Efficacy, Safety, and Durability of Faricimab in Macular Oedema Due to Retinal Vein Occlusion: 72-Week Results From the Phase 3 BALATON and COMINO Trials

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Objective

To evaluate the long-term efficacy, safety, and durability of faricimab in patients with macular oedema due to retinal vein occlusion (RVO)

Conclusions

Dual angiopoeitin-2 (Ang-2)/vascular endothelial growth factor (VEGF)-A inhibition with faricimab offers disease control in patients with RVO

- Best-corrected visual acuity (BCVA) gains at week 24 were maintained through week 72
- Central subfield thickness (CST) reductions at week 24 were maintained through week 72
- > 45% of patients were on ≥ every 12 weeks faricimab dosing at week 68

Faricimab was well tolerated with no change in safety profile

Financial Disclosures

- MW: Support for travel and speakers' fees: AbbVie, Alimera, Bayer, Novartis, Roche
- FA, YL, LPP, JRW: Employee: Genentech, Inc.
- PA, AK, A-CR: Employee: Roche Products Ltd.

Study and Product Disclosures

- In the UK, faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular oedema. Faricimab is not currently approved for use outside these indications in the UK
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by F. Hoffmann-La Roche Ltd. for the study and third-party writing assistance, which was provided by Luke Carey, PhD, CMPP, of Envision Pharma Group
- Roche conducted a factual accuracy check on the final article but any decision to incorporate comments was made solely at the discretion of the authors

Presented at the Royal College of Ophthalmologists Annual Congress Belfast, UK | 20–23 May 2024

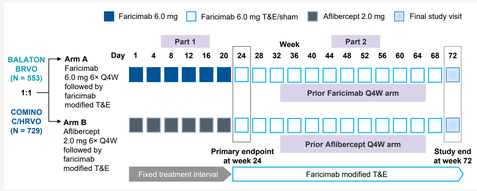
Background

- Faricimab is a dual Ang-2/VEGF-A inhibitor and the first bispecific antibody designed for intraocular use
- Week 24 results from the phase 3 BALATON (NCT04740905) and COMINO (NCT04740931) trials support the efficacy and safety of faricimab for the treatment of macular oedema due to RVO[1]
  - BCVA gains from baseline at week 24 with faricimab were noninferior to aflibercept
  - CST reductions from baseline were comparable across treatment arms
  - Faricimab was well tolerated through week 24, with a safety profile comparable to aflibercept

Methods

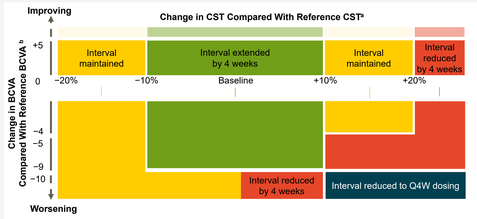
Phase 3 Study Design (BALATON, N = 553; COMINO, N = 729)

- **Population:** Age ≥ 18 years; treatment-naïve macular oedema due to RVO; BCVA 73–19 letters (20/40–20/400)
- **Primary endpoint:** Change from baseline in BCVA at week 24



BALATON (NCT04740905); COMINO (NCT04740931).
BCVA, best-corrected visual acuity; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; HRVO, hemiretinal vein occlusion; Q4W, every 4 weeks; RVO, retinal vein occlusion; T&E, treat-and-extend.

RVO Modified T&E Regimen



Modified T&E regimen: Once reduced, the treatment interval could no longer be extended, except for patients who were on longer intervals and were directly reduced to Q4W (eg, Q16W → Q4W; such patients could be extended to Q12W, but not to Q16W)

[a] 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. [b] Reference BCVA was defined as the mean of the 3 best BCVA values achieved at any prior active dosing visit. BCVA, best-corrected visual acuity; CST, central subfield thickness; Q4W, every 4 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; RVO, retinal vein occlusion; T&E, treat-and-extend.

