

**EFIKASI ANTI IL-6 RECEPTOR MONOCLONAL ANTIBODY SEBAGAI
TERAPI ADJUVAN PASIEN COVID-19 DENGAN CYTOKINE RELEASE
SYNDROME: SEBUAH TINJAUAN SISTEMATIS**

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ABSTRAK

Pendahuluan: *Cytokine release syndrome* (CRS) memainkan peran penting dalam onset dan progresi gangguan pernapasan akut ataupun kerusakan multi-organ pada pasien COVID-19 derajat berat. Beberapa studi menyebutkan interleukin 6 termasuk sitokin utama dalam terjadinya CRS. Penulis tertarik menilai anti IL-6 *receptor monoclonal antibody* seperti tocilizumab dan sarilumab yang berpotensi sebagai immunomodulator dalam terapi adjuvan pasien COVID-19. **Metode:** Penulis menelaah studi relevan dari PubMed, EBSCO MEDLINE, dan Google Scholar dengan desain *Randomized Controlled Trial* (RCT). Hasil utama ialah kebutuhan ventilasi mekanik invasif/*organ life-support* lainnya, dengan hasil sekunder berupa keamanan penggunaan obat. Kualitas setiap studi diuji dengan *Cochrane Risk-of-Bias Tool for Randomized Trials* (RoB 2). **Hasil:** Dari 16 studi RCT yang ditinjau dengan melibatkan 6.762 pasien, didapatkan hubungan antara Anti IL-6 *receptor monoclonal antibody* dengan kebutuhan VMI/*organ life support* lainnya (602/3641 [16.5%] di kelompok intervensi versus 777/3394 [23%] di kelompok kontrol, RR = 0.77; 95% CI [0.72, 1.21]; $P < 0.00001$; $I^2 = 20\%$). Tidak ditemukan efek samping serius terkait pengobatan. **Kesimpulan:** Anti IL-6 *receptor monoclonal antibody* (tocilizumab dan sarilumab) aman dan berpotensi memberikan perbaikan klinis bila diberikan bersamaan dengan steroid pada pasien COVID-19 dengan CRS.

Kata kunci: COVID-19, *Cytokine Release Syndrome*, Antibodi Monoklonal, Interleukin 6 (IL-6)

EFFICACY OF ANTI IL-6 RECEPTOR MONOCLONAL ANTIBODY AS ADJUVANT THERAPY IN COVID-19 PATIENTS WITH CYTOKINE RELEASE SYNDROME: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Cytokine release syndrome (CRS) take an important role in the progression of acute respiratory distress syndrome or multi-organ damage in severe COVID-19 patients. Several studies stated interleukin 6 including the main cytokine in the occurrence of CRS. We are interested in assessing anti-IL-6 receptor monoclonal antibodies, such as tocilizumab and sarilumab, which have potential as immunomodulators in adjuvant therapy for COVID-19 patients. **Methods:** We reviewed relevant Randomized Controlled Trial (RCT) studies from PubMed, Google Scholar, and EBSCO MEDLINE up to December 2021. The primary outcome included the requirement for invasive mechanical ventilation/other organ life-support, with the secondary outcome was incidence of adverse events. The risk of bias of each study was assessed using the Cochrane Risk-of-Bias Tool for Randomized Trials (RoB 2). **Results:** Sixteen RCT studies met the eligibility criteria involving 6,762 patients. There was an association between anti IL-6 receptor monoclonal antibodies and the requirement for IVM/other organ life support (602/3641 [16.5%] in the intervention group vs 777/3394 [23%] in the control group, RR = 0.77; 95% CI [0.72, 1.21]; P < 0.00001; I2 = 20%). There were no serious adverse events associated with the treatment. **Conclusion:** Anti-IL-6 receptor monoclonal antibodies are potentially safe and reduce the requirement for intubation when given concomitantly with steroids in COVID-19 patients with CRS. However, further recommendations of anti-IL-6 receptor monoclonal antibodies for COVID-19 patients, particularly sarilumab, should continue to be corroborated by high-quality evidence from randomized controlled trials.

Keywords: COVID-19, Cytokine Release Syndrome, Monoclonal Antibody, Interleukin 6 (IL-6)