Poster P272

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Immune response to influenza vaccine in patients with relapsing multiple sclerosis treated with ofatumumab: results from an open-label, multicenter, phase 4 study

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KEY FINDINGS & CONCLUSIONS

- Ofatumumab (OMB)-treated patients with relapsing multiple sclerosis (RMS) are able to mount an immune response following inactivated influenza vaccination
- These results are consistent with current European and US product labeling guidelines, which recommend inactivated vaccines be administered 2 weeks prior to starting OMB
- T-cell immunologic responses were not obtained in this study

INTRODUCTION

- Ofatumumab (OMB) is a fully human anti-CD20 monoclonal antibody administered by monthly subcutaneous injection (20 mg in 0.4 mL)[1,2]
- OMB is approved for the treatment of adults with relapsing multiple sclerosis (RMS) in the European Union and the United States[1,2]
- Vaccinations comprise an important component of MS management, and there is a need for data regarding whether treatment with OMB impacts the humoral immune response to vaccines, including the influenza vaccine, in patients with RMS
- The objective of this prospective phase 4 study (NCT04667117) was to assess whether patients with RMS treated with OMB 20 mg every 4 weeks could mount a humoral immune response to the 2020-2021, 2021-2022, or 2022-2023 inactivated influenza vaccine compared with patients treated with interferon or glatiramer acetate (IFN/GA)

METHODS

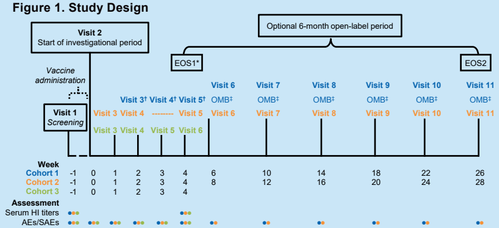
Study Design

- A 3-cohort, open-label, multicenter, prospective, phase 4 study (NCT04667117; **Figure 1**)
  - Cohort 1: vaccinated ≥2 weeks before starting OMB
  - Cohort 2: vaccinated ≥4 weeks after starting OMB
  - Cohort 3: vaccinated ≥4 weeks after enrollment and currently being treated with IFN/GA
- Cohort 1 received OMB 2, 3, and 4 weeks after vaccination, followed by monthly doses from Week 6; Cohorts 2 and 3 continued OMB or other disease-modifying therapy (DMT) per their current dosing schedule
- Patients in all cohorts underwent humoral immunity titer evaluations before vaccination (baseline) and 4 weeks (Week 4) post vaccination
- Patients in Cohorts 1 and 2 could continue receiving monthly doses of OMB during an optional extension period
- Patients with recent major infections or who had been or were being treated with certain immunosuppressive or immunomodulatory therapies were excluded from the trial
- Only patients who had pre- and post-vaccination antibody titers (observed cases) were included in this analysis

Study Endpoints

- **Primary endpoint:**
  - Patients achieving seroprotection to influenza at Week 4 (defined as a post-vaccination antibody titer ≥40)
- **Secondary endpoints:**
  - Achieving seroconversion (defined as post-vaccination humoral immunity titers ≥4-fold increase or ≥40 in those with pre-vaccination titers ≥10 or <10, respectively)
  - Safety (any adverse events [AEs], serious AEs [SAEs], and AEs leading to discontinuation)

Figure 1. Study Design



AE, adverse event; EOS, end of study; HI, hemagglutination inhibition; OMB, ofatumumab; SAE, serious adverse event
*Participants in Cohort 3 will not enter the extension; †Weekly OMB loading dose; ‡Monthly OMB dose

RESULTS

Patients

- This study included a total of 63 patients with a mean (range) age of 41 (22-54) years
- The majority of patients were female (76%) and White (86%), and 67% had used a previous DMT for MS treatment (**Table 1**)
- The mean (standard deviation) duration of exposure to the study treatment was 15 (1.5) days for Cohort 1, 320 (192.4) days for Cohort 2, and 2519 (1720.5) days for Cohort 3

