NACI rapid response: Recommended use of AstraZeneca COVID-19 vaccine in younger adults

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Recommendation

NACI recommends that AstraZeneca COVID-19 vaccine should not be used in adults under 55 years of age at this time while the safety signal of Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) following vaccination with AstraZeneca COVID-19 vaccine is investigated further.

Summary of rationale

Rare cases of serious blood clots, including cerebral venous sinus thrombosis, associated with thrombocytopenia have been recently reported in Europe following post-licensure use of AstraZeneca COVID-19 vaccine [1] [2]. Cases identified so far have been primarily in women under the

age of 55 years; although cases in men have also been reported and have mostly occurred between 4 and 16 days after receipt of vaccine. This adverse event is being referred to as Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) [3]. This entity is associated with the development of antibodies that "activate" platelets, which stimulate the formation of clots and result in thrombocytopenia. The mechanism of action is similar to heparin-induced thrombocytopenia (HIT). The exact mechanism by which the AstraZeneca vaccine triggers VIPIT is still under investigation. At this time, no other risk factors have consistently been identified in patients who develop VIPIT. This adverse event has not been identified following receipt of mRNA COVID-19 vaccines to date.

The rate of this adverse event is still to be confirmed. Based on information from the European Medicines Agency on March 18, 2021 it was originally estimated at approximately 1 per 1,000,000 people vaccinated with the AstraZeneca vaccine, however a higher rate of 1 per 100,000 was reported by the Paul-Ehrlich Institut in Germany [4]. Additional information is currently being gathered to characterize more accurately the rate of VIPIT. Based on available information, the case fatality of VIPIT is approximately 40%, however, the case fatality may decrease with increased awareness of the adverse event and appropriate early treatment.

Following population-based analyses of VIPIT assessing risk of COVID-19 disease by age, and considering that alternate products are available (i.e., mRNA vaccines), from what is known at this time, there is substantial uncertainty about the benefit of providing AstraZeneca COVID-19 vaccine to adults under 55 years of age given that the potential risks associated with VIPIT, particularly at the lower estimated rates. As a precautionary measure, while Health Canada carries out an updated benefit/risk analysis based on emerging data, NACI recommends that the vaccine not be offered to adults under the age of 55. Adults 55 years of age and older may

still be offered the AstraZeneca vaccine with informed consent, given the increased risk of hospitalization and death due to COVID-19 disease in this population [5] and since VIPIT appears to be a rarer event in that age group [6]. Since the current cases have occurred primarily in women, men may be less at risk of this adverse event and could potentially have a different benefit/risk assessment, however investigations are ongoing as it is possible that the reported female predominance of VIPIT is because more women received the AstraZeneca vaccine, making it difficult to assess risk based on sex. Young healthcare workers, one of the early priority groups receiving this vaccine globally, include a higher proportion of females.

Anyone receiving the AstraZeneca COVID-19 vaccine should be informed of this potential adverse event and advised to seek immediate medical attention if they develop symptoms of thromboembolism and/or thrombocytopenia between days 4 and 20 following receipt of the AstraZeneca vaccine [3]. Symptoms to be vigilant for include: shortness of breath, chest pain, leg swelling, persistent abdominal pain, neurological symptoms including sudden onset of severe or persistent worsening headaches or blurred vision, skin bruising (other than at the site of vaccination) or petechiae [3] [6]. In addition, healthcare professionals should be aware of VIPIT including how to diagnose and treat the condition (see Ontario Science Table guidelines [3]).

Canada is expected to receive sufficient mRNA COVID-19 vaccines to fully vaccinate the population with two doses of mRNA vaccine before fall 2021. AstraZeneca COVID-19 vaccine was expected to make up a small proportion of the COVID-19 vaccines available for use in Canada; therefore, COVID-19 vaccinations will not be significantly delayed without using AstraZeneca COVID-19 vaccine in younger adults.

Based on the international data that continues to emerge regarding VIPIT following receipt of AstraZeneca COVID-19 vaccine, the precautionary principle, and Canada's expected supply of mRNA COVID-19 vaccines, NACI has made a recommendation that will continue to be reassessed based on the rapidly evolving evidence.

Given the rare but severe VIPIT events reported in Europe, mainly in women under 55 years of age, and a plausible causal mechanistic explanation, NACI has evaluated the benefit/risk ratio comparing this adverse event to the risk of COVID-19 deaths for individuals in Canada in various age strata and considering the supply of alternate COVID-19 vaccines available in Canada (mRNA vaccines). While awaiting the results from Health Canada inquiries and the overall risk assessment, NACI recommends immediately pausing the use of the AstraZeneca vaccine in all individuals less than 55 years of age in Canada.

Decisions on the type of second dose that will be offered to those individuals under 55 years of age who have been vaccinated with AstraZeneca COVID-19 vaccine will be determined based on the latest evidence and research. NACI will continue to review evidence as it emerges, including evidence on mixed COVID-19 vaccine schedules, to provide advice to public health programs on the potential for completing the series with other vaccine products.

Further information on signs and symptoms of this adverse event and treatment can be found on Health Canada's website.

References

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