

Interim Results of an Open-Label Study to Assess Humoral Immune Response to COVID-19 mRNA Vaccine in Participants with Relapsing Multiple Sclerosis Treated with Ofatumumab

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SUMMARY

- Although these are interim results with a limited number of patients, most patients in this study developed an antibody response to COVID-19 mRNA vaccination ≥ 4 weeks after starting ofatumumab treatment
- All ofatumumab-treated patients <50 years who received a third dose developed an antibody response after COVID-19 mRNA vaccination
- This study is ongoing and will continue to collect data on ofatumumab-treated RMS patients and humoral immune response to a COVID-19 mRNA vaccine. Other studies are also currently underway to describe humoral and cell-mediated immune response



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BACKGROUND

- Ofatumumab (OMB, Kesimpta®) is a fully human anti-CD20 monoclonal Ab approved for the treatment of relapsing multiple sclerosis (RMS) in adults in the US¹ and other countries
- Recently reported open-label extension data (ALITHIOS) showed 94% (n=139) of COVID-19 cases were mild or moderate in severity in adults treated with OMB²
- Ocrelizumab (OCR) and rituximab (RTX) have shown diminished humoral response but robust cellular (T cell) response³; data on OMB immune responses are accumulating

OBJECTIVE

- To report interim results of a Phase 4 study (NCT04847596) assessing the effects of OMB on humoral immune response to COVID-19 mRNA vaccine in participants with RMS

RESULTS

PATIENT DEMOGRAPHICS AND DISPOSITION

- Patient demographics and disposition are described in **Table 1**

Table 1. Patient demographics and disposition

	Total (N=26)
Disposition / Reason, n (%)	
Completed study	14 (53.9)
Ongoing	9 (34.6)
Discontinued	3 (11.5)
AE (herpes zoster)*	1 (3.85)
Subject decision†,‡	2 (7.69)
Age, median (range), years	42.0 (27–54)
Female, n (%)	21 (80.8)
Race, n (%)	
White	25 (96.15)
Black or African American	1 (3.85)
Ethnicity, n (%)	
Hispanic or Latino	9 (34.6)
Not Hispanic or Latino	16 (61.5)
Not reported	1 (3.9)
OMB treatment duration at screening, median (range), days	239.0 (52–367)
Prior MS DMT before OMB treatment	
Any MS DMT (excluding OMB)	22 (84.6)
Treatment-naïve prior to OMB start‡	4 (15.4)
Number of vaccine doses	
2	16 (61.5)
3	10 (38.5)

*Subject came to site at Visit 3 but did not perform Visit 3 assay (last assay performed at Visit 2)

†One subject (age 43, who received 3 Moderna vaccine doses, with prior OCR treatment) discontinued after screening visit

‡One subject discontinued after Visit 2 (last assay performed at Visit 2)

