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An expert Delphi panel to understand potential ofatumumab injection–related reactions among patients with relapsing forms of multiple sclerosis

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KEY FINDINGS & CONCLUSIONS

- An expert panel of US-based neurologists and advanced practitioners experienced with ofatumumab therapy in people with relapsing forms of multiple sclerosis (PwRMS) agreed that local or systemic injection-related reactions (IRRs) with ofatumumab were unlikely in clinical practice
- Participants were also unlikely to recommend pre- and/or post-treatment options
- This study provides insights for health care providers into the potential occurrence and management of IRRs with ofatumumab in the clinical practice setting

INTRODUCTION

- Ofatumumab (OMB) is a fully human anti-CD20 monoclonal antibody used to treat people with relapsing forms of multiple sclerosis (PwRMS) and is administered as a once-monthly subcutaneous injection in adults[1,2]
- PwRMS treated with OMB can experience local and systemic injection-related reactions (IRRs)[2]
- In the phase 3 ASCLEPIOS I/II clinical studies of OMB, reported systemic IRRs, such as headache and flushing, were mostly mild to moderate in severity, and most occurred at first dose[2]
- Although systemic OMB IRRs have been examined in clinical trials, data on the potential occurrence and management of IRRs reported in real-world clinical settings are limited
- The objective of this study was to better understand clinicians' perspectives regarding the occurrence and management of local and systemic IRRs among PwRMS treated with OMB in clinical practice

METHODS

Study Design

- To obtain insights and consensus regarding the occurrence and management of potential OMB IRRs, a panel of US-based neurologists and advanced practitioners (physician assistants and nurse practitioners) experienced with OMB therapy in PwRMS were invited to take part in a 3-round online modified Delphi study (Table 1)
- Data were collected in a double-blinded manner; thus, the sponsor did not have access to identifiable participant information and participants were not provided information on the study sponsor
- Planning for this modified Delphi consensus-building process began in 2022, and the 3 rounds were conducted from April (Round 1) through September 2023 (Round 3)
- During Round 1, participants completed a survey that included a questionnaire designed to characterize the expert sample and the Delphi questionnaire on IRR management to establish a baseline assessment
- Round 2 involved live webinars to obtain feedback on the Round 1 Delphi questionnaire results
- In Round 3, participants were asked to review Round 1 results and Round 2 feedback before providing their final Delphi questionnaire responses

Table 1. Study Participant Inclusion/Exclusion Criteria

Inclusion criteria
• Age ≥18 years
• Board-certified US-based neurologist in MS and/or neurology specialist or board-certified physician assistant or nurse practitioner with a neurology/MS specialty
• Current or previous clinical practice for ≥2 years in neurology
• ≥50% of the time/effort treating patients
• Have ever prescribed OMB to ≥5 patients
• Able to speak, read, and understand English
• Willing to take part in all study procedures that take ~4 hours over 12 weeks to complete all 3 Delphi rounds
• Willing to participate in the study using an online (web-based) survey platform
• Willing to provide informed consent to participate in this study

Exclusion criteria
• Not prescribed OMB in the last 12 months
• Did not have experience treating patients receiving OMB
• Unwilling to provide informed consent

