Trial Results "Lay" Summary

Immune responses and clinical outcomes following COVID-19 vaccination in patients with immune suppressive diseases (The OCTAVE Study)

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Background

Vaccines against COVID-19 have saved millions of lives across the world since the pandemic with the SARS-CoV-2 virus began in late 2019. COVID-19 vaccines continue to protect most people in the population from severe disease, but not necessarily from SARS-CoV-2 infection.

Clinical trials and population studies that measure how effective the COVID-19 vaccines are, have largely focused on people without known chronic disease. However, UK Government estimates suggest 500,000 people have diseases that reduce their immune response. Early on in the pandemic it became clear that patients who were immune suppressed (either by the medicines they were taking, or because of their underlying disease) had especially high rates of severe COVID-19, leading to hospitalisation, intensive care admissions and death. Unfortunately, these very same patient groups remained vulnerable to COVID-19 after vaccines were rolled out as the immune system of these patients was not able to respond to vaccines in the same way as other people.

In OCTAVE, we measured the immune response to COVID-19 vaccines in patients who had immune systems that were suppressed either because of medicines that were taken for specific diseases, or because of the disease itself. Patients were recruited from 11 hospitals across the United Kingdom. We measured the two parts of the immune response that we know are important in protecting people from disease before and after vaccinations — antibodies and T cells. In general, antibodies are the first line of defence against new virus infection and react to the outer coat of the virus, whereas T cells react later and target/kill cells that become infected. We also measured the immune response of some patients after vaccination, to the new SARS-CoV-2 variants (e.g. Omicron) that are now widely circulating in the population. We then assessed whether the size of the immune response after vaccination, was associated with subsequently becoming infected with SARS-CoV-2 infection and the severity of COVID-19.

The OCTAVE Trial

The OCTAVE trial included 2,686 patients with immune suppressive conditions and measured the immune response to SARS-CoV-2 before, during and after two COVID-19 vaccines. We included patients with cancer, joint disease and other diseases of the immune system, kidney disease including those patients on dialysis, liver disease, liver and kidney transplant patients, inflammatory bowel disease and patients with blood cancer, some of whom had stem cell transplants.

Patients received mRNA or Oxford-Astrazeneca vaccine according to government recommendations and local availability of vaccines. We compared the immune response in patients with healthy volunteers who had been included in government or charity-funded studies of health-care workers (PITCH). Importantly, in the OCTAVE study the antibody and T cell responses were each measured in the same laboratory. This meant that for the first time we could make direct comparisons between patient groups to better understand who is most vulnerable to vaccine non-response, infection and severe COVID-19.

Although the main aim of the study was to look at immune responses to the vaccines themselves we were also able to measure how these immune responses might work against some of the new SARS-CoV-2 variants that have emerged over the last 2 years. We assessed this using both blood and saliva samples. Looking at immune responses in saliva is important, as the nose and mouth are the first places the body encounters airborne viruses like SARS-CoV-2.

Through this study we worked out which factors were associated with a low or absent immune response to vaccines.

Results

Overall, we showed that more than 88% of patients developed antibodies after vaccination. However, 27% of all patients (approximately a quarter of our patients) generated low levels of antibodies compared to the healthy group of volunteers, and 12% of patients (around 1 in 10 patients) failed to develop any measurable COVID-19 antibodies. Vaccines were less effective for patients taking drugs that we know prevent antibodies from being made effectively, patients with kidney disease on haemodialysis, and patients who had received kidney and liver transplants. T cells against COVID-19 were detected in 88% of patients. However, patients with kidney disease and transplant recipients had lower T cells compared to the healthy group.

Antibody responses to the new COVID-19 variant viruses measured in blood and saliva were lower compared to responses against the original COVID-19 virus — antibodies were especially low against the Omicron variant, whereas T cell responses against this variant was largely maintained. We found that the mRNA vaccine was associated with higher antibody, but lower T cell responses compared to Oxford-AstraZeneca vaccines. The type of immune suppressing medications that patients were taking seemed to have more of an effect on the antibody responses than on the T cells. During the study, we found that 474 patients became infected with the SARS-CoV-2 virus. Of these, 33 patients were admitted to hospital and 15 patients died from COVID-19. We found that the strength of both the antibody and the T cell response was associated with severe COVID-19 or death.

Overall, this study identifies patient groups that may not respond to COVID-19 vaccines and shows that both parts of the immune system (antibodies and T cells) protect patients from severe COVID-19.

As part of OCTAVE, an additional study, looking at the immune responses of children with reduced immune systems, is underway and we hope to publish the results of that work later this year.

To access the published paper please see https://www.nature.com/articles/s41591-023-02414-4