

Evolutionary Therapeutic Strategies

**e Expanded Umbilical Cord Mesenchymal Stem Cells (UC-MSCs) as a Therapeutic Strategy In Managing Critically Ill COVID-19 Patients: The Case for Compassionate Use**

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COVID-19 has affected the United States leading to a national emergency with health care and economic impact, propelling the country into a recession with disrupted lifestyles not seen in recent history. COVID-19 is a serious illness leading to multiple deaths in various countries including the United States. Several million Americans satisfy the Center for Disease Control and Prevention (CDC) criteria for being high risk. Unfortunately, the available supply of medical beds and equipment for mechanical ventilation are much less than is projected to be needed. The World Health Organization (WHO) and multiple agencies led by the CDC in the United States have attempted to organize intensive outbreak investigation programs utilizing appropriate preventive measures, evaluation, and treatment.

The clinical spectrum of COVID-19 varies from asymptomatic forms to conditions encompassing multiorgan and systemic manifestations in terms of septic shock, and multiple organ dysfunction (MOD) syndromes. The presently approved treatments are supportive but not curative for the disease. There are multiple treatments being studied. These include vaccines, medications Remdesivir and hydroxychloroquine and potentially combination therapy. Finally, expanded umbilical cord mesenchymal stem cells or (UC-MSCs) may have a role and are being studied.

The cure of COVID-19 is essentially dependent on the patients' own immune system. When the immune system is over activated in an attempt to kill the virus, this can lead to the production of a large number of inflammatory factors, resulting in severe cytokine storm. The cytokine storm may induce organ damage followed by the edema, dysfunction of air exchange, acute respiratory distress syndrome (ARDS), acute cardiac injury, and secondary infection, which may lead to death. Thus, at this point, the avoidance of the cytokine storm may be the key for the treatment of HCOV-19 infected patients.

In China, where there was limited availability of effective modalities to manage COVID-19 several patients were treated with expanded UC-MSCs. Additionally, the Italian College of Anesthesia, Analgesia, Resuscitation and Intensive Care have reported guidelines to treat coronavirus patients with stem cells in the hope of decreasing the number of patients going to the ICU, and, also relatively quickly getting them out of ICU.

In this manuscript, we describe the urgent need for various solutions, pathogenesis of coronavirus and the clinical evidence for treatment of COVID-19 with stem cells. The limited but emerging evidence regarding UC MSC in managing COVID-19 suggests that it might be considered for compassionate use in critically ill patients to reduce morbidity and mortality in the United States.

The administration and Coronavirus Task Force might wish to approach the potential of expanded UC-MSCs as an evolutionary therapeutic strategy in managing COVID-19 illness with a 3-pronged approach: If proven safe and effective on a specific and limited basis...

1. Minimize regulatory burden by all agencies so that critically ill COVID-19 patients will have access regardless of their financial circumstance.

2. Institute appropriate safeguards to avoid negative consequences from unscrupulous actors.
3. With proper informed consent from patients or proxy when necessary, and subject to accumulation of data in that cohort, allow the procedure to be initiated in critically ill patients who are not responding to conventional therapies.

**Key words:** Coronavirus, COVID-19, cytokine storm, multiorgan failure, expanded umbilical cord mesenchymal stem cells

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