References

1. Tadayoni R et al. *Ophthalmology* 2024; doi: 10.1016/j.ophtha.2024.01.029

Results

Baseline Characteristics Were Generally Well Balanced Across Treatment Arms Within Each Trial

ITT Population	BALATON (BRVO)		COMINO (H/CRVO)	
	Aflibercept 2.0 mg n = 277	Faricimab 6.0 mg n = 276	Aflibercept 2.0 mg n = 363	Faricimab 6.0 mg n = 366
Age, mean (SD)	63.8 (10.6)	64.3 (10.7)	64.7 (13.3)	65.6 (13.1)
Sex, female, n (%)	147 (53.1)	133 (48.2)	163 (44.9)	173 (47.3)
Ethnicity: Hispanic or Latino, n (%)	51 (18.4)	47 (17.0)	73 (20.1)	66 (18.0)
Race,[a] n (%)				
American Indian or Alaska Native	0	3 (1.1)	3 (0.8)	2 (0.5)
White	172 (62.1)	172 (62.3)	253 (69.7)	243 (66.4)
Asian	94 (33.9)	90 (32.6)	88 (24.2)	89 (24.3)
Black or African American	7 (2.5)	6 (2.2)	13 (3.6)	10 (2.7)
Region, n (%)				
Rest of the world	128 (46.2)	129 (46.7)	187 (51.5)	187 (51.1)
Asia	85 (30.7)	85 (30.8)	83 (22.9)	84 (23.0)
United States and Canada	64 (23.1)	62 (22.5)	93 (25.6)	95 (26.0)
BMI, kg/m^2, mean (SD)	28.58 (7.37)	28.61 (7.42)	28.64 (5.97)	27.38 (5.19)
Systolic blood pressure, mmHg, mean (SD)	137.22 (14.11)	137.39 (14.61)	136.63 (15.78)	135.62 (15.55)
Diastolic blood pressure, mmHg, mean (SD)	82.19 (9.25)	83.00 (9.72)	81.24 (10.35)	80.44 (9.79)
BCVA (letters), mean (SD)	57.64 (12.15)	57.50 (13.04)	50.71 (16.34)	50.25 (16.25)
BCVA category, n (%)[b]				
≤ 34 letters (20/200 or worse)	90 (32.5)	89 (32.2)	80 (22.0)	79 (21.6)
> 34 to < 55 letters (between 20/200 and 20/80)			105 (28.9)	106 (29.0)
≥ 55 letters (20/80 or better)	187 (67.5)	187 (67.8)	178 (49.0)	181 (49.5)
CST, µm, mean (SD)	558.12 (180.26)	558.32 (177.03)	721.07 (242.86)	702.21 (244.00)
Months since RVO diagnosis in the study eye, mean (SD)	1.65 (7.27)	1.26 (1.88)	1.10 (0.95)	1.57 (6.39)
Intraocular pressure, mmHg, mean (SD)	14.48 (2.94)	14.57 (2.88)	14.97 (3.17)	14.89 (3.06)
Lens status: Phakic, n (%)	239 (86.3)	236 (85.5)	314 (86.5)	308 (84.2)

[a] Not all race categories are presented; percentages do not add up to 100. Age is at randomisation. [b] Stratification factors: BALATON: ≤ 54 letters (20/80 or worse) ≥ 55 letters (20/80 or better); COMINO: ≤ 34 letters (20/200 or worse), 34 to < 55 letters (between 20/200 and 20/80), ≥ 55 letters (20/80 or better). Percentages are based on the n in the column headings. BCVA, best-corrected visual acuity; BMI, body mass index; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; CST, central subfield thickness; HRVO, hemiretinal vein occlusion; ITT, intent to treat; RVO, retinal vein occlusion; SD, standard deviation.

