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**Pharmacological Immunomodulation in Covid 19**

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Covid 19 is characterized by hyperresponsiveness of immune system and when disease progresses, systemic proinflammatory cytokines and biomarkers are elevated and immune modulators have the potential to inhibit cytokines and to treat the cytokine storm. The cytokine dysregulation and influx of inflammatory myeloid cells can lead acute respiratory distress syndrome (ARDS), multiorgan dysfunction and death [1]. The macrophage activation syndrome (MAS)-like pulmonary immunopathology and the direct endothelial damage leads to micro- and macrothrombotic episodes. Immunomodulator drugs either stimulate or suppress the immune system, modulate the immune response, including both adaptive and innate immunity, may significantly reduce hyperinflammation. Specific Immune Modulators such as anti-cytokines, the Interleukin (IL)-1 Receptor antagonists by inhibiting the proinflammatory cytokines IL-1 $\alpha$  and IL-1 $\beta$  is effective in treating MAS[2]. IL-6 Receptor Antagonists, Tocilizumab (Actemra<sup>®</sup>) is a recombinant humanized anti-human IL-6 receptor monoclonal antibody can specifically bind the membrane-bound IL-6 receptor (mIL6R) and soluble IL-6 receptor (sIL6R), thereby inhibiting signal transduction, a possible therapeutic option for CRS of severely ill COVID-19 patients who have extensive lung lesions and high IL-6 levels [3]. Ruxolitinib (Jakafi<sup>®</sup>), a potent and selective oral inhibitor of both JAK1 and JAK2 protein kinases, interrupts signaling downstream of multiple proinflammatory cytokines, which constitute the cytokine storm and increased activation of the JAK-STAT pathway. Nebulized sargramostim 125  $\mu$ g twice daily for 5 days is an effective strategy for pneumonia-associated ARDS. High-dose IVIG at a dose of 0.3–0.5 g/kg/day for 5 days normalize body temperature within 1–2 days but thromboembolic complications were reported in some cases. Low-dose dexamethasone (6 mg once daily, orally or intravenously) for 10 days reduced deaths by one-third in patients on mechanical ventilation in RECOVERY trial. Triple antiviral therapy of lopinavir/ritonavir, ribavirin, and nebulized IFN $\beta$ -1b could shorten the duration of viral shedding. Statins inhibit MyD88 pathway and tend to preserve MyD88 levels during hypoxia and stress confer a protective effect in COVID-19 patients. Recombinant human ACE (rhACE2) is a novel therapy for acute lung injury. Macrolides, azithromycin and clarithromycin, are antibiotics with immunomodulatory and anti-inflammatory effects, downregulate proinflammatory cytokines and known to prolong the QT interval and potentially increase the risk of sudden cardiac death in combination with other QT-prolonging therapies such as chloroquine. Patients with elevated CRP and/or lymphopenia are most benefit from hydroxychloroquine. By increasing endosomal pH and disturbing the glycosylation of cell surface receptors, these medications provide an important defense against viral entry and replication, may bind to gangliosides with high affinity, thus preventing SARS-CoV-2 from binding with the ACE-2 receptor, but RECOVERY trial & ORCHID study showed a lack of evidence of efficacy and patients receiving hydroxychloroquine plus azithromycin were more likely to have cardiac arrest. Targeting PGD2/DP2 signaling as an immunotherapeutic approach for immune dysfunction and lymphopenia, characteristic features of COVID-19 disease. Ramatroban (Baynas<sup>®</sup>) is a potent, reversible, and selective antagonist of PGD2/DP2 receptors that has been shown to inhibit PGD2-stimulated IL-13 secretion, used orally as a therapeutic agent in the context of COVID-19.

SARS patients who received convalescent plasma within 14 days after the onset of symptoms manifested better outcomes. Immunomodulatory (mesenchymal stem cell transplantation) improves pulmonary function within 2 days after MSCs transplantation, having anti-inflammatory and anti-fibrotic effects with regenerative potential in vascular dysfunction of Covid-19. These cells are ACE2 and TMPRSS2 negative, making them a good cell target not influenced by SARS-CoV-2 infection and used to treat covid-19 intubated-ventilated patients presenting with Acute Respiratory Distress Syndrome of less than 96 h. (very small embryonic like stem cells (VSELs) have the ability to support endothelial cells angiogenic potential and counteract lymphopenia. Both immunosuppression and immunomodulation could serve as potent COVID-19 pharmacotherapies when they are administered in an appropriate disease stage/severity. Complement C5a inhibition with vilobelimab in a single placebo-controlled trial showed a mortality benefit Of the JAK inhibitors, baricitinib is the most thoroughly studied with the largest survival benefit effect and low risk of serious adverse events [4].

### Biography

Ramachandran Muthiah, Consultant at Zion hospital, Azhagamandapam and Morning Star hospital, Marthandam, Kanyakumari District, India. Born on 10/5/1966 at keezhkulam village and father Muthiah belongs to enayam thoppu and mother Swornam belongs to Palaninta vilai, keezhkulam-629193 (+914651 203014) and both were farmers. Got married with an agricultural scientist Rajula shanthy and has one son R. Jeremy and now living with R.Russulsy. Completed primary education at Anaan vilai, keezhkulam and secondary education at Concordia Higher secondary school, Pootteti, MBBS in 1988 (Madurai Kamaraj), M.D. in 1996, D.M. in 2003, Dr.MGR Medical University, Chennai, 6 months course in Interventional cardiology at Batra Hospital, New Delhi in 2006 (Ministry of health, Govt of India). Worked as medical officer in Rural health services for 5 years (keezhachekkarakudi, Aryappapuram Primary health centres, ESI hospital, Singanallur, coimbatore), teaching category as Assistant Professor at Madras, Coimbatore and Thoothukudi medical colleges. Marital life and job position get troubled with police arrests, brutal assaults, killing attempts and jail imprisonments happened in kerala state and police arrest, mental hospital transfer and psychiatric custody happened in tamil nadu state. Published papers in Cardiosource, American College of Cardiology Foundation, Case Reports in Clinical Medicine (SCIRP) and Journal of Saudi Heart Association.

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