SUMMARY OF STUDY PROTOCOL

TITLE: IMPACT OF TREATMENT WITH IMMUNOSUPRESIVE DRUGS IN COVID-19 PATIENTS WITH MAS-LIKE PROFILE: A RETROSPECTIVE COHORT STUDY (SAM-COVID PROJECT)

PROTOCOL CODE: FIS-INM-2020-03
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1. Promoter

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2. Study title.

IMPACT OF TREATMENT WITH IMMUNOSUPRESIVE DRUGS IN COVID-19 PATIENTS WITH MAS-LIKE PROFILE: A RETROSPECTIVE COHORT STUDY (SAM-COVID PROJECT)

3. Protocol code.

FIS-INM-2020-03

4. Principal investigator.

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5. Sites.

Multicentre study - in at least 14 Spanish hospitals

6. IRB.

IRB of University Hospitals Virgen Macarena-Virgen del Rocío de Sevilla.

7. Main objetive.

To evaluate the efficacy and safety of immunosupressive drugs in COVID-19 patients without mechanical ventilation, with clinical and laboratory data suggestive of macrophagic activation syndrome.

8. Design.

Retrospective, multicentre cohort study.

9. Disease under investigation.

COVID-19

10. Variables.

Main exposure: High-dose corticosteroids, tocilizumab, sarilumab, anakimra, gammaglobulins vs no treatment with these drugs.

Other exposures: age, gender, underlying conditions, duration of symptoms until admission and day 0, radiographic pulmonary involvement, severity of acute disease, oxygen requirements at admission and day 0, laboratory data at admission and day 0, other treatments received, site.

11. Study population

Inclusion criteria

- Adult patient (18 years or more) admitted because of COVID-1, confirmed by PCR in a nasopharyngeal swab or from lower respiratory tract sample.
- Presenting in a specific date (day 0), at least one clinical and one laboratory criteria among these:
    - Clinical criteria: temperature 38ºC or more, and worsening of respiratory insufficiency (increase in oxygen needs to achieve O2 saturation >92%).
    - Laboratory criteria: ferritin >2000 ng/mL (or >1000 increase), d-dimers >1500 µg/mL (or double fold increase in 24h) and IL6 >50 pg/mL.

Exclusion criteria

- Mechanical ventilation in day 0.
- Palliative care.
- Previous treatment with corticosteroids, tocilizumab, other immunusuppresive drugs or immunoglobulins.

12. Endpoints

Primary: time until mechanical ventilation or death up to day 21

Secondary: time until mechanical ventilation up to day 21, time until death up to day 21, proportion of patients with secondary infections up to day 21, proportion of patients with digestive tract haemorrhage up to day 21, proportion of patients with improvement in 2 or more points in the 7 point WHO scale in day 21.

13. Funding source.

Submitted for funding to Instituto de Salud Carlos III.

14. Statistical analysis

Patients treated with immunosuppressive drugs (overall, and specific drugs) will be compared to those not treated with any of those not receiving these drugs in proportion and time to reach the primary endpoint. The effect of confounders will be controlled by Cox (for time-dependent outcomes) or logistic regression (for categorical outcomes), and by calculating a propensity score for receiving immunosuppressive drugs, for which the inverse probability weighting and matching will be used.