Interim Results of Open-label Multicenter Phase 4 Study Assessing Immune Response to Influenza Vaccine in Patients With Relapsing Multiple Sclerosis Treated With Ofatumumab

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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
- OMB, administered as monthly 20 mg (in 0.4 ml) subcutaneous injection, demonstrated superior efficacy versus teriflunomide and a favorable safety profile in RMS patients in the Phase 3 ASCLEPIOS I and II trials[1,2]
- Vaccinations comprise an important component of MS management. Data are needed regarding whether OMB impacts humoral immune response to vaccines, including the influenza vaccine, in RMS patients

Objective

- **To assess whether RMS patients treated with subcutaneous OMB 20 mg every 4 weeks can mount an immune response to the 2020-2021 inactivated influenza vaccine compared to those on IFN/GA**

Methods

Study design

- This is an ongoing 3-cohort, open-label, multicenter, prospective, Phase 4 study (NCT04667117; **Figure 1**)
  - Cohort 1 received the influenza vaccine ≥2 weeks prior to starting OMB
  - Cohort 2 received the vaccine ≥4 weeks after starting OMB
  - Cohort 3 received the vaccine ≥4 weeks after starting IFN/GA
- Patients in Cohort 1 will receive OMB 20 mg at 2, 3, and 4 weeks after vaccination, followed by subsequent OMB 20 mg doses once monthly starting at Week 6
- Patients in Cohorts 2 and 3 will continue taking their prescribed therapy per their current dosing schedule
- Key exclusion criteria:
  - Patients with recent infections
  - Prior treatment with B-cell targeted therapies, lymphocyte-trafficking blockers, alemtuzumab, anti-CD4, cladribine, cyclophosphamide, mitoxantrone, azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, total body irradiation, bone marrow transplantation; treatment with a natalizumab within 6 months of week 0; treatment with an S1P modulator within 60 days prior to Week 0
- All groups underwent a HI titer prior to and 4 weeks after vaccination
- Number and percentage of patients with AEs were reported
- Patients in Cohorts 1 and 2 can continue into the optional Extension Period and take monthly doses of OMB

Study endpoints

- **Primary endpoint:** achieving seroprotection to influenza at Week 4 (postvaccination antibody titer ≥40)
- **Secondary endpoints:**
  - Achieving seroconversion (postvaccination HI titers ≥4-fold increase or ≥40 in those with prevaccination titers ≥10 or <10, respectively)
  - Safety (any AEs, SAEs, and AEs leading to discontinuation)

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Figure 1. Study Design

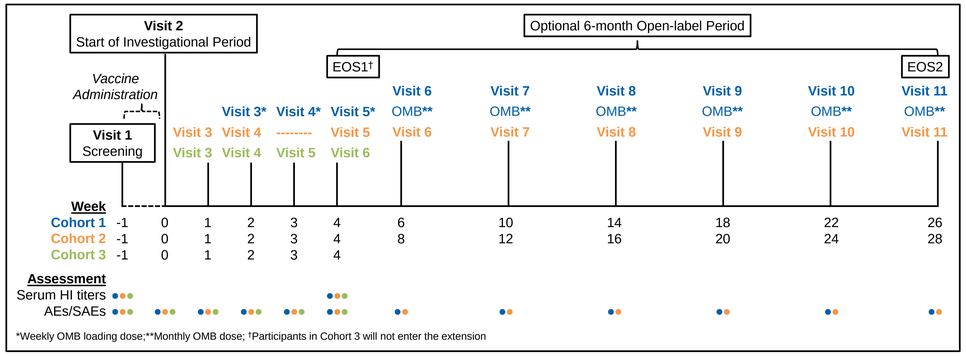

Table 1. Immune response of Cohort 1 (n=5; vaccine ≥2 weeks prior to starting OMB)