MS, multiple sclerosis; OMB, ofatumumab
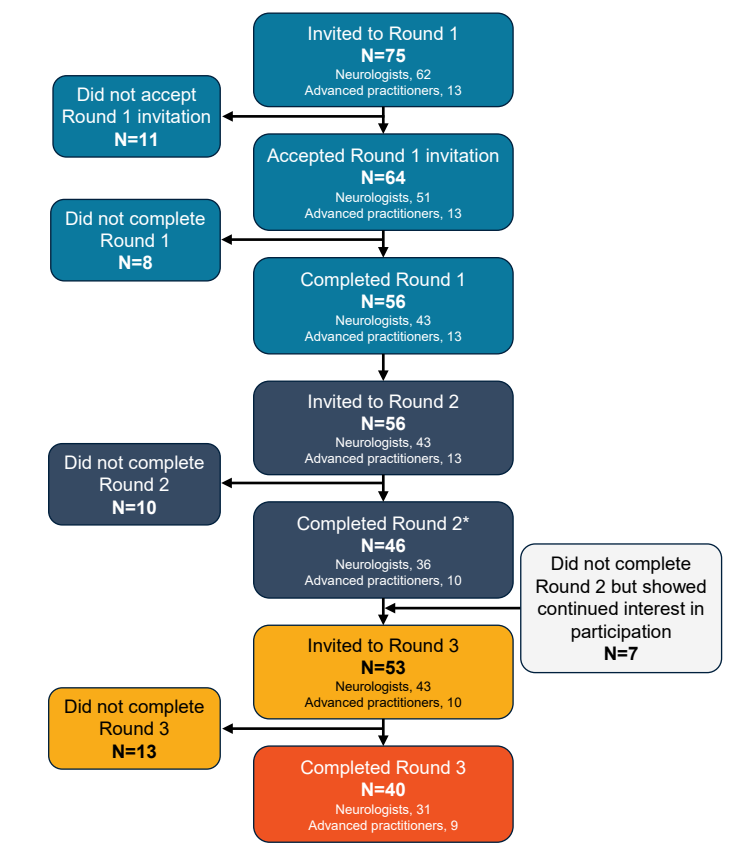
Delphi Questionnaire

- The Delphi questionnaire included 20 questions in 4 sections presenting a series of likelihood (scale: highly unlikely [0] to highly likely [100]), proportion, and ranking queries:
  - Section 1 (questions [Qs] 1-9): likelihood of IRRs among PwRMS (local and systemic)
  - Section 2 (Qs 10-11): systemic IRR treatment options and management for PwRMS
  - Section 3 (Qs 12-15): systemic IRR prevention management—pre-treatment decision making for PwRMS
  - Section 4 (Qs 16-17): systemic IRR rescue management—post-treatment decision making for PwRMS
- Consensus was deemed to be met in likelihood/proportion questions if interquartile ranges (75th-25th percentiles) around the median (0-100) responses were <25 and in ranking questions if >75% of respondents ranked an option among the top 2 in Round 3

RESULTS

Participants

- Forty participants (neurologists, n=31; nurse practitioners, n=5; physician assistants, n=4) completed all 3 Delphi rounds (Figure 1)
- The majority of participants were male (55.0%), White (62.5%), and had ≥10 years of clinical practice experience (72.5%); all participants treated ≥6 patients with OMB, and 37.5% treated ≥26 patients (Table 2)
- All 40 participants spent more than 74% of their time providing direct patient care in a clinical setting

Figure 1. Delphi Round Flow Chart

- Invited to Round 1 — N=75 (Neurologists, 62; Advanced practitioners, 13)
- Did not accept Round 1 invitation N=11
- Accepted Round 1 invitation N=64 (Neurologists, 51; Advanced practitioners, 13)
- Did not complete Round 1 N=8
- Completed Round 1 N=56 (Neurologists, 43; Advanced practitioners, 13)
- Invited to Round 2 N=56 (Neurologists, 43; Advanced practitioners, 13)
- Did not complete Round 2 N=10
- Completed Round 2* N=46 (Neurologists, 36; Advanced practitioners, 10)
- Did not complete Round 2 but showed continued interest in participation N=7
- Invited to Round 3 N=53 (Neurologists, 43; Advanced practitioners, 10)
- Did not complete Round 3 N=13
- Completed Round 3 N=40 (Neurologists, 31; Advanced practitioners, 9)

*Of the 56 experts invited to Round 2, 45 were able to attend the live webinar; a further 8 showed continued interest in participation but were unable to join the scheduled sessions and were therefore provided with an offline version of the webinar. Of these, 1 provided their responses

