CATALYST Trial Summary

Researchers look at the results of many studies to understand which drugs work and how they work. It takes a lot of people in many studies all around the world to advance medical science. This summary only shows the results from this one study known as the CATALYST trial. Other studies may find different results. We thank all patients who participated in the CATALYST trial.

Study name:

CATALYST: A randomised multicentre, multi-arm multi-stage, open label, adaptive, proof of concept trial designed to guide the selection of interventions for phase 3 trials in hospitalised patients with COVID-19 infection.

Trial Registration Number:
ISRCTN registry number 40580903
EudraCT Number: 2020-001684-89

General Information about the study

Severe COVID-19 is associated with a high risk of death and disability in some of those who recover. Poorly controlled inflammation contributes to severe COVID-19. There are a large number of different drugs capable of reducing inflammation in different ways. It is possible that some of these drugs may help patients with severe COVID-19. However, proving that a drug can reduce death often requires clinical trials with hundreds or even thousands of patients. The CATALYST trial was designed to look at how a sensitive marker of inflammation changes over time to give an early indication of whether a drug may or may not work in severe COVID-19. By testing drugs in a smaller number of patients (known as a phase 2 study), we aimed to prioritise which drugs to study in larger studies (known as phase 3 studies).
The study was sponsored by the University of Birmingham and was run though the Cancer Research UK Clinical Trials Unit Birmingham. It was publically funded by the Medical Research Council and the study drugs were provided free of charge by Izana Bioscience and Celltrion. Izana Bioscience and Celltrion had no role in the design, running or interpretation of the study. Patients who had survived serious illness with COVID-19 were asked to comment on the design of the study. The study recruited patients at 9 hospital sites in the UK between 15th June 2020 and 18th February 2021.

Who participated in the study?

We recruited patients who were admitted to hospital with COVID-19 infection that was affecting their lungs. To take part, patients also had to have evidence of elevated inflammation as measured by a blood test. The biomarker used to indicate this is called C-Reactive Protein (CRP), and for this study CRP had to be at least 40 mg/L for a patient to be eligible to take part.

What treatments were given?

Participants were randomly allocated to one of three treatment groups. Patients allocated to usual care received the standard care they would have received if they were not part of the trial. Usual care may have differed slightly between hospitals and will have changed over time during the course of the pandemic. Patients allocated to namilumab received usual care plus a single dose of a drug that blocks a specific protein, known as GM-CSF, that works to increase inflammation. Namilumab is being developed to treat various inflammatory disorders, but is currently an unlicensed mediation. Patients allocated to infliximab received usual care plus a single dose of a drug that blocks another protein, known as TNF, that also increases inflammation. Infliximab is widely used in the treatment of several inflammatory diseases such as rheumatoid arthritis. Both study drugs were given by a drip.

What happened in the study?

CRP levels were followed over time in all patients until day 14, discharge or death dependent on which event happened earlier. The patients' clinical state was followed until day 28. Once more than 20 patients were allocated to each treatment group, the CRP data was looked at by an independent committee to advise on whether the treatments should continue to be given in the study or whether it should be stopped. This is known as an interim analysis. If there was a 90% probability or greater that the study drug was better than usual care at reducing CRP, then the study drug could either continue to be given in the current study to collect more clinical data (up to a maximum of 60 patients per arm) and/or be recommended to a phase 3 study. If the probability of a study drug being better than usual care at reducing CRP was less than 50% (an equal chance that it was better or worse) then the drug would no longer be given.

We randomised 146 participants to the study; usual care (n=54), namilumab (n=57) and infliximab (n=35).

What are the results of the study?

The probability that namilumab was superior to usual care alone in reducing CRP over time was 97%. At the interim analysis it was decided that recruitment to namilumab should be continued to collect more clinical data. Recruitment to the namilumab arm was stopped before 60 patients were recruited into both the namilumab and usual care arms, as a change in standard of care outside of the study would affect CRP measurements and therefore make it harder to interpret the effectiveness of the study drugs. Deaths occurred in 6 out of 55 (11%) namilumab treated patients and 10 out of 54 (19%) usual care patients. Using a statistical modelling approach that took into account other factors such as patient age, we calculated that for participants recruited on the intensive care unit, the probability of being discharged at day 28 was 47% for usual care alone and 66% for usual care plus namilumab. For participants recruited on the ward, the probability of being discharged at day 28 was 64% for usual care alone, and 77% for patients treated with namilumab. However, as expected, the study was too small to conclude if these differences in death and discharge were real or a chance finding. The probability of infliximab being better than usual care alone in reducing CRP over time was only 15%. Allocation to infliximab was therefore stopped for futility following the interim analysis. Deaths occurred in 4 out of 29 (14%) infliximab treated patients and 5 out of 34 (15%) usual care patients.

What medical problems (adverse reactions) did the participants have?

Adverse events were reported at a similar rate in the namilumab and usual care groups, and between infliximab and usual care. Non-COVID-19 infections were reported in a similar number of patients in the namilumab (8 out of 55 patients; 15% of those included) and usual care arms (7 out of 54 patients; 13% of those included). However a greater number of infection events were seen in affected patients treated with namilumab compared to usual care alone (20 events compared to 10 events).

How has this study helped patents and researchers?

The study suggests that, out of the drugs tested, namilumab should be prioritised for further study in severe COVID-19.

Details of any further research planned

Namilumab has been recommended for further study in phase 3 trials.

Where can I learn more about this study?

The CATALYST trial results are published in The Lancet Respiratory Medicine doi: 10.1016/S2213-2600(21)00460-4