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USE OF COMBINATION THERAPY WITH REMDESIVIR, NIRMATRELVIR/RITONAVIR AND SOTROVIMAB IN AN IMMUNOCOMPROMISED PATIENT WITH PERSISTENT SEVERE SARS-Cov-2 ACUTE RESPIRATORY SYNDROME

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Background: The different clinical manifestations by the SARS-Cov-2 infection are related to the specific immune response to virus. Immunocompromised hosts have higher risk of progression into severe forms and greater mortality than the general population and they have higher probability of infection prolonged, viral reactivation or clinical rebound. Delaying oncological treatments until viral clearance, they have a worse prognosis. Humoral immunity deficiency may be due to the depletion of B for hematological disease or for specific therapy (anti-CD 20). These patients may develop a persistent COVID-related chronic inflammatory state due to the lack of an antibody response induced by the infection. The persistence of the SARS-Cov-2 infection over time in the immunocompromised subject could therefore justify the prolonged use of combination therapy. We report a case of combination therapy in an immunocompromised patient with prolonged severe COVID.

Case Presentation: 66-year-old woman, diabetic, hypertensive, lobectomy for pulmonary mucinous adenocarcinoma, not vaccinated for SARS-Cov-2, affected by follicular mature B-cell lymphoma stage IV A treated with the G-CHOP regime, was admitted to our I.D.D for pneumonia and persistence of SARS-Cov-2 infection for one month, treated with nirmatrelvir/ritonavir for 5 days at home. We diagnosed the Omicron variant, XXBB1.5 and no anti-Capsid immune response and for S2, but for RBD and S1. For the clinical worsening, the therapy was administered with oxygen in HFNC, heparin, dexamethasone, remdesivir for 46 days, nirmatrelvir/ritonavir for 15 days and sotrovimab 500 mg, in off label regime. The patient was discharged after 50 days, asymptomatic, with reduction of the ground glass areas, but appearance of fibrotic areas and with only the N gene positive CT 36 by nasal swab.

Discussion: After 4 years from the onset of the SARS-Cov-2 pandemic, with numerous viral variants having a progressively lower impact on the global health, immunocompromised hosts have still high risk of disease progression in a severe form due to the possible poor humoral response to the vaccination and/or to infection. The mAbs and antivirals are the drugs currently approved for the prevention of progression of severe disease, but they're not authorized in patients hospitalized for COVID on oxygen. The use of two antiviral drugs in combination with sotrovimab, the only one monoclonal antibody that still seems to be effective on the Omicron variant and subvariants, may have a potential advantage thanks to the combination of the three different antiviral mechanisms. Its combination and prolonged use seem effective and safe for immunocompromised hosts at risk of evolving into a severe form and with prolonged COVID or viral reactivation (despite there are few studies about that). So, more studies about antiviral combination therapy in immunocompromised hosts are necessary.

1. Guidelines, Update 2023;

2. Triple combination Therapy with 2 antivirals and monoclonal antibodies for persistent or relapsed severe acute respiratory coronavirus 2 infection in immunocompromised Patients, M. Mikulska, Bassetti et al, CID 2023;

3. Early combination with remdesivir, nirmatrelvir/ritonavir and sotrovimab for the treatment of Covid 19 in immunocompromised hosts, I.Gentile, G.Viceconte et al (Giornale di virologia 20, 2023)

4. The unique presentation of SARS COV 2 infection in patients with B cell depletion: definition of "persistent infiammatory sero-negative Covid", Belkin A.et Al Clinical Micorbiology and Infection 2023;

5. Sars Cov2 in immunocompromised individuals. DeWolf S., Immuni 2022;

6. Novel treatment combing antiviral and neutralizing antibody-based therapies with monitoring pf spike -specific antibody and viral load for immunocompromised patients with persistent COVID 19 infection. Wada D, Experimenta Hematology and Oncology 2022