Table 2. Participant Characteristics

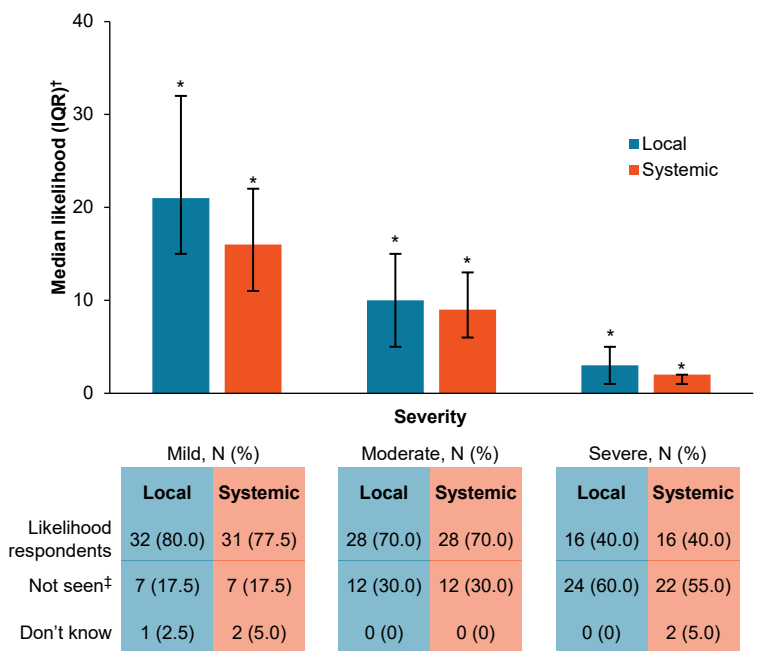| Characteristic	Participants (N=40)
Sex, n (%)	
Male	22 (55.0)
Female	16 (40.0)
Prefer not to answer	2 (5.0)
Age, years	
20-29	1 (2.5)
30-39	11 (27.5)
40-49	9 (22.5)
50-59	11 (27.5)
60-69	7 (17.5)
≥70	1 (2.5)
Race, n (%)	
White	25 (62.5)
Asian	5 (12.5)
Black or African American	2 (5.0)
Native Hawaiian or Other Pacific Islander	1 (2.5)
≥2 races	2 (5.0)
Prefer not to answer	5 (12.5)
Experience in clinical practice, years	
<10	11 (27.5)
10-19	11 (27.5)
20-29	15 (37.5)
30-39	2 (5.0)
≥40	1 (2.5)
Primary clinical practice setting, n (%)	
University hospital or university-affiliated clinic	13 (32.5)
Private medical practice	12 (30.0)
Specialty/multispecialty group practice	14 (35.0)
Hospital or clinic not associated with a university*	1 (2.5)
Proportion of PwRMS seen monthly, n (%)	
1-20%	11 (27.5)
21-40%	11 (27.5)
41-60%	7 (17.5)
61-80%	3 (7.5)
81-100%	8 (20.0)
Number of PwRMS prescribed ofatumumab, n (%)	
6-10	16 (40.0)
11-25	9 (22.5)
26-50	8 (20.0)
51-75	3 (7.5)
≥75	4 (10.0)

PwRMS, people with relapsing forms of multiple sclerosis
*Including community health clinics

Delphi Questionnaire Results

- Participants strongly agreed that local and systemic IRRs, regardless of severity, were unlikely (Figure 2)
- Participants also agreed that pre- or post-treatment of systemic IRRs was not uniformly needed for PwRMS receiving OMB
- When asked to rank factors that are important when considering pre-treatment for potential systemic IRRs, participants agreed that prior adverse reactions is a top factor and ranked it highest priority on average
- Most participants ranked severity and type of side effect in the top 5 most important factors to consider when deciding whether to post-treat systemic IRRs, although consensus was not achieved for any of the individual ranked factors

Figure 2. Likelihood of OMB IRRs
What is the likelihood that local/systemic OMB IRRs, if any, occur among your patients with RMS?

