OCTAVE-DUO Trial

A Phase III, Multicentre, Randomised Trial Comparing SARS-CoV-2 Re-Boost Vaccine Strategies in Immunocompromised Participants

Lay Summary of Clinical Trial Results

Introduction

This summary shares the main findings from the OCTAVE-DUO trial, which looked at how well a third vaccination dose of COVID-19 vaccines worked for people who had low or no response to the first two vaccinations. It's important to remember that other studies might find different results or add new information.

The research team want to thank all the participants and their caregivers for their crucial role in helping us learn more about vaccine responses. Their involvement is really important for advancing medical research.

The trial was sponsored by the University of Birmingham and coordinated by the Cancer Research Clinical Trials Unit (CRCTU) at the University of Birmingham. The research was funded by the Medical Research Council and Blood Cancer UK.

This summary is for information purposes only. If you have medical questions, please contact your doctor. If you participated in this trial and have questions about the results, please speak with a doctor or other staff member at your trial site.

Why the research was needed

The investigators' previous study (OCTAVE) showed that almost a third (30%) of immune compromised patients had either a low or no immune response after their first two COVID-19 vaccines. This raised the question of the potential benefit of a third vaccine dose in these clinically vulnerable patients. The strategy of a vaccine re-boost had previously been successful for other vaccines, but the limited COVID-19 vaccine research performed prior to this trial gave variable results and therefore additional research was needed.

What were the main questions studied?

The questions the researchers wanted to answer in this trial were:

1. Whether a third vaccine dose of either the Pfizer or Moderna COVID-19 vaccines would boost the immune response in people with certain immune-related conditions that had low or no antibodies after their first two vaccine doses;
2. In participants with lymphoid malignancies, whether a third vaccine dose of the Pfizer Moderna or Novavax COVID-19 vaccines would boost the immune response in people that had low or no antibodies after their first two vaccine doses;
3. To compare if the type of vaccine used for the third vaccination would make a difference to the immune response across different diseases and treatments.

Who participated in the trial?

The people who took part in the OCTAVE-DUO trial were adults aged 18 and over with low or no response to two previous doses of COVID-19 vaccine based on their antibody levels measured at least 14 days after receipt of the second vaccine dose.

The participants' medical conditions included:

- immune-mediated rheumatic diseases
- solid cancer
- chronic kidney disease
- inflammatory bowel disease on immune suppressive therapy
- chronic liver disease
- stem cell transplant
- CAR-T cell therapy
- lymphoid malignancy
- primary immunodeficiency

What intervention did the participants receive?

This was a randomised trial. The people taking part received a vaccine randomly chosen by a computer.

The vaccines the participants were allocated to were one of the following**:**

- Pfizer SARS-CoV-2 vaccine (371 participants)
- Moderna SARS-CoV-2 vaccine (363 participants)
- Novavax SARS-CoV-2 vaccine (51 participants with lymphoid malignancy)

What happened during the trial?

Before deciding to take part in the trial, all the participants were provided with detailed information about it. They could also discuss it with their families and clinical team before agreeing to take part. This is called "informed consent", which is an important part of any trial. The doctors and nurses then asked the participants about their medical history and checked their health to make sure they could join the trial and that it was safe for them to do so.

Participants were required to attend clinic for the collection of a blood sample prior to receiving the third vaccine dose. Participants returned to clinic between three and five weeks after receiving their third vaccine dose for the collection of another blood sample.

The immune response was measured in each blood sample.

Where possible, participants were followed up during their regular hospital visits for their underlying medical condition or via telephone call.

Information was also collected retrospectively from the clinical records three months after the third vaccine dose, to see if they had received a further COVID-19 booster, had caught COVID-19, or whether they had been admitted to hospital.

What were the results of the trial?

This is a summary of the main results from this trial for all the participants combined.

The OCTAVE-DUO trial was a UK based trial, recruiting 804 participants between 4th August 2021 and 31st March 2022. Of the participants, 45% were women and 55% men; and 85% were of white ethnicity.

Numbers of participants by medical condition:

- immune-mediated rheumatic diseases, 189
- solid cancer, 10
- chronic kidney disease, 164
- inflammatory bowel disease on immune suppressive therapy, 95
- chronic liver disease, 82
- stem cell transplant, 44
- CAR-T cell therapy, 2
- lymphoid malignancy, 178
- primary immunodeficiency, 40

15 participants (2%) withdrew from the trial prior to receiving their third vaccine dose and were not included in the final analysis.

