Design and Rationale for an Open-label Multicenter Phase 4 Study Assessing Immune Response to COVID-19 Vaccine in Patients With RMS Treated With Ofatumumab

Tanuja Chitnis,[1] Barry Hendin,[2] Kottil Rammohan,[3] Stephen Yeung,[4] Xiangyi Meng,[4] Elisabeth B. Lucassen,[4] James Stankiewicz,[4] Amit Bar-Or[5]

[1]Brigham Multiple Sclerosis Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [2]Banner - University Medicine Neurosciences Clinic, Phoenix, AZ, USA; [3]University of Miami School of Medicine, Miami, FL, USA; [4]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [5]Center for Neuroinflammation and Experimental Therapeutics and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

P777

Scan this QR code

Presenter email address: tchitnis@rics.bwh.harvard.edu

Background

- OMB, a fully human anti-CD20 monoclonal antibody, is indicated for the treatment of adults with RMS in the US[1]
- It is important to assess if OMB-treated patients can mount a protective immune response to the COVID-19 vaccine

Objective

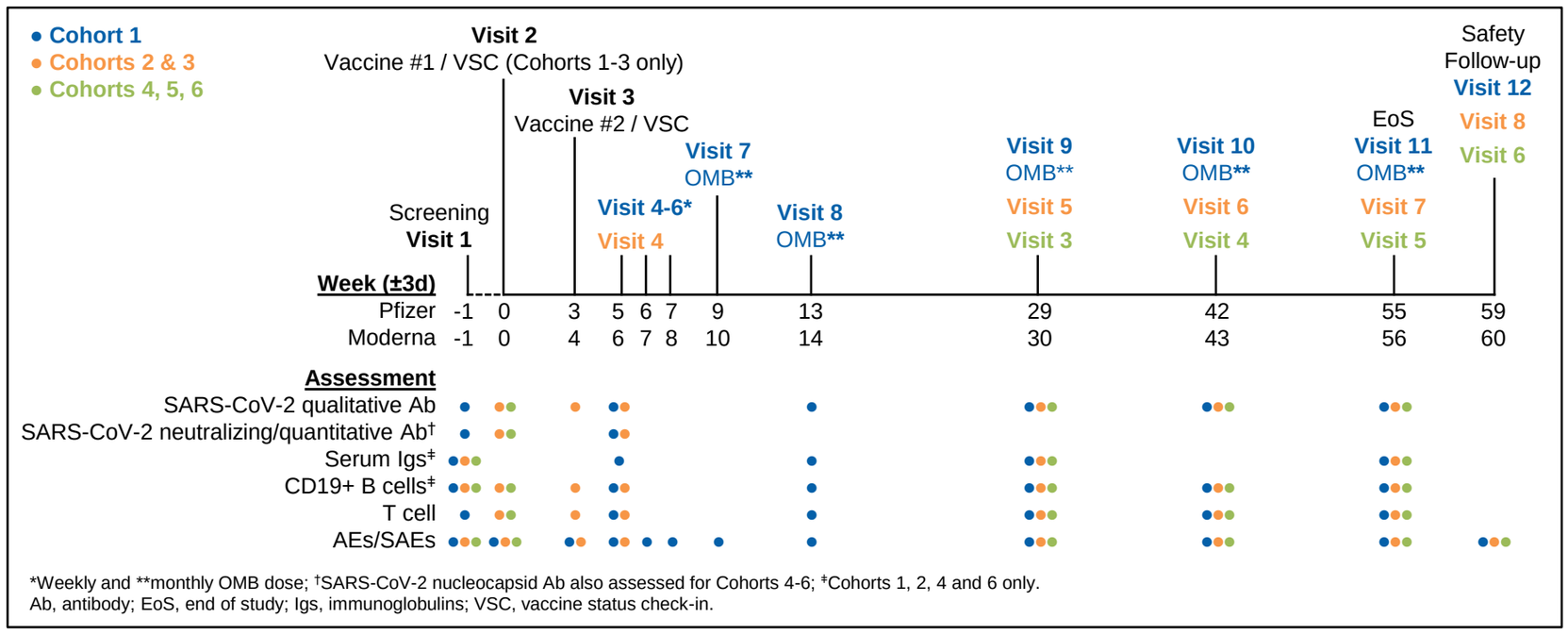
- **To assess the immune response to COVID-19 mRNA vaccines (Pfizer or Moderna), and the impact of a booster dose, in RMS patients treated monthly with subcutaneous OMB**