METHODS

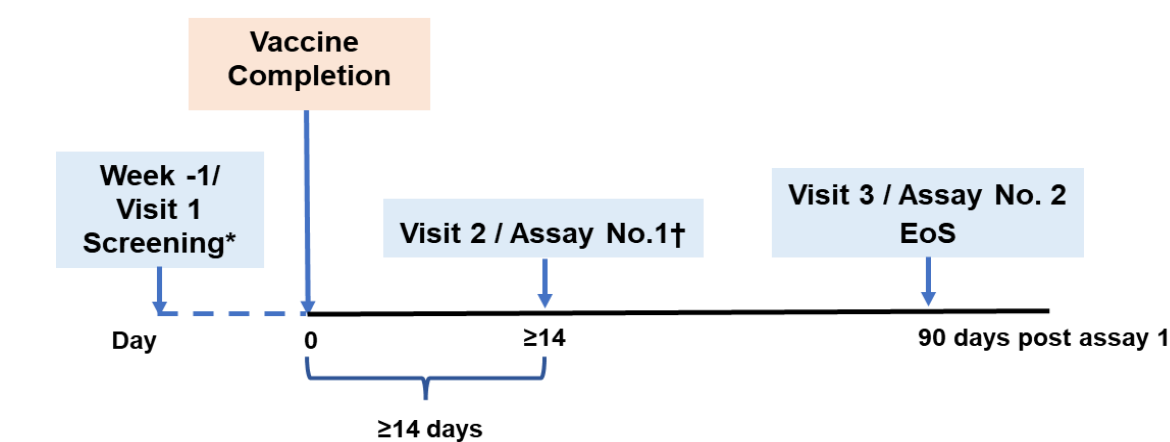
STUDY DESIGN

- This is an ongoing open-label, multicenter, single cohort, prospective study that enrolled RMS patients (aged 18–55) who are currently receiving OMB for ≥ 1 month (**Figure 1**)
- Patients who received 2 or 3 doses of a COVID-19 mRNA (Pfizer/Moderna) vaccine were eligible for enrollment
- Patients with prior COVID-19 diagnosis, contraindication to receiving an COVID-19 mRNA vaccine, recent major infections, and prior treatment with S1P receptor modulators or natalizumab <2 months prior to enrollment were excluded
- First post-vaccination serologic assessment occurred ≥ 14 days after 2nd or 3rd dose followed by a second assessment 90 days thereafter
- Qualitative IgG Ab (spike or RBD) assays were done or facilitated by local institutional laboratories. As such, determination of positive or negative result was by local laboratory threshold

STUDY ENDPOINTS

- Primary endpoint:** Achieving immune response to non-live COVID-19 mRNA vaccine as defined by a positive SARS-CoV-2 qualitative IgG Ab assay (Assay No. 1)
- Secondary endpoints:** AEs/SAEs reporting

Figure 1. Study Design



*Vaccine scheduled or first dose already received; †If entry criteria met at screening, Assay No.1 may be done at Visit 1

EFFECT OF OMB TREATMENT ON HUMORAL IMMUNE RESPONSE TO COVID-19 mRNA VACCINE

- A scheduled interim analysis was conducted in 26 participants
 - Serologic data for Assay No. 1 (first post-vaccination assessment) available for 25 patients due to one screen failure; characteristics described in **Table 2**
- 56.0% (14/25) achieved a positive humoral immune response to COVID-19 vaccine at Assay No. 1 (responders) (**Table 2**)
- Humoral immune response appears to be increased with three doses vs two (**Table 3**)
- Prior DMT, particularly OCR, appears to affect humoral immune response (**Table 2**)
- Age ≥ 50 appears to lead to decreased humoral response (**Table 2**)
- Length of OMB treatment and brand of vaccine do not appear to impact likelihood of achieving a positive humoral response (**Table 2**)

Table 2. Immune response to non-live COVID-19 mRNA vaccine

	Responders, n/M (%)
Overall response rate	14/25 (56.0) 95% CI: (35.3, 75.0)
Prior MS DMT before OMB treatment	
OCR	1/5 (20.0)
Other*	13/18 (72.2)
Treatment-naïve prior to OMB start	2/4 (50.0)
Age (years)	
<50	13/18 (72.2)
≥ 50	1/7 (14.3)
Length of OMB treatment at time of Assay No.1 (days)	
<182	5/9 (55.6)
≥ 182	9/16 (56.3)
Type of COVID-19 mRNA vaccine	
Moderna	4/7 (57.1)
Pfizer	10/18 (55.6)

n=number of patients with positive; M=number of patients with lab data

*Other: Fingolimod hydrochloride, Siponimod fumarate, Glatiramer Acetate, Natalizumab, Dimethyl Fumarate, Interferon β -1a, Immunoglobulins Nos, Teriflunomide

Table 3. Positive qualitative Ab response by number of COVID-19 mRNA vaccinations

