OCTAVE study reveals vaccine responses in patients with impaired immune systems

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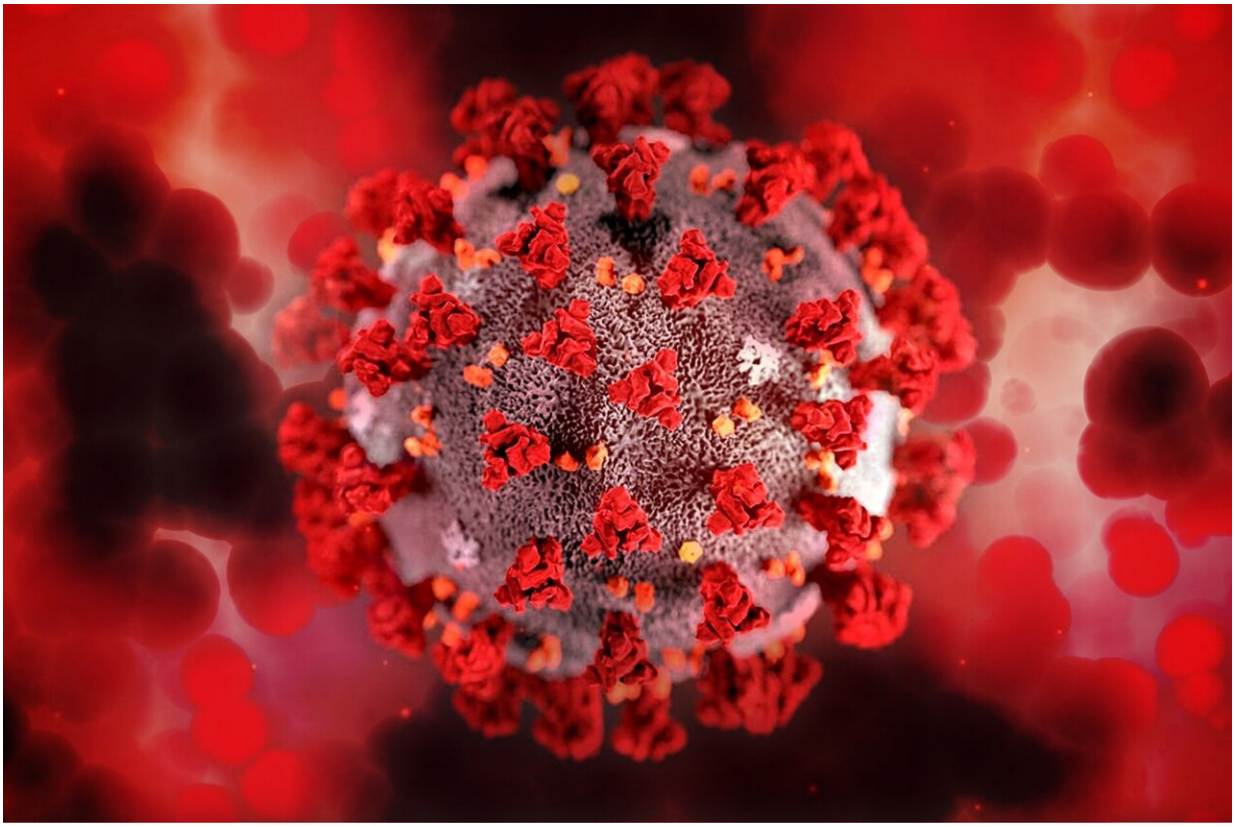

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The OCTAVE study—a multi-center, UK-wide trial, led by the University of Glasgow and co-ordinated by the University of Birmingham's Cancer Research UK Clinical Trials Unit—is evaluating

the immune responses following COVID-19 vaccination in patients with immune-mediated inflammatory diseases such as cancer, inflammatory arthritis, diseases of the kidney or liver, or patients who are having a stem cell transplant.

These first data from the study are published today at 5pm UK time as a pre-print on the *The Lancet* pre-print site.

The OCTAVE trial is one of the largest studies in the world so far into post-SARS-CoV-2 vaccination in immunocompromised patients and is funded by the Medical Research Council (MRC). OCTAVE is a collaborative research project involving groups in the Universities of Glasgow, Birmingham, Oxford, Liverpool, Imperial College London and Leeds Teaching Hospitals NHS Trust.

