Blood cancer and arthritis patients taking Rituximab show impaired antibody response to COVID vaccine

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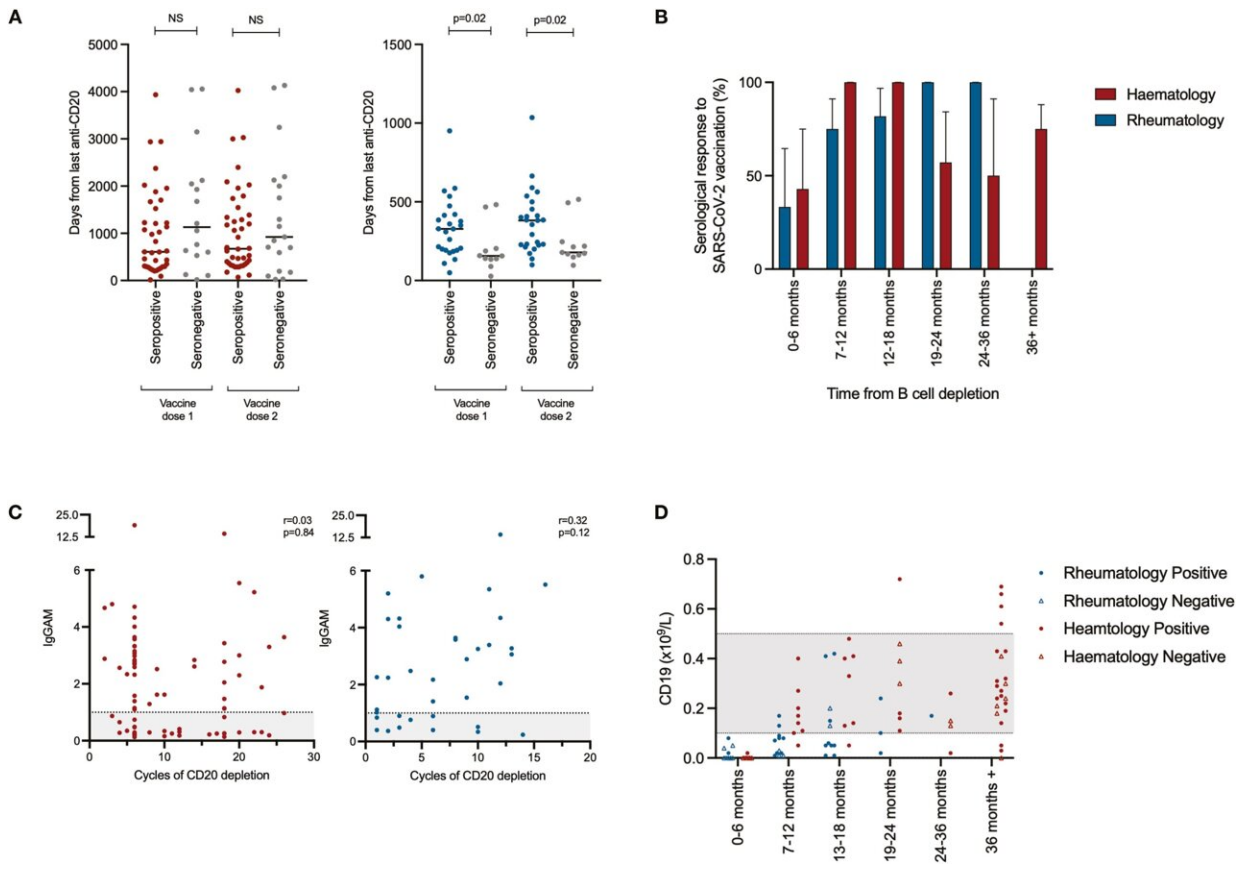

Immune reconstitution following CD20 depletion and vaccine responsiveness. (A) Time between last administration of anti-CD20 B-cell-depleting treatment and vaccine administration (left panel—haemato-oncology patients [red], right panel—rheumatology patients [blue]). (B) Seropositivity following SARS-CoV-2 vaccination with respect to time from last administration of anti-CD20 B-cell depletion. (C) Association between the magnitude of antibody responses and

total prior exposure to anti-CD20 B-cell-depleting agents. IgGAM ratios less than 1.0 are considered negative and represented by the gray zone on the graph. (D) B-cell reconstitution and its association with vaccine responsiveness following treatment with anti-CD20 B-cell-depleting agents. Gray zones represent normal range for cellular populations. Credit: DOI: 10.1093/cei/uxab018

Certain blood cancer and arthritis patients have a significantly reduced antibody response to double COVID-19 vaccination in the first six months of being treated with a widely used drug, reveals a new study.