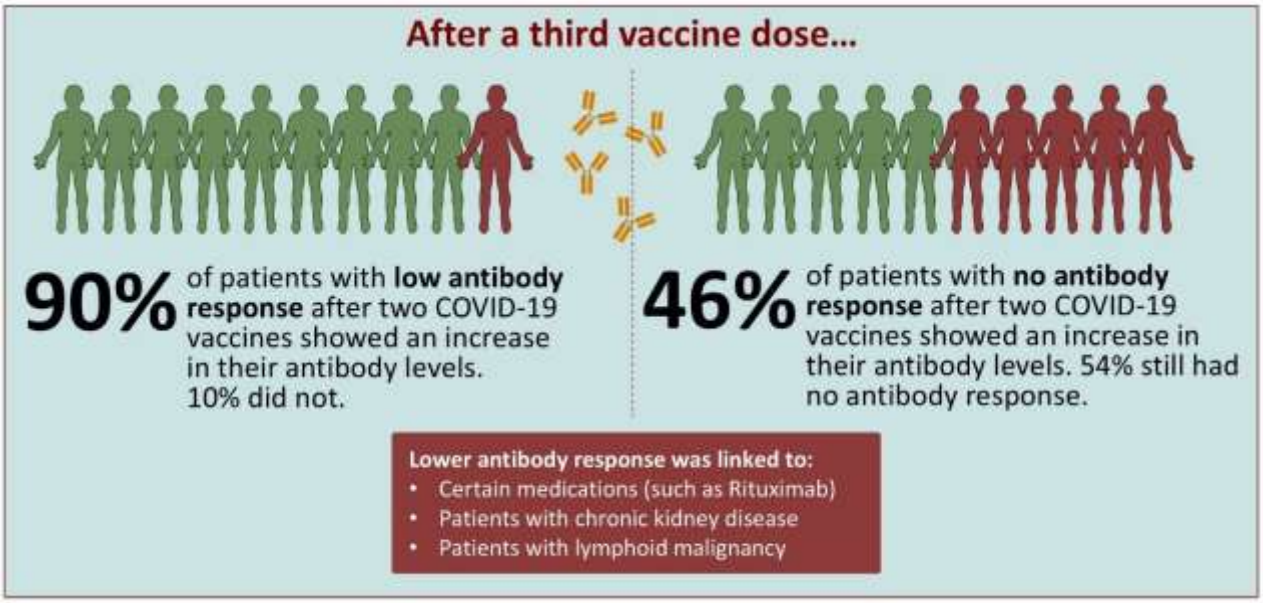
Both antibodies and T-cell responses were measured.

Antibodies, produced by a type of white blood cell called B-cells, are released by a healthy immune system and attack the outer coat of the virus.

T-cells, a different type of white blood cell, target infected cells and destroy them. This happens later in the immune response to the infection.

Of the 804 participants that joined the study, antibody level results from before and after the third COVID-19 vaccine dose were obtained for 729 people. Participants were grouped into either low responders (423 participants) or non-responders (306 participants) based on their antibody response to the first two vaccine doses.

