Asthma drug shortens recovery time in COVID-19 patients at home

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Early treatment with an asthma drug budesonide shortens recovery time in COVID-19 patients aged over 50 who are treated at home or in other community settings.

The Platform Randomized Trial of Interventions against COVID-19 in Older People (PRINCIPLE) trial is led by the University of Oxford. It is funded by UK Research and Innovation and the National Institute for Health Research (NIHR) through the COVID-19 Rapid Response rolling call.

It is the world's largest Phase 3 platform randomized controlled trial to find clear evidence of an effective COVID-19 treatment for use in primary care that can significantly shorten recovery time.

The latest findings have the potential to change how COVID-19 is treated in its early stages in non-hospital, community settings both in the UK and internationally.

Inhaled budesonide is a safe, relatively inexpensive and readily available corticosteroid commonly used around the world in inhalers to treat asthma and chronic obstructive pulmonary disease. It was added to the PRINCIPLE trial on 28 November 2020.

To provide real-time information in the pandemic, these preliminary results will be posted on the medRxiv preprint server and submitted to a journal to undergo peer review.

Shortened recovery by up to three days

For the interim report, a total of 961 patients were randomly assigned to receive inhaled budesonide at home. These were compared with 1819 patients randomly assigned to the usual standard of NHS care alone.

Of these, 751 people in the budesonide group, and 1028 in the usual care group were SARS-CoV-2 positive and included in the primary interim analysis.

Based on the interim analysis using the latest data from 25 March 2021, the results showed the estimated median time to self-reported recovery for inhaled budesonide was:

- 3.01 days shorter compared to usual care (95% Bayesian credible interval 1.13 to 5.42 days)
- with a high probability (0.999) of being superior to the usual standard of care.

32% of those taking inhaled budesonide, compared to 22% in the usual care group, recovered within the first 14 days since being randomized into the trial. And they have subsequently remained well until 28 days (relative risk 1.46, 95% CI 1.23—1.74).

Participants in the budesonide group also reported greater wellbeing after two weeks (mean difference in WHO-5 Wellbeing score + 3.37, 95% CI 0.97—5.76, p = 0.006).

Unclear if drug reduces hospitalisations

Among patients who had completed all 28 days of study follow up by 25 March 2021:

- 8.5% (59/692) in the budesonide group were hospitalized with COVID-19
- 10.3% (100/968) in the usual care group (estimated percentage benefit, 2.1% [95% BCI -0.7% – 4.8%], probability of superiority 0.928).

Fewer people than expected were admitted to hospital in the trial, and COVID-19 cases and hospitalisations continue to drop in the UK. Therefore, it is unclear from this interim analysis whether budesonide reduces hospitalisations.

Patients with COVID-19 symptoms that started within 14 days and who are at higher risk of a poor outcome from the illness could join the trial. In addition, those with a positive SARS-CoV-2 result were included in the main analysis.

Patients treated with inhaled budesonide were asked to inhale 800 micrograms twice a day for 14 days and were followed-up for 28 days.

All patients were aged over 50 with an underlying health condition that put them at more risk of serious COVID-19 illness, or aged over 65.

Could help people all around the world

Joint Chief Investigator Professor Richard Hobbs, head of Oxford University's Nuffield Department of Primary Care Health Sciences, said: "For the first time we have high-quality evidence of an effective treatment that can be rolled out across the community for people who are at most risk of developing more severe illness from COVID-19. Unlike other proven treatments, budesonide is effective as a treatment at home and during the early stages of the illness. This is a significant milestone for this pandemic and a major achievement for community-based research."

Professor Fiona Watt, executive chair of the Medical Research Council, which co-funded the study, said: "Researchers involved in the PRINCIPLE trial have overcome considerable logistical hurdles to set up a world-leading rigorous drug trial in people's homes. We are now rewarded with the first inexpensive and widely available drug that can shorten recovery times for COVID-19 patients in the community. People around the world will be helped to recover faster thanks to these exciting new results."

Not possible without patients who volunteered

Joint Chief Investigator Professor Chris Butler, a South Wales GP and professor of primary care from the University of Oxford's Nuffield Department of Primary Care Health Sciences, said: "PRINCIPLE, the world's largest platform trial of community-based treatments for COVID-19, has found evidence that a relatively cheap, widely available drug with very few side effects helps people at higher risk of worse outcomes from COVID-19 recover quicker, stay better once they feel recovered, and improves their wellbeing.

"We therefore anticipate that medical practitioners around the world caring for people with COVID-19 in the community may wish to consider this evidence when making treatment decisions, as it should help people with COVID-19 recover quicker.

"This exciting finding about the beneficial effects of inhaled budesonide would not have been possible without the contribution of those patients who volunteered to participate. Your gift of taking part will help doctors and nurses provide better evidence-based care for people with COVID-19 worldwide.

"It also stands as a monument to the far-sighted funders of PRINCIPLE, the UK-wide clinical research networks who have been absolutely key to the successful implementation of the trial, all the general practices and clinicians who support PRINCIPLE, NHS Digital, HDRUK, the Therapeutics Task Force and the hard work and dedication of our study team and oversight committees in the Primary Care Clinical Trials Unit."

HDRUK, as part of the UKRI-funded COVID-19 Data and Connectivity National Core Study, has helped increase recruitment by linking the trial to the test and trace data. This has enabled PRINCIPLE to recruit PCR positive individuals in the community soon after they test positive.

More information: undefined undefined et al. Inhaled budesonide for COVID-19 in people at higher risk of adverse outcomes in the community: interim analyses from the PRINCIPLE trial, *medrxiv* (2021). DOI: 10.1101/2021.04.10.21254672