Methods

Study design

- This is a 6-cohort, open-label, multicenter, prospective, Phase 4 study (NCT04878211; **Figure 1**)
  - Cohorts 1-3 assess patient's serum before and after vaccination
  - Cohorts 4-6 include fully vaccinated patients, with or without a booster
  - Cohort 1 will receive full course (2 doses) of COVID-19 mRNA vaccine ≥2 weeks prior to starting OMB
  - Cohorts 2-6 include those who will or have received the full vaccine course ≥4 weeks after starting OMB or IFN/GA

Figure 1. Study design



*Weekly and **monthly OMB dose; †SARS-CoV-2 nucleocapsid Ab also assessed for Cohorts 4-6; ‡Cohorts 1, 2, 4 and 6 only.
Ab, antibody; EoS, end of study; Igs, immunoglobulins; VSC, vaccine status check-in.

- All groups will undergo serologic testing
- Patients in Cohort 1 will receive OMB 20 mg at 2, 3, and 4 weeks after full course vaccination, followed by subsequent OMB 20 mg doses once monthly throughout treatment period (360 days after completion of full course vaccination)
- Patients in Cohorts 2-6 will continue taking their prescribed therapy per their current dosing schedule throughout treatment period

Study objectives

- **Primary objective**: To assess immune response to COVID-19 vaccine in OMB-treated participants
- **Secondary objectives**:
  - Assess sustained immune response and immune conversion to vaccine in OMB-treated participants
  - Assess AEs and SAEs
- **Exploratory objectives**:
  - Assess differential T cell response and reactivity to vaccination
  - Assess neutralizing antibody development

Participants and setting

- This study plans to enroll up to 88 RMS patients (up to 66 to begin or already on OMB, and 22 on IFN/GA) at up to 30 US centers
- Inclusion and exclusion criteria are described in **Table 1**

Remote procedures

- Qualifying study participants may be offered the option to have certain study procedures performed remotely under the oversight of the Investigator

Table 1. Key inclusion and exclusion criteria

Key inclusion criteria	Cohort 1	2	3	4	5	6
Male or female patients, aged 18 to 55 years at screening	•	•	•	•	•	•
Diagnosis of RMS by 2017 revised McDonald criteria	•	•	•	•	•	•
Vaccination status						
Naïve to mRNA COVID-19 vaccine (Pfizer or Moderna)	•	•	•			
Fully vaccinated* with mRNA COVID-19 vaccine				•	•	•
Received an mRNA booster ≥4 weeks prior to enrollment†						•
Study treatment						
Eligible to receive and plan to be started on OMB according to the approved labeling	•					
Currently on OMB for ≥4 weeks for RMS treatment		•		•		•
Currently on IFN/GA for ≥4 weeks for RMS treatment			•		•	

Key exclusion criteria
Already received J&J COVID-19 vaccine
Known clinical diagnosis of COVID-19 prior to study
Any major episode of infection requiring hospitalization or treatment with IV antibiotics or oral antibiotics within 4 or 2 weeks prior to the first vaccination visit, respectively
Prior treatment with B-cell targeted therapies, alemtuzumab, anti-CD4, cladribine, cyclophosphamide, mitoxantrone, azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, total body irradiation, or bone marrow transplantation; prior treatment with S1P agent or natalizumab within 2 or 6 months of study enrollment, respectively
Baseline total serum IgG <400 mg/dl

