Submission Id: 3859

Title

Inhaled budesonide for COVID-19 in people at higher risk of complications in the community: the UK national community randomi

Priority 1 (Research Category)

Acute respiratory infections

Presenters

Richard Hobbs, , FMedSci, Oghenekome Gbinigie, MBChB, Emma Ogburn, PhD, Ly-Mee Yu, Oliver van Hecke, MD, PhD, Jienchi Dorward, MBChB, Chris Butler, FRCGP, FMedSci, Benjamin Saville, PhD

Abstract

Background

The effectiveness of repurposed treatments with supportive evidence for higher risk individuals with COVID-19 in the community is unknown. In the UK PRINCIPLE national platform trial we aimed to determine whether 're-purposed medicines' (hydroxychloroquine, azithromycin, doxycycline, colchicine, inhaled budesonide, and other interventions) reduced time to recovery and COVID-19 related hospitalisations/deaths among people at higher risk of COVID-19 complications in the community. We mainly report the findings for budesonide arm here.

Methods

Participants in this multicentre, open-label, multi-arm, adaptive platform randomised controlled trial were aged ≥65, or ≥50 years with comorbidities, and unwell ≤14 days with suspected COVID-19 in the community, and were randomised to usual care, usual care plus inhaled budesonide (800µg twice daily for 14 days), or usual care plus other interventions. The co-primary endpoints are time to first self-reported recovery, and hospitalisation/death related to COVID-19, within 28 days, analysed using Bayesian models. Trial registration: ISRCTN86534580. Funded by United Kingdom Research Innovation (MC_PC_19079).

Findings

The trial opened on April 2, 2020, with the first 4 intervention arms stopped on futility grounds. Randomisation to the budesonide arm occurred from November 27, 2020 until March 31, 2021, when the pre-specified time to recovery superiority criterion was met. The primary analysis model includes 2530 SARS-CoV-2 positive participants, randomised to budesonide (n=787), usual care (n=1069), and other treatments (n=674). Time to first self-reported recovery was shorter in the budesonide group

versus usual care (hazard ratio 1·21 [95% credible interval 1·08 to 1·36], probability of superiority >0·999, estimated benefit 2·94 [95% credible interval 1·19 to 5·12] days). An estimated 6·8% COVID-19 related hospitalisations/deaths occurred in the budesonide group versus 8·8% in usual care (estimated absolute difference, 2·0% [95% credible interval -0·2% to 4·5%], probability of superiority 0·963). In the main secondary analysis of admissions using only concurrent controls, admissions occurred in 6.6% (3.8 to 10.1%) in the budesonide group versus 8.8% (95% CI 5.2 to 13.1%), with an absolute difference of 2.2% (0.0 to 4.9%) and a hazard ratio of 0.73 (0.53 to 1.00), meeting the pre-specified superiority probability of 0.975. Three serious adverse events occurred in the budesonide group and three in usual care.