Received: 1 March 2021 | Accepted: 12 March 2021

DOI: 10.1111/bcp.14828

LETTER TO THE EDITOR

# Will AstraZeneca be able to provide clinical trial data on its COVID-19 vaccine efficacy in older adults?

The UK MHRA granted emergency authorization to the AstraZeneca COVID-19 vaccine on December 30, 2020. Two standard doses of this vaccine must be given 4–12 weeks apart to ≥18-year-old individuals.[1] The EU Commission granted conditional authorization on January 29, 2021. With regard to dosing interval and target population, the EU label states that it was impossible to estimate the vaccine efficacy in older adults (≥56-year-olds) due to insufficient number of participants and COVID-19 cases in this population group.[2] With the information available at the time the EU granted the authorization, many EU countries decided to limit its administration to, for instance, ≤55-year-old individuals (e.g., Italy and Spain) or ≤65-year-olds (e.g., France and Germany). On February 15, the World Health Organization included this vaccine in its Emergency Use Listing for adults and the elderly, although acknowledging the lack of efficacy data in this latter population group.[3]

In the first report published on December 8, 2020, Voysey et al.[4] evaluated the AstraZeneca COVID-19 vaccine efficacy on two placebo-controlled randomized controlled trials (RCTs) conducted in the United Kingdom and Brazil. For the primary efficacy analysis of two standard doses given 4–12 weeks apart, 4440 (vaccine) and 4455 (control) participants were assessed. Since the number of older adults (≥56-year-olds) and the time for COVID-19 cases to accrue were limited, it was impossible to estimate the vaccine efficacy in this population group: investigators believed that "additional data will be available in future analyses."[4]

On February 19, 2021, Voysey et al.[5] published the second report on the efficacy of the AstraZeneca COVID-19 vaccine. Pooling data of four placebo-controlled RCTs conducted in the United Kingdom, Brazil, and South Africa that received two standard doses with a 4-12-week interval, 7201 (vaccine) and 7179 (control) participants were assessed. No data on the efficacy of this vaccine in older adults was mentioned. It follows that the number of COVID-19 cases accrued in ≥56-year-old individuals was still limited to draw any estimation on vaccine efficacy. So currently, with the data of four RCTs and a remarkable higher number of participants, the situation regarding the efficacy in older adults has not changed since the temporary authorizations of this vaccine in the United Kingdom and other jurisdictions were granted: AstraZeneca has yet to prove its efficacy in older adults.

Although the AstraZeneca COVID-19 vaccine has been authorized in some 60 jurisdictions, two important countries with stringent regulatory requirements, Switzerland and the United States, have not yet. The Swiss Agency has already assessed the data submitted by this company.[6] Conversely, AstraZeneca has not applied for emergency-use authorization at the USA FDA yet. Seems likely that this vaccine will not be authorized in these two countries until the large ($N$ = 32 459; NCT04516746) placebo-controlled RCT—that is being run in the United States, France, and in four South American countries—shows positive efficacy results, something expected by March 2021. This, however, could be in jeopardy since, to comply with participants' rights,[7] all participants must be timely informed that COVID-19 vaccines are being deployed in the countries where the trial is being conducted. Since 73% of participating sites of this large RCT are in the United States, it is worth mentioning that as of February 26, 40 and 3 of the 45 U.S. states where this trial is being run were vaccinating ≥65- and ≥70-year-old persons, respectively.[8] Hopefully, at the time these participants have started to withdraw from the trial to be vaccinated with an authorized vaccine, the number of COVID-19 cases have reached the minimum number to allow estimating the vaccine efficacy in this population group. If this is the case, the AstraZeneca COVID-19 vaccine labels temporarily authorized in the United Kingdom and elsewhere must be amended to include the efficacy data in older adults. Similarly, this vaccine could then be assessed and eventually authorized in Switzerland and the United States. However, its limited efficacy (10%) against all COVID-19 due to the B.1.351 variant[9]—that forced the South African authorities to suspend its deployment—and the authorization for emergency use for ≥18-year-old individuals of the one-dose Janssen vaccine in the United States could make the authorization of the AstraZeneca vaccine somewhat difficult. The large ongoing trial might be the last opportunity for this vaccine to show its efficacy in older adults in a placebo-controlled RCT.

However, vaccine effectiveness in the real world—that could be shown in observational studies conducted in countries where this vaccine is being rolled out[10]—will shed light on this weak point of this, otherwise, cheap and useful vaccine to address this pandemic. If the AstraZeneca COVID-19 vaccine shows robust effectiveness results in the real world, health authorities of those European countries that have limited its administration to individuals up to a certain age will have scientific reasons to change their minds, even if efficacy data in placebo-controlled RCTs are still lacking.

KEYWORDS

AstraZeneca vaccine, COVID-19, efficacy, elderly, placebo-controlled trials, SARS-CoV-2

  

## ACKNOWLEDGEMENT

This work required no funding.

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## REFERENCES

1. Gov.UK. Regulatory approval of COVID-19 vaccines AstraZeneca. MHRA. Information for healthcare professionals and the public about the COVID-19 vaccine AstraZeneca. Published 30 December 2020. Last update 23 February 2021. Accessed 26 February 2021 https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca
2. European Medicines Agency. COVID-19 vaccine AstraZeneca. 29 January 2021. EMA/57617/2021. EMEA/H/C/005675. Accessed 26 February 2021 https://www.ema.europa.eu/sites/default/files/documents/2021/01/29/positive_opinion-_covid-19_vaccine_astrazeneca_en.pdf
3. World Health Organization. SAGE (Strategic Advisory Group of Experts) on Immunization Working Group on COVID-19 vaccines. AZD1222 vaccine against COVID-19 developed by Oxford University and Astra Zeneca: Background paper. Draft. 10 February 2021. Accessed 26 February 2021 https://apps.who.int/iris/handle/10665/339474
4. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet*. 2020;397:99–111.
5. Voysey M, Clemens SAC, Madhi SA, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet*. 2021;397(10277):881–891. https://doi.org/10.1016/S0140-6736(21)00432-3 Online ahead of print
6. Swissmedic. Rolling authorisation application for COVID-19 vaccines Swissmedic requests additional data. Swissmedic examines the data on the vaccine from AstraZeneca it receives on an ongoing basis. February 2021. Accessed 26 February 2021 https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/coronavirus-impfstoff-astrazeneca-weitere-daten-verlangt.html
7. Dal-Ré R, Orenstein W, Caplan AL. Trial participants' right after authorization of COVID-19 vaccines. *Lancet Respir Med*. 2021. https://doi.org/10.1016/S2213-2600(21)00044-8 Online ahead of print
8. See how the vaccine rollout is going in your state. The New York Times. Updated Feb 21, 2021. Accessed 26 February 2021 https://www.nytimes.com/interactive/2020/us/covid-19-vaccine-doses.html
9. Madhi SA, Baille V, Cutland CL, et al. Safety and efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine against the B.1.351 variant in South Africa. *N Engl J Med*. 2021. https://doi.org/10.1056/NEJMoa2102214 Online ahead of print
10. Vasileiou E, Simpson CR, Robertson C, 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. www.ed.ac.uk/files/atoms/files/scotland_firstvaccinedata_preprint.pdf