

New study to test third COVID-19 vaccine for people with weakened immune systems

- Participants will be given either Pfizer, Moderna or Novavax as a third dose of vaccine
- The government-funded study follows the results of the OCTAVE trial showing that 89% of people who are immunocompromised or immunosuppressed generate antibodies, and 60% generate a strong antibody response after 2 doses

A new clinical trial to determine whether a third dose of vaccine will improve the immune response for people who have weakened immune systems is launching in the UK.

The study, OCTAVE DUO, will offer people who are immunosuppressed or immunocompromised a Pfizer, Moderna or Novavax vaccine to determine whether this will give a stronger immune response than 2 doses.

The £2.2 million study will build on the OCTAVE trial, led by the University of Glasgow and co-ordinated by the University of Birmingham's Cancer Research UK Clinical Trials Unit.

The OCTAVE trial has published preliminary data today showing that 89% of people who are immunocompromised or immunosuppressed generate antibodies following vaccination, and 60% generated a strong antibody response following 2 doses of a vaccine.

However, 40% of people in these groups mounted a low, or undetectable, immune response after 2 doses, and the level of antibody response varies between the groups studied.

The level of antibodies required for protection from COVID-19 is still not known, and it is likely that T cells also play an important role in protecting people from the virus. These findings therefore do not provide a conclusive assessment of the protection vaccines offer people with weakened immune systems.

Up to 1,200 patients who are already involved in the OCTAVE study or those with other at-risk conditions involved in parallel studies will be recruited to the OCTAVE DUO trial.

The OCTAVE DUO study, co-funded by the government's Vaccines Taskforce and UK Research and Innovation (UKRI) and led by the University of Glasgow and University of Birmingham, will analyse in detail the immune response of this

group to the vaccine and the durability of this protection. It will also use healthcare records to determine whether any participants are later diagnosed with COVID-19.

Initial results are expected later this year to inform the UK's COVID-19 vaccine deployment in these specific at-risk groups. The trial will follow the patients to mid-2022 and offer more detailed information at that stage about the immune responses that develop in these groups.

The government is carefully considering the findings of the OCTAVE trial and will also consider any further appropriate advice – including from the independent Joint Committee on Vaccination and Immunisation (JCVI) – for those who are immunosuppressed as part of regular reviews of the latest data and evidence on vaccine efficacy and effectiveness.

Health and Social Care Secretary Sajid Javid said:

Vaccines have built a strong wall of defence in the UK and this is allowing most of us to learn to live safely with COVID-19.

We know some people may get less protection from the vaccine than others, so we are planning for a booster programme in the autumn, prioritising those most at risk.

This new study will play an important role in helping to shape the deployment of future vaccines doses for these specific at-risk groups.

A separate study by Public Health England (PHE) in July which looked at antibody response and vaccine effectiveness against symptomatic infection also showed that those who were immunocompromised had lower antibody responses.

It also found that protection from COVID (vaccine effectiveness against symptomatic disease) for those who are immunosuppressed of all ages after one dose was 4%, but after 2 doses it was 74%, providing similar protection to those who are not in an at-risk group. Again vaccine effectiveness may vary by specific condition and severity of that condition.

Patients included in the OCTAVE DUO study are people with:

- lymphoid malignancies
- immune mediated inflammatory diseases (including rheumatoid arthritis, psoriatic arthritis, vasculitis and inflammatory bowel disease)
- renal disease
- solid tumours (including breast and lung cancers)
- haematopoietic stem-cell transplantation
- hepatic and intestinal disease
- primary immune deficiency

Professor Iain McInnes, Head of the College of Medical, Veterinary and Life

Sciences at the University of Glasgow who leads the OCTAVE and OCTAVE DUO studies, said:

It is hugely important for us to urgently understand the effectiveness of COVID-19 vaccines in people who have immune-mediated inflammatory diseases, cancer, and diseases of the kidney or liver.

Our first study to answer this question is the OCTAVE study which has shown that there is a group of patients who may not mount a sufficient immune response.

We are pleased to now roll-out the OCTAVE DUO trial, to investigate the effects of a third dose on this particular group of patients who have shown an undetectable or low vaccine response. We hope to provide answers to this very important unanswered question.

Professor Pam Kearns, Director of the University of Birmingham's Cancer Research UK Clinical Trials Unit which is co-ordinating both OCTAVE and OCTAVE DUO, said:

The pandemic has been particularly concerning for millions of people in the UK who have conditions or long term illnesses which place them at greater risk of severe illness and death from COVID-19.

Together with our preliminary findings from OCTAVE, this new study will be instrumental in helping inform how best to vaccinate patients with chronic conditions, and protect them from COVID-19 infection in the future.

Dr Rob Buckle, Chief Scientist of the Medical Research Council, part of UKRI, which co-funded the trial, said:

While most of us are relieved to be vaccinated to protect ourselves and those around us, today's results investigating the outcome for people with immunosuppression will be of concern to the subset for whom the vaccine didn't trigger a large protective response.

This new study of giving third jabs to this group is critical research which we hope will demonstrate a much-needed immunity boost or identify those who could benefit from other interventions.

One of the real strengths of the UK's scientific response to the pandemic has been the way that we've assembled teams of experts to lead cutting-edge studies like this, to inform our vaccine roll-out and government decision-making in real time.

More than 89 million doses have been administered in the UK, including more than 47 million people with a first dose and more than 41 million people with a second dose.

Data from PHE shows COVID-19 vaccines are highly effective against hospitalisation from the Delta (B.1.617.2) variant, the dominant strain in the UK. The analysis shows that, across all adults, the Pfizer-BioNTech vaccine is 96% effective and the Oxford-AstraZeneca vaccine is 92% effective against hospitalisation after 2 doses.

COVID-19 vaccines have saved around 95,200 lives and prevented 82,100 hospitalisations and 23.9 million infections in England alone, the latest data from PHE and Cambridge University shows.

Further advice on vaccination, including on whether a third dose should be given to the immunocompromised, is not dependent on the OCTAVE DUO, the results of which are expected later this year.

Recruitment to the OCTAVE DUO study will be only from the cohort of people involved in the initial OCTAVE study, and similar studies.

Hospital study sites that recruited patients for OCTAVE:

- QEH Birmingham
- Glasgow
- St James's Leeds
- Imperial London (Hammersmith)
- Oxford
- Addenbrooke's
- Southampton
- King's College London
- Sheffield
- St George's London
- Freeman Hospital