COVID-19 Pathophysiologic leading to the drugs to be used

**MAVRILIMUMAB IMPROVES OUTCOMES IN SEVERE COVID-19 PNEUMONIA AND SYSTEMIC HYPER-INFLAMMATION**

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**Background:** Patients with severe COVID-19 pneumonia and hyperinflammation face increased mortality. There is an urgent need for effective treatments to reduce the burden of the COVID-19 pandemic.

**Objectives:** Our protocol aimed at evaluating the potential improvement in clinical outcomes with mavrilimumab, an anti-Granulocyte/Macrophage Colony-Stimulating Factor Receptor alpha (GM-CSFRA) monoclonal antibody, in patients with COVID-19 pneumonia and systemic hyperinflammation.

**Methods:** Single-center, open-label, single active arm intervention; Adult patients with severe COVID-19 pneumonia (as evaluated by CT scanning), hypoxia (PaO2:FIO2 ratio ≤ 300 mmHg), and systemic hyper-inflammation (increased C-reactive protein [CRP] ≥ 100 mg/mL and/or ferritin ≥ 900 µL, increased lactate dehydrogenase [LDH]) received a single intravenous dose of mavrilimumab added to standard of care; follow-up 28 days. Main outcomes were the main outcomes were the rate of mortality, fever (temperature > 38°C), hospitalization time; % of pts achieving a clinical improvement; hospital stay; time to discharge from hospital; % of pts achieving a clinical improvement; others included of mavrilimumab added to standard of care; follow-up 28 days. Main outcomes included: death, fever > 38°C, hospital stay; % of pts achieving a clinical improvement; hospital stay; time to discharge from hospital; % of pts achieving a clinical improvement (7-point WHO clinical status scale, 1=discharge, 7=death); others included: time to clinical improvement (≥ 2 categories on the 7-point WHO clinical status scale, 1=discharge, 7=death); others included: time to discharge from hospital; % of pts achieving a clinical improvement; survival; mechanical-ventilation-free survival; time to fever resolution; CRP; PaO2:FIO2 ratio.

**Results:** A mavrilimumab group (n=13 COVID-19 patients, non-mechanically ventilated, median age 57 [IQR, 52-58], males 12 [92%], febrile 11 [85%]; time to discharge from hospital; % of pts achieving a clinical improvement; 7-point WHO clinical status scale, 1=discharge, 7=death); others included: time to clinical improvement (≥ 2 categories on the 7-point WHO clinical status scale, 1=discharge, 7=death); others included: time to discharge from hospital; % of pts achieving a clinical improvement; survival; mechanical-ventilation-free survival; time to fever resolution; CRP; PaO2:FIO2 ratio.

**Conclusion:** Mavrilimumab was well tolerated in all patients. Randomized controlled trials are warranted to confirm our findings.

**References:**


**Disclosure of Interests:** Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, Pfizer, MSD, Giulio Cavalli Speakers bureau: SOBI, Novartis, Pfizer, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Emanuela Dell Di Torre: None declared, Piera Angelillo: None declared, Alessandro Tomelleri: None declared, Nicola Boffini: None declared, Stefano Tentori: None declared, Francesca Mette: None declared, Patricia Rovere-Querin: None declared, Annalisa Ruggeri: None declared, Teresa D'Aliberti: None declared, Paolo Scarpellini: None declared, Giovanni Landoni: None declared, Francesco De Cobelli: None declared, John F. Paolini Shareholder of: Kiniksa, speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Consultant of: Abvigen, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, SOBI, DOl: 10.1136/annrheumdis-2020-eular.6858

**COO0002**

**LOSS OF SELF-TOLERANCE IN SARS-COV-2 INFECTION: IMMUNOLOGICAL ASSESSMENT OF A CONVALESCENT COHORT**

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**Background:** Some infectious agents may act as inducers of autoimmune conditions. Despite SARS-CoV-2 infection can induce autoimmune phenomena in infected people6, individual risk factors or underlying mechanisms leading to loss of immunological tolerance are still unknown.