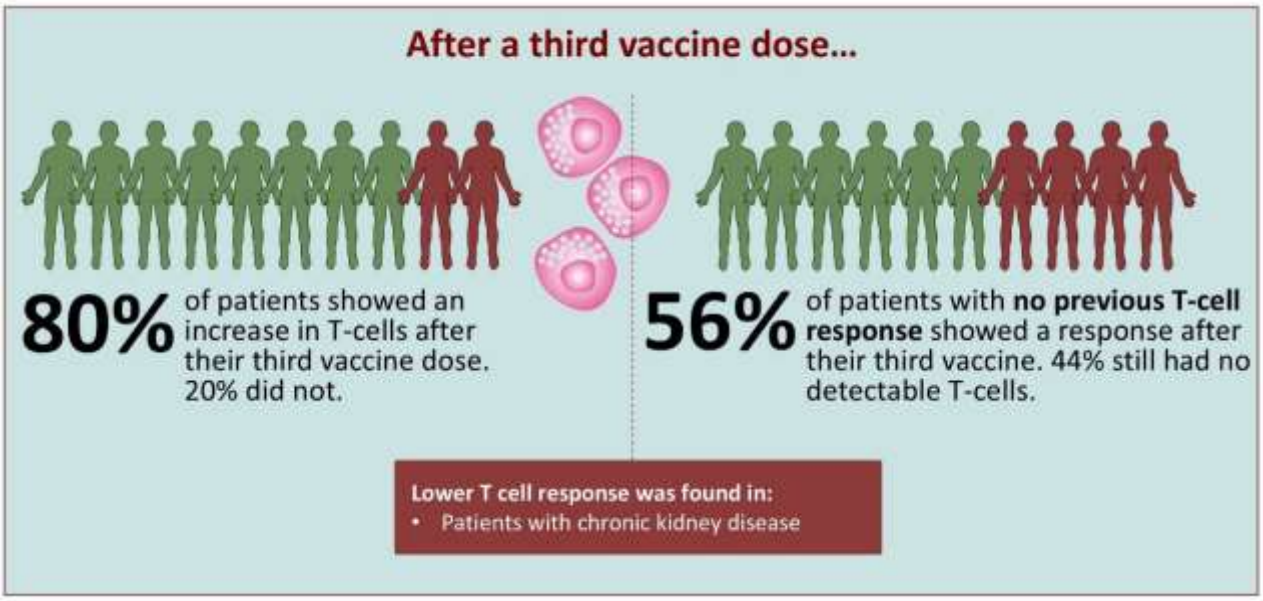
The results after the third vaccine dose showed that most participants had a significant increase in their antibody levels:



In those with a low antibody response to two vaccine doses, a third dose enhanced their antibody levels to similar amounts as seen in healthy individuals after two vaccine doses.

Some groups, like those with chronic kidney disease or lymphoid malignancy, had lower antibody responses to the third vaccine dose. This may be due to their underlying medical condition or the treatments they were receiving. Older age (especially over 75) and certain treatments targeting B-cells also increased the chance of not responding to the booster vaccination.

T-cell response results were available for 616 participants. Overall, 80% of participants had detectable responses after the third vaccine dose, including 56% of people who previously did not have a T-cell response.



There were 24 serious adverse events reported of which two were related to the vaccines.

There were seven deaths (1% of participants), but none were caused by the vaccines.

In summary

- Novavax vaccine was less effective at boosting antibody levels compared to Pfizer or Moderna vaccines for patients with lymphoid malignancies.
- For other patients, both Pfizer and Moderna were equally effective.
- All three vaccines led to similar T-cell responses.

How this trial has helped participants and researchers

The OCTAVE-DUO study showed that giving a third COVID-19 vaccine dose to people with weakened immune systems can significantly improve their immune response. Many patients who did not respond well to two previous doses were able to produce antibodies and T-cells, which help fight the virus, after a third dose, to levels similar to those in healthy individuals who had had two doses.

Importantly, the study also identified a group of people who still do not respond well, even after multiple doses, leaving them vulnerable to COVID-19. Researchers found key factors that can help predict who may not benefit from vaccines, suggesting that an alternative approach to COVID-19 should be considered.

The trial was launched when it was not clear how valuable a third dose would be. The UK Government used early data from the trial when deciding about the booster vaccine programme, which began in September 2021 for people with weak immune systems and which has continued every 6-12 months since then.

Details of further research

Some participants went on to join the ongoing Stravinsky study (Stratification of Clinically Vulnerable People for COVID-19 Risk Using Antibody Testing) which aims to establish if antibody testing can identify who remains at greatest risk of severe COVID-19 infection after vaccinations. (https://www.immunology.org/partnerships/stravinsky).

Where can I learn more about this trial?

You can find more information about this trial at the websites listed below:

OCTAVE-DUO - University of Birmingham
Cancer Research UK's website
https://www.isrctn.com/ISRCTN15354495

If you have questions about this trial, you can also contact the trial team by e-mail at:
OCTAVE-DUO@trials.bham.ac.uk

Trial information

Short trial title:	OCTAVE-DUO
Full trial title:	A Phase III, Multicentre, Randomised Trial Comparing SARS-CoV-2 Re-Boost Vaccine Strategies in Immunocompromised Participants
Research sponsor:	University of Birmingham, UK
Name of Research Ethics Committee:	London - Fulham
Research Ethics Committee reference number:	21/HRA/3072
IRAS ID:	302634
EudraCT number:	2021-003632-87
ISRCTN:	15354495
Date trial commenced:	31st July 2021
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