Faricimab in Diabetic Macular Edema: Two-Year Results From the Phase 3 YOSEMITE and RHINE Trials

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On behalf of the YOSEMITE and RHINE Investigators

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2 Genentech, Inc., South San Francisco, CA
3 Roche Products Ltd., Welwyn Garden City, UK

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Disclosures

Financial Disclosures
► JAW: Consultant: Genentech, Inc.; Research Support: Adverum, Alimera, Bayer, Clover Therapeutics, Genentech, Inc., Iveric Bio, Kodiak, Lowy Medical Research Institute, Neurotech, NIH National Eye Institute, Opthea, Regeneron
► KA, ZH, YT, HL: Employee: Genentech, Inc.
► JI, DS: Employee: Roche Products Ltd.

Study and Product Disclosures
► Faricimab has been approved by the US Food and Drug Administration for the treatment of neovascular age-related macular degeneration and diabetic macular edema in adults. Please note that faricimab has not been approved for use outside of the United States
► This study includes research conducted on human subjects
► Institutional Review Board approval was obtained prior to study initiation
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YOSEMITE and RHINE Investigated Faricimab Q8W or Treat-and-Extend–Based PTI Dosing With Up to Q16W Intervals

YOSEMITE and RHINE
Phase 3, randomized, double-masked, active comparator–controlled trials
Patients with center-involving DME (CST ≥ 325 µm)a
BCVA 25–73 ETDRS letters (Snellen BCVA ~20/320–20/40)b

YOSEMITE: N = 940
RHINE: N = 951

Anti-VEGF treatment-naïve or previously treated patients with DMEc (1 eye per patient)

Primary Endpointd

<table>
<thead>
<tr>
<th>Time, Weeks</th>
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<tbody>
<tr>
<td>D1</td>
</tr>
<tr>
<td>Active treatment (faricimab 6.0 mg or aflibercept 2.0 mg)</td>
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<tr>
<td>Sham</td>
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<tr>
<td>PTI visit (sham or faricimab 6.0 mg)</td>
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<tr>
<td>Final study visit</td>
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<table>
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<tr>
<th>Faricimab 6.0 mg Q8W</th>
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<td>D1</td>
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<th>Faricimab 6.0 mg PTI</th>
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<tr>
<th>Aflibercept 2.0 mg Q8W</th>
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<td>D1</td>
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Study End

YOSEMITE: NCT03622580; RHINE: NCT03622593. a CST was measured as the distance from the internal limiting membrane to Bruch's membrane. b BCVA was measured using the ETDRS visual acuity chart at a starting distance of 4 m. c Previously anti-VEGF–treated eyes (treated ≥ 3 months before day 1) were limited to 25% of the total enrolment. d Primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52, and 56. DME, diabetic macular edema; CST, central subfield thickness; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; VEGF, vascular endothelial growth factor.
The PTI Algorithm Is a Protocol-Driven Treat-and-Extend Regimen, With Decisions Based on Changes in CST and BCVA

Initiation Phase
- 4 initial Q4W doses through week 12
- Q4W dosing maintained until the first achievement of CST < 325 µm

Anti-VEGF treatment-naive or previously treated patients with DME (1 eye per patient)
- YOSEMITE: N = 940
- RHINE: N = 951

YOSEMITE: N = 940
RHINE: N = 951

PTI Phase

<table>
<thead>
<tr>
<th>Change in CST From Reference CST, %</th>
<th>Improved CST</th>
<th>Stable CST</th>
<th>Worsened CST</th>
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<tbody>
<tr>
<td></td>
<td>+5%</td>
<td>+10%</td>
<td>+20%</td>
</tr>
<tr>
<td></td>
<td>−20%</td>
<td>−10%</td>
<td>0%</td>
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<tr>
<td></td>
<td>−10%</td>
<td>0%</td>
<td>+10%</td>
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</tbody>
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Change in BCVA From Reference BCVA, ETDRS Letters
- Extend interval by 4 weeks (up to Q16W)
- Maintain interval
- Reduce interval by 4 weeks (as low as Q4W)
- Reduce interval by 8 weeks (as low as Q4W)

