Faricimab vs standard of care in naive neovascular age-related macular degeneration patients

An indirect treatment comparison using individual level

Lanzetta P[1], Parravano MC[2], Nicolò M[3], Staurenghi G[4], Viola F[5], Vujosevic S[6], Galeone C[7,8], Bianchino L[9], Sicari E[9], Villa G[9]

1 Department of Ophthalmology, University of Udine, Udine, Italy; 2 IRCCS Fondazione Bietti, Rome, Italy; 3 University Eye Clinic, Ospedale Policlinico San Martino IRCCS, Genoa, Italy; 4 Eye Clinic, Department of Biomedical and Clinical Sciences "Luigi Sacco", Luigi Sacco Hospital, University of Milan, Milan, Italy; 5 Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy; Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; 6 Eye Clinic, IRCCS MultiMedica, Milan, Italy; 7 Bicocca Applied Statistics Center (B-ASC), Università degli Studi di Milano-Bicocca, Milan, Italy; 8 Biostatistics & Outcome Research, Statinfo, Milan, Italy; 9 Roche S.p.A., Monza, Italy

CO71

AIMS

To evaluate the potential benefit of faricimab, a new targeting vascular endothelial growth factor A (VEGF-A) and Angiopoietin-2, versus the current intravitreal a-VEGF Standard of Care (SoC) in neovascular age-related macular degeneration (nAMD) patients.

METHODS

Patient-level data from the companion phase III clinical trials TENAYA (NCT03823287) and LUCERNE (NCT03823300) (for a total of 513 patients treated with faricimab) and the RADIANCE Italian observational study (SoC: n=263; including aflibercept: n=101, bevacizumab: n=53, ranibizumab: n=59) were used. The investigation included naïve nAMD patients with effectiveness data at one year follow-up available. Effectiveness was assessed in terms of change from baseline in best-corrected visual acuity (BCVA) and central subfield thickness (CST). Propensity score weighting (PSW) was used to balance demographic and clinical patients' characteristics between the faricimab and the SoC cohorts. Weighted one-way ANOVA was applied to compare changes in BCVA and CST between groups. A sensitivity analysis to adjust for injections' number was conducted using weighted ANCOVA.

RESULTS

Propensity Score Analysis

Before weighting using the calculation of propensity scores, significant differences in baseline patients' characteristics between the two cohorts were observed. As shown in Table 1 and 2, after PSW, the cohorts resulted well-balanced.

MAIN OUTCOME RESULTS

Primary endpoint: change in BCVA

After PSW (*Table 1*), mean vision gains in BCVA after 1 year of treatment were 6.5 letters in the faricimab cohort and 1.0 in the real-world cohort (*Table 3*), with a corresponding treatment difference of 5.4 letters in favour of faricimab (*Figure 1*). After adjusting for the number of injections, the treatment difference remained statistically significant, and was equal to 4.0 letters.

Secondary endpoint: change in CST

After PSW (*Table2*), mean CST change from baseline was -143.2 µm in the faricimab cohort and -71.4 µm in the real world cohort (*Table 4*), with a corresponding treatment difference of -71.8 µm in favour of faricimab (*Figure 2*). A very similar estimated treatment difference was found after adjusting for the number of injections, with a reduction equal to -71.5 µm.

Table 1. Baseline demographic and clinical characteristics in the pivotal and Radiance studies before and after PSW as performed in the analysis on the change in BCVA from baseline after 1 year of treatment

	Before weighting				After weighting			
	Pivotal faricimab (N=513)	Radiance SoC (N=263)	SMD	p-value for comparison	Pivotal faricimab	Radiance SoC	SMD	p-value for comparison
Age, median (IQR)	76 (70-81)	78 (73-82)	-0.254	0.0007	77 (71-82)	76 (71-81)	0.040	0.601
Sex, n (%)								
Men	187 (36.5)	115 (43.7)	-0.149	0.049	315.2 (40.8)	319.7 (40.1)	0.014	0.778
Women	326 (63.6)	148 (56.3)			457.2 (59.2)	477.6 (59.9)		
Lesion type, n (%)								
Occult	275 (54.6)	103 (40.9)	0.292		395.7 (52.3)	406.4 (52.1)	0.005	
Classic*	210 (41.7)	121 (48.0)	-0.102	<0.001	316.6 (41.8)	323.6 (41.5)	0.008	0.951
RAP	19 (3.8)	28 (11.1)	-0.271		45.1 (6.0)	49.4 (6.3)	-0.014	
Missing	*9*	*11*			*14.9*	*17.8*		
IRF at baseline, n (%)								
No	276 (54.9)	84 (42.6)	0.026	0.004	359.2 (51.5)	371.8 (51.5)	-0.003	0.998
Yes	227 (45.1)	113 (57.4)			337.9 (48.5)	349.9 (48.5)		
Missing	*10*	*66*			75.3	75.4		
SRF at baseline, n (%)								
No	172 (34.0)	58 (29.2)	0.236	0.217	233.4 (33.3)	264.5 (36.4)	0.055	0.211
Yes	334 (66.0)	141 (70.8)			468.2 (66.7)	461.7 (63.6)		
Missing	*7*	*64*			70.8	71.0		
VA at baseline, mean±SD	60.5 ± 13.1	57.1 ± 21.1	0.219	0.004	59.6 ± 16.5	61.1 ± 34.3	-0.088	0.244

IQR, interquartile range; IRF, intraretinal fluid; SMD, standardized mean difference; SRF, subretinal fluid; * Including "minimally" e "predominantly" classic lesions.

