# Evidence Search Service Results of your search request

## Use of tocilizumab or alternative interleukin 6 (IL6) inhibitor in treating covid-19

**ID of request:** 28595  
**Date of request:** 1st April, 2021  
**Date of completion:** 13th April, 2021

If you would like to request any articles or any further help, please contact:  Nicola Salliss at [nicola.salliss@nhs.net](mailto:nicola.salliss@nhs.net)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: Use of tocilizumab or alternative interleukin 6 (IL6) inhibitor in treating covid-19. Nicola Salliss. (13th April, 2021). HAYWARDS HEATH, UK: Brighton and Sussex Library and Knowledge Service.

**Sources searched**  
Citation tracking (4)  
Cochrane Library (1)  
EMBASE (125)  
Europe PubMed Central (49)  
UpToDate (1)

**Date range used** (5 years, 10 years): 1 Jan 2021 -   
**Limits used** (gender, article/study type, etc.): English language   
**Search terms and notes** (full search strategy for database searches below):

Embase was searched via OVID using relevant natural language and controlled vocabulary terms. A scoping search found frequent mentions of sarilumab as a treatment therefore this was included as a separate search term.  Europe PMC was searched to find additional articles including preprints. Searches were limited to English language material published since 1st January 2021. Results were reviewed for relevance and then de-duplicated in EndNote. Due to the large number of results retrieved no further resources were searched other than those listed above.

For more information about the resources please go to: <https://www.bsuh.nhs.uk/library/>.

## Summary of Results

This evidence search looked at the use of tocilizumab or alternative interleukin 6 inhibitors in the treatment of Covid-19.  A large body of research has been published since 1st January 2021, including several systematic reviews. As this is very much a live topic, Europe PubMed Central was searched to find the most recent articles which means that the report includes many preprint articles that have not yet been peer-reviewed.

## Contents

[A. Synopses or Summaries](#Content2)

UpToDate

[COVID-19: Management in hospitalized adults](#Research895388)

[B. Systematic Reviews](#Content3)

Cochrane Database of Systematic Reviews

[Interleukin‐6 blocking agents for treating COVID‐19: a living systematic review](#Research895635)

Drug Research

[Efficacy and Safety of Tocilizumab for Coronavirus Disease 2019 (Covid-19) Patients: A Systematic Review and Meta-analysis](#Research899085)

Expert review of anti infective therapy

[Pharmacological interventions for COVID-19: a systematic review of observational studies and clinical trials](#Research899047)

Expert review of clinical immunology

[Efficacy and safety of Tocilizumab in severe and critical COVID-19: A Systematic Review and Meta-Analysis](#Research899150)

F1000Research

[Optimal use of tocilizumab for severe and critical COVID-19: A systematic review and meta-analysis](#Research899138)

International immunopharmacology

[The effect of tocilizumab on COVID-19 patient mortality: A systematic review and meta-analysis of randomized controlled trials](#Research899115)

Journal of Medical Virology

[Efficacy of tocilizumab in COVID-19: A systematic review and meta-analysis](#Research899036)

MedRxiv

[Efficacy and safety of tocilizumab in the management of COVID-19: A systematic review and meta-analysis of observational studies](#Research899184)

Pulmonology

[Rationale and evidence on the use of tocilizumab in COVID-19: a systematic review](#Research899062)

Research Square

[Efficacy and Safety of Tocilizumab in Patients with COVID-19: A Systematic Review and Meta-Analysis](#Research899114)

Systematic Reviews in Pharmacy

[Immunosuppression drugs seize the overacting immune system by preventing the cytokine storm in covid-19 symptoms](#Research899059)

Thorax

[Systematic review and meta-analysis of anakinra, sarilumab, siltuximab and tocilizumab for COVID-19](#Research899097)

[C. Original Research](#Content5)