**Change in CST From Reference CST, %**

- Improved CST
- Stable CST
- Worsened CST

**Time, Weeks**

- D1
- 4
- 8
- 12
- 16
- 20
- 24
- 28
- 32
- 36
- 40
- 44
- 48
- 52
- 56
- 60
- 64
- 68
- 72
- 76
- 80
- 84
- 88
- 92
- 96
- 100

- Active treatment (faricimab 6.0 mg or aflibercept 2.0 mg)
- Sham
- PTI visit (sham or faricimab 6.0 mg)
- Final study visit

**Note:**
- CST was measured as the distance from the internal limiting membrane to Bruch's membrane.
- Reference BCVA was defined as the mean of the 3 best BCVA values achieved at any prior active dosing visit.
- Reference CST was defined as the CST value when the original reference value (CST < 325 µm) was achieved. Reference CST was adjusted if CST decreased by > 10% from the previous reference CST for 2 consecutive active dosing visits and the values obtained were within 30 µm. The CST value obtained at the latter visit served as the new reference CST.
- BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q16W, every 16 weeks; VEGF, vascular endothelial growth factor.
Patient Disposition Through Study End: YOSEMITE

1532 patients screened
- 592 excluded

940 enrolled and randomized

Faricimab Q8W
- n = 315
- 313 patients treated
  - 261 (83.4%) completed study treatment
  - 52 (16.6%) discontinued treatment
    - 16 death
    - 12 lost to follow-up
    - 10 withdrawal by patient
    - 8 adverse event
    - 3 physician decision
    - 1 lack of efficacy
    - 2 other

Faricimab PTI
- n = 313
- 313 patients treated
  - 266 (85.0%) completed study treatment
  - 47 (15.0%) discontinued treatment
    - 19 death
    - 9 adverse event
    - 9 lost to follow-up
    - 8 withdrawal by patient
    - 1 physician decision
    - 1 pregnancy

Aflibercept Q8W
- n = 312
- 311 patients treated
  - 259 (83.3%) completed study treatment
  - 52 (16.7%) discontinued treatment
    - 19 withdrawal by patient
    - 12 death
    - 9 lost to follow-up
    - 5 adverse event
    - 2 physician decision
    - 1 lack of efficacy
    - 1 protocol deviation
    - 3 other
Patient Disposition Through Study End: RHINE

- 1715 patients screened
- 951 enrolled and randomized
- 764 excluded

Faricimab Q8W
- n = 317
- 317 patients treated
- 273 (86.1%) completed study treatment
- 44 (13.9%) discontinued treatment
  - 12 death
  - 11 withdrawal by patient
  - 10 lost to follow-up
  - 7 adverse event
  - 2 physician decision
  - 2 other

Faricimab PTI
- n = 319
- 319 patients treated
- 285 (89.3%) completed study treatment
- 34 (10.7%) discontinued treatment
  - 9 death
  - 9 withdrawal by patient
  - 8 adverse event
  - 5 lost to follow-up
  - 1 physician decision
  - 2 other

Aflibercept Q8W
- n = 315
- 314 patients treated
- 267 (85.0%) completed study treatment
- 47 (15.0%) discontinued treatment
  - 13 withdrawal by patient
  - 10 death
  - 7 lost to follow-up
  - 7 physician decision
  - 5 adverse event
  - 1 pregnancy
  - 1 protocol deviation
  - 3 other
During the 2-year studies, major protocol deviations related to COVID-19 were reported for 191 (20.3%) and 279 (29.3%) patients in YOSEMITE and RHINE, respectively.

