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Presenter: J. Korich

ACKNOWLEDGMENTS

Medical writing assistance was provided by Claire Snaith and Joseph Ward of inScience Communications, Springer Healthcare Ltd, UK, and was funded by the healthcare business of Merck KGaA, Darmstadt, Germany.

DISCLOSURES

MSF has received honoraria or consultation fees from Alexion, Atara Biotherapeutics, Bayer, BeiGene, Celgene (BMS), the healthcare business of Merck KGaA (Darmstadt, Germany), Novartis, Pendopharm, Roche, and Sanofi; was a member of a company advisory board, board of directors, or other similar group for Alexion, Atara Biotherapeutics, Bayer, BeiGene, Celgene (BMS), Clene Nanomedicine, Janssen (J&J), McKesson, the healthcare business of Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Sanofi; has been a participant in a company sponsored speaker's bureau for the healthcare business of Merck KGaA (Darmstadt, Germany) and Sanofi; and has received research or educational grants from Sanofi. **MT** is a former employee of the healthcare business of Merck KGaA, Darmstadt, Germany. **ZM** is an employee of Merck spol. s r.o., Bratislava, Slovakia (an affiliate of Merck KGaA, Darmstadt, Germany). **DJ** is an employee of Merck Serono Ltd, Feltham, UK (an affiliate of Merck KGaA, Darmstadt, Germany). **JK** is an employee of EMD Serono, Inc., Rockland, MA, USA.

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Presenter: J. Korich[5]

[1]University of Ottawa, Department of Medicine and the Ottawa Hospital Research Institute, Ottawa, ON, Canada; [2]the healthcare business of Merck KGaA, Darmstadt, Germany; [3]Merck spol. s r.o., Bratislava, Slovakia (an affiliate of Merck KGaA, Darmstadt, Germany); [4]Merck Serono Ltd, Feltham, UK (an affiliate of Merck KGaA, Darmstadt, Germany); [5]EMD Serono, Inc., Rockland, MA, USA.

CONCLUSION

Cumulatively to May 2021, no new safety concerns have been identified from the post-approval data of sc IFN β-1a.

To date (04 January 2022) there has been no suggestion of an increased risk of respiratory viral infection in patients treated with sc IFN β-1a for relapsing MS, and approximately 48% of COVID-19 confirmed adverse events were resolved or resolving.

INTRODUCTION

- sc IFN β-1a is a well-established DMT for relapsing MS.
- Since its introduction to the market, the estimated cumulative exposure to sc IFN β-1a amounts to 1,831,698 patient-years (as of May 2021).
- The COVID-19 pandemic has become a concern for MS patients and their healthcare providers in terms of its effect on the associated safety of their DMT.
  - Preliminary evidence suggests IFN-treated patients report fewer infections and better recovery per infection.[1,2]

OBJECTIVE

To report on the post-approval safety profile of sc IFN β-1a in patients with relapsing MS, including COVID-19 and other respiratory viral infections.

METHODS

Post-approval data

- Serious and non-serious AEs/ADRs from post-approval spontaneous individual case safety reports are presented cumulative to May 2021.
- AEs of special interest
  - Rates are shown as estimated cumulative reporting rate per 10,000 patient-years.
- Respiratory viral infections
  - ADR are shown as cumulative number of patients.

COVID-19 data

- COVID-19 cases in sc IFN β-1a-treated patients with MS were sourced from the Merck KGaA, Darmstadt, Germany Global Patient Safety Database.
- COVID-19 findings are summarized, as of 04 January 2022.

RESULTS

Table 1. AEs of special interest (cumulative to 03 May 2021)

AE of special interest*	Estimated cumulative† reporting rate per 10,000 patient-years	Most frequently reported preferred terms
Autoimmune disorders	95	• Multiple sclerosis • Rheumatoid arthritis
Acute coronary syndrome	7.1	• Myocardial infarction • Coronary artery occlusion
Pulmonary arterial hypertension	0.8	• Pulmonary hypertension • Pulmonary arterial hypertension
Panniculitis	0.45	• Panniculitis • Erythema nodosum
Chronic lymphocytic leukaemia	0.18	• Chronic lymphocytic leukaemia

Table 2. Respiratory viral infections (cumulative to 03 May 2021)

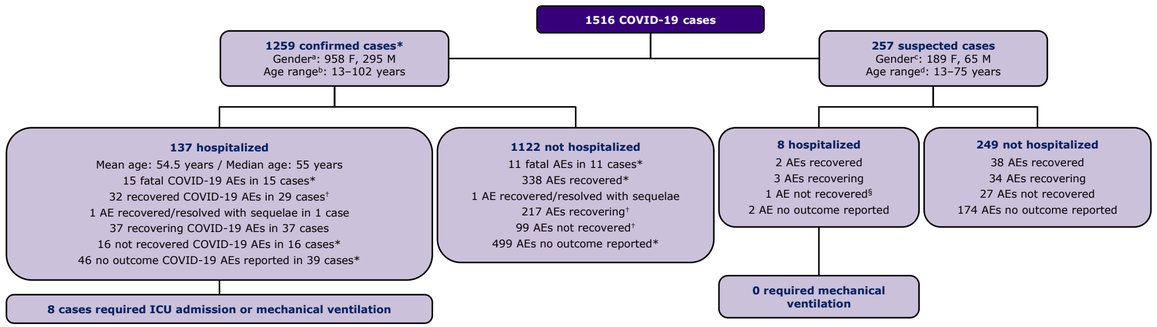
Preferred term	Cumulative† serious ADR (number of patients)	Cumulative† non-serious ADR (number of patients)	Cumulative† total (number of patients)
Influenza	47	2327	2374
Viral infection	49	270	319
H1N1 influenza	4	11	15
Viral bronchitis		6	6
Viral upper respiratory tract infection	1	4	5
Viral pharyngitis		4	4
Pneumonia viral	3	1	4
Pneumonia respiratory syncytial viral	2		2
Viral sinusitis		2	2
Viral rhinitis		1	1
Laryngitis viral		1	1
Respiratory tract infection viral		1	1