*Completed full vaccine course (two doses) ≥4 weeks after start of commercially prescribed OMB or IFN/GA for RMS treatment
†Cohort 5 booster is optional

Table 2. Study endpoints

Primary endpoint
Achieving positive SARS-CoV-2 qualitative IgG antibody assay* (yes/no)
Secondary endpoints
Achieve immune response at other assessment time points (yes/no)
Immune conversion to COVID-19 vaccine (yes/no)
AEs and SAEs
Exploratory endpoints
Frequency of IFNγ positive CD4+ or CD8+ T cells by flow cytometry after stimulation with SARS-CoV-2 peptide*
Positive T cell reactivity by IFNγ ELISPOT after stimulation with SARS-CoV-2 peptide* (yes/no)
Achieving positive SARS-CoV-2 neutralization antibody assay* (yes/no)

*14 days after full course vaccination

Endpoints and assessments

- Study endpoints are summarized in **Table 2**
- AEs will be monitored for at least 30 days following the last dose of study treatment

Data analyses

- The number and percentage of responders will be presented
- The 95% confidence interval for the proportion of responders will be calculated by using exact method

Results

- The planned first patient first visit was on May 31, 2021
- Study completion is expected by Q4 2022
- An interim analysis will be performed once Cohorts 2 and 4 have ≥10 patients total that have had serum drawn ≥14 days after full course vaccination
  - Second interim analysis once Cohort 6 has ≥10 patients, and third interim analysis once Cohorts 2-5 have full enrollment with blood drawn ≥14 days after full course vaccination

Conclusions

- This study will contribute to a better understanding of immune responses that occur in OMB-treated RMS patients given a COVID-19 mRNA vaccine

References

1. KESIMPTA® (ofatumumab) Prescribing Information. https://www.novartis.us/sites/www.novartis.us/files/kesimpta.pdf. Accessed: September 9, 2021

Abbreviations

Ab, antibody; AE, adverse event; bpm, beats per minute; CI, confidence interval; CIS, clinically isolated syndrome; COVID-19, coronavirus disease 2019; DMT, disease modifying therapy; EDSS, Expanded Disability Status Scale; EoS, end of study; EoT, end of treatment; HCP, healthcare professional; IFN, interferon; Igs, immunoglobulins; MS, multiple sclerosis; N, number of patients; n, number of observations; PI, principal investigator; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; S1P, sphingosine 1-phosphate; SAE, serious adverse event; SD, standard deviation; SPMS, secondary progressive multiple sclerosis; VSC, vaccine status check-in.

Disclosures

Tanuja Chitnis has provided advisory board/consulting services to Biogen Idec, Merck Serono, Novartis, Sanofi, Bayer, Celgene (Bristol Myers Squibb), and Alexion; has received research support from Verily, Merck Serono, and Novartis; and is employed by Brigham and Women's Hospital. **Barry Hendin** has received advisory and speaking honoraria from Biogen, Genentech, Genzyme, EMD Serono, Novartis and Alexion. **Kottil Rammohan** has consulted for and received honorarium from Biogen, Novartis, Genzyme, Genentech, and EMD Serono, and received grants from Biogen, Novartis, EMD Serono, Genzyme and Roche Genentech; no salary, stocks, or intellectual property. **Stephen Yeung, Xiangyi Meng, Elisabeth B. Lucassen,** and **James Stankiewicz** are employees of Novartis Pharmaceuticals Corporation. **Amit Bar-Or** has participated as a speaker in meetings sponsored by, and received consulting fees and/or grant support from, Actelion, Atara Biotherapeutics, Biogen Idec, Celgene/ Receptos, Genentech/Roche, Mapi, MedImmune, Merck/EMD Serono, Novartis and Sanofi.

Acknowledgements

The study was supported by Novartis Pharmaceuticals Corporation. Medical writing support was provided by Grace Jeong, PhD (Alphabet Health) 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 publication.

Poster Presentation at the Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), 2021.