- 167 (17.8%) and 210 (22.1%) patients missed ≥ 1 visit around the primary endpoint and/or final study visits

However, not all missed visits had a potential impact on efficacy:

- 63 (6.7%) and 76 (8.0%) patients missed ≥ 1 dose around the primary endpoint visits
- 15 (1.6%) and 48 (5.0%) patients missed ≥ 1 dose around the final study visits

Sensitivity and supplemental analyses to test the robustness of the primary results were consistent across different methods for handling missing data and intercurrent events.

Percentages are based on the intent-to-treat population (YOSEMITE, N = 940; RHINE, N = 951).

- Included missed visits at weeks 44, 48, 52, 56, 88, 92, 96, and/or 100.
- Included missed doses at weeks 44, 48, and/or 52.
- Included missed doses at weeks 88, 92, and/or 96.
### Baseline Patient Characteristics Were Well Balanced Across Treatment Arms

<table>
<thead>
<tr>
<th></th>
<th>YOSEMITE</th>
<th>RHINE</th>
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<tr>
<td></td>
<td>Faricimab Q8W (n = 315)</td>
<td>Faricimab PTI (n = 313)</td>
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<tr>
<td>Age, years, mean (SD)</td>
<td>61.6 (9.5)</td>
<td>62.8 (10.0)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>128 (40.6%)</td>
<td>116 (37.1%)</td>
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<tr>
<td>White, n (%)</td>
<td>241 (76.5%)</td>
<td>240 (76.7%)</td>
</tr>
<tr>
<td>BCVA, ETDRS letters, mean (SD)</td>
<td>62.0 (9.9)</td>
<td>61.9 (10.2)</td>
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<tr>
<td>CST, µm, mean (SD)</td>
<td>492.3 (135.8)</td>
<td>485.8 (130.8)</td>
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<tr>
<td>Previously anti-VEGF treated, n (%)</td>
<td>77 (24.4%)</td>
<td>68 (21.7%)</td>
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<td>Baseline DR severity status, n (%):</td>
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<tr>
<td>DR questionable, mild to moderate NPDR (ETDRS-DRSS level 10/12, 14/20, 35, 43)</td>
<td>174 (55.2%)</td>
<td>187 (59.7%)</td>
</tr>
<tr>
<td>Moderately severe and severe NPDR (ETDRS-DRSS level 47, 53)</td>
<td>113 (35.9%)</td>
<td>99 (31.6%)</td>
</tr>
<tr>
<td>PDR (ETDRS-DRSS level 61, 65, 71/75)</td>
<td>22 (7.0%)</td>
<td>21 (6.7%)</td>
</tr>
<tr>
<td>Cannot grade (ETDRS-DRSS level 90)</td>
<td>4 (1.3%)</td>
<td>5 (1.6%)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (0.6%)</td>
<td>1 (0.3%)</td>
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</table>

Results are presented for the intent-to-treat population. *Age at randomization. CST was measured as the distance from the internal limiting membrane to Bruch's membrane. BCVA, best-corrected visual acuity; CST, central subfield thickness; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; ETDRS, Early Treatment Diabetic Retinopathy Study; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PTI, personalized treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor.
Vision Gains With Faricimab Q8W and PTI Up to Q16W Were Noninferior to Aflibercept Q8W at 1 Year

Results are based on a mixed model for repeated measures analysis; 95.04% CI error bars are shown.

*a Primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52, and 56.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks.
Vision Gains With Faricimab Q8W and PTI Up to Q16W Were Noninferior to Aflibercept Q8W at 1 Year and Maintained Through Year 2

**YOSEMITE**

**Average of weeks 92–100\(^a\)**
- Faricimab Q8W: +10.7 ETDRS letters
- Faricimab PTI: +10.7 ETDRS letters
- Aflibercept Q8W: +11.4 ETDRS letters

**Time, Weeks**

**Adjusted Mean BCVA Change From Baseline, ETDRS Letters**

- Aflibercept Q8W (n = 312)
- Faricimab Q8W (n = 315)
- Faricimab PTI (n = 313)