	Mild, N (%)		Moderate, N (%)		Severe, N (%)	
	Local	**Systemic**	**Local**	**Systemic**	**Local**	**Systemic**
Likelihood respondents	32 (80.0)	31 (77.5)	28 (70.0)	28 (70.0)	16 (40.0)	16 (40.0)
Not seen‡	7 (17.5)	7 (17.5)	12 (30.0)	12 (30.0)	24 (60.0)	22 (55.0)
Don't know	1 (2.5)	2 (5.0)	0 (0)	0 (0)	0 (0)	2 (5.0)

IQR, interquartile range; IRR, injection-related reaction; OMB, ofatumumab; RMS, relapsing multiple sclerosis
*Reached consensus (IQR, 75th-25th percentile, around median responses were <25 out of 100)
†Median likelihood toward 0 means highly unlikely and toward 100 means highly likely. Threshold median values for the level of likelihood were <25 for unlikely, 25-75 for moderately likely, and >75 for likely
‡"Not seen" was an opt-out for likelihood responses but should not be equated to zero likelihood

- Participants indicated that the most common challenge in effectively managing systemic OMB IRRs in their clinical practice was a "lack of communication with patient, patient not reporting IRRs" (Figure 3)
- Conversely, there was limited consensus on various aspects of systemic IRR prevention and management, including specific interventions, barriers, and pre- and post-treatment options
- There were minimal changes in consensus between Rounds 1 and 3

Figure 3. Common Challenges to Effectively Managing OMB IRRs
Of the following, which would you rank as the most common challenges or barriers to effectively managing systemic OMB IRRs in your clinical practice or in the clinical setting more generally?
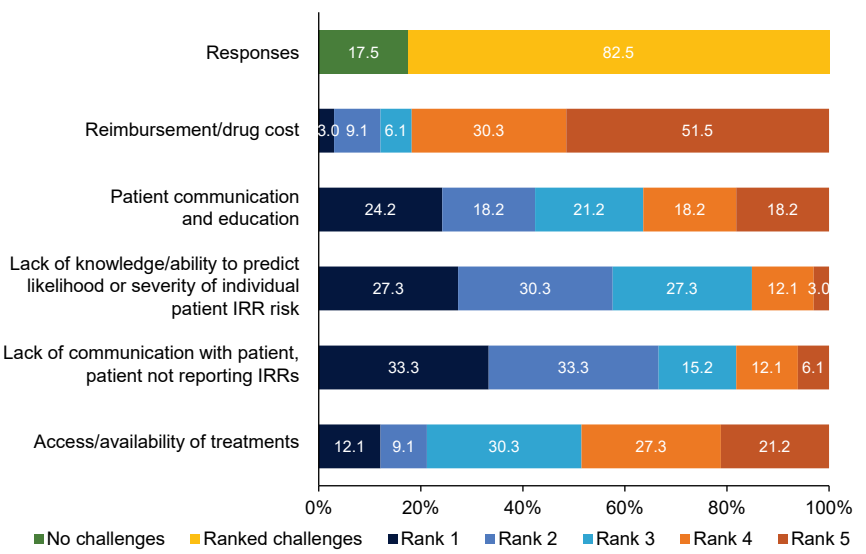
IRR, injection-related reaction; OMB, ofatumumab
Percentages for each challenge are calculated out of the total number of participants who provided ranking responses (N=33/40)
Percentages may not always add up to 100 due to rounding
1 is the most challenging and 5 is the least challenging

Limitations

- Results of this study may have been impacted by lower reporting of IRRs by patients in clinical practice compared with clinical trials
- The small sample size and US-based panel may limit the generalizability of these results
- As participants volunteered and were compensated for their participation, these results may be impacted by self-selection bias

References

1. Novartis Pharmaceuticals Corporation. Prescribing information. Kesimpta® 2020. Accessed January 11, 2024. https://www.novartis.com/us-en/sites/novartis_us/files/kesimpta.pdf;
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