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Cardiovascular, neurological, and pulmonary events following vaccination with the BNT162b2, ChAdOx1 nCoV-19, and Ad26.COV2.S vaccines: An analysis of European data

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ABSTRACT

The ChAdOx1 nCoV-19 (ChA) (AstraZeneca) and Ad26.COV2.S (AD26) (Janssen) vaccines are virus-based coronavirus disease 2019 (COVID-19) vaccines used worldwide. In spring 2021, venous blood clots and thrombocytopenia were described in some vaccine recipients. We evaluated the frequency of severe adverse events (SAEs) documented in the EudraVigilance European database in young adult (18–64 years old) and older (≥65 years old) vaccine recipients up to 23 June 2021 and related them to coagulation disorders and arterial, cardiac, and nervous system events. Comparison between the frequency of SAEs and SAE-related deaths in ChA and AD26 vs. BNT162b2 COVID-19 (BNT) (Pfizer/BioNTech) vaccine recipients demonstrated: 1) ChA and AD26 recipients than BNT recipients had higher frequencies of not only SAEs caused by venous blood clots and hemorrhage, but also thromboembolic disease and arterial events, including myocardial infarction and stroke; 2) a corresponding higher frequency of SAE-related deaths. The frequency was higher in both young adults and older adults. Comparison between the frequency of SAEs and SAE-related deaths in AD26 vs. ChA recipients demonstrated in AD26 recipients: 1) lower frequency of thrombocytopenia; 2) lower frequency of SAEs in young adult recipients; 3) higher frequency of SAEs in older recipients. Interestingly, most of the venous thrombotic SAEs associated with ChA and AD26 vaccines were not associated with thrombocytopenia, suggesting that TTS (thrombosis with thrombocytopenia syndrome) is not the only type of thrombosis observed following virus-based vaccines. In conclusion, both virus-based COVID-19 vaccines show more SAEs than BNT, but the frequency of the SAE type in the different age groups differs, suggesting that the mechanisms responsible of SAEs overlap only partly.

1. Introduction

Vaccines against severe acute respiratory syndrome coronavirus (SARS-CoV)-2 that cause an immune response against the SARS-CoV-2 spike protein are, at present, the primary method of fighting the coronavirus disease 2019 (COVID-19) pandemic. Real-world studies have described similar vaccine efficacy in preventing COVID-19 and severe COVID-19 [1–3]. To evaluate the benefit–risk profile of each vaccine, it is crucial to know the adverse events (AEs) each vaccine causes not only in the short-term but also in the mid/long-term, with particular reference to severe AEs (SAEs) and death. SAEs, consisting of events that occur extremely rarely in the healthy population, are promptly detected by pharmacovigilance, but SAEs consisting of events that happen relatively frequently in the population may be more challenging to discover because attributed to underlying disease and underreported [4–7].

In March 2021, the ChAdOx1 nCoV-19 COVID-19 adenovirus-based vaccine (ChA) produced by AstraZeneca was associated with blood clots in unusual sites and bleeding events [8]. Subsequently, Greinacher and colleagues demonstrated thrombocyte aggregation in the presence of anti-platelet factor 4 antibodies (anti-PF4) [9] that were produced in response to SARS-CoV-2 spike protein, adenovirus proteins, and a co-factor present in ChA but not in the Ad26.COV2.S vaccine (AD26)

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