Comparable Ofatumumab Treatment Outcomes in Patients across Racial/Ethnic Groups in the ASCLEPIOS I/II and APOLITOS studies

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Introduction

- Ofatumumab is a fully human anti-CD20 monoclonal antibody approved for the treatment of RMS in adults in the US[1] and other countries[a]
- Ofatumumab, administered as monthly 20 mg (in 0.4 ml) subcutaneous (s.c.) injection, demonstrated superior efficacy and a favorable safety profile versus teriflunomide in RMS patients in the Phase 3 ASCLEPIOS I/II trials[1,2]
- Ofatumumab is amongst the most efficacious medications in RMS, according to a network meta-analysis[3]
- The MS disease course varies between racial/ethnic groups.[4] However, differences in response to treatment outcomes may exist

Objective

- To compare ofatumumab treatment outcomes in RMS patients across different racial/ethnic groups in the ASCLEPIOS I/II and APOLITOS trials

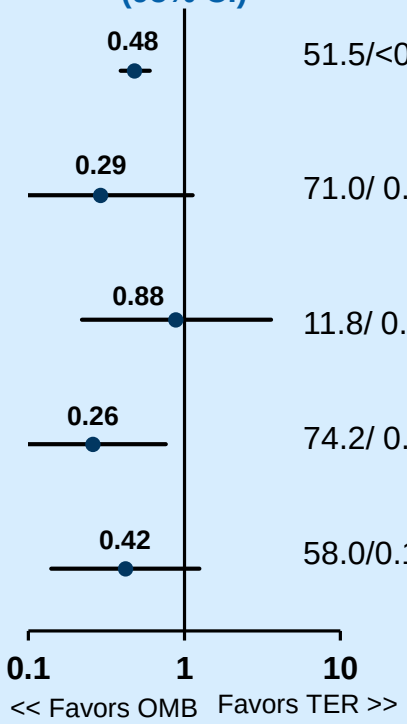
Methods

- Post hoc analysis included data from patients who received ofatumumab 20 mg s.c.
- Subgroup analyses were planned to check for numerical consistency between racial/ethical groups (subgroups are not powered)
- Study outcomes: Efficacy (ARR), pharmacokinetics (PK), pharmacodynamics (PD), and safety

[a]Australia, Canada, Singapore, Switzerland, UAE, Albania, Argentina, Japan and India; ARR, annualized relapse rate; MS, multiple sclerosis; RMS, relapsing multiple sclerosis; [1]KESIMPTA® [Prescribing Information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; Aug 2020. [2]Hauser SL, et al. *N Engl J Med.* 2020;383:546–57. [3]Samjoo A, et al. *J Comp Eff Res.* 2021;9:1255-1274. . [4]Amezcua, L and McCauley J. *Mult Scler* 2020; 26: 561–567.

Results: Efficacy (Annualized Relapse Rate)

	Group	Adjusted ARR (95% CI)	Rate ratio (95% CI)	RR (%)/p-value
ASCLEPIOS I/II (up to 30 months)	**Caucasian**			
	OMB 20 mg (N=829)	0.13 (0.11, 0.15)	0.48	51.5/<0.001
	TER 14 mg (N=829)	0.26 (0.23, 0.30)		
	African/American			
	OMB 20 mg (N=28)	0.07 (0.02, 0.22)	0.29	71.0/ 0.075
	TER 14 mg (N=38)	0.23 (0.12, 0.45)		
	Asian			
	OMB 20 mg (N=36)	0.08 (0.03, 0.24)	0.88	11.8/ 0.862
	TER 14 mg (N=35)	0.09 (0.04, 0.24)		
	Other			
	OMB 20 mg (N=53)	0.08 (0.03, 0.18)	0.26	74.2/ 0.014
	TER 14 mg (N=34)	0.30 (0.15, 0.57)		
APOLITOS up to 24 weeks	**Japanese*/Caucasian**			
	OMB 20 mg (N=43)	0.264 (0.11, 0.63)	0.42	58.0/0.119
	Placebo (N=21)	0.629 (0.28, 1.43)		