**Treatment difference versus aflibercept Q8W at 2 years\(^a\) (ETDRS letters), mean (95.04% CI)**
- Faricimab Q8W: −0.7 (−2.6, +1.2)
- Faricimab PTI: −0.7 (−2.5, +1.2)

**RHINE**

**Average of weeks 92–100\(^a\)**
- Faricimab Q8W: +10.9 ETDRS letters
- Faricimab PTI: +10.1 ETDRS letters
- Aflibercept Q8W: +9.4 ETDRS letters

**Time, Weeks**

**Adjusted Mean BCVA Change From Baseline, ETDRS Letters**

- Aflibercept Q8W (n = 315)
- Faricimab Q8W (n = 317)
- Faricimab PTI (n = 319)

**Treatment difference versus aflibercept Q8W at 2 years\(^a\) (ETDRS letters), mean (95.04% CI)**
- Faricimab Q8W: +1.5 (−0.5, +3.6)
- Faricimab PTI: +0.7 (−1.3, +2.7)

Results are based on a mixed model for repeated measures analysis; 95.04% CI error bars are shown.

\(^a\) Adjusted mean BCVA change from baseline at 2 years, averaged over weeks 92, 96, and 100.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks.
More Than 50% of Patients in the Faricimab PTI Arms Achieved Q16W Dosing at Week 52

Analyses included patients in the faricimab PTI arms who had not discontinued the study at the week 52 visit (YOSEMITE, n = 286; RHINE, n = 308). Treatment interval at week 52 was defined as the treatment interval decision made at that visit. Percentage is based on the pooled number of patients in the faricimab PTI arms with dosing interval data at week 56 (n = 592).

PTI, personalized treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

- **YOSEMITE Week 52**:
  - Q4W: 10.8%
  - Q8W: 15.4%
  - Q12W: 21.0%
  - Q16W: 52.8%
  - Q12W + Q16W: 73.8%

- **RHINE Week 52**:  
  - Q4W: 13.3%
  - Q8W: 15.6%
  - Q12W: 20.1%
  - Q16W: 51.0%
  - Q12W + Q16W: 71.1%

- **YOSEMITE Week 52**
  - 11% of patients were on Q8W dosing or a combination of Q4W and Q8W dosing through week 56
  - 7% of patients remained on Q4W dosing through week 56

- **RHINE Week 52**
  - 62% of patients completed one full Q12W dosing cycle and maintained Q12W or Q16W dosing without an interval reduction below Q12W through week 56

*Analyses included patients in the faricimab PTI arms who had not discontinued the study at the week 52 visit (YOSEMITE, n = 286; RHINE, n = 308). Treatment interval at week 52 was defined as the treatment interval decision made at that visit. Percentage is based on the pooled number of patients in the faricimab PTI arms with dosing interval data at week 56 (n = 592). PTI, personalized treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.
Proportion of Patients Who Achieved Faricimab Q16W Dosing Increased to ≥ 60% at Week 96

YOSEMITE Week 96a

- Q4W: 7.0%
- Q8W: 14.8%
- Q12W: 18.1%
- Q16W: 60.0%

Q12W + Q16W: 78.1%

RHINE Week 96a

- Q4W: 10.1%
- Q8W: 11.8%
- Q12W: 13.6%
- Q16W: 64.5%

Q12W + Q16W: 78.1%b

- Median number of injections in year 2 (weeks 60–96)c
  - Faricimab PTI: 3 injections
  - Faricimab Q8W: 5 injections
  - Aflibercept Q8W: 5 injections

79% of patients who achieved Q12W or Q16W dosing at week 52 maintained ≥ Q12W dosing without an interval reduction below Q12W through week 96d

76% of patients who achieved Q16W dosing at week 52 maintained Q16W dosing without an interval reduction through week 96e

