscale Scores at Week 24 by Subgroups of IRF Exposure

The reported difference represents the comparison between G2 (2-3 visits with IRF) or G3 (4-7 visits with IRF) versus G1 (0-1 visits with IRF). LS mean and inference were calculated from an MMRM model. The model included subgroups of IRF exposure, study, baseline BCVA, and subgroups of IRF exposure-by-visits interaction.

Outcomes by Exposure to Residual IRF Through Week 52: GALILEO Analysis
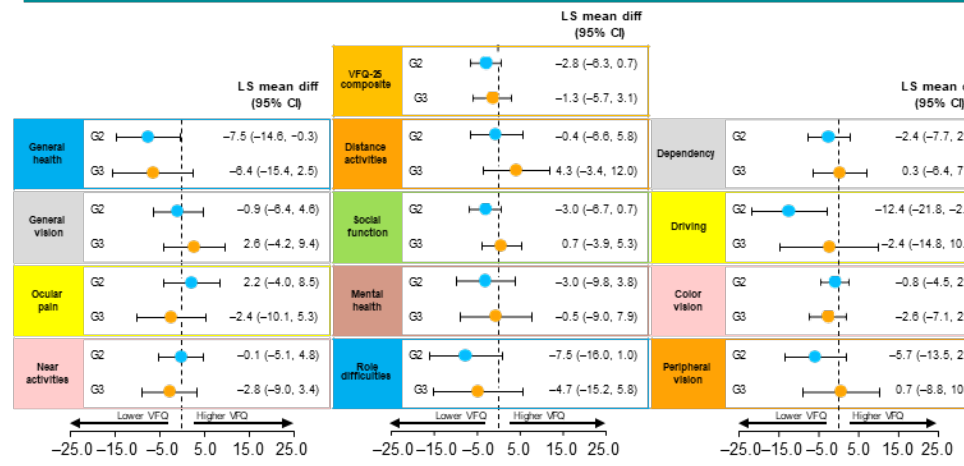
- Eyes in G3 had numerically lower BCVA gains over 52 weeks compared with patients in G1 and G2, while CST decreased to a similar extent across groups (**Figure 3**)

Figure 3. Outcomes Through Week 52 by Subgroups of IRF Exposure

G1: 0-3 visits with IRF (n=32)　G2: 4-7 visits with IRF (n=36)　G3: 8-14 visits with IRF (n=20)

LS mean and inference were calculated from an MMRM model. The model included subgroups of IRF exposure, baseline BCVA or CST, and subgroups of IRF exposure-by-visits interaction.

- At Week 52, VFQ-25 composite and subscale scores were overall similar between subgroups of residual IRF exposure (**Figure 4**)

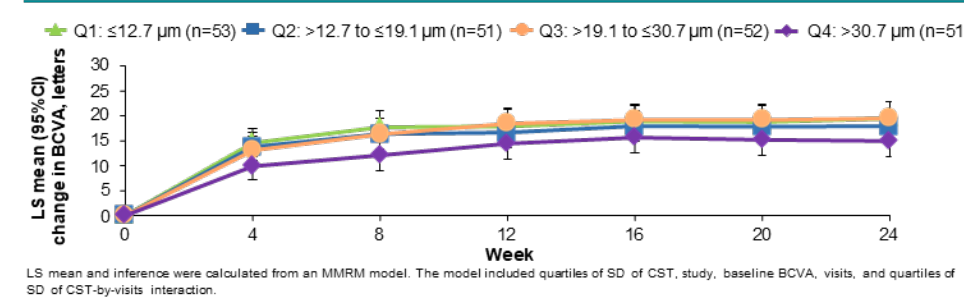**Figure 4. Difference in VFQ-25 Composite and Subscale Scores at Week 52 by Subgroups of IRF Exposure**

The reported difference represents the comparison between G2 (4-7 visits with IRF) or G3 (8-14 visits with IRF) versus G1 (0-3 visits with IRF). LS mean and inference were calculated from an MMRM model. The model included subgroups of IRF exposure, baseline BCVA, and subgroups of IRF exposure-by-visits interaction.