The research, published today in journal *Clinical & Experimental Immunology*, was carried out by experts across the Universities of Birmingham and Wolverhampton, The Royal Wolverhampton NHS Trust, University Hospitals

Birmingham NHS Foundation Trust (UHB), Worcestershire Acute Hospitals NHS Trust, and NIHR Clinical Research Network West Midlands (NIHR CRN West Midlands). It aimed to establish whether a drug called Rituximab—typically used to treat patients with haemato-oncological disease (e.g., certain blood cancers) or rheumatological disease (e.g., certain types of arthritis)—may hinder the effectiveness of COVID-19 vaccines. Treatments such as Rituximab work by killing B cells, which are part of our immune system.

The study involved 80 patients receiving treatment for blood cancers and 36 being treated for diseases such as arthritis. Blood samples were taken before and after vaccination with two doses of either the Pfizer/BioNTech or Oxford/AstraZeneca COVID-19 vaccine between December 2020 and April 2021. The results were then compared with a control group of healthy age-matched healthcare workers participating in

other University of Birmingham-led COVID-19 studies.

The results showed that in the first six months following treatment with Rituximab, only 42.2 percent of patients with blood cancers and 33.3 percent of patients with arthritis developed an antibody response to double vaccination—and this was reduced further to 22.7 percent in patients vaccinated while actively receiving anti-lymphoma chemotherapy.

Also, in those that did have an antibody response to vaccination, the strength of the response was much lower in those with blood cancer or arthritis compared to those in the healthy cohort.

The study showed that six months after treatment, as patients' bodies began rebuilding B cells, vaccine responsiveness increased to 100 percent in blood cancer patients, while in arthritis patients there were also 'progressive increases' in overall vaccine responsiveness the greater the gap between vaccine and drug treatment.

The research showed similar quality and strength in antibody response with both types of COVID-19 vaccines and across both groups of patients. However, the data also show that shorter intervals (of less than a month) between the first and second vaccine significantly improved both quality and strength of antibody response in blood cancer patients.

Co-corresponding author Professor Supratik Basu, Consultant Haematologist at The Royal Wolverhampton NHS Trust and a researcher at the University of Wolverhampton, explained: "Rituximab targets B cells, which normally produce antibodies. Our hypothesis was that the drug might inadvertently affect the response to COVID-19 vaccination, which may leave patients very vulnerable to serious illness. These patients are already considered to be high-risk, and therefore it seemed sensible to determine whether the treatment for their pre-existing

condition was stopping the body from producing the antibodies it needs to fight the virus. Here we could establish if further vaccination was required or if alternative protection was needed. As the rate of antibodies in this cohort was extremely low, this should alert clinicians to prioritize these patients for their third booster COVID-19 vaccine, while also giving important reminders about precautions such as hand-washing and social distancing."

First and co-corresponding author Dr. Adrian Shields, a Clinical Immunologist at the University of Birmingham, said: "Rituximab is used all over the world to treat blood cancers and inflammatory diseases. We now know that its use is associated with poor responses to new vaccines. The results from our study emphasize how important it is to undertake further research to improve our understanding of how to use vaccines to achieve the best possible protection for our most clinically vulnerable patients."

Co-corresponding author Mark Drayson, Professor of Clinical Immunodiagnostics at the University of Birmingham and Honorary Consultant Immunologist at UHB, added: "Our research provides important observations, which suggest that additional immunisations could be necessary at least six months after treatment with drugs that deplete B cells to optimize vaccine responsiveness. The monitoring of how a patient's immune response is rebuilding following treatment may also help to ensure optimal vaccine timing. We recommend that individuals who do not respond to COVID-19 vaccines should be evaluated further for secondary immunodeficiency, particularly if treatments that deplete B cells were last administered 18 months or more prior to vaccination."

More information: Adrian M Shields et al, SARS-CoV-2 vaccine responses following CD20-depletion treatment in patients with haematological and rheumatological disease: a West Midlands Research

Consortium study, *Clinical and Experimental Immunology* (2022). DOI: 10.1093/cei/uxab018