OCTAVE study FAQs

Q. Can you tell me more about the OCTAVE study and how it was carried out?

A. The OCTAVE (Observational Cohort Trial-T-cells Antibodies and Vaccine Efficacy in SARS-CoV-2) study is a multi-centre, UK-wide trial, led by the University of Glasgow and co-ordinated by the University of Birmingham's Cancer Research UK Clinical Trials Unit. The trial is funded by the Medical Research Council (MRC) and is a collaborative research project involving groups in the Universities of Glasgow, Birmingham, Oxford, Liverpool, Imperial College London and Leeds Teaching Hospitals NHS Trust.

OCTAVE is designed to examine vaccination responses in people with conditions, or who are receiving therapies, that could reduce the function of the immune system. Our key question is to ask how well COVID vaccines work in people with such conditions. To address this issue, the study used a series of state-of-the-art immune tests, performed on blood samples from consenting immunocompromised patients from across the UK, taken before and after COVID-19 vaccination.

The OCTAVE study looks at those with immune mediated inflammatory diseases including rheumatoid arthritis, psoriatic arthritis, ANCA-Associated Vasculitis, inflammatory bowel disease, as well as people with solid tissue and blood cancers, hepatic disease and renal disease. So far, 2,583 patients have been recruited to the trial making it one of the largest global studies in which detailed immune response is being assessed post-SARS-CoV-2 vaccination. Here we describe data only from the first 600 of these recruited patients.

Q. What did the study find?

A. OCTAVE's early data show that a majority, around 60%, of patients in the study groups mount an immune response that looks similar to that seen in healthy control subjects. However, a proportion of our study subjects mount a lower than expected antibody response after two SARS-CoV-2 vaccines – overall around 40% of OCTAVE study subjects. Indeed, approximately 11% of our patients fail to generate any antibodies 4 weeks after two vaccines. Failure to generate antibodies is found at higher proportion in some specific patient subgroups, in particular in patients with ANCA-Associated Vasculitis who have received B cell depleting therapy.

Communications and Public Affairs Office
University of Glasgow
Glasgow G12 8QQ
Tel: +44 (0)141 330 3535
Email: media@gla.ac.uk
www.glasgow.ac.uk

The proportion of patients with lower levels of antibody reactivity was found to vary across different diseases. For instance, the percentage of patients responding less well than the lowest levels seen in healthy subjects was as follows:

- *87% of those with ANCA-associated vasculitis*
- *51% of those with inflammatory arthritis (rheumatoid arthritis and psoriatic arthritis)*
- *36% of patients with hepatic disease*
- *29% of patients with renal failure, on dialysis*
- *42% of patients with renal failure on dialysis and also receiving medicines associated with immunosuppression*
- *10% of patients with solid cancer (breast and lung)*
- *33% of patients with hematological malignancies (acute myeloid leukaemia and multiple myeloma)*
- *17 % of patients with haemopoietic stem cell transplant*

The OCTAVE study looked not only at antibody levels in blood, but also examined the ability of a particular form of white blood cell, called a T cell, to respond to the vaccine. In contrast to the observed antibody response, evaluation of the T cell response revealed that patients generated a similar response to that observed within healthy controls. For instance, even though the ANCA-associated vasculitis did not generate a robust antibody response they did mount a comparable T cell response. This shows that examination of different parts of the immune system is vital to properly understand what may be happening after vaccination of these patients subgroups.

Q. What do these results mean for people with underlying health conditions?

A. Initial data from the ongoing OCTAVE study show that a significant proportion of clinically at-risk patients with conditions that can lead to an immunocompromised or immunosuppressed state, mount a low, or undetectable, antibody response after two doses of the same SARS-CoV-2 vaccine, when compared with healthy subjects who have received two SARS-CoV-2 vaccines. However, blood antibody levels and clinical protection are not synonymous. The clinical significance of these findings in terms of vaccines providing protection from exposure to SARS-CoV-2 itself is not known, as there is, as yet, no currently agreed clinical cut off in blood antibody test levels that can effectively predict protection from future infection risk by SARS-CoV-2, or the clinical seriousness of such infection were it to occur. Further study is therefore required to better understand the levels of response which will provide protection against COVID-19.