Positive Qualitative Ab Response	Two doses, n/M (%)	Three doses, n/M (%)
Overall	7/16 (43.8%)	7/9 (77.8%)
No prior OCR	7/13 (53.8%)	6/7 (85.7%)
Age<50	7/12 (58.3%)	6/6 (100.0%)
Age<50, no prior OCR	7/10 (70.0%)	6/6 (100.0%)

n=number of patients with positive; M=number of patients with lab data

SAFETY

- Four (15.4%) patients experienced AEs related to OMB treatment or vaccination
 - AEs by preferred term included COVID-19, cough, fatigue, headache, herpes zoster, oropharyngeal pain, rhinorrhea, SARS-CoV-2 Ab test negative, each by n=1 (3.9%)
- No SAEs were reported

LIMITATIONS

- Assays were performed by local labs using local procedures
- The population studied was heterogeneous and sample size was limited

CONCLUSIONS

- Albeit limited by population heterogeneity and small sample size, these interim results offer preliminary data on humoral immune response in OMB-treated RMS patients given a COVID-19 mRNA vaccine
 - Three vaccine doses may elicit a stronger humoral immune response than two doses in OMB-treated RMS patients
 - Prior OCR or age ≥ 50 may lead to a decreased humoral immune response while length of OMB treatment and COVID-19 mRNA vaccine type may not impact humoral immune response
- As both cellular and humoral responses contribute to immunity against COVID-19, further data are needed on OMB T cell response to COVID-19 mRNA vaccines in OMB-treated RMS patients; a subsequent study to assess this is currently ongoing (NCT04869358)
- Full results will be available once longitudinal data has been acquired and analyzed

ABBREVIATIONS: AE, adverse event; Ab, antibody; COVID-19, coronavirus disease 2019; DMT, disease-modifying therapy; EoS, end of study; HCP, healthcare professional; IgG, immunoglobulin G; MS, multiple sclerosis; OCR, ocrelizumab; OMB, ofatumumab; RMS, relapsing multiple sclerosis; RTX, rituximab; SAE, serious adverse event; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; S1P, sphingosine-1-phosphate.

DISCLOSURES: AH Cross has received consulting fees, support and honoraria from Biogen, Celgene, Bristol Myers Squibb, EMD fees from Biogen Idec, Celgene/Receptos, Janssen/Actelion, Merck/EMD Serono, Horizon, Novartis, Genentech/Roche and TG Therapeutics. A Chinae is a speaker for Sanofi-Genzyme, Biogen, Teva, Novartis, Genentech, EMD Serono, and Allergan. B Hendin has received advisory and speaking honoraria from Biogen, Genentech, Genzyme, EMD Serono, Novartis and Alexion. MJ Tullman has received consulting fees, research support, and/or speaking honoraria from Biogen, Bristol Myers Squibb, EMD Serono, Genzyme, Genentech, Novartis, TG Therapeutics, Horizon, and Banner Life Sciences. R Aburashed has received consulting fees and/or speaker honoraria from and served on scientific advisory boards for Bayer, Biogen, Genentech, Sanofi, Teva, and Novartis (also received research grants). J Stankiewicz, E Lucassen, and X Meng are employees of Novartis Pharmaceuticals Corporation. A Bar-Or has participated as a speaker in meetings sponsored by and received consulting fees and/or grant support from: Atara Biotherapeutics, Biogen Idec, Celgene/Receptos, Janssen/Actelion, MAPI, Medimmune, Merck/EMD Serono, Novartis, Roche/Genentech and Sanofi-Genzyme.

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ACKNOWLEDGEMENTS: The study was supported by Novartis Pharmaceuticals Corporation. Medical writing support was provided by Julie Espinosa, PhD, of Alphabet Health (New York, NY) and was funded by Novartis Pharmaceuticals Corporation. This poster was developed in accordance with Good Publication Practice (GPP3) guidelines. Authors had full control of the content and made the final decision on all aspects of this poster.