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# Post-approval Safety of Subcutaneous Interferon $\beta$ -1a in the Treatment of Multiple Sclerosis, with Particular Reference to Respiratory Viral Infections

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**MT, ZM,** and **DJ** are employees of Merck KGaA, Darmstadt, Germany



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**CONCLUSIONS**

Cumulatively to May 2021, no new safety concerns have been identified from the post-approval data of sc IFN β-1a. To date (20 July 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 49% 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<sup>1,2</sup>

**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

**METHODS (CONTINUED)**

**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 20 July 2021

**RESULTS**

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

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

\*Identified close monitoring events for sc IFN β-1a as part of the Merck KGaA/EMD Serono risk management plan.  
<sup>†</sup>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.

**RESULTS**

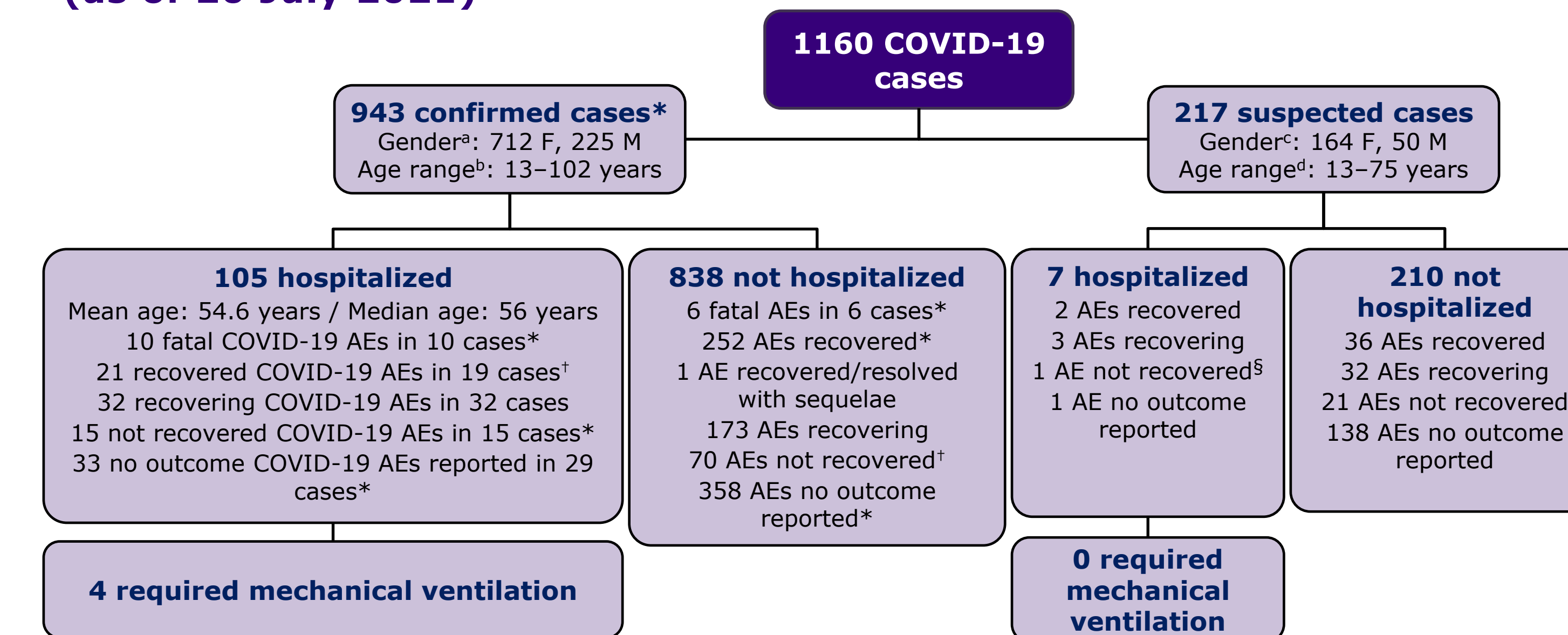
**Table 2. Respiratory viral infections (cumulative to 03 May 2021)**

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

Cumulative sc IFN β-1a exposure from February 1998 to May 2021 is approximately 1,831,698 patient-years.