*Identified close monitoring events for sc IFN β-1a as part of the Merck KGaA, Darmstadt, Germany/EMD Serono risk management plan; †Cumulative sc IFN β-1a exposure from February 1998 to May 2021 is approximately 1,831,698 patient-years.

A total of **527,833 ADRs** have been reported spontaneously, with **6.6%** of events classified as serious. No new safety concern has been identified.

Safety analysis of the top five most common respiratory viral infection ADRs reported spontaneously (excluding COVID-19 related terms) did not reveal any difference from the known safety profile of sc IFN β-1a, and cases were typically non-serious.

Figure 1. COVID-19 cases in sc IFN β-1a-treated patients with MS (as of 04 January 2022)



*32 fatal cases: 26 fatal COVID-19 events in 26 cases (COVID-19 in 21 cases and COVID-19 pneumonia as the cause of death in 5 cases) and 6 unknown causes of death in 6 cases;†2 AEs in 1 case; §1 fatal case comprising 1 non-fatal suspected COVID-19 event; [a]Unknown gender for 6 patients; [b]Unknown age for 81 patients; [c]Unknown gender for 3 patients; [d]Unknown age for 38 patients.

COVID-19 in IFN-treated patients with MS

- In a multivariate analysis of Italian and French patients with MS, the use of IFN appeared to **decrease the risk** of severe COVID-19
  - Anti-CD20 therapies were significantly associated (OR=2.05, 95% CI=1.39–3.02, p<0.001) with COVID-19 severity, whereas IFN indicated a decreased risk (OR=0.42, 95% CI=0.18–0.99, p=0.047)[1]
  - In the French MS registry, in a univariate analysis IFN-treated patients were associated with a **lower risk** of a severe outcome due to COVID-19 (OR=0.07, 95% CI [0.02-0.25])[3]

REFERENCES
1. Sormani MP, et al. *Ann Clin Transl Neurol*. 2021;8:1738–1744. **2**. MS International Federation, updated 4 February 2021, available at: https://www.msif.org/news/2020/02/10/the-coronavirus-and-ms-what-you-need-to-know/ [Accessed 22/4/21]. **3**. Louapre C, et al. *JAMA Neurol*. 2020;77:1079–1088.

Abbreviations: ADR, adverse drug reaction; **AE**, adverse event; **CI**, confidence interval; **DMT**, disease-modifying therapy; **IFN**, interferon; **MS**, multiple sclerosis; **OR**, odds ratio; **PwMS**, patients with MS; **sc**, subcutaneous.

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Presented at AAN 2022 | April 2–7 | Seattle, Washington, USA

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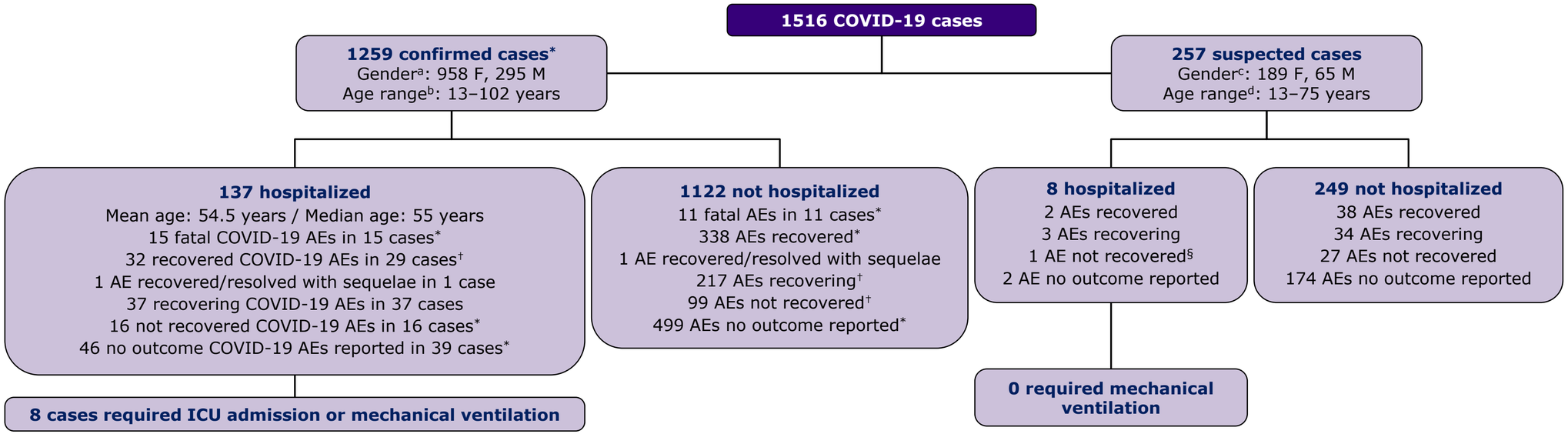

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