Table 2. Baseline demographic and clinical characteristics in the pivotal and Radiance studies before and after PSW as performed in the analysis on the change in CST from baseline after 1 year of treatment

	Before weighting				After weighting			
	Pivotal faricimab (N=513)	Radiance SoC (N=263)	SMD	p-value for comparison	Pivotal faricimab	Radiance SoC	SMD	p-value for comparison
Age, median (IQR)	76 (70-81)	77 (72-82)	-0.155	0.077	76 (70-81)	76 (70-80)	0.030	0.739
Sex, n (%)								
Men	184 (36.2)	80 (48.2)	-0.246	0.006	365.4 (39.4)	275.7 (40.4)	-0.019	0.727
Women	325 (63.8)	86 (51.8)			407.8 (60.6)	407.6 (59.7)		
Lesion type, n (%)								
Occult	274 (54.8)	76 (47.2)	0.161		350.5 (53.1)	363.1 (54.2)	-0.022	
Classic*	207 (41.4)	63 (39.1)	0.056	<0.001	268.4 (40.7)	265.4 (39.6)	0.022	0.916
RAP	19 (3.8)	22 (13.7)	-0.346		40.8 (6.2)	41.9 (6.5)	-0.002	
Missing	*9*	*5*			*13.3*	*12.8*		
IRF at baseline, n (%)								
No	276 (55.2)	68 (43.9)	-0.168	0.004	343.4 (52.4)	342.6 (51.6)	-0.016	0.755
Yes	224 (44.8)	87 (56.1)			311.8 (47.6)	321.8 (48.4)		
Missing	*9*	*11*			*18.0*	*18.8*		
SRF at baseline, n (%)								
No	170 (33.9)	46 (29.5)	-0.022	0.309	219.3 (33.3)	242.6 (36.4)	0.065	0.244
Yes	332 (66.1)	110 (70.5)			438.8 (66.7)	424.4 (63.6)		
Missing	*7*	*10*			*15.1*	*16.2*		
VA at baseline, mean±SD	360 ± 121	392 ± 163	-0.223	0.021	366 ± 144	362 ± 288	0.030	0.725

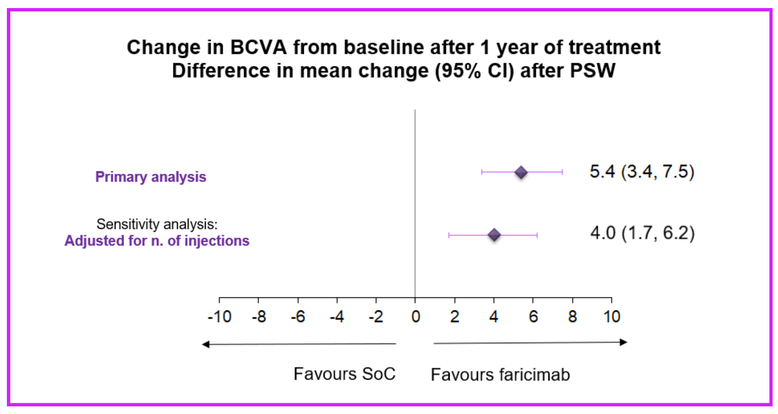
IQR, interquartile range; IRF, intraretinal fluid; SMD, standardized mean difference; SRF, subretinal fluid.* Including "minimally" e "predominantly" classic lesions.

Table 3. BCVA changes between faricimab and SoC, after and before PSW and after adjusting for the number of injections

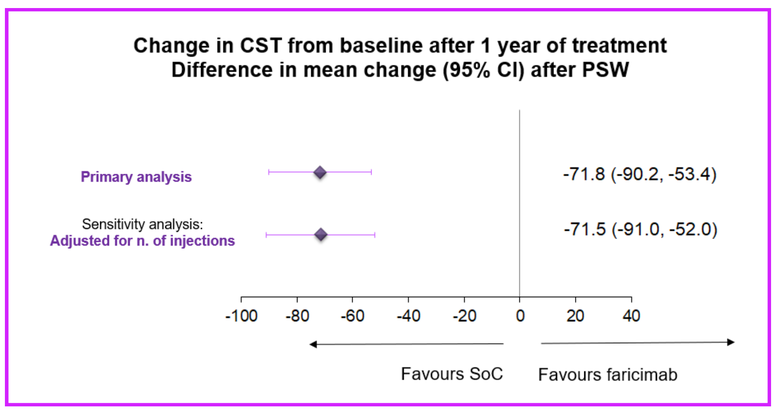
	faricimab	SoC
Weighted BCVA at baseline Mean ± SD	59.6 ± 16.5	61.1 ± 34.3
Weighted BCVA change from baseline Mean (95% CI)	6.5 (5.0, 7.9)	1.0 (-0.4, 2.5)
Weighted BCVA change from baseline *adjusted for n. of injection* Mean (95% CI)	5.9 (4.4, 7.4)	1.9 (0.4, 3.5)

Table 4. CST changes between faricimab and SoC, after and before PSW and after adjusting for the number of injections

	faricimab	SoC
Weighted CST at baseline Mean ± SD	366 ± 144	362 ± 288
Weighted CST change from baseline Mean (95% CI)	-143 (-156, -130)	-71 (-84, -58)
Weighted CST change from baseline adjusted for n. of injection Mean (95% CI)	-143 (-156, -130)	-72 (-85, -58)



Fugure 1. Main efficacy results



Fugure 2. Main efficacy results

CONCLUSION

In naive nAMD patients, first line treatment with faricimab resulted in a greater vision gain and in CST reduction compared with current intravitreal a-VEGF Standard of Care. Despite limitations of indirect treatment comparisons, which call for specific post-marketing real world studies, the present analysis supports potential benefits in nAMD patients treated with faricimab.

corresponding author: emilia.sicari@roche.com