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 20 July 2021)**



\*22 fatal cases: 16 fatal COVID-19 events in 16 cases (COVID-19 in 13 cases and COVID-19 pneumonia as the cause of death in 3 cases) and 6 unknown causes of death in 6 cases.  
<sup>†</sup>2 AEs in 1 case.  
<sup>§</sup>1 fatal case comprising 1 non-fatal suspected COVID-19 event.  
<sup>¶</sup>Unknown gender for 6 patients; <sup>‡</sup>Unknown age for 53 patients; <sup>•</sup>Unknown gender for 3 patients; <sup>•</sup>Unknown age for 28 patients.

**COVID-19 in IFN-treated patients with MS**

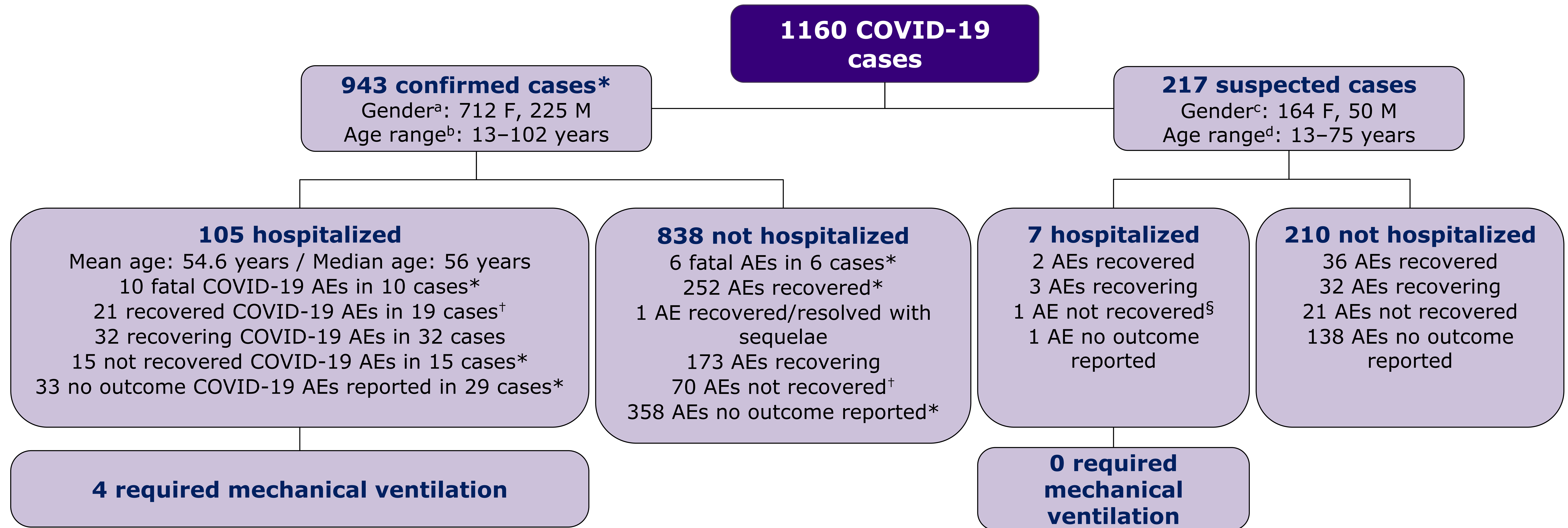
- In a multivariate analysis of Italian and French patients with MS, the use of IFN appeared to **decrease the risk** of severe COVID-19
- Anti-CD20 therapies were significantly associated (OR=2.05, 95% CI=1.39-3.02, p<0.001) with Covid-19 severity, whereas IFN indicated a decreased risk (OR=0.42, 95% CI=0.18-0.99, p=0.047)<sup>1</sup>
- 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])<sup>3</sup>

SCAN FOR FULL AUTHOR DISCLOSURE DETAILS





**Figure 1. COVID-19 cases in sc IFN  $\beta$ -1a-treated patients with MS (as of 20 July 2021)**



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