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Q. What was the vaccine response in the control group?

A. For the healthy control group, serum samples from the UK PITCH (Protective Immunity from T cells in Healthcare workers) consortium were used. PITCH is a prospective multi-centre study, with the goal of undertaking a deeper mechanistic study, including T cell responses, of immunity induced by natural infection and vaccination. 100% of participants had measurable vaccine response in the healthy control group examined in the PITCH study.

Q. What vaccines did participants receive?

A. Subjects received either COVID-19 mRNA Vaccine BNT162b2 (Pfizer/BioNTech) or ChAdOx1 Vaccine (AstraZeneca formerly AZD1222) as part of the National COVID19 vaccination programme.

Q. Are there plans to now offer booster vaccinations to immunocompromised patients?

A. It is possible that even partial protection from lower level of vaccine response may be clinically beneficial, and this is something OCTAVE scientists will closely monitor. There are also imminent plans in place to investigate the effects of administrating an alternate vaccine type as a third dose to the group of people in OCTAVE with an undetectable or low vaccine immune response. They will be included in a new study called, the OCTAVE DUO study, that will investigate the potential benefits of an immunological screening programme for vulnerable patients to identify those who will benefit from a subsequent vaccine boost.

Q Why is there such differences between serological and/or T Cell immune responses between each of the different health conditions? Is this connected to certain medications/treatments?

A. *Further analysis is required to determine not only the disconnect between the antibody and T cell response but also how disease/medications/treatments differentially impact the subsequent immune responses observed.*

Q: Can people ask to sign up to OCTAVE and is it still ongoing?

A*: Patients in the OCTAVE trial are invited to participate through attending clinics at hospitals taking part in the trial and by speaking to their consultant. Hospital study*

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sites that recruit patients for OCTAVE: QEH Birmingham, Glasgow, St James Leeds, Imperial London, Oxford, Addenbrookes, Southampton, Kings College London, Sheffield, St Georges London, Velindre, Freeman Hospital.

Patient cohorts included in the study are people with: lymphoid malignancies, immune mediated inflammatory diseases (including rheumatoid arthritis, psoriatic arthritis, vasculitis and inflammatory bowel disease), end stage renal disease, solid tumours (including breast and lung cancers), haematopoietic stem-cell transplantation, and hepatic disease.

There will be a follow on study, called OCTAVE DUO, which is already underway and will recruit up to 1,200 patients who are already involved in the OCTAVE study, or who have other at risk conditions and are already participating in parallel studies, and who had a low or absent immune response after two doses of vaccine.

Q: If an immunocompromised member of the public contacts me, who can I suggest they talk to?

A: *They should speak to their doctor. If they would like other support, or to find out more about other trials for people with their condition, a useful place to direct them to could be if there is a charity related to their disease, e.g. Cancer Research UK, Blood Cancer UK, Versus Arthritis, Kidney Research UK.*

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For more information contact Elizabeth McMeekin or Ali Howard in the University of Glasgow Communications and Public Affairs Office on 0141 330 4831 or 0141 330 6557; or email Elizabeth.mcmeekin@glasgow.ac.uk or ali.howard@glasgow.ac.uk

To interview Professor Pam Kearns, contact Emma McKinney, Media Relations Manager, University of Birmingham, e.j.mckinney@bham.ac.uk or +44 7815607157.

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Communications and Public Affairs Office
University of Glasgow
Glasgow G12 8QQ
Tel: +44 (0)141 330 3535
Email: media@gla.ac.uk
www.glasgow.ac.uk

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Glasgow G12 8QQ
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