Outcomes by Quartiles of CST Fluctuation From Week 4 to Week 24: COPERNICUS and GALILEO Integrated Analysis
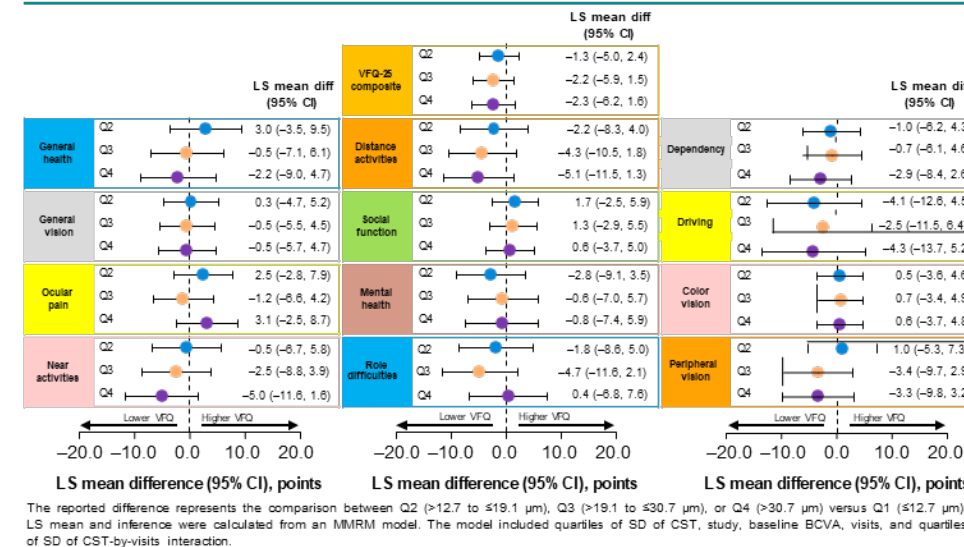
- BCVA gains through 24 weeks were lowest in Q4 compared with Q1 (**Figure 5**)

Figure 5. Mean Change in BCVA From Baseline Through Week 24 by Quartiles of CST Fluctuation

Q1: ≤12.7 µm (n=53)　Q2: >12.7 to ≤19.1 µm (n=51)　Q3: >19.1 to ≤30.7 µm (n=52)　Q4: >30.7 µm (n=51)

LS mean and inference were calculated from an MMRM model. The model included quartiles of SD of CST-by-visits interaction.

- VFQ-25 composite score at Week 24 was similar across quartiles of CST fluctuation (**Figure 6**)
  - Subscale scores were overall similar across quartiles of CST fluctuation, with a trend of lower scores in Q4 in the near activities subscale
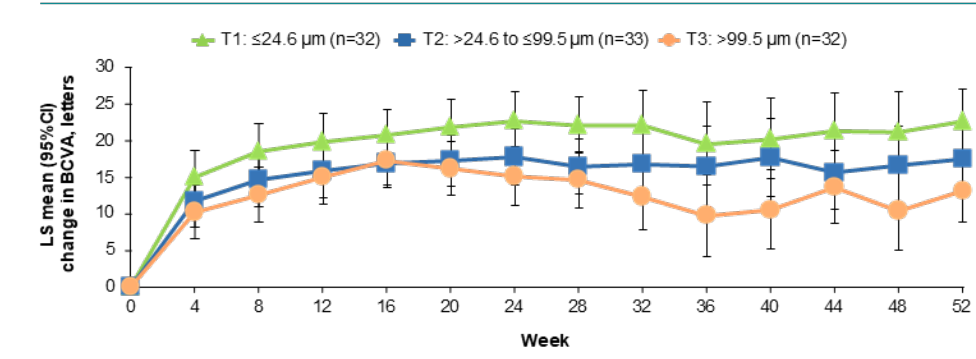
Figure 6. Difference in VFQ-25 Composite and Subscale Scores at Week 24 by Quartiles of CST Fluctuation

The reported difference represents the comparison between Q2 (>12.7 to ≤19.1 µm), Q3 (>19.1 to ≤30.7 µm), or Q4 (>30.7 µm) versus Q1 (≤12.7 µm). LS mean and inference were calculated from an MMRM model. The model included quartiles of SD of CST, study, baseline BCVA, visits, and quartiles of SD of CST-by-visits interaction.