ARR was low in all racial/ethnic patient groups on ofatumumab treatment

*In the APOLITOS extension, ARR in the continuous ofatumumab group (0.081) was similar to that of Phase 3 trial and other ethnic groups (Saida T, et al. Poster presentation at AAN 2021)
ARR, annualized relapse rate; CI, confidence interval; OMB, ofatumumab; RR, rate reduction; TER, teriflunomide

Results: PK and PD

PK: Pre-dose ofatumumab concentration and B cell levels

	Group	n	Concentration (µg/mL) Median (95% range)	n	B cell levels at 6 months (cells/ µL) Median (95% range)
ASCLEPIOS I/II	Caucasian	753	0.44 (0.05, 2.53)	762	0.0 (0.0, 20.0)
	African/American	23	0.11 (0.05, 1.67)	25	0.0 (0.0, 24.0)
	Asian	29	0.13 (0.05, 1.20)	30	0.0 (0.0, 31.0)
	Other	33	0.45 (0.05, 2.53)	35	0.0 (0.0, 0.0)
APOLITOS	Japanese	20	0.71 (0.14, 2.0)	19	0.0 (0.0, 3.55)
	Caucasian	20	0.42 (0.11, 1.48)	17	1.0 (0.0, 11.8)

Ofatumumab pre-dose concentrations were comparable across groups in the ASCLEPIOS trials and slightly higher in Japanese patients in the APOLITOS trial, consistent with the lower mean body weight in this subgroup

PK

- A population-PK analysis of PK data of RMS patients showed minor but not clinically significant differences between racial/ ethnic groups and PK parameters

PD

- No clinically relevant difference in the level of B-cell depletion was observed among these populations
- In the APOLITOS trial, ofatumumab was associated with a consistent depletion of CD19+ B-cells and CD3+CD20+ T-cells in Asian and Caucasian patients, indicating a similar PD response

PD, pharmacodynamics; PK, pharmacokinetics

Results: Safety

	ASCLEPIOS I/II*				APOLITOS* (24 weeks)	
	Caucasian n=829 n (%)	Black/African American n=28 n (%)	Asian n=36 n (%)	Other n=53 n (%)	Japanese n=21 n (%)	Caucasian n=22 n (%)
Patients with ≥1 AE	704 (84.9)	26 (92.9)	24 (66.7)	37 (69.8)	17 (81.0)	13 (59.1)
Patients with ≥1 SAE	78 (9.4)	3 (10.7)	1 (2.8)	4 (7.5)	1 (4.8)	0 (0.0)
AEs of special interest						
Injection systemic reaction	171 (20.6)	5 (17.9)	7 (19.4)	6 (14.3)	4 (19.0)	6 (27.3)
Injection site reaction	88 (10.6)	4 (14.3)	1 (2.8)	5 (11.9)	1 (4.8)	0 (0.0)
Infections	443 (53.4)	16 (57.1)	8 (22.2)	21 (39.6)	10 (47.6)	6 (27.3)
Neoplasm	22 (2.7)	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	0 (0.0)
Hepatic safety	42 (5.1)	0 (0.0)	2 (5.6)	0 (0.0)	0 (0.0)	1 (4.5)
Neutropenia	9 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

No meaningful differences were observed in the pattern, incidence, severity of AEs

*included patients who received ofatumumab in the trial
AE adverse event; SAE, serious adverse event

Conclusions

- This post hoc analysis revealed no clinically relevant differences in ofatumumab treatment outcomes for RMS patients of different racial/ethnic groups in the ASCLEPIOS I/II and APOLITOS trials
  - Ofatumumab showed a comparable reduction in annualized relapse rate
  - No clinically significant difference was observed regarding pharmacokinetics, B-cell depletion and the safety profile
  - The safety profile was consistent with the overall population with no discernible trends/safety signals[1]
- The approved dosing regimen of ofatumumab s.c. has been justified across racial/ethnic groups and collection of safety and efficacy data will be continued in future studies

[1]Hauser SL, et al. *N Engl J Med.* 2020;383:546–57.

Disclosures

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