Methylprednisolone Pulses In Hospitalized Patients With Severe Covid-19 Pneumonia

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BACKGROUND

Pulse glucocorticoid therapy (> 250 mg of prednisone equivalent per day for 1 or a few days) is used in many immuno-inflammatory diseases for its quick and strong anti-inflammatory effect in emergency situations. It was used during SARS-CoV-1 epidemics with no consistent data regarding its benefits. The efficacy and safety of this therapy associated to dexamethasone in coronavirus disease 2019 (Covid-19) pneumonia are unclear.

We hypothesized that high-dose pulse steroids might quickly decrease the hyperinflammatory reaction involved in COVID-19 pathogenesis and subsequently improve patients' recovery time.

Trial registration number: EudraCT Number: 2020-004323-16; ClinicalTrials.gov Identifier: NCT04673162.

METHODS

We conducted a double-blind, randomized, placebo-controlled, multicentric trial in hospitalized patients with COVID19-pneumonia.

PICO:

- **Patients** hospitalized for recent-onset Covid-19 pneumonia requiring supplemental oxygen in any delivery mode, except invasive mechanical ventilation, with PaO_2/FiO_2 between 100 mmHg and 300 mmHg, and a serum C-reactive protein greater than 5 mg/dl.
- **Intervention**: 1 gram of methylprednisolone for 3 consecutive days in addition to standard dexamethasone.
- **Comparison**: placebo (100 ml of 0.9% normal saline) in addition to standard dexamethasone.
- **Outcomes**: The primary outcome was the time interval between randomization and hospital discharge without the need of supplementary oxygen at 28 days of follow-up. All-cause mortality, survival free from invasive ventilation and safety were also evaluated.

RESULTS

Primary outcome

A total of 304 patients underwent randomization (*Figure 1*) in 19 Italian sites between December 21, 2020, and March 10, 2021. Three patients retired the consent to the study one day after randomization, leaving 301 patients eligible for intention to treat analyses.

112 of 151 (74.2%) patients in the pulse methylprednisolone arm and 111 of 150 (74.0%) patients in the placebo arm were discharged from hospital without oxygen (p = 0.528) within 28 days from randomization (*Figure 2*).

Methylprednisolone pulse therapy in addition to standard dose dexamethasone **did not improve** time to hospital discharge nor death rate in patients with SARS-CoV-2 pneumonia.

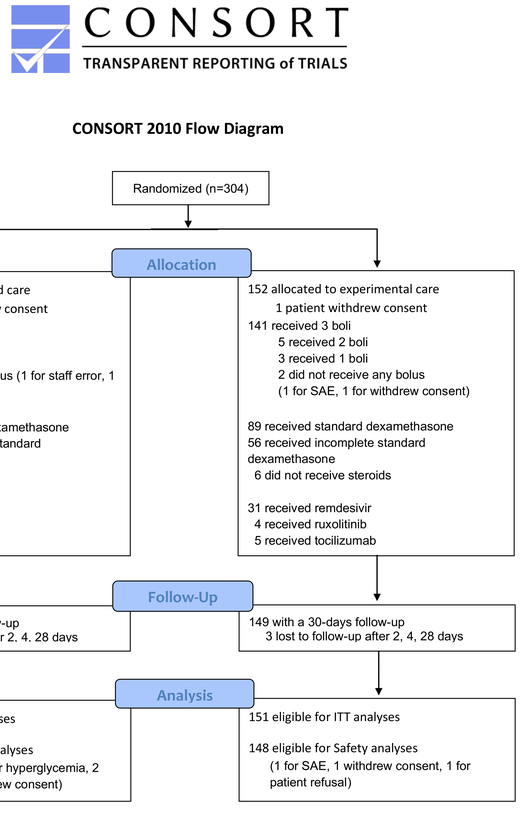


Figure 1. CONSORT flow diagram

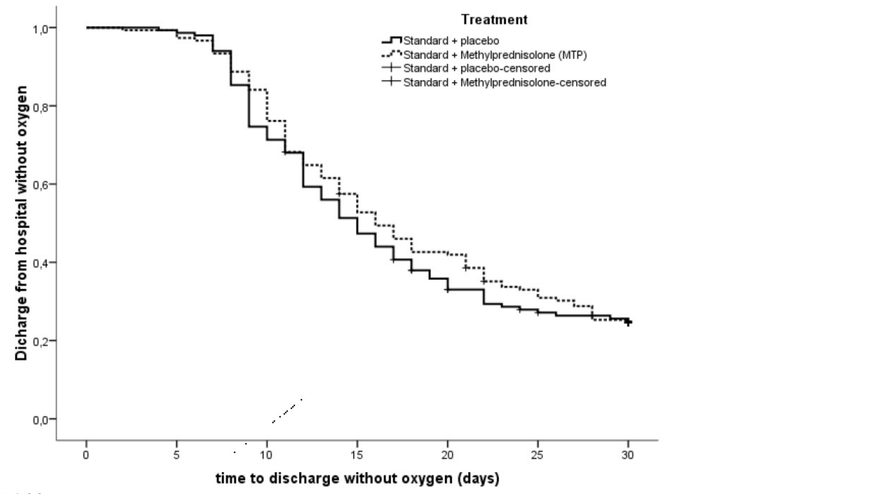


Figure 2. Kaplan-Meier estimates of hospital discharge without oxygen

Secondary outcomes

We did not observe any significant differences the two arms in terms of admission to Intensive Care Unit with orotracheal intubation or death (19.9% vs 16.0% respectively; HR 1.27; 95%CI, 0.74-2.16), or in terms of overall mortality (9.3% vs 11.3% respectively; HR 0.82; 95%CI, 0.40-1.66).

Serious adverse events occurred in 9 patients (6.0%) in the methylprednisolone pulse group and in 12 patients (8.0%) in the placebo group.

CONCLUSIONS

Methylprednisolone pulse therapy in addition to standard dose 6 mg dexamethasone did not provide any benefit compared to the standard of care in this randomized controlled trial.