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M.S. Freedman, H. Guehring, Z. Murgasova, D. Jack

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CONCLUSIONS

Cumulatively to May 2020, no new safety concern has been identified from the post-approval data of sc IFN β-1a.

To date (19 January 2021) 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 54% of COVID-19 confirmed adverse events were resolved or resolving.

INTRODUCTION

- sc IFN β-1a is a well-established disease-modifying therapy for relapsing MS.
- Since its introduction to the market, the estimated cumulative exposure to sc IFN β-1a amounts to 1,766,525 patient-years (as of May 2020).
- In recent months 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 disease-modifying therapy.
  - Preliminary evidence suggests IFN-treated patients report fewer infections and better recovery per infection.[1,2]

IFN, interferon; **MS**, multiple sclerosis; **sc**, subcutaneous

OBJECTIVES

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.

IFN, interferon; **MS**, multiple sclerosis; **sc**, subcutaneous

METHODS

Post-approval Data

- Serious and non-serious AEs from post-approval spontaneous individual case safety reports are presented cumulative to May 2020.
- AEs of special interest
  - Rates are shown as estimated cumulative reporting rate per 10,000 patient-years.
- Respiratory viral infections
  - AE rates 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 Global Safety Database.
- COVID-19 findings are summarized, as of 19 January 2021.

AE, adverse events; **IFN**, interferon; **MS**, multiple sclerosis; **sc**, subcutaneous; **sc**, subcutaneous

RESULTS

Table 1. AEs of Special Interest (Cumulative to 03 May 2020)

AE of special interest*	Estimated cumulative** reporting rate per 10,000 patient-years	Most frequently reported preferred terms
Autoimmune disorders	80	• Multiple sclerosis • Optic neuritis
Acute coronary syndrome	7.05	• Myocardial infarction • Acute myocardial infarction
Pulmonary arterial hypertension	0.8	• Pulmonary hypertension • Pulmonary arterial hypertension
Panniculitis	0.45	• Panniculitis • Erythema nodosum • Erythema induratum
Chronic lymphocytic leukemia	0.17	• Chronic lymphocytic leukaemia

*Identified close monitoring events for sc IFN β-1a as part of the Merck KGaA/EMD Serono risk management plan. **Cumulative sc IFN β-1a exposure from February 1998 to May 2020 is approximately 1,766,525 patient-years.

- A total of **525,268 AEs** have been reported, with **6.6%** of events classified as serious.
- No new safety concern has been identified.

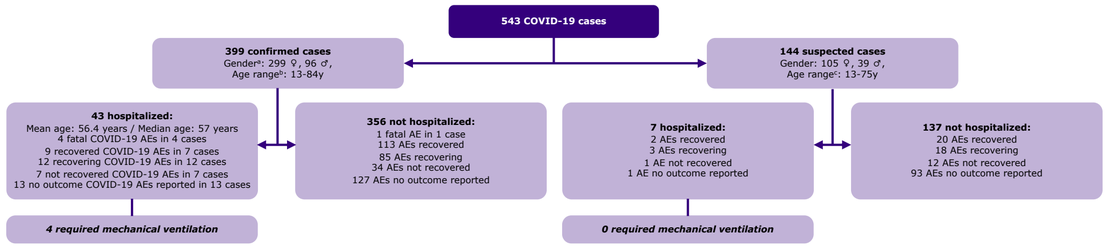
Table 2. Respiratory Viral Infections (Cumulative to 03 May 2020)

Preferred term	Cumulative Serious AE (number of patients)	Cumulative Non-serious AE (number of patients)	Cumulative Total (number of patients)
Influenza	47	2322	2369
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

Cumulative sc IFN β-1a exposure from February 1998 to May 2020 is approximately 1,766,525 patient-years.

- Safety analysis of the top five most common respiratory viral infection AEs reported spontaneously 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 19 January 2021)



In some instances, the number of AEs does not correspond to the number of cases because multiple events were reported. Nine fatal cases were reported among patients with confirmed COVID-19: 5 fatal COVID-19 events in 5 cases (COVID-19 infection as the cause of death in 3 cases; COVID-19 pneumonia as the cause of death in 4th case; and COVID-19, sepsis, and bilateral pneumonia as the causes of death in the 5th case) and 4 unknown causes of death in 4 cases. Among those with suspected COVID-19, there was 1 fatal case comprising 1 non-fatal suspected COVID-19 event. [a]Unknown gender for 4 patients; [b]Unknown age for 27 patients; [c]Unknown age for 15 patients.