**Objectives:** To assess the rate of development of autoantibodies in convalescent SARS-CoV-2 patients and their relation on infection clinical course and disease parameters.

**Methods:** One-hundred and nine convalescent SARS-CoV-2 patients were studied and underwent multidisciplinary assessment in a Day Hospital clinical setting. For each patient, demographic, clinical and immunological data were collected and, at study entry, autoimmune profile (antinuclear antibodies (ANAs), antibodies reacting with extractable nuclear antigens (anti-ENA), antineutrophil cytoplasmic antibodies (ANCAs), Lupus anticoagulant (LA), antichondrit antibodies (aCL) IgM and IgG, anti-Sj-glycoprotein I (anti-Sj2-GP) IgM and IgG) was assessed by Fluorescent immunoassay. Moreover, IL-6 plasma levels were assessed by ELISA (ELLA).

**Results:** After a median time from hospitalization for SARS-CoV-2 infection of 53.3 ± 9.0 days, 55 (50.5%) SARS-CoV-2 convalescent patients showed the positivity (ABpos) of at least one autoantibody. In particular, 31 (28.4%) were positive for LA, 11 (10.1%) for IgM-RF, 8 (7.3%) for ANA and 6 (5.5%) for IgG-aCL while less than 2% showed other autoantibody positivity (IgM-aCL, IgG-an-ti-Sj2-GP, ENA, ACA, c-ANCA, Sc170 and RNP). Analyzing the patient-related characteristics associated with the development of autoimmunity, convalescent male patients were more likely characterized by the development of antiphospholipid antibodies (aPL) (37.3%) than female (16.7%; p=0.02). Considering the disease-related characteristics, convalescent SARS-CoV-2 patients who experienced severe pneumonia (i.e., oxygen support need) during hospitalization, more likely received IL-6R-inhibitor administration (47.3%) and developed more than one autoantibody (87.5%) (aPL + another AB) than convalescent SARS-CoV-2 patients who did not need oxygen support (12.5%; p=0.02) [OR=95%CI: 9.5(1.4-109.1)] or IL-6R-inhibitor (13.5%; p<0.001). Finally, assessing cytokines plasma levels in convalescent SARS-CoV-2 patients stratified based on the development of autoantibodies we found that, despite a significant reduction of IL-6 plasma levels from hospitalization, convalescent SARS-CoV-2 patients who developed autoantibody positivity had higher IL-6 plasma levels (8.5 ± 2.5 pg/ml) than convalescent SARS-CoV-2 AB-positives patients (5.6 ± 1.5 pg/ml; p=0.07), mostly if considered autoantibodies other than aPIL (15.4 ± 7.7 pg/ml; p=0.01).

**Conclusion:** Loss of self-tolerance is a common phenomenon in the medium-term convalescent SARS-CoV-2 convalescent patients whose occurrence is dependent by a severe disease course and by an aberrant host inflammatory response. Long-term follow-up will reveal AB persistence and their clinical impact.

**References:**


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**COO0005**

**C-C CHEMOKINE RECEPTOR TYPE 5 AND ITS LIGANDS CCL4, 8 AND 11 CAN LINK COVID-19, RHEUMATOID ARTHRITIS AND HYDROXYCHLOROQUINE**

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**Background:** Coronavirus disease (COVID-19) caused by SARS-CoV-2 represents an unprecedented global public health concern with a particular burden on patients with chronic diseases and those on immune-modulating drugs. It is especially worrisome to patients with rheumatoid arthritis (RA) who are on immune suppression regimens1. On the other side, many reports showed and recommended the use of some Disease-Modifying Drugs commonly used to treat rheumatic diseases like hydroxychloroquine. However, the general understanding of COVID-19 characteristics in this population and the mechanism of action of these drugs in COVID-19 is still unknown[2].