The study used a variety of state-of-the-art immune tests performed on blood samples taken before and/or after COVID-19 vaccination in around 600 people recruited across the UK. OCTAVE's early data show that 40% of people in the patient groups studied mounted a low serological immune response after two SARS-CoV-2 vaccines.

In addition to this, the initial data shows that approximately 11% of immunocompromised patients fail to generate any antibodies 4 weeks after two vaccines. Failure to generate antibodies is found at higher proportion in some specific patient sub-groups; in particular, in patients with ANCA-associated vasculitis who have received Rituximab treatment.

Looking in detail at patient vaccine response within each of the disease subgroups included in the study, researchers found that a significant proportion of patients studied as part of OCTAVE generate lower levels of SARS-CoV-2 antibody reactivity, when compared with healthy subjects after two SARS-CoV-2 vaccines.

The proportion of patients with lower levels of antibody reactivity was dependent on the disease cohort, with 90% of those with Rituximab treated ANCA-Associated Vasculitis, 54% of those with inflammatory arthritis, 21% of those on haemodialysis, 42% of those on haemodialysis receiving immunosuppressive therapy, 51% of those with Hepatic disease, 17% of those with solid cancer, 39% of those with hematological malignancies, and 33% of patients who have undergone haemopoietic stem cell transplant responding less well than the baseline for healthy subjects.

Importantly, however, the significance of these findings in terms of what they can tell us about vaccine protection from exposure to COVID-19 is not currently known, as there is no current agreed clinical cut off to measure COVID-19 vaccination response.

Prof Iain McInnes, lead of the OCTAVE trial, and vice principal and head of the College of MVLS at the University of Glasgow, said: "The roll-out of the vaccine program was extremely important for these vulnerable groups of patients, however due to their underlying medical conditions and treatments, which can weaken their immune systems, we were concerned that people with these medical conditions may not receive optimal protection, so it was, and remains, extremely important to investigate this unanswered question.

"While 40% of these clinically at-risk patent groups were found to have a low or undetectable immune response after a double dose of the vaccine, we are encouraged that this figure isn't higher. However, it is possible even partial protection may be clinically beneficial, and this is something we will closely monitor.

"There are also imminent plans in place to investigate the effects of administrating an alternate vaccine dose to the group with an undetectable or low vaccine immune response; and we hope these

findings will support the role out of an immunological screening program for vulnerable patients to identify those who will benefit from a subsequent vaccine boost.

"We would continue to encourage all people and especially those patients within these clinically at-risk groups to make sure they receive their vaccine doses if they haven't done so already."

Professor Pam Kearns, director of the University of Birmingham's Cancer Research UK Clinical Trials Unit which is co-ordinating OCTAVE, said: "A significant number of people in the UK were advised to shield because they have conditions or long term illnesses which place them at greater risk of severe illness and death from COVID-19.

"The rapid development of vaccines for COVID-19 has been a major step forward in the battle against this global pandemic, and the most clinically-at-risk people were among the first in the UK to be offered one. However, while we know COVID-19 vaccines are highly effective in healthy individuals, questions have remained as to how effective they are in protecting the chronically ill.

"These preliminary results of OCTAVE and the results of our continuing and forthcoming research 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: "Today's results will be of concern for the subset of people within those who are immunosuppressed for whom the vaccine didn't trigger a large protective response. We're funding an extension to the OCTAVE study to give third jabs to this group, which we hope will deliver 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 and responsive studies like this, to inform our vaccine roll-out and government decision-making in real time."

The OCTAVE (Observational Cohort Trial-T-cells Antibodies and Vaccine Efficacy in SARS-CoV-2) study looks at those with immune mediated inflammatory diseases including rheumatoid arthritis, psoriatic arthritis, ANCA-associated vasculitis, inflammatory bowel disease, as well as hepatic disease and renal failure. So far more than 2,500 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.

The data reported in this pre-print includes the post-vaccine immune response results from the first 600 patients recruited four weeks post-second dose.

More information: Examining the Immunological Effects of COVID-19 Vaccination in Patients with Conditions Potentially Leading to Diminished Immune Response Capacity – The OCTAVE Trial: ssrn.com/abstract=3910058

Provided by University of Glasgow