Comparative Efficacy of Faricimab for the Treatment of Diabetic Macular Edema (DME): A Systematic Literature Review (SLR) and Network Meta-Analysis (NMA)

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► FM, DT: Employee: Genentech, Inc.
► KG: Employee: Roche Products Ltd.
► TP, CB: Employee: F. Hoffmann-La Roche Ltd.

Study and Product Disclosures

► Faricimab is approved for the treatment of retinal vein occlusion in the USA, and neovascular age-related macular degeneration and diabetic macular edema in multiple countries worldwide. Faricimab is not currently approved for use outside these indications
► This study includes research conducted on human subjects
► Institutional Review Board approval was obtained prior to study initiation
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**Introduction**

Flexible dosing regimens have been used to reduce treatment burden after the initial dosing phase, including\(^1,2\):

- **T&E** – dosing intervals determined by findings at last dosing visit
- **PRN** – injections as needed based on outcomes at regular monitoring visits

*Faricimab* is a dual inhibitor of VEGF-A and Ang-2 associated with improved vascular stability and potential for extended durability up to Q16W in clinical trials for DME and nAMD\(^2,3\).

**Objective:**

To evaluate the comparative efficacy, injection frequency, and safety of faricimab T&E regimen (6 mg Q4W–Q16W) relative to other anti-VEGF therapies and regimens for DME/nAMD treatment.

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Ang-2, angiopoietin-2; DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; NMA, network meta-analysis; PRN, pro re nata; Q4W, every 4 weeks; Q16W, every 16 weeks; SLR, systematic literature review; T&E, treat-and-extend; VEGF, vascular endothelial growth factor.

Outcomes assessed following 12 months of treatment:

- Change in BCVA from baseline
- Change in CST from baseline
- Injection frequency
- All-cause discontinuations and safety outcomes

Bayesian network meta-analysis performed using a random effects model

\[ p(\theta | \text{Data}) = \frac{p(\text{Data} | \theta) \cdot p(\theta)}{p(\text{Data})} \]

Faricimab data extracted from CSRs from 2 RCTs in patients with DME:

- YOSEMITE (NCT03622580)
- RHINE (NCT03622593)

SLR identified RCTs for anti-VEGF monotherapies in patients with DME published before August 2021:

- Bevacizumab: 1.25 mg PRN
- Ranibizumab: 0.3/0.5 mg PRN and 0.3/0.5 mg T&E
- Aflibercept: 2 mg PRN

26 RCTs were included in the network meta-analysis
Outcomes assessed following 12 months of treatment:

- Comparative change in BCVA from baseline
- Change in CST from baseline
- Injection frequency
- All-cause discontinuations and adverse events

26 RCTs were included in the network meta-analysis
Faricimab T&E Was Associated With Comparable or Greater Visual Acuity Improvements at 12 Months in DME

Mean difference in change in BCVA, ETDRS letters (95% CrI) for faricimab 6.0 mg T&E vs:

- Bevacizumab 1.25 mg PRN: +4.78 (+8.28, +0.58)
- Ranibizumab 0.3/0.5 mg PRN: +4.38 (+7.42, +1.10)
- Ranibizumab 0.3/0.5 mg T&E: +4.83 (+9.02, +0.21)
- Afibercept 2 mg PRN: +1.99 (+5.37, −1.80)

BCVA, best-corrected visual acuity; CrI, credible interval; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; PRN, pro re nata; T&E, treat-and-extend.
Faricimab T&E Was Associated With a Greater Decrease in CST vs Comparators at 12 Months in DME

Mean difference in change in CST, µm (95% CrI) for faricimab 6.0 mg T&E vs:

- Bevacizumab 1.25 mg PRN: −125 (−91, −158)
- Ranibizumab 0.3/0.5 mg PRN: −75 (−46, −103)
- Ranibizumab 0.3/0.5 mg T&E: −66 (−34, −98)
- Aflibercept 2 mg PRN: −55 (−23, −87)

- **Injection frequency** with faricimab T&E was numerically lower vs anti-VEGF monotherapy flexible dosing
- The rate of **all-cause discontinuations** and **safety outcomes** were similar between faricimab T&E and comparators*

* Data not available for ranibizumab 0.3/0.5 mg T&E. CrI, credible interval; CST, central subfield thickness; DME, diabetic macular edema; PRN, pro re nata; T&E, treat-and-extend; VEGF, vascular endothelial growth factor.
Network Meta-Analysis Comparing Faricimab vs Aflibercept at 12 Weeks of Treatment (Matched Dosing Phase)

