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

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Background

- OMB is a fully human anti-CD20 monoclonal antibody approved for the treatment of RMS in adults in the US[1] and other countries[a]
- OMB, 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]
- OMB 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 OMB 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 OMB 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

Results

Efficacy (Annualized Relapse Rate)

- ARR was low in all racial/ethnic patient groups on ofatumumab treatment (**Figure 1**)

PK and PD

- OMB 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 (**Figure 2**)

PK:

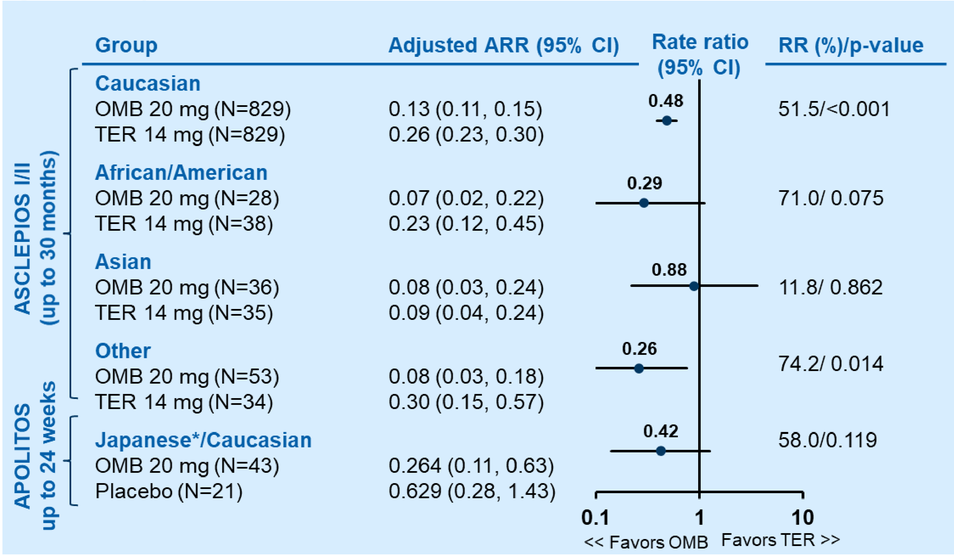
- A population-PK analysis of PK data of RMS patients showed minor but not clinically significant differences between racial/ ethnic groups and PK parameters

PD:

- No clinically relevant difference in the level of B-cell depletion was observed among these populations
- In the APOLITOS trial, OMB 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

[a]Australia, Canada, Singapore, Switzerland, UAE, Albania, Argentina, Japan and India

Figure 1. Efficacy of OMB



*In the APOLITOS extension, ARR in the continuous OMB group (0.081) was similar to that of Phase 3 trial and other ethnic groups (Saida T, et al. Poster presentation at AAN 2021)

Figure 2. PK: Pre-dose OMB 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)

Safety

- No meaningful differences were observed in the pattern, incidence, and severity of AEs (**Figure 3**)

Figure 3. Safety of OMB

	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)

*included patients who received OMB in the trial

Conclusions

- This post hoc analysis revealed no clinically relevant differences in OMB treatment outcomes for RMS patients of different racial/ethnic groups in the ASCLEPIOS I/II and APOLITOS trials
  - OMB showed a comparable reduction in ARR
  - No clinically significant difference was observed regarding PK, B-cell depletion and the safety profile
  - The safety profile was consistent with the overall population with no discernible trends/safety signals[2]
- The approved dosing regimen of OMB s.c. has been justified across racial/ethnic groups and collection of safety and efficacy data will be continued in future studies

Abbreviations

AE, adverse event; ARR, annualized relapse rate; CI, confidence interval; MS, multiple sclerosis; OMB, ofatumumab; PD, pharmacodynamics; PK, pharmacokinetics; RR, rate reduction; RMS, relapsing multiple sclerosis; SAE, serious adverse event; TER, teriflunomide.

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