1. ["Tocilizumab-an option for patients with COVID-19 associated cytokine release syndrome: A single center experience", a retrospective study-original article](#Research899053)
2. [A Case Series of Severe Hospitalized COVID-19 Patients Treated with Tocilizumab and Glucocorticoids: A Report from Saudi Arabian Hospital](#Research899027)
3. [A retrospective matched cohort single-center study evaluating outcomes of COVID-19 and the impact of immunomodulation on COVID-19-related cytokine release syndrome in solid organ transplant recipients](#Research899153)
4. [Administration of tocilizumab to patients with high concentrations of IL-6 in the course of COVID-19 is associated with a better prognosis](#Research899072)
5. [An unfavourable outcome following switching intravenous abatacept and tocilizumab to subcutaneous forms during the COVID-19 pandemic](#Research899082)
6. [Anakinra after treatment with corticosteroids alone or with tocilizumab in patients with severe COVID-19 pneumonia and moderate hyperinflammation. A retrospective cohort study](#Research899033)
7. [Anti-IL6 treatment of serious COVID-19 disease: A monocentric retrospective experience](#Research899051)
8. [Association between Early Treatment with Tocilizumab and Mortality among Critically Ill Patients with COVID-19](#Research899084)
9. [Benefits of early aggressive immunomodulatory therapy (tocilizumab and methylprednisolone) in COVID-19: Single center cohort study of 685 patients](#Research899117)
10. [Biological agents for rheumatic diseases in the outbreak of COVID-19: Friend or foe?](#Research899166)
11. [Characteristics of the First 102 Severe COVID-19 Cases Treated With Convalescent Plasma or Tocilizumab or Both in Al-Nahdha Hospital, Oman](#Research899026)
12. [Clinical course of severe COVID19 treated with tocilizumab and antivirals post-allogeneic stem cell transplant with extensive chronic GVHD](#Research899129)
13. [Clinical course of severe patients with COVID-19 treated with tocilizumab: report from a cohort study in Spain](#Research899054)
14. [Combination of Tocilizumab and Steroids to Improve Mortality in Patients with Severe COVID-19 Infection: A Spanish, Multicenter, Cohort Study](#Research899161)
15. [Combination therapy of Tocilizumab and steroid for management of COVID-19 associated cytokine release syndrome: A single center experience from Pune, Western India](#Research899067)
16. [Combination therapy with tocilizumab and corticosteroids for aged patients with severe COVID-19 pneumonia: A single-center retrospective study](#Research899116)
17. [Comparative Survival Analysis of Immunomodulatory Therapy for Coronavirus Disease 2019 Cytokine Storm](#Research899135)
18. [Compassionate use of tocilizumab in severe SARS-CoV2 pneumonia](#Research899079)
19. [Corrigendum to: Outcomes in patients with severe COVID-19 disease treated with tocilizumab: a case-controlled study](#Research899156)
20. [Corticosteroids and tocilizumab reduce in-hospital mortality in severe COVID-19 pneumonia: a retrospective study in a Spanish hospital](#Research899182)
21. [COVID-19 and IL-6: Why vitamin D (probably) helps but tocilizumab might not](#Research899172)
22. [Covid-19 controversies: the tocilizumab chapter](#Research899124)
23. [COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network](#Research899049)
24. [COVID-19 treatment options: a difficult journey between failed attempts and experimental drugs](#Research899042)
25. [Covid-19: Arthritis drug tocilizumab reduces deaths in hospitalised patients, study shows](#Research899190)
26. [COVID-19: Still a place for tocilizumab?](#Research899152)
27. [COVIDOSE: A Phase II Clinical Trial of Low-Dose Tocilizumab in the Treatment of Noncritical COVID-19 Pneumonia](#Research899176)
28. [Cytokine Profiles Before and After Immune Modulation in Hospitalized Patients with COVID-19](#Research899037)
29. [Decreased serum levels of the inflammaging marker miR-146a are associated with non-clinical response to tocilizumab in COVID-19 patients](#Research899162)
30. [Development and validation of a prediction model for tocilizumab failure in hospitalized patients with SARS-CoV-2 infection](#Research899134)
31. [Does timing matter on tocilizumab administration? Clinical, analytical and radiological outcomes in COVID-19](#Research899131)
32. [Dynamic changes in serum IL-6, IL-8, and IL-10 predict the outcome of ICU patients with severe COVID-19](#Research899112)
33. [Early clinical outcomes with tocilizumab for severe COVID-19: a two-centre retrospective study](#Research899174)
34. [Early Tocilizumab Dosing Is Associated With Improved Survival in Critically Ill Patients Infected With Severe Acute Respiratory Syndrome Coronavirus-2](#Research899143)
35. [Early use of tocilizumab in the prevention of adult respiratory failure in SARS-CoV-2 infections and the utilization of interleukin-6 levels in the management](#Research899032)
36. [Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: Randomised controlled trial](#Research899183)