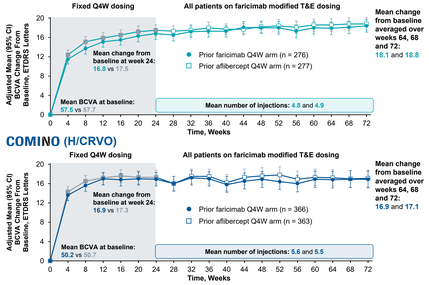
Consistent Proportion of Patients Gaining/Avoiding a Loss of Vision Averaged Over Weeks 64, 68 and 72

CMH Weighted % Averaged Over Weeks 64, 68, 72	BALATON (BRVO)		COMINO (H/CRVO)	
	Aflibercept Q4W switched to faricimab modified T&E n = 277	Faricimab Q4W switched to faricimab modified T&E n = 276	Aflibercept Q4W switched to faricimab modified T&E n = 363	Faricimab Q4W switched to faricimab modified T&E n = 366
Gaining ≥ 15 letters in BCVA	65.8%	61.5%	59.5%	57.6%
Gaining ≥ 10 letters in BCVA	79.1%	78.9%	70.5%	71.3%
Avoiding a loss of ≥ 15 letters in BCVA	98.2%	98.9%	95.6%	93.7%

Percentages are based on the n in the column headings. Missing assessments were imputed by LOCF.
BCVA, best-corrected visual acuity; BRVO, branch retinal vein occlusion; CMH, Cochran-Mantel-Haenszel; CRVO, central retinal vein occlusion; HRVO, hemiretinal vein occlusion; LOCF, last observation carried forward; Q4W, every 4 weeks; T&E, treat-and-extend.

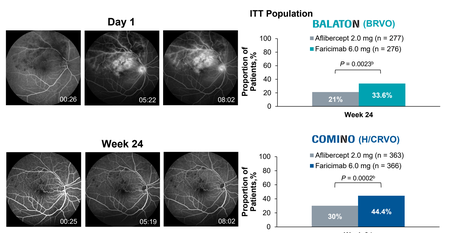
Change in BCVA Over Time: Robust BCVA Gains at Week 24 Maintained Through Week 72 for Both Arms

ITT Population



Faricimab modified T&E regimen started at week 24 but not all patients received faricimab at week 24. Mean change from baseline at week 24 and mean BCVA at baseline differ slightly from primary analysis due to updates before database lock. All observed values are used regardless of the occurrence of the intercurrent events. Results are based on a MMRM analysis in the ITT population. Missing data were implicitly imputed by MMRM. Invalid BCVA values were excluded from analysis. 95% CI is a rounding of 95.03% CI. BCVA, best-corrected visual acuity; BRVO, branch retinal vein occlusion; CI, confidence interval; CRVO, central retinal vein occlusion; ETDRS, Early Treatment Diabetic Retinopathy Study; HRVO, hemiretinal vein occlusion; ITT, intent to treat; MMRM, mixed model repeated measures; Q4W, every 4 weeks; T&E, treat-and-extend.

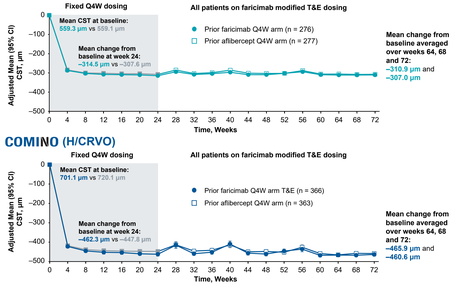
More Patients Achieved Absence of Macular Leakage[a] With Faricimab vs Aflibercept at Week 24



[a] Macular leakage area within ETDRS grid was assessed by the reading centre based on FA images obtained at baseline and predefined follow-up intervals. Absence is defined as area of leakage within the macula of 0 mm^2 per FA. The prespecified exploratory analysis only included patients with evaluable FA data (BALATON: aflibercept, n = 224; faricimab, n = 229; COMINO: aflibercept, n = 297; faricimab, n = 311). All observed values are used regardless of the occurrence of the intercurrent events. 95.03% CIs are shown. [b] Nominal *P* value based on risk difference test (Wald method), not adjusted for multiplicity. No formal statistical conclusions should be made based on the *P* values. BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; ETDRS, Early Treatment Diabetic Retinopathy Study; FA, fluorescein angiography; HRVO, hemiretinal vein occlusion; ITT, intent to treat.

