tolerated, with no new safety risks identified. These data inform physicians on the longer-term safety profile of ofatumumab in people living with RMS.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

Adverse event	Core, ASCLEPIOS OMB (N=946)		Core + extension, Overall OMB, (N=1969)	
	n (%)	EAIR (95% CI)	n (%)	EAIR (95% CI)
Patients with at least one AE	791 (83.61)	188.55 [175.86, 202.16]	1771 (89.9)	124.65 [118.97, 130.59]
Patients with at least one SAE	86 (9.10)	5.39 [4.36, 6.65]	289 (14.7)	4.68 [4.17, 5.26]
AEs leading to discontinuation	54 (5.70)	–	139 (7.1)	–
Infections and infestations	488 (51.58)	51.14 [46.80, 55.88]	1334 (67.75)	40.99 [38.85, 43.25]
Serious infections	24 (2.54)	1.44 [0.97, 2.15]	106 (5.38)	1.63 [1.35, 1.97]
Injection-related systemic reactions	195 (20.61)	15.49 [13.46, 17.83]	508 (25.79)	10.06 [9.22, 10.98]
Injection site reactions	103 (10.88)	7.21 [5.94, 8.74]	243 (12.34)	4.08 [3.60, 4.63]
Malignancies	5 (0.53)	0.32 [0.13, 0.77]	21 (1.06)	0.32 [0.21, 0.48]
Deaths	0	0	9 (0.46)	–

Safety Profile of Ofatumumab for Up to 5 years of Treatment

EPO-643

International Consensus on Smoldering Disease in Multiple Sclerosis using the Delphi Method

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Background and aims: Despite the successful therapeutic suppression of relapses and new MRI lesions, most people with multiple sclerosis (pwMS) experience neurological deterioration. Accumulating data suggest that multiple sclerosis (MS) in addition to being a disease related to acute focal inflammation, involves more widespread, smoldering pathogenic processes that impact the entire central nervous system from early stages of the disease. Understanding and better defining the biology underlying the clinical and radiological manifestations of smoldering pathological processes remain important unmet needs. Greater comprehension of smoldering disease will improve clinical management, promote drug research by identifying new targets, stratifying pwMS for clinical trials and aid pwMS in understanding the causes of disease worsening.

Methods: Fifteen MS experts from eight countries across Europe, US, and Canada convened to develop consensus-driven statements on smoldering disease across multiple domains. They employed the Delphi method to anonymously establish agreement on a 5-point scale with "consensus" defined a priori as >75% who agree or strongly agree.

Results: See Table

Table 1

Statements relating to definition of smoldering disease	Statements relating to disease worsening due to smoldering disease
Smoldering disease is considered an umbrella term characterizing chronic pathobiological processes occurring in the CNS, beyond acute focal inflammation, associated with neurodegeneration leading to clinical worsening in pwMS, that may start early and continues throughout the disease course.	Clinical disease worsening is not just associated with progressive stages of the disease but may be observed at early stages of the disease and throughout the course of MS
Progression independent of relapse activity (PIRA) should be considered primarily a clinical manifestation of smoldering disease and therefore those terms should not be used interchangeably	Disease worsening may be driven by smoldering disease activity, which may be present throughout the disease course (even before clinical features manifest) and may account for physical as well as cognitive dysfunction

Table

Conclusion: This expert panel aims to provide further definitions and recommendations to help raise awareness and educate the neurology community on smoldering disease as well as advise on its implementation into routine clinical practice. Full presentation and publication of all statements with supporting evidence are expected in 2023.

Disclosure: The concepts and contents of this abstract emerged from several meetings facilitated by Sanofi. The experts involved are paid for attending the meetings but not for any writing efforts. Medical writing support was provided by Lionel Thevathasan, MD from LT Associates Ltd who was funded by Sanofi.