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| **Title** | Low-dose hydrocortisone in patients with COVID-19 and severe hypoxia – the COVID STEROID trial |
| **Objectives** | To assess the effects of low-dose intravenous hydrocortisone on the number of days alive without life-support in adult patients with COVID-19 and severe hypoxia.  |
| **Design** | Multicentre, parallel-group, centrally randomised, stratified, blinded, clinical trial. |
| **Population** | Adult patients with COVID-19 and severe hypoxia |
| **Experimental intervention** | Continuous IV infusion of hydrocortisone 200 mg daily will be given for 7 days in addition to standard care.  |
| **Control intervention** | Continuous IV infusion of matching placebo (0.9% saline) will be given in addition to standard care (no corticosteroids). |
| **Outcomes** | **Primary outcome**Days alive without life support (mechanical ventilation, circulatory support, or renal replacement therapy) at day 28 **Secondary outcomes**- Serious adverse reactions (anaphylactic reaction to hydrocortisone, new episode of septic shock, invasive fungal infection or clinically important gastrointestinal bleeding)- 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 1 year- Health-related quality of life at 1 year |
| **Inclusion criteria** | Adult patients (≥ 18 yr.) with documented COVID-19 receiving mechanical ventilation OR non-invasive ventilation or continuous use of continuous positive airway pressure for hypoxia OR at least 10 L/min of oxygen independent of delivery system |
| **Exclusion criteria** | Systemic use of corticosteroids for other causes than COVID-19, invasive mechanical ventilation > 48 hours, documented invasive fungal infection, fertile women (< 50 yr.) with positive urine or plasma-hCG, hypersensitivity to hydrocortisone, a patient for whom the clinical team has decided not to use mechanical ventilation, previously randomised into the COVID STEROID trial, informed consent not obtainable.  |
| **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 time on life support among the survivors assuming a baseline 28-day mortality of 30%.  |
| **Trial duration** | The trial intervention will continue for 7 days after randomisation or until death (whichever comes first). Follow up: 28 days, 90 days and 1 yearEstimated recruitment period: April 2020 – December 2020.  |