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a Analyses included patients in the faricimab PTI arms who had not discontinued the study at the week 96 visit (YOSEMITE, n = 270; RHINE, n = 287). Treatment interval at week 96 was defined as the treatment interval decision made at that visit.
b Sum of Q12W and Q16W percentages shown; calculated proportion of patients who achieved Q12W or Q16W dosing at week 96 is 78.049%. Results are presented for the pooled YOSEMITE/RHINE safety-evaluable population (faricimab Q8W, n = 630; faricimab PTI, n = 632; aflibercept Q8W, n = 625).
c Percentage is based on the pooled number of patients in the faricimab PTI arms who achieved Q12W or Q16W dosing at week 52 and had not discontinued the study at the week 96 visit (n = 406).
d PTI, personalized treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.
e Percentage is based on the pooled number of patients in the faricimab PTI arms who achieved Q16W dosing at week 52 and had not discontinued the study at the week 96 visit (n = 291).
Comparable Proportion of Patients Gained or Avoided Loss of Vision With Faricimab Q8W and PTI Up to Q16W vs Aflibercept Q8W at 2 Years

- **Proportion of patients who gained or avoided a loss of ≥ 15 ETDRS letters at 2 years, averaged over weeks 92, 96, and 100.** Analyses included patients with ≥ 1 nonmissing assessment at weeks 92, 96, and 100. Weighted proportions were estimated using the CMH method, stratified by baseline characteristics: BCVA score (< 64 vs ≥ 64 ETDRS letters), prior intravitreal anti-VEGF therapy (yes vs no), and region (United States and Canada vs rest of the world).

- Weighted proportion for the aflibercept Q8W arm presented for the faricimab Q8W versus aflibercept Q8W comparison. 95.04% CI error bars are shown.

### Patients Who Gained ≥ 15 ETDRS Letters at 2 Years, %

<table>
<thead>
<tr>
<th></th>
<th>YOSEMITE</th>
<th>RHINE</th>
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</thead>
<tbody>
<tr>
<td>Aflibercept Q8W</td>
<td>37% (n = 259)</td>
<td>39% (n = 254)</td>
</tr>
<tr>
<td>Faricimab Q8W</td>
<td>37% (n = 262)</td>
<td>40% (n = 259)</td>
</tr>
<tr>
<td>Faricimab PTI</td>
<td>38% (n = 270)</td>
<td>31% (n = 282)</td>
</tr>
</tbody>
</table>

### Patients Who Avoided a Loss of ≥ 15 ETDRS Letters at 2 Years, %

<table>
<thead>
<tr>
<th></th>
<th>YOSEMITE</th>
<th>RHINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflibercept Q8W</td>
<td>98% (n = 259)</td>
<td>98% (n = 262)</td>
</tr>
<tr>
<td>Faricimab Q8W</td>
<td>98% (n = 270)</td>
<td>98% (n = 259)</td>
</tr>
<tr>
<td>Faricimab PTI</td>
<td>97% (n = 282)</td>
<td>97% (n = 254)</td>
</tr>
</tbody>
</table>

*a* Proportion of patients who gained or avoided a loss of ≥ 15 ETDRS letters at 2 years, averaged over weeks 92, 96, and 100. Analyses included patients with ≥ 1 nonmissing assessment at weeks 92, 96, and 100. Weighted proportions were estimated using the CMH method, stratified by baseline characteristics: BCVA score (< 64 vs ≥ 64 ETDRS letters), prior intravitreal anti-VEGF therapy (yes vs no), and region (United States and Canada vs rest of the world). Weighted proportion for the aflibercept Q8W arm presented for the faricimab Q8W versus aflibercept Q8W comparison. 95.04% CI error bars are shown.

BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor.
Greater Reductions in CST With Faricimab Q8W and PTI Up to Q16W vs Aflibercept Q8W at 1 Year

**YOSEMITE**

- Faricimab Q8W: $-206.6 \, \mu m^*$
- Faricimab PTI: $-196.5 \, \mu m^*$
- Aflibercept Q8W: $-170.3 \, \mu m$

**RHINE**

- Faricimab Q8W: $-195.8 \, \mu m^*$
- Faricimab PTI: $-187.6 \, \mu m^*$
- Aflibercept Q8W: $-170.1 \, \mu m$

Test for superiority: * Nominal $P < 0.05$ versus aflibercept Q8W. *Adjusted mean CST change from baseline at 1 year, averaged over weeks 48, 52, and 56.

Adjusted mean CST change from baseline was estimated using a mixed model for repeated measures analysis; 95.04% CI error bars are shown.

CST, central subfield thickness; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks.
Greater Reductions in CST With Faricimab Q8W and PTI Up to Q16W vs Aflibercept Q8W at 1 Year Were Maintained Through Year 2

**Adjusted Mean CST Change From Baseline, µm**

**YOSEMITE**

- Faricimab Q8W: $-216.0$ µm*
- Faricimab PTI: $-204.5$ µm
- Aflibercept Q8W: $-196.3$ µm

**RHINE**

- Faricimab Q8W: $-202.6$ µm*
- Faricimab PTI: $-197.1$ µm
- Aflibercept Q8W: $-185.6$ µm

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Test for superiority: * Nominal $P < 0.05$ versus aflibercept Q8W.
*Adjusted mean CST change from baseline at 2 years, averaged over weeks 92, 96, and 100.

Adjusted mean CST change from baseline was estimated using a mixed model for repeated measures analysis; 95.04% CI error bars are shown. CST, central subfield thickness; PTI, personalized treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks.
More Patients Achieved Absence of DME With Faricimab Q8W and PTI Up to Q16W vs Aflibercept Q8W Through Year 2

CMH test for superiority: * Nominal $P < 0.05$ versus aflibercept Q8W; nominal $P > 0.05$ where no asterisk is shown. *Absence of DME was defined as CST $< 325$ μm, measured as the distance from the internal limiting membrane to Bruch’s membrane.

Weighted proportions were estimated using the CMH method, stratified by baseline BCVA (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no) and region (United States and Canada vs rest of the world). Baseline values are not weighted; 0% of patients had absence of DME at screening, which was up to 28 days ahead of baseline. Weighted proportions for the aflibercept Q8W arm presented for the faricimab Q8W versus aflibercept Q8W comparison. 95.04% CI error bars are shown.

BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; CST, central subfield thickness; DME, diabetic macular edema; PTI, personalized treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor.
More Patients Achieved Absence of IRF With Faricimab Q8W and PTI Up to Q16W vs Aflibercept Q8W Through Year 2

CMH test for superiority: * Nominal P < 0.05 versus aflibercept Q8W; nominal P > 0.05 where no asterisk is shown.
Weighted proportions were estimated using the CMH method, stratified by baseline BCVA (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no) and region (United States and Canada vs rest of the world); baseline values are not weighted. Weighted proportion for the aflibercept Q8W arm presented for the faricimab Q8W versus aflibercept Q8W comparison. 95.04% CI error bars are shown.
BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; IRF, intraretinal fluid; PTI, personalized treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor.
Rates of Absence of SRF Through Year 2 Were High and Comparable With Faricimab Q8W and PTI Up to Q16W vs Aflibercept Q8W

CMH test for superiority: * Nominal $P < 0.05$ versus aflibercept Q8W; nominal $P > 0.05$ where no asterisk is shown.

Weighted proportions were estimated using the CMH method, stratified by baseline BCVA (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no) and region (United States and Canada vs rest of the world); baseline values are not weighted. Weighted proportion for the aflibercept Q8W arm presented for the faricimab Q8W versus aflibercept Q8W comparison. 95.04% CI error bars are shown.

BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; PTI, personalized treatment interval; Q8W, every 8 weeks; SRF, subretinal fluid; VEGF, vascular endothelial growth factor.
Analyses included patients with evaluable color fundus photograph images at baseline and week 52 and/or week 96. Weighted proportions were estimated using the CMH method, stratified by baseline BCVA (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no), and region (United States and Canada vs rest of the world). Weighted proportions for the aflibercept Q8W arm presented for the faricimab Q8W versus aflibercept Q8W comparison. 97.52% CI error bars are shown at week 52; 95.04% CI error bars are shown at week 96. BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; DRSS, Diabetic Retinopathy Severity Scale; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor.
Faricimab Was Well Tolerated Through Study End

<table>
<thead>
<tr>
<th>Exposure-Adjusted Incidence Rates Through Study End, Events Per 100 Patient-Years (95% CI)(^a)</th>
<th>YOSEMITE/RHINE Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Faricimab Q8W (n = 630)</strong></td>
<td><strong>Faricimab PTI (n = 632)</strong></td>
</tr>
<tr>
<td>Total patient-years at risk(^b)</td>
<td>1138.9</td>
</tr>
<tr>
<td>Ocular AEs(^c)</td>
<td>58.65 (54.29, 63.27)</td>
</tr>
<tr>
<td>Serious ocular AEs(^c)</td>
<td>2.99 (2.07, 4.17)</td>
</tr>
<tr>
<td>Ocular AEs of special interest(^c)</td>
<td>2.81 (1.92, 3.97)</td>
</tr>
<tr>
<td>Associated with BCVA loss of ≥ 30 ETDRS letters for &gt; 1 hour</td>
<td>2.02</td>
</tr>
<tr>
<td>Requiring surgical or medical intervention to prevent permanent loss of sight</td>
<td>0.53</td>
</tr>
<tr>
<td>Associated with severe intraocular inflammation</td>
<td>0.26</td>
</tr>
<tr>
<td>Nonocular AEs</td>
<td>180.53 (172.81, 188.50)</td>
</tr>
<tr>
<td>Serious nonocular AEs</td>
<td>30.56 (27.43, 33.94)</td>
</tr>
<tr>
<td>APTC events(^d)</td>
<td>2.99 (2.07, 4.17)</td>
</tr>
<tr>
<td>Death</td>
<td>1.40</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>0.97</td>
</tr>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Results are presented for the pooled YOSEMITE/RHINE safety-evaluable population.\(^4\) Events per 100 patient-years is calculated as the number of events/total patient-years at risk x 100.\(^5\) Total patient-years at risk is the sum of all time intervals (in years) for all patients, from the first dose of study treatment until the patient completes or withdraws from the study.\(^6\) Ocular AEs in the study eye only are presented.\(^7\) APTC events were adjudicated by an external independent committee; all other events were investigator reported. Multiple occurrences of the same AE in an individual are counted as separate events. Includes AEs with onset from the first dose of study drug through study end. AE, adverse event; APTC, Anti-Platelet Trialists’ Collaboration; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PTI, personalized treatment interval; Q8W, every 8 weeks.
### Inflammation Events Through Study End Were Low and Comparable Across Treatment Arms

