COVID STEROID 2 trial synopsis

Title	Higher vs. Lower Doses of Dexamethasone in Patients with COVID-19 and Severe Hypoxia: the COVID STEROID 2 trial
Objectives	To assess the effects of higher (12 mg) vs lower doses (6 mg) of intravenous dexamethasone on the number of days alive without life-support in adult patients with COVID-19 and severe hypoxia.
Design	International, parallel-group, centrally randomised, stratified, blinded, clinical trial.
Population	Adult patients with COVID-19 and severe hypoxia
Experimental intervention	Dexamethasone 12 mg once daily for up to 10 days will be given as bolus injection in addition to standard care.
Control intervention	Dexamethasone 6 mg once daily for up to 10 days will be given as bolus injection in addition to standard care.
Outcomes	**Primary outcome** Days alive without life support (i.e. mechanical ventilation, circulatory support, or renal replacement therapy) at day 28 **Secondary outcomes** - Serious adverse reactions (new episode of septic shock, invasive fungal infection, clinically important gastrointestinal bleeding, or anaphylactic reaction to dexamethasone) at day 28 - Days alive without life support at day 90 - Days alive and out of hospital at day 90 - All-cause mortality at day 28, day 90 and day 180 - Health-related quality of life at day 180
Inclusion criteria	Adult patients (≥ 18 yr.) with documented COVID-19 receiving mechanical ventilation OR non-invasive ventilation (NIV) or continuous use of continuous positive airway pressure (CPAP) for hypoxia OR at least 10 L/min of oxygen independent of delivery system
Exclusion criteria	We will exclude patients who have an indication for systemic use of higher doses of corticosteroids (above 6 mg dexamethasone or equivalent) for other indications than COVID-19, who have received corticosteroids for COVID-19 for 5 consecutive days or more, who have invasive fungal infection, who have active tuberculosis, who have known hypersensitivity to dexamethasone, who are pregnant, and those in whom informed consent cannot be obtained.
Sample size	1000 (2 x 500 patients). The trial has 85% power to detect a 15% relative reduction in 28-day mortality combined with a 10% reduction in days on life support among the survivors assuming a baseline 28-day mortality of 30%.
Trial duration	The trial intervention will continue for up to 10 days after randomisation or until discharge or death (whichever comes first). Follow up: 28 days, 90 days and 180 days Estimated recruitment period: August 2020 – February 2022.