First in Human Clinical Trial of a T Cell Therapy for COVID-19

AIMS

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the virus that causes COVID-19. In this study, a cell therapy, SARS-CoV-2 Virus Specific T cells (SARS-CoV-2 VST), was developed using donor immune cells collected from people who had recovered from COVID-19. The aim of the project was to undertake a phase Ib/IIa First in Human (FIH) clinical trial to establish the safety and feasibility of SARS-CoV-2 VST for the treatment of COVID-19 in hospitalised patients.

KEY FINDINGS

- 1090 patients were screened in total. Due to a policy change in the mandatory testing of SARS-CoV-2, there was a significant drop in the identification of SARS-CoV-2 positive cases.
- Two patients of our target of eleven patients were recruited to the phase Ib/IIa FIH clinical trial and were administered SARS-CoV-2 VST, with no reported adverse events.
- The clinical trial could not be completed due to insufficient patient recruitment.

WHAT DID THE STUDY INVOLVE?

This study was part of the DEFINE trial platform, designed to evaluate new or repurposed treatments for COVID-19.

The study involved:

- A dose escalation phase Ib/IIa clinical trial to assess the safety and feasibility of treatment with SARS-CoV-2 VST and to examine a range of clinical and immunological responses to the infused cells.
- Patient eligibility criteria included: patients over 16, SARS-CoV-2 positive, must have oxygen levels of 92% or higher prior to infusion, no vaccinations up to 3 weeks prior to infusion and must not be pregnant or breastfeeding.
- Patients provided blood samples prior to infusion to establish viral load, human leukocyte antigens (HLA) type to ensure the donor and patient have closely matched immune system markers, and to identify baseline values for clinical parameters (physical, electrolyte, haematological and liver function).
- Seven SARS-CoV-2 VST batches were available for clinical use.
- Patients were administered a single infusion of HLA-matched SARS-CoV-2 VST. The clinical trial design included 3 cohorts to test dose escalation, with the first 3 participants receiving the lowest dose (group 1, 1.5x106 cells total), the next 3 participants receiving the middle dose (group 2, 1.5x107 cells total), and the last five participants receiving the highest dose (group 3, 1.5x108 cells total).
- Following completion of the infusion, patients were sampled after 2-3 hours, then subsequently at 24h and 48h (patients remained in hospital for a minimum of 48 hours), with full patient monitoring run for 6-weeks post infusion.

- The patient information sheet was reviewed by a patient representative, and their suggestions were included in the final document. Feedback from participants from earlier arms of the trial was taken into consideration when developing the protocol, and sampling requirements and frequency were amended to reduce the burden on patients.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Two of eleven patients were recruited to the clinical trial and administered SARS-CoV-2 VST, with no reported adverse events. Early in the study (September 2022), a policy change from the Scottish government resulted in the cessation of routine SARS-CoV-2 testing in NHS Lothian, with only symptomatic patients being tested for SARS-CoV-2. This resulted in a significant drop in SARS-CoV-2-positive cases being identified within the hospital and impacted the number of patients that could be screened for recruitment to the trial. The trial strategy had been to approach patients in the hospital setting who had coincidentally tested positive for SARS-CoV-2 but were otherwise well regarding COVID-19. Due to removal of asymptomatic COVID-19 testing, many patients identified did not meet the inclusion/exclusion criteria for the trial. Several mitigations were put in place, including opening a second site, establishing a mechanism to help identify SARS-CoV-2 positive patients and changing the eligibility criteria to include patients maintaining saturations at ≥92% on a minimum of 28% supplemental oxygen therapy. Despite the mitigations, we were unable to reach our recruitment target and fully demonstrate product safety.

WHAT IMPACT COULD THE FINDINGS HAVE?

The manufacturing process developed for SARS-CoV-2 VST is applicable in principle to adaptation to SARS-CoV-2 variants and to a wide range of other viral infections including other coronaviruses and influenza which have caused previous pandemics. Development of new treatment options would particularly benefit those patients who are immunocompromised and are at risk of persistent infection or more serious disease.

HOW WILL THE OUTCOMES BE DISSEMINATED?

Details of the study can be found on the ISRCTN registry (ISRCTN14212905) and the EU Clinical Trials Register (EudraCT 2020-002230-32).

CONCLUSION

The clinical trial could not be completed because we were unable to reach our recruitment target. The initial strategy of this study was to validate SARS-CoV-2 VST safety in a generally healthy patient group. Despite rapid development and manufacturing of the SARS-CoV-2 VST, during the study a policy change resulting in the cessation of routine SARS-CoV-2 testing led to a significant drop in the identification of SARS-CoV-2 positive cases. This raises an important challenge in designing trials for treatments of emerging viruses.

RESEARCH TEAM & CONTACT

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Additional Information
The study ended on the 30th April 25 and received £280,403 of funding from the Chief Scientist Office.