<table>
<thead>
<tr>
<th>Exposure-Adjusted Incidence Rates Through Study End, Events Per 100 Patient-Years (95% CI)a</th>
<th>YOSEMITE/RHINE Pooled</th>
<th></th>
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<tr>
<td></td>
<td>Faricimab Q8W (n = 630)</td>
<td>Faricimab PTI (n = 632)</td>
</tr>
<tr>
<td>Total patient-years at riskb</td>
<td>1138.9</td>
<td>1157.2</td>
</tr>
<tr>
<td><strong>Intraocular inflammation eventsc</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uveitis</td>
<td>0.35 (0.42, 1.61)</td>
<td>0.43 (0.79, 2.25)</td>
</tr>
<tr>
<td>Iritis</td>
<td>0.09</td>
<td>0.35</td>
</tr>
<tr>
<td>Iridocyclitis</td>
<td>0.18</td>
<td>0.26</td>
</tr>
<tr>
<td>Vitritis</td>
<td>0.18</td>
<td>0.09</td>
</tr>
<tr>
<td>Post procedural inflammation</td>
<td>0.09</td>
<td>0.09</td>
</tr>
<tr>
<td>Chorioretinitis</td>
<td>0</td>
<td>0.09</td>
</tr>
<tr>
<td>Keratic precipitates</td>
<td>0</td>
<td>0.09</td>
</tr>
<tr>
<td>Keratouveitis</td>
<td>0</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Endophthalmitis events</strong></td>
<td>0.18</td>
<td>0.35</td>
</tr>
<tr>
<td>Retinal vasculitis events</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Occlusive retinal vasculitis events</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Results are presented for the pooled YOSEMITE/RHINE safety-evaluable population. *Events per 100 patient-years is calculated as the number of events/total patient-years at risk x 100. bTotal patient-years at risk is the sum of all time intervals (in years) for all patients, from the first dose of study treatment until the patient completes or withdraws from the study. cExcluding endophthalmitis. All events are investigator reported; multiple occurrences of the same AE in an individual are counted as separate events. Includes AEs with onset from the first dose of study drug through study end. AE, adverse event; PTI, personalized treatment interval; Q8W, every 8 weeks.
Retinal Occlusive Events Through Study End Were Low Across Treatment Arms

| Exposure-Adjusted Incidence Rates Through Study End, Events Per 100 Patient-Years (95% CI)a | YOSEMITE/RHINE Pooled |
|---|---|---|
|  | Faricimab Q8W (n = 630) | Faricimab PTI (n = 632) | Aflibercept Q8W (n = 625) |
| Total patient-years at riskb | 1138.9 | 1157.2 | 1138.2 |
| Retinal vein occlusion events | 0.09 | 0.43 | 0 |
| Retinal artery occlusion events | 0.09 | 0.17 | 0.18 |
| Retinal artery embolism events | 0 | 0 | 0.09 |

Results are presented for the pooled YOSEMITE/RHINE safety-evaluable population. a Events per 100 patient-years is calculated as the number of events/total patient-years at risk x 100. b Total patient-years at risk is the sum of all time intervals (in years) for all patients, from the first dose of study treatment until the patient completes or withdraws from the study. All events are investigator reported; multiple occurrences of the same AE in an individual are counted as separate events. Includes AEs with onset from the first dose of study drug through study end. AE, adverse event; PTI, personalized treatment interval; Q8W, every 8 weeks.
Over 2 Years, Faricimab Demonstrated Durable Efficacy Through Disease Control With Up to Q16W Dosing

**Faricimab**

Faricimab targets **2 distinct disease pathways** to promote **vascular stability**, which may lead to a **more durable therapy** while maintaining **long-term vision gains**.

**Durable vision gains**

**Comparable 1-year BCVA gains** with faricimab up to Q16W versus aflibercept Q8W were **maintained through year 2**.

**DME disease control**

**Improved anatomic outcomes** with faricimab up to Q16W versus aflibercept Q8W were **maintained over 2 years**:

- **Change in CST** favored faricimab
- More patients achieved **absence of DME**
- More patients achieved **absence of IRF**

**Safety outcomes**

Faricimab was well tolerated, and **no cases of retinal vasculitis or occlusive retinal vasculitis** were reported.

**Long-term outcomes**

The ongoing RHONE-X long-term extension study will generate 4-year data.

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*a* Absence of DME was defined as CST < 325 μm, measured as the distance from the internal limiting membrane to Bruch’s membrane.

*b* Proportion of patients in the pooled faricimab PTI arms who achieved ≥ Q12W or Q16W dosing at week 96, among those who had not discontinued the study at the week 96 visit (YOSEMITE, n = 270; RHINE, n = 287).

BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; IRF, intraretinal fluid; PTI, personalized treatment interval; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.