Table 1. Patient Demographics and Clinical Characteristics

Characteristic	Cohort 1 (n=22)	Cohort 2 (n=22)	Cohort 3 (n=19)	Overall (N=63)
Age, years				
Mean (range)	41.4 (24-53)	38.9 (22-54)	43.3 (27-53)	41.1 (22-54)
Sex, n (%)				
Female	19 (86.4)	15 (68.2)	14 (73.7)	48 (76.2)
Male	3 (13.6)	7 (31.8)	5 (26.3)	15 (23.8)
Race, n (%)				
White	21 (95.5)	18.8 (81.8)	15 (78.9)	54 (85.7)
Black or African American	1 (4.5)	4 (18.2)	4 (21.1)	9 (14.3)
Ethnicity, n (%)				
Hispanic or Latino	6 (27.3)	4 (18.2)	0	10 (15.9)
Not Hispanic or Latino	16 (72.7)	18 (81.8)	19 (100.0)	53 (84.1)
Any previous MS DMT, n (%)	1 (4.5)	22 (100.0)	19 (100.0)	42 (66.7)
Glatiramer acetate	1 (4.5)	0	12 (63.2)	13 (20.6)
Interferon beta-1a	0	0	4 (21.1)	4 (6.3)
Interferon beta-1b	0	0	1 (5.3)	1 (1.6)
Ofatumumab	0	22 (100.0)	0	22 (34.9)
Peginterferon beta-1a	0	0	2 (10.5)	2 (3.2)

DMT, disease-modifying therapy; MS, multiple sclerosis

Seroprotection at Week 4

- At Week 4, seroprotection was generally high across strains and consistent between Cohorts (**Table 2**). Lower seroprotection rates were observed for all Influenza B strains and for Influenza A Wisconsin

Table 2. Percentages of Patients With Seroprotection at Week 4 by Influenza Strain

Strain	% of Patients With Seroprotection at Week 4		
	Cohort 1 (n=22)	Cohort 2 (n=22)	Cohort 3 (n=19)
Influenza A Brisbane	100% (5/5)	100% (2/2)	100% (1/1)
Influenza A Cambodia	100% (13/13)	80% (4/5)	85.7% (6/7)
Influenza A Kansas	100% (5/5)	100% (2/2)	100% (1/1)
Influenza A Michigan	100% (5/5)	100% (2/2)	100% (1/1)
Influenza A Singapore	100% (5/5)	100% (2/2)	100% (1/1)
Influenza A Victoria	100% (13/13)	100% (5/5)	100% (7/7)
Influenza A Wisconsin	61.5% (8/13)	40% (8/20)	68.8% (11/16)
Influenza B Colorado	60% (3/5)	50% (1/2)	100% (1/1)
Influenza B Phuket	77.8% (14/18)	68.2% (15/22)	76.5% (13/17)
Influenza B Washington	76.9% (10/13)	20% (1/5)	71.4% (5/7)

- The most commonly assessed strains (Wisconsin and Phuket) showed comparability of seroprotection between Cohorts 1 and 3 with a somewhat reduced response in Cohort 2. Of the next most tested groups (Cambodia, Victoria, and Washington), Washington also showed similarities between Cohorts 1 and 3, with a reduced response in Cohort 2, whereas Cambodia showed a diminished response in both Cohorts 2 and 3 compared with Cohort 1. Response to Victoria was uniformly robust
- The seroprotection rates presented here are similar to those previously reported for IFN/GA and ocrelizumab, another anti-CD20 DMT[3,4]

Seroconversion at Week 4

- The rates of seroconversion at Week 4 were variable across vaccine influenza strains (**Table 3**); however, trends for lower rates of seroconversion in Cohort 2 vs Cohorts 1 and 3 were broadly consistent across individual influenza A and B strains