Strain	Seroprotection (%)		Seroconversion (%)	Mean change in HI titer (SD)
	Screening	Week 4	Week 4	Week 4 from Baseline
Influenza A Brisbane	100.00	100.00	80.00	432.00 (354.85)
Influenza A Kansas	100.00	100.00	40.00	160.00 (228.04)
Influenza A Michigan	80.00	100.00	60.00	490.00 (447.33)
Influenza A Singapore	80.00	100.00	40.00	444.00 (489.98)
Influenza B Colorado	0.00	60.00	60.00	48.00 (56.30)
Influenza B Phuket	0.00	80.00	60.00	44.00 (32.09)

Table 2. Immune response of Cohort 2 (n=2; vaccine ≥4 weeks after starting OMB)

Strain	Seroprotection (%)		Seroconversion (%)	Mean change in HI titer (SD)
	Screening	Week 4	Week 4	Week 4 from Baseline
Influenza A Brisbane	100.00	100.00	0.00	20.00 (28.28)
Influenza A Kansas	100.00	100.00	0.00	0.00 (0.00)
Influenza A Michigan	100.00	100.00	0.00	-40 (56.57)
Influenza A Singapore	100.00	100.00	0.00	0.00 (0.00)
Influenza B Colorado	50.00	50.00	0.00	40.00 (56.57)
Influenza B Phuket	50.00	50.00	0.00	-5.00 (7.07)

Table 3. Immune response of Cohort 3 (n=1; vaccine ≥4 weeks after starting IFN/GA)

Strain	Seroprotection (%)		Seroconversion (%)	Mean change in HI titer (SD)
	Screening	Week 4	Week 4	Week 4 from Baseline
Influenza A Brisbane	100.00	100.00	0.00	160.00
Influenza A Kansas	100.00	100.00	0.00	40.00
Influenza A Michigan	100.00	100.00	100.00	480.00
Influenza A Singapore	100.00	100.00	0.00	40.00
Influenza B Colorado	0.00	100.00	100.00	60.00
Influenza B Phuket	0.00	0.00	0.00	0.00

Results

Patient characteristics

- 8 patients were included in this interim analysis; mean age was 35 years (range: 22–48), 75% female, and 87.5% White

Immune response

- **Tables 1-3** show percentage of patients in Cohorts 1-3 with seroprotection at Screening and at Week 4; percentage of patients with seroconversion at Week 4; and the mean (SD) change in HI titers from Baseline, by strain name

Safety

- 4 out 5 (80%) patients in Cohort 1 experienced ≥1 AE, including:
  - Nausea (40%), pain (40%), asymptomatic COVID-19 (20%), back pain (20%), hypoesthesia (20%), migraine (20%), muscle spasms (20%), polydipsia (20%), and pyrexia (20%)
- No AEs were reported in Cohorts 2 and 3
- No serious AE was reported
- There were no study discontinuations due to AE

Conclusions

- This study plans to enroll up to 66 patients and study completion is expected by Q3 2022; additional data forthcoming
- Despite small sample size which limits data interpretation, these interim results offer the first preliminary data of immune response in OMB-treated RMS patients given an inactivated vaccine.

Abbreviations

AE, adverse event; COVID-19, coronavirus disease 2019; EOS, end of study; GA, glatiramer acetate; HI, hemagglutination inhibition; IFN, interferon; MS, multiple sclerosis; OMB, ofatumumab; RMS, relapsing multiple sclerosis; S1P, sphingosine-1-phosphate; SD, standard deviation; SAE, serious adverse event.

References

1. KESIMPTA® (ofatumumab) Prescribing Information. https://www.novartis.us/sites/www.novartis.us/files/kesimpta.pdf. Accessed: March 15, 2021.
2. Hauser SL, et al. N Engl J Med 2020;383:546-557.

Disclosures

Jeffrey Gitt receives honoraria for promotional programs from Biogen, Bristol Myers Squibb, Genentech, Allergan, and Alexion Pharmaceuticals companies. **Elisabeth B. Lucassen, James Stankiewicz,** and **Xiangyi Meng** are employees of Novartis Pharmaceuticals Corporation. **Bianca Weinstock-Guttman** has received consulting fees from Biogen, Celgene, EMD Serono, Genentech and Janssen, and research support from Biogen, Celgene, EMD Serono, Genentech and Novartis.

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