Change in CST Over Time: CST Reductions Maintained From Week 24 Through Week 72 For Both Arms

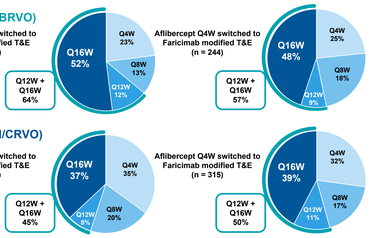
ITT Population



Faricimab modified T&E regimen started at week 24 but not all patients received faricimab at week 24. Mean change from baseline at week 24 and mean CST at baseline differ slightly from primary analysis due to updates before database lock. All observed values are used regardless of the occurrence of the intercurrent events. Results are based on an MMRM analysis in the ITT population. Missing data were implicitly imputed by MMRM. 95% CI is a rounding of 95.03% CI. CST is measured as ILM-RM, as graded by central reading centre. BM, Bruch's membrane; BRVO, branch retinal vein occlusion; CI, confidence interval; CRVO, central retinal vein occlusion; CST, central subfield thickness; HRVO, hemiretinal vein occlusion; ILM, internal limiting membrane; ITT, intent to treat; MMRM, mixed model repeated measures; Q4W, every 4 weeks; T&E, treat-and-extend.

Proportion of Patients on Modified T&E Intervals at Week 68: More Than 57% of Patients in BALATON and More Than 45% in COMINO Achieved ≥ Q12W Dosing

ITT Population



Once reduced, the treatment interval could no longer be extended, except for patients who were on longer intervals and were directly reduced to Q4W (eg, Q16W → Q4W; such patients could be extended to Q12W, but not to Q16W). Treatment interval at a given visit was defined as the treatment interval decision made at that visit. Percentages are based on n: the number of randomised patients who had not discontinued the study at week 68. Descriptive summary is presented. BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; HRVO, hemiretinal vein occlusion; ITT, intent to treat; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

Faricimab Was Well Tolerated From Week 24 to 72, With no Change in Safety Profile

AEs From Week 24 to 72, Patients With ≥ 1 AE, n (%)	BALATON (BRVO)		COMINO (H/CRVO)	
	Aflibercept Q4W to Faricimab modified T&E n = 267	Faricimab Q4W to Faricimab modified T&E n = 270	Aflibercept Q4W to Faricimab modified T&E n = 342	Faricimab Q4W to Faricimab modified T&E n = 359
Ocular AEs	81 (30.3)	76 (28.1)	118 (34.5)	130 (36.2)
Serious ocular AEs	3 (1.1)	4 (1.5)	12 (3.5)	26 (7.2)
Ocular AEs of special interest	1 (0.4)	1 (0.4)	9 (2.6)	21 (5.8)
Intraocular inflammation events	3 (1.1)	2 (0.7)	5 (1.5)	10 (2.8)
Iridocyclitis	1 (0.4)	1 (0.4)	4 (1.2)	3 (0.8)
Iritis	2 (0.7)	0	1 (0.3)	3 (0.8)
Vitritis	0	1 (0.4)	0	4 (1.1)
Uveitis	0	0	0	1 (0.3)
Noninfectious endophthalmitis	0	0	0	1 (0.3)
Keratic precipitates	0	0	0	1 (0.3)
Endophthalmitis events	0	0	1 (0.3)	0
Retinal vasculitis events	0	0	0	0
Retinal artery occlusion/embolism	0	0	1 (0.3)	0
Serious nonocular AEs	23 (8.6)	25 (9.3)	41 (12.0)	30 (8.4)
APTC events	8 (3.0)	2 (0.7)	6 (1.8)	8 (2.2)
AEs leading to treatment discontinuation through week 24	4 (1.5)	0	6 (1.8)	8 (2.2)

Percentages are based on the n in the column headings. For prior faricimab, includes AEs with onset on or after the week 24 treatment or dose hold or if none onset on or after day 168 through week 72. For prior aflibercept, includes AEs with an onset on or after the date of the first faricimab dose through week 72. Multiple occurrences of the same AE in 1 individual are counted only once. AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; HRVO, hemiretinal vein occlusion; Q4W, every 4 weeks; T&E, treat-and-extend.