Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Ofatumumab

Trial Indication(s)

Relapsing Multiple Sclerosis

Protocol Number

COMB157GUS18

Protocol Title

An open-label multicenter single-arm pilot study to assess immune response to COVID-19 vaccine in participants with relapsing multiple sclerosis treated with ofatumumab 20 mg subcutaneously

Clinical Trial Phase

Phase IV

Phase of Drug Development

Approval

Study Start/End Dates

Study Start Date: 21 May 2021

End of data collection: 18 Feb 2022

Reason for Termination

Not Applicable

Study Design/Methodology

This was a single-arm, pilot, multicenter, prospective study in participants with relapsing MS treated with ofatumumab for a month or longer. Patients screened for the study could either be scheduled for the COVID-19 vaccine, have received the first dose of the vaccine with the second dose scheduled, or have already completed the full-course vaccination. Fully vaccinated participants were to be able to complete Immune Assay No. 1 after the second dose of the vaccine.
The study aimed to enroll up to 22 participants at 5 study sites in the United States. A total of 26 participants were enrolled and analyzed.

There were 3 possibilities with regards to the timing of receiving the vaccine:

- Already received both doses of an mRNA vaccine (Pfizer or Moderna):
  The Screening Visit (Visit 1) had to take place at least 14 days after the second dose of the vaccine.
  Immune Assay No. 1 (Visit 2) had to be done after the second dose of the vaccine.
  Participants who had received the 2 doses of the mRNA vaccine, and met all entry criteria at the Screening Visit (Visit 1), could complete all assessments for both Visit 1 and Visit 2 on the same date.
- Participants who had received the initial dose of an mRNA vaccine and had their second dose scheduled:
  Immune Assay No. 1 (Visit 2) had to occur $\geq$ 14 days after the documented date of the second dose of the vaccine.
- Participants who had been scheduled to receive their initial dose of the mRNA vaccine:
  Immune Assay No. 1 (Visit 2) was to occur within $\geq$ 14 days after the date of the second dose of the vaccine.

Immune Assay No. 2 was to be conducted 90 days after Immune Assay No. 1.

Centers

Five study sites in the United States

Objectives:

Primary objective
The primary objective was to assess immune response to non-live mRNA COVID-19 vaccine in ofatumumab-treated participants with relapsing MS.

Secondary objective
The secondary objective was to assess AEs and SAEs.

Test Product (s), Dose(s), and Mode(s) of Administration

Ofatumumab 20 mg subcutaneously

Statistical Methods
The statistical analysis was performed by Novartis or a designated CRO using SAS® version 9.4 or higher.
The Safety Set was the only analysis set defined and comprised all participants who signed the informed consent and met all entry criteria.
The number and percentage of participants with immune response to the mRNA vaccine were presented. A 95% confidence interval for the proportion of responders was calculated using an exact method. No hypothesis was tested in this study.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

Patients eligible for inclusion had to meet all of the following criteria:
1. Signed informed consent had to be obtained prior to participation in the study

2. Aged 18-55 years inclusive at Screening
3. Diagnosis of relapsing MS by 2017 revised McDonald criteria
4. Willing to comply with the study schedule
5. Had received/scheduled vaccination with an FDA-approved for emergency use COVID-19 mRNA vaccine (Pfizer or Moderna). Either had been scheduled for vaccine, received a single vaccine with a scheduled second dose, or already completed full-course vaccination. Fully vaccinated patients had to be able to complete Immune Assay No. 1 after the second dose of the vaccine
6. Currently receiving ofatumumab for the treatment of relapsing MS for a month or longer (pre-ofatumumab serology with hepatitis B testing showing no active or latent infection, as well as serum IgG results to be recorded in the database if available)

Exclusion Criteria:

