



Between the essential precautions and the undesirable confusion

Press Release of the French National Academy of Medicine

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Reports of thrombo-embolic adverse events led France, like several other countries of the European community, to suspend the use of the COVID-19 AstraZeneca[®] vaccine on March 15, 2021, pending an opinion from the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency (EMA) [1]. This opinion was issued on March 18; It confirmed that the benefits of the AstraZeneca[®] COVID-19 vaccine outweigh the potential risks associated with it, stating that "it is a safe, effective vaccine not associated with an increased risk of thrombosis formation". However, it added that uncertainties regarding the very rare cases of cerebral venous thrombosis with thrombocytopenia observed in younger patients require a special attention.

On 19 March, considering 18 cases of cerebral venous thrombosis and 7 cases of disseminated intravascular coagulation reported for a total of 20 million people vaccinated in Europe with the AstraZeneca[®] COVID-19 vaccine, and estimating that a link between these 25 events (resulting in 9 deaths) and the vaccination could not be formally excluded, the French National Authority for Health (HAS) recommended to only use this vaccine for people aged 55 or over [2].

This opinion, quickly relayed by the French General Directorate of Health, goes against the recommendation issued on February 2 by the same HAS, which recommended to preferentially use the AstraZeneca[®] COVID-19 vaccine in people under 65 [3]. Initially motivated by the lack of data after the age of 65 in the pivotal Phase 3 clinical study, this reservation was lifted by the large Scottish study showing the efficacy of the AstraZeneca[®] COVID-19 vaccine in the elderly [4].

Such a reversal, which can only be justified by the precautionary principle, has two major drawbacks:

1. it has seriously disturbed the progress of the national vaccination campaign, as this decision led vaccination centers and general practitioners to cancel appointments, to modify appointment plans and to throw away unused doses of vaccine, increasing the regrettable rate of waste;
2. it raises doubts about the approvals issued by the EMA and thus creates public mistrust of the various vaccines against Covid-19 put on the market. The current epidemic resurgence of Covid-19 observed in several French departments makes it necessary to achieve an effective vaccination coverage in the entire population as quickly as possible. Aware of the need to adapt the vaccination campaign to the sometimes unpredictable rate of delivery of vaccine doses

while maintaining a reinforced pharmacovigilance, **the French National Academy of Medicine recommends :**

- not to suspend the use of a vaccine benefiting from Marketing Authorization on the basis of very rare adverse event reports whose incidence in the vaccinated population is not significantly higher than the expected incidence in the general population;
- not to override the EMA's opinions in the name of a precautionary principle that should first apply to the very real risk of Covid-19;
- to do everything possible to reduce the rate of wastage of vaccine doses;
- to strengthen the resources of the national vaccine pharmacovigilance monitoring system to ensure an in-depth clinical evaluation of each reported adverse event, with a particular attention to thrombotic events;
- to share with the general public updated data on the efficacy and safety of the anti-Covid-19 vaccines used in France through a sustained, clear, transparent and non-anxiety-inducing communication.

1. Communiqué of the French National Academy of Medicine "European plans for enhanced pharmacovigilance: safety or restraint?" March 17, 2021

2. HAS. Opinion n° 2021.0018/AC/SEESP on the place of the AstraZeneca® vaccine in the vaccination strategy following the opinion of the European Medicines Agency concerning adverse events that occurred in several European countries in vaccinated persons. March 19, 2021

3. HAS. Recommendation " Covid-19 Vaccination Strategy: Covid-19 Astra-Zeneca® Vaccine Place ". February 2, 2021

4. Vasileiou E et al. Effectiveness of first dose of Covid-19 vaccines against hospital admissions in Scotland: national prospective cohort study of 5.4 million people (preprint), 2021