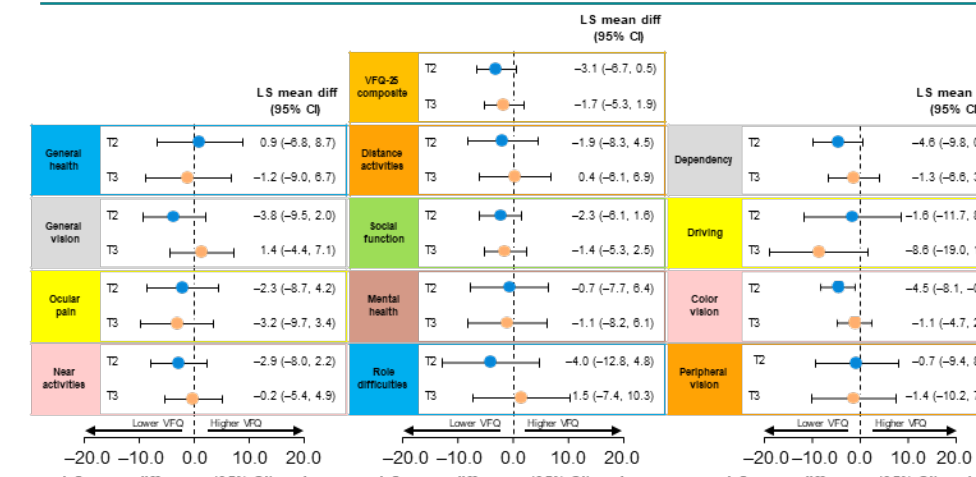### Outcomes by Tertiles of CST Fluctuation From Week 4 to Week 52: GALILEO Analysis

- Eyes in T3 had lower BCVA gains through Week 52 versus those in T1 (**Figure 7**)

Figure 7. Mean Change in BCVA From Baseline Through Week 52 by Tertiles of CST Fluctuation

T1: ≤24.6 µm (n=32)　T2: >24.6 to ≤99.5 µm (n=33)　T3: >99.5 µm (n=32)

LS mean and inference were calculated from an MMRM model. The model included tertiles of SD of CST, baseline BCVA, and tertile of SD of CST-by-visit interaction from Week 4 to Week 52.

- VFQ-25 composite and subscale scores at Week 52 was similar across tertiles of CST fluctuation (**Figure 8**)

Figure 8. Difference in VFQ-25 Composite and Subscale Scores at Week 52 by Tertiles of CST Fluctuation

The reported difference represents the comparison between T2 (>24.6 to ≤99.5 µm) or T3 (>99.5 µm) versus T1 (≤24.6 µm). LS mean and inference were calculated from an MMRM model. The model included tertiles of SD of CST, baseline BCVA, and tertiles of SD of CST-by-visits interaction.

CONCLUSIONS

- Greater exposure to residual IRF was associated with a trend towards lower BCVA gains through Week 24 and Week 52
- Higher CST fluctuation was associated with a trend towards lower BCVA gains through Week 24 and Week 52
- Similar vision-related quality of life responses (composite and subscale) were observed across subgroups of residual IRF and CST fluctuation, potentially driven by the better-seeing eye, in patients with macular edema following CRVO[5]
- Minimizing IRF and CST fluctuations could optimize outcomes in the treatment of eyes with macular edema following CRVO using IAI