Drug could more effectively treat patients hospitalised with COVID-19 pneumonia, early stage research finds

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A proof-of-concept trial led by the Universities of Birmingham and University Hospitals Birmingham NHS Foundation Trust has identified a

drug that may offer benefit some patients hospitalised with COVID-19 pneumonia.

The CATALYST trial tested UK-based bio-pharmaceutical company Izana Bioscience's namilumab (IZN-101) as a potential therapeutic to treat patients who are hospitalised with COVID-19 pneumonia, and receiving 'usual' care, as well as having high levels in their blood of a marker of inflammation known as C reactive protein (CRP). CRP levels rise when there is inflammation in the body, and elevated levels of CRP have been found to be a potential early marker to predict risk for severity of COVID-19.

An antibody already in late-stage trials to treat rheumatoid arthritis, namilumab targets a 'cytokine' which is naturally secreted by immune cells in the body but, in uncontrolled levels, is believed to be a key driver of the excessive and dangerous lung inflammation seen in COVID-19 patients.

The trial, carried out in collaboration with the University of Oxford and funded by the Medical Research Council and carried out between June 2020 and February 2021, involved patients aged over 16 with COVID-19 pneumonia either being treated on a ward or Intensive Care Unit (ICU) at nine NHS hospitals across the UK.

The study, published today in *The Lancet Respiratory Medicine*, involved 54 patients receiving 'usual care' (steroids and oxygen or ventilation, depending on the severity of disease) and 57 patients given usual care as well as a single intravenous dose of 150mg of namilumab.

As well as COVID-19 pneumonia, all study participants had CRP levels greater than 40mg/l. The researchers compared the probability of the reduction of levels of CRP in patients. Compared to usual care alone, the researchers found there was a 97% probability of CRP being reduced

over time in those given namilumab when compared with usual care alone.

The patients were monitored, and after 28 days the study also showed there were fewer deaths and more discharges from hospital or ICU in those who had been given namilumab compared to those receiving usual care alone.

By day 28, 78% (43) of the patients receiving namilumab were discharged from hospital or ICU, compared to 61% (33) of the patients given usual care. In the namilumab group, 11% (6) were still in hospital by day 28, compared to 20% (11) in the usual care group. Of those in the namilumab group, 11% (6) patients died compared to 19% (10) who died in the usual care group by day 28.

The team calculated the differences between the two cohorts in overall probability of those being discharged from ICU or a ward at 28 days. Of those on a ward, the probability of discharge at day 28 was 64% in the usual care cohort, compared to 77% in the Namilumab cohort. Of those in ICU, probability of discharge at day 28 was 47% in the usual care group, compared to 66% in the Namilumab cohort.

Dr. Ben Fisher, co-chief investigator of the CATALYST trial at the University of Birmingham's Institute of Inflammation and Ageing, and Consultant Rheumatologist at University Hospitals Birmingham NHS Foundation Trust (UHB), said: "Our research has provided important proof-of-concept evidence that namilumab reduces inflammation in hospitalised patients with COVID-19 pneumonia. However, our sample size is too small for a definitive assessment of clinical outcomes and further studies are required for this, as well as to understand better the population that may benefit most. Our results may not generalise to hospitalised patients without evidence of pneumonia or raised CRP or patients not requiring hospitalisation. It is important, therefore, that

namilumab is now prioritised for further COVID-19 research in a much larger national Phase III clinical trial."

Dr. Someit Sidhu, Co-founder of Izana Bioscience, said: "We are proud to support the CATALYST trial led by the highly experienced team at the University of Birmingham and UHB, Europe's largest integrated critical care centre. "We believe namilumab can play a significant role in dampening the hyper-inflammation seen in patients with severe COVID-19 infection and are committed to working with regulators and partners across the world to ensure this potential therapy can be developed for patients with COVID-19 who urgently need treatments. This is a particularly significant moment for me, supporting the global response to this pandemic through the work of the team at University Hospital Birmingham—the hospital where I trained as a junior doctor before going on to found Izana."

The CATALYST team also tested a second drug called infliximab (CT-P13), currently used as a treatment for inflammatory conditions. They compared the same patients with COVID-19 pneumonia and CRP levels greater than 40mg/l receiving 'usual care', to 35 patients receiving usual care and a single intravenous dose of 5mg/kg of infliximab. However, the study found infliximab was not more effective than usual care, with just a 15% probability of CRP being reduced.

Dr. Fisher added: "Our findings relating to infliximab, while disappointing, are also important as we continue to investigate and identify existing and new anti-inflammatory drugs that may play a critical role in targeting and reducing the most serious symptoms of COVID-19."

Designed by the Inflammation—Advanced and Cell Therapy Trials Team (I-ACT) at the University of Birmingham's Cancer Research UK Clinical Trials Unit, CATALYST is being run in close partnership with

UHB and the Birmingham National Institute for Health Research Biomedical Research Centres (NIHR BRC) and delivered in close collaboration with the NIHR BRCs at Oxford, Imperial College London and University College London.

More information: Namilumab or infliximab compared with standard of care in hospitalised patients with COVID-19 (CATALYST): a randomised, multicentre, multi-arm, multistage, open-label, adaptive, phase 2, proof-of-concept trial, *The Lancet Respiratory Medicine*, DOI: 10.1016/S2213-2600(21)00460-4 , www.thelancet.com/journals/lan … (21)00460-4/fulltext

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