

TPE-Nabs Combination Therapy for Severe COVID-19

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The pandemic spread of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) requires very urgently to identify effective therapies and prophylaxis. This appears perhaps even more imperative, after remdesivir, seemingly the most promising antiviral drug with very potent *in vitro* activity against SARS-CoV-2, was tested in adults with severe COVID-19 in a randomized, double-blind, placebo-controlled, multi-centre trial with somewhat disappointing results [1] (quote): “*In this study of adult patients admitted to hospital for severe COVID-19, remdesivir was not associated with statistically significant clinical benefits.*”

Therapeutic Plasma Exchange (TPE) is an effective treatment in many clinical situations and a typical single TPE treatment takes about 2 hours and replaces 1 to 1.5 blood volumes; the plasma is discarded and replaced by an isotonic solution of ~5% human albumin, which typically does not induce any detectable hypersensitivity or toxic reactions. Recent COVID-19 studies suggested that no individual anti-inflammatory treatment had any clinically significant therapeutic effects (Giuseppe Ippolito, personal communication). Indeed, many COVID-19 patients develop sepsis-like syndromes, in which TPE may significantly reduce the levels of key proinflammatory cytokines and permeability factors [2]. This part of the combination therapy may have beneficial effects particularly in Acute Respiratory Distress Syndrome (ARDS) patients.

Subsequently, replacing 400 ml of the isotonic human albumin solution with 400 ml of ABO-matched convalescent plasma [3] containing high titres of anti-SARS-CoV-2 neutralizing antibodies (nAbs) would complement this approximately 2-hour treatment of severely ill COVID-19 patients. It is noteworthy that significantly higher titres of nAbs are present in elderly and middle-age than in young recovered patients [4].

Many hospitals probably cannot perform the virus-neutralization assay, which requires a BSL-3 or 4 lab. Therefore, plasmas with high titers of antibodies binding to the S1-RBD, S1-NTD and S2 should be selected. Testing by ELISA (or another suitable assay) can replace the virus neutralization assay, because practically all known nAbs are binding to one of these three SARS-CoV-2 regions and interfering with binding to ACE2 or with S2-mediated membrane fusion [5]. Alternatively, nAbs-containing allogeneic plasma could be substituted by cross-neutralizing SARS-CoV RBD-specific (human or ‘humanized’) antibodies [6] or SARS-CoV-2-specific monoclonal nAbs [7] and the whole TPE-nAbs procedure can be repeated as needed.

This combination TPE-nAbs treatment of COVID-19 patients could be very effective, free of most toxic side effects associated with many antiviral drugs currently tested and the only potential side effect could be an allergic reaction (these reactions are known to occur, but are not

extremely frequent) towards an unknown component in the allogeneic plasma. This possible TPE-nAbs combination therapy for COVID-19 may be of interest to the broad *World Journal of Medical Oncology* readership.

References:

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