1. Known clinical diagnosis of COVID-19 prior to screening based on investigator's or patient's personal physician's judgement
2. Has a contraindication to receiving an mRNA COVID-19 vaccine
3. Has an immediate allergic reaction to past vaccine or injection
4. Any safety finding including low IgG and/or low IgM levels requiring an ofatumumab treatment interruption within the 12 weeks immediately prior to vaccination as determined by the HCP
5. Any major episode of infection requiring hospitalization or treatment with intravenous antibiotics within 2 weeks prior to the screening visit
6. Prior treatment with sphingosine 1-phosphate agent within 2 months of study enrollment
7. Prior treatment with natalizumab within 6 months of study enrollment
8. Contraindications to ofatumumab treatment as per the United States Prescribing Information will be adhered to which include active infection hepatitis B infection, progressive multifocal leukoencephalopathy and pregnancy.
9. Participation in another interventional clinical trial within 14 days before enrollment.
10. Have been treated with any of the medications as described in the full protocol

11. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception while taking study treatment and for 6 months after stopping medication

Participant Flow Table

Table 10-1 Disposition (Safety Set)

Disposition/reason	Total N=26 n (%n)
Completed study	23 (88.46)
Discontinued	3 (11.54)
Primary reason for not completing study	
Adverse event [a]	1 (3.85)
Participant decision	2 (7.69)

a) One participant was listed as discontinued from the study due to an AE. However, the reason for discontinuation was the use of prohibited medication taken to treat the AE.

Baseline Characteristics

Table 10-2 Demographic summary (Safety Set)

Characteristic	Total N=26
Age (year)	
n	26
Mean	42.9
Standard deviation	7.91
Minimum	27
Median	42.0
Maximum	54
Age group - n (%)	
< 40 year	11 (42.31)
≥ 40 year	15 (57.69)
< 50 year	19 (73.08)
≥ 50 year	7 (26.92)
Sex - n (%)	
Female	21 (80.77)
Male	5 (19.23)
Race - n (%)	
Black or African American	1 (3.85)
White	25 (96.15)
Ethnicity - n (%)	
Hispanic or Latino	9 (34.62)
Not Hispanic or Latino	16 (61.54)
Not reported	1 (3.85)

Primary Outcome Result(s)

Proportion of participants achieving immune response

Table 11-1 Percentage of participants achieving immune response [a] by visit (non-responder imputation) (Safety Set)

Visit	N=26 n/M (%)	95% confidence interval [b]
Visit 2	14/26 (53.85)	(33.37,73.41)
Visit 3/EOS	13/26 (50.00)	(29.93,70.07)

a) Immune response defined by a positive SARS-CoV-2 qualitative IgG test
b) Calculated using an exact method (Clopper and Pearson 1934)
n = number of participants with positive SARS-CoV-2 qualitative IgG test

M = number of all participants in the study

Table 11-2 Percentage of participants achieving immune response [a] by visit (observed data) (Safety Set)

Visit	N=26 n/M (%)	95% confidence interval [b]
Visit 2	14/25 (56.00)	(34.93,75.60)
Visit 3/EOS	13/23 (56.52)	(34.49,76.81)

a) Immune response defined by a positive SARS-CoV-2 qualitative IgG test
b) Calculated using an exact method (Clopper and Pearson 1934)
n = number of participants with positive SARS-CoV-2 qualitative IgG test

M = number of all participants in the study

Secondary Outcome Result(s)

See Adverse Events section

Safety Results

Adverse Events by System Organ Class

Table 12-1 Number (%) of participants with adverse events by primary system organ class and preferred term (Safety Set)

System organ class Preferred term	N=26 n (%)
Any adverse event	5 (19.23)
Infections and infestations	5 (19.23)
COVID-19	4 (15.38)
Herpes zoster	1 (3.85)
Pharyngitis streptococcal	1 (3.85)
Investigations	1 (3.85)
SARS-CoV-2 antibody test negative	1 (3.85)
Nervous system disorders	1 (3.85)
Headache	1 (3.85)

Serious Adverse Events and Deaths

There were no deaths during the study

Other Relevant Findings

Not applicable

Conclusion:

- Participants with relapsing MS who received ofatumumab treatment mounted an immune response to non-live mRNA COVID-19 vaccine. The proportion of participants achieving immune response was 53.85% at Immune Assay 1
- Adverse events were reported for less than 20% of participants in the study. The most commonly reported preferred term was COVID-19. No deaths or SAEs occurred

Date of Clinical Study Report

17 November 2022