Background
OMB, a fully human anti-CD20 monoclonal antibody, is indicated for the treatment of adults with RMS in the US.

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 (NCT04978211; 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

Table 1. Key inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Key inclusion criteria</th>
<th>Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male or female patients, aged 18 to 55 years at screening</td>
<td>1 2 3 4 5 6</td>
</tr>
<tr>
<td>Diagnosis of RMS by 2019 revised McDonald criteria</td>
<td>✔ ✔ ✔ ✔ ✔ ✔</td>
</tr>
<tr>
<td>Vaccination status</td>
<td>✔ ✔ ✔ ✔ ✔ ✔</td>
</tr>
<tr>
<td>Naive to mRNA COVID-19 vaccine (Pfizer or Moderna)</td>
<td>✔ ✔ ✔ ✔ ✔ ✔</td>
</tr>
<tr>
<td>Fully vaccinated* with mRNA COVID-19 vaccine</td>
<td>✔ ✔ ✔ ✔ ✔ ✔</td>
</tr>
<tr>
<td>Received an mRNA booster ≥4 weeks prior to enrollment</td>
<td>✔ ✔ ✔ ✔ ✔ ✔</td>
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</tbody>
</table>

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 ≥1 IP 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

Figure 1. Study design

Table 2. Study endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Primary endpoint</th>
<th>Secondary endpoint</th>
<th>Exploratory endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune conversion to COVID-19 vaccine</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔</td>
<td>✔ ✔</td>
</tr>
<tr>
<td>AEs and SAEs</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔</td>
<td>✔ ✔</td>
</tr>
</tbody>
</table>

AEs and SAEs

Positive T cell reactivity by IFNy ELISPOT after stimulation with SARS-CoV-2 peptide (yes/no)

Positive SARS-CoV-2 neutralizing antibody assay (yes/no)

Clinical trial registration number: NCT04978211

References


Abbreviations

AE, 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; ELISPOT, end of study; EoT, end of treatment; HCP, healthcare professional; IFN, interferon; IgG, immunoglobulin G; 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; S19, S19 phosphate; SAE, serious adverse event; SD, standard deviation; SPMS, secondary progressive multiple sclerosis; VSC, vaccine status check.

Disclosures

Tanjana Chitnis has provided advisory board/consulting services to Biogen, Genentech, Merck Serono, Novartis, Sanofi, Bayer, Celgene (Bristol Myers Squibb), and Alexion; has received research support from Merck Serono, and Novartis; and has been employed by Brigham and Women’s Hospital. Barry Hendin has received advisory and speaking honoraria from Biogen, Genentech, Genmab, EMD Serono, Novartis, and Alexion. Kottil Rammohan has consulted for and received honorarium from Biogen, Novartis, Genmab, Genentech, and EMD Serono, and received grants from Biogen, Novartis, EMD Serono, GentaC rea, 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, MapBiomed, MedImmune, EMD Serono, Novartis, and Sanofi.

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