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UNIVERSITÀ DI ROMA



UMBERTO I
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AZIENDA POLICLINICO UMBERTO I

U.O.D. SMID02

CENTRO DI RIFERIMENTO REGIONALE PER LE IMMUNODEFICIENZE PRIMITIVE

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Title: High dose intravenous polyvalent immunoglobulin in patients with early inflammatory COVID-19

Rationale

To determine the effect of treatment with high doses IVIG in a population of hospitalized COVID-19 patients at an early stage of disease showing progression of inflammatory markers by a pilot prospective, longitudinal, interventional study. The study sought to generate information for an early treatment approach able to protect from COVID-19 progression of inflammation, and on immune-mediated mechanisms of inflammatory disease in COVID-19 patients.

Design: Six-month pilot interventional, prospective, multicenter cohort study.

Setting: Hospital-based COVID-19 Units in three University hospitals (Coordinator Centre AUO Policlinico Umberto I Rome: Quinti, Milito, Palange, Mezzaroma, Mastroianni, Sapienza University of Rome; Azienda Ospedaliera Ca' Foncello, Treviso: Agostini, Cinetto. University of Padua; AOU Federico II, Napoli: Spadaro).

Endpoints of the study

Primary endpoint: Survival at 3, and 6 months from the first dose of IVIG.

Secondary endpoints: Imaging progression on chest CT; Arterial Blood Gas Analysis; Number of Intensive Care Unit admissions; Assessment of adverse events; Drug prescriptions; Emergency room and out patients visits and hospitalizations. Inflammatory laboratory indexes: lymphocyte absolute count, ferritin serum levels, CRP, PT, PTT, INR, D-dimer, serum levels of pro-inflammatory

cytokines and chemokines including: tumor necrosis factor (TNF) α , interleukin 1 β (IL-1 β), IL-6, interferon gamma. Flow cytometry analysis of peripheral blood mononuclear cells: inflammatory monocytes, monocyte/lymphocyte ratio, NK cells, CD3 positive T cells.

Methods

Timing: From the time of study approval, we will enroll COVID-19 patients consecutively admitted to our units. Analyses will be done in all treated patients with available data.

Patients: 30 adult patients with COVID-19 early stage respiratory disease will be enrolled in this pilot prospective six-months study. All patients will undergo to clinical and immunological follow-up for six-months.

Study Drug. Polyvalent immunoglobulins for Intravenous (IVIG) use (contract manufacturing, Italy).

Study drug administration. IVIG will be administered at a dose of 0.3 g/kg/day for 5 consecutive days.

Study design. Pilot, prospective, interventional 6-month study in patients with Stage I early infection COVID-19 disease. All patients will be screened if aged >18 years and having a confirmed SARS-CoV-2 infection. At the first day of hospital admission (baseline, T0), blood samples will be collected for baseline parameters assessment, Arterial Blood Gas Analysis. All subjects will be assessed to identify those patients showing a progression (3x normal values) of serum inflammatory markers (D-dimers, ferritin and CRP, IL-6) and selected for the inclusion in the interventional drug study. All patients will be informed on the study, including its safety profile and supply procedures, and will sign the written informed consent. All parameters will be tested the first day before study drug administration (T1), at day 5 (T2) after completing the first cycle of study drug administration, and at day 30 from T1 (T3). During the study time patients will be allowed to continue their therapies, and they will continue to be monitored for their clinical status until day 180 from T1 (T4). All patients may receive low molecular weight heparins, azithromycin, anti-viral drugs limited to the combinations darunavir / cobicistat and lopinavir / ritonavir and hydroxychloroquine. They will NOT be able to take therapy with anti-IL1R, IL6R or other therapies subject to current clinical trials in progress. Data from clinical visit (T0-T4) will be reported, following our consolidated clinical practice. Patients who will ask to leave the study will be considered as drop out.

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