**Outcomes of interest:**
- Change in BCVA and in CST from baseline through week 12
- Differences and the probability of faricimab leading to better outcomes

**DME**
- YOSEMITE (N = 940)
- RHINE (N = 951)
- PHOTON (N = 658)

**nAMD**
- TENAYA (N = 671)
- LUCERNE (N = 658)
- PULSAR (N = 1009)
- CANDELA (N = 106)

**Product Dosing**
- **Aflibercept 2 mg IVT Q4W**
- **Aflibercept 8 mg IVT Q4W**
- **Faricimab 6 mg IVT Q4W**

**Bayesian network meta-analysis**
- performed on 7 studies using RE and FE models

BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; FE, fixed-effect; IVT, intravitreal; nAMD, neovascular age-related macular degeneration; Q4W, every 4 weeks; RE, random effects.
Faricimab was associated with comparable or numerically greater change in visual acuity vs aflibercept 2 mg and 8 mg at 12 weeks.

Mean difference in BCVA change from baseline, ETDRS letters (RE model 95% CrI) for faricimab 6.0 mg IVT Q4W vs:

- **Aflibercept 2 mg IVT Q4W**
  - nAMD & DME: +0.4 (+2.0, –1.3)
  - DME: 0.0 (+1.8, –1.9)
  - nAMD: +0.9 (+2.5, –0.9)

- **Aflibercept 8 mg IVT Q4W**
  - nAMD & DME: +1.3 (+4.1, –1.4)
  - DME: +1.0 (+4.2, –2.1)
  - nAMD: +1.8 (+4.3, –0.8)

Mean change in BCVA was numerically greater or similar for faricimab across all analysis vs 2 mg or 8 mg aflibercept.

Comparative benefit of faricimab vs aflibercept for this period was 1–2 letters.

BCVA, best-corrected visual acuity; CrI, credible interval; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; IVT, intravitreal; nAMD, neovascular age-related macular degeneration; Q4W, every 4 weeks; RE, random effects.
Faricimab Was Associated With Greater CST Improvements vs Aflibercept 2 mg or 8 mg at 12 Weeks

Mean difference in CST change from baseline, µm (RE model, 95% CrI) for faricimab 6.0 mg IVT Q4W vs:

- **Aflibercept 2 mg IVT Q4W**
  - nAMD & DME: -15 (−6.8, −22.0)
  - DME: -15 (−5.4, −25.0)
  - nAMD: -13 (−0.6, −26.0)

- **Aflibercept 8 mg IVT Q4W**
  - nAMD & DME: -18 (−4.5, −32.0)
  - DME: -22 (−1.0, −43.0)
  - nAMD: -15 (−0.6, −26.0)

Greater mean change in CST in the pooled nAMD & DME analysis with faricimab vs. 2 mg and 8 mg aflibercept. Comparative benefit of faricimab during this period was 13–22 µm and was consistent across analyses.

Crl, credible interval; CST, central subfield thickness; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; IVT, intravitreal; nAMD, neovascular age-related macular degeneration; Q4W, every 4 weeks; RE, random effects.
≥93% Probability of Greater CST Reduction and ≥77% Probability of Greater BCVA Gains With Faricimab vs Aflibercept 8 mg

Probability of Faricimab Achieving Increased BCVA or CST Reduction Compared With Aflibercept 8 mg at 12 Weeks (Random Effects Model)

BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration.
In an NMA, Dual VEGF-A/Ang-2 Inhibition With Faricimab Provides Improved Anatomic Results Compared With Anti-VEGF Monotherapies, Including Aflibercept 8 mg

**At 12 months:** Compared with anti-VEGF monotherapy flexible regimens in DME, faricimab T&E showed:
- Comparable or improved efficacy in BCVA
- Greater CST improvement

**At 12 weeks:** Compared with aflibercept 8 mg or 2 mg for treatment of nAMD or DME, faricimab showed:
- Greater CST improvements
- ≥ 77% probability of greater BCVA gains

Ang-2, angiopoietin-2; BCVA, best-corrected visual acuity; DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; NMA, network meta-analysis; T&E, treat-and-extend; VEGF(-A), vascular endothelial growth factor-A.