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P101

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

1 **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**

2 **All ofatumumab-treated patients <50 years who received a third dose developed an antibody response after COVID-19 mRNA vaccination**

3 **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**

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 US[1] 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 OMB[2]
- Ocrelizumab (OCR) and rituximab (RTX) have shown diminished humoral response but robust cellular (T cell) response[3]; 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

METHODS

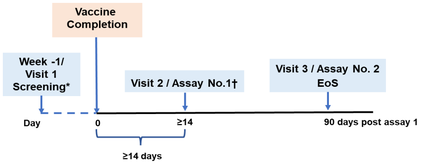
STUDY DESIGN

- 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

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 of 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)

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 heterogenous 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 Chinea** 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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