Table 3. Percentages of Patients Achieving Seroconversion at Week 4 by Influenza Strain

Strain	% of Patients Achieving Seroconversion		
	Cohort 1 (n=22)	Cohort 2 (n=22)	Cohort 3 (n=19)
Influenza A Brisbane	80% (4/5)	0% (0/2)	0% (0/1)
Influenza A Cambodia	84.6% (11/13)	20% (1/5)	42.9% (3/7)
Influenza A Kansas	40% (2/5)	0% (0/2)	0% (0/1)
Influenza A Michigan	60% (3/5)	0% (0/2)	100% (1/1)
Influenza A Singapore	40% (2/5)	0% (0/2)	0% (0/1)
Influenza A Victoria	92.3% (12/13)	20% (1/5)	42.9% (3/7)
Influenza A Wisconsin	46.2% (6/13)	10% (2/20)	37.5% (6/16)
Influenza B Colorado	60% (3/5)	0% (0/2)	100% (1/1)
Influenza B Phuket	50% (9/18)	18.2% (4/22)	41.2% (7/17)
Influenza B Washington	38.5% (5/13)	0% (0/5)	42.9% (3/7)

- The seroconversion rates presented here are similar to those previously reported for IFN/GA and ocrelizumab, another anti-CD20 DMT[3,4]

Safety

- Overall, 38.1% (24/63) of patients experienced ≥1 AE (**Table 4**)
- AEs were most frequent in Cohort 1, where 72.7% (16/22) of patients experienced an AE vs 27.3% (6/22) in Cohort 2 and 10.5% (2/19) in Cohort 3
- The higher frequency of AEs in Cohort 1 is likely related to ofatumumab initiation (ie, IRRs)
- 1 SAE (MS pseudo relapse) was reported in Cohort 2
- No AEs resulting in discontinuation were reported

Table 4. AEs That Occurred in ≥4% of Patients and SAEs

AE, n (%)	Cohort 1 (n=22)	Cohort 2 (n=22)	Cohort 3 (n=19)	Overall (N=63)
Any AE	16 (72.7)	6 (27.3)	2 (10.5)	24 (38.1)
IRR	4 (18.2)	0	0	4 (6.3)
Headache	3 (13.6)	1 (4.5)	0	4 (6.3)
Nausea	3 (13.6)	0	0	3 (4.8)
COVID-19	2 (9.1)	0	1 (5.3)	3 (4.8)
Influenza-like illness	2 (9.1)	1 (4.5)	0	3 (4.8)
Pain	3 (13.6)	0	0	3 (4.8)
Pyrexia	2 (9.1)	0	1 (5.3)	3 (4.8)
SAE	0	1 (4.5)	0	1 (1.6)
MS pseudo relapse	0	1 (4.5)	0	1 (1.6)

AE, adverse event; COVID-19, coronavirus disease 2019; IRR, injection-related reaction; MS, multiple sclerosis; SAE, serious adverse event
IRRs were coded to the preferred term of "injection-related reaction" if specified by the investigator as related to the injection; all IRRs may not have been captured as IRRs

Limitations

- This study was conducted over multiple flu seasons, with participants receiving several different vaccines
- Previous exposure to vaccine strains may influence seroconversion rates, with greater responses seen with novel strains than in strains included in the vaccine in more than 1 consecutive year[5]
- The maximum age for this study was 55 years; therefore, the impact of immunosenescence in older patients with MS was not examined
- This study only examines the humoral immune response to the vaccine; therefore, we cannot draw conclusions regarding cell-mediated immunity. However, studies investigating response to coronavirus disease 2019 (COVID-19) mRNA vaccines in patients treated with OMB showed that, although antibody response was diminished, 100% of patients vaccinated for COVID-19 while receiving OMB treatment had severe acute respiratory syndrome coronavirus 2–specific T cells[6]

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Disclosures

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