COVID-19 in IFN-treated Patients With MS

- In the Italian MS population, the use of IFN appeared to **decrease the risk** of COVID-19.
  - PwMS with suspected or confirmed COVID-19 were treated with IFN at a significantly lower frequency (OR=0·47, 95% CI [0·33-0·67], p<0·001) than the Italian MS population.[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]

AE, adverse event; **CI**, confidence interval; **IFN**, interferon; **MS**, multiple sclerosis; **OR**, odds ratio; **PwMS**, patients with MS; **sc**, subcutaneous

1. Sormani MP, et al. *SSRN Electronic J.* 2020; doi:10.2139/ssrn.3631244. 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.

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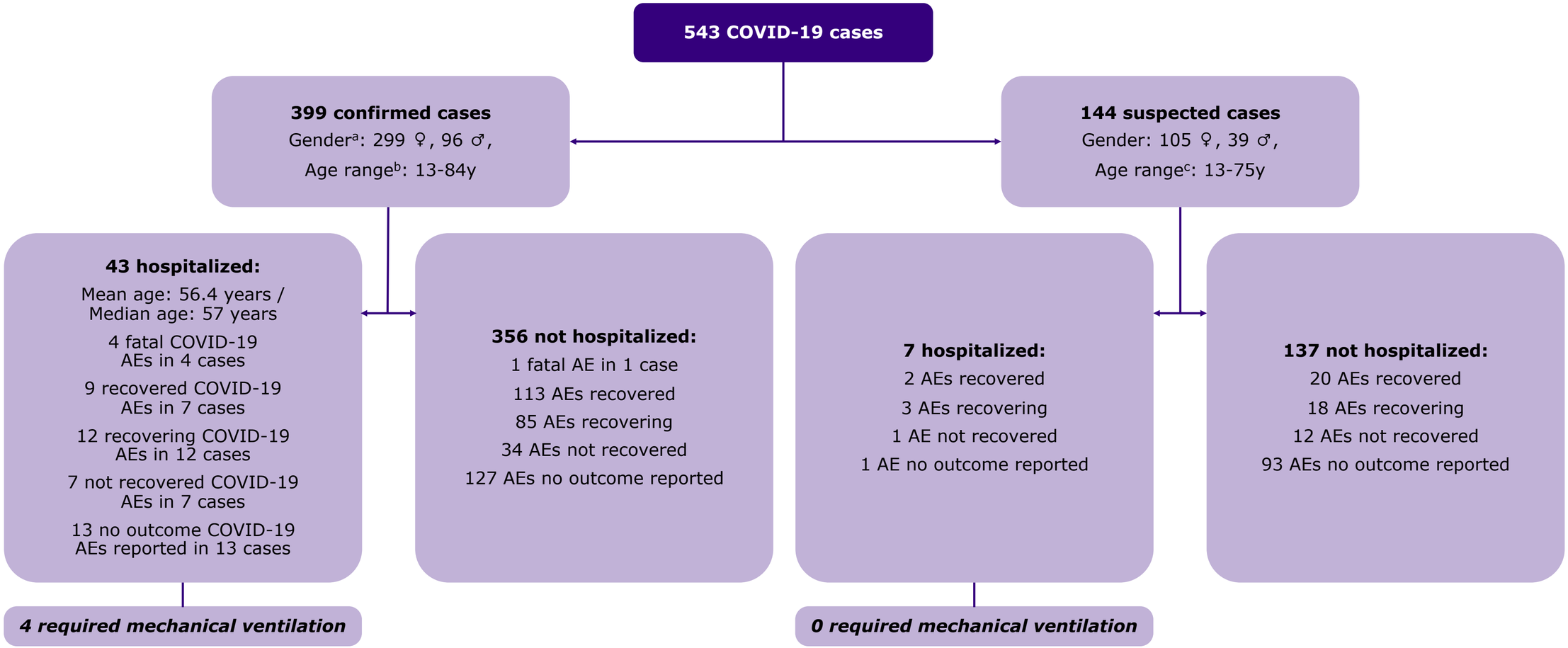

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