37. [Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized with COVID-19 Pneumonia: A Randomized Clinical Trial](#Research899163)
38. [Effect of Tocilizumab vs Usual Care in Adults Hospitalized with COVID-19 and Moderate or Severe Pneumonia: A Randomized Clinical Trial](#Research899087)
39. [Effective treatment with Tocilizumab in a COVID-19 patient on maintenance hemodialysis: A case report](#Research899137)
40. [Effectiveness and safety of intravenous tocilizumab to treat COVID-19-associated hyperinflammatory syndrome: Covizumab-6 observational cohort](#Research899061)
41. [Effectiveness of anakinra for tocilizumab-refractory severe COVID-19: A single-centre retrospective comparative study](#Research899063)
42. [Effects of tocilizumab on mortality in hospitalized patients with COVID-19: a multicentre cohort study](#Research899122)
43. [Effects of tocilizumab versus hemoadsorption combined with tocilizumab in patients with SARS-CoV-2 pneumonia: Preliminary results](#Research899045)
44. [Experience of using tocilizumab for treatment in Indonesian patients with severe COVID-19](#Research899189)
45. [Feasibility of tocilizumab in ICU patients with COVID-19](#Research899090)
46. [Fighting the storm: could novel anti-TNFα and anti-IL-6 C. sativa cultivars tame cytokine storm in COVID-19?](#Research899101)
47. [Genetically proxied interleukin-6 receptor inhibition: Opposing associations with COVID-19 and pneumonia](#Research899107)
48. [Glucocorticoids alone versus tocilizumab alone or glucocorticoids plus tocilizumab in patients with severe SARS-CoV-2 pneumonia and mild inflammation](#Research899034)
49. [High expression of ace2 in the human lung leads to the release of il6 by suppressing cellular immunity: Il6 plays a key role in covid-19](#Research899041)
50. [Host-directed therapies for COVID-19](#Research899120)
51. [IL-6 blockade for COVID-19: a global scientific call to arms](#Research899133)
52. [IL-6 inhibition in the treatment of COVID-19: a meta-analysis and meta-regression](#Research899179)
53. [IL-6 modulation for COVID-19: the right patients at the right time?](#Research899035)
54. [IL-6 serum levels predict severity and response to tocilizumab in COVID-19: An observational study](#Research899074)
55. [Immediate amelioration of severe respiratory distress in sjogren's syndrome with covid-19 treated with a single dose of off-label tocilizumab](#Research899093)
56. [Immunomodulation for the management of severe SARS-CoV2 infections. State of the art and review of the literature](#Research899038)
57. [Impact of Interleukin-6 Receptor Blockade With Tocilizumab on Cardiac Injury in Patients With COVID-19: A Retrospective Cohort Study](#Research899188)
58. [Influence of Cytokine Release Syndrome in Severe COVID-19 Patients Treated With Tocilizumab Over the Quantiferon TB Gold Plus Results](#Research899164)
59. [Insights from compassionate use of tocilizumab for COVID-19 to inform appropriate design of randomised controlled trials](#Research899039)
60. [Interleukin-1 and interleukin-6 inhibition compared with standard management in patients with COVID-19 and hyperinflammation: a cohort study](#Research899052)
61. [Interleukin-6 Antagonists: Lessons From Cytokine Release Syndrome to the Therapeutic Application in Severe COVID-19 Infection](#Research899126)
62. [Interleukin-6 blockade with tocilizumab in COVID-19: Does it live up to its hype?](#Research899103)
63. [Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19](#Research895390)
64. [Interleukin-6 receptor blockade with subcutaneous tocilizumab improves coagulation activity in patients with COVID-19](#Research899066)
65. [Interleukin-6 receptor blockade with subcutaneous tocilizumab in severe COVID-19 pneumonia and hyperinflammation: a case-control study](#Research899147)
66. [Interleukin-6 Receptor Inhibition in Covid-19 - Cooling the Inflammatory Soup](#Research899160)
67. [Interleukin-6 signaling blockade treatment for cytokine release syndrome in COVID-19 (Review)](#Research899055)
68. [Interleukin-6: From arthritis to CAR-T cell therapy and COVID-19](#Research899099)
69. [Intestinal perforation in patient with COVID-19 infection treated with tocilizumab and corticosteroids. Report of a clinical case☆ Perforación intestinal en paciente COVID-19 en tratamiento con tocilizumab y corticoides. A propósito de un caso](#Research899078)
70. [Invasive pulmonary aspergillosis after treatment with tocilizumab in a patient with COVID-19 ARDS: a case report](#Research899191)
71. [Investigation of the disease process and drug combinations in patients with suspected/confirmed Covid-19 using favipiravir](#Research899140)
72. [Is There Still a Place for Tocilizumab in Coronavirus Disease 2019?](#Research899100)
73. [Late onset infectious complications and safety of tocilizumab in the management of COVID-19](#Research899144)
74. [Matched cohort study on the efficacy of tocilizumab in patients with COVID-19](#Research899155)
75. [Metabolomic/lipidomic profiling of COVID-19 and individual response to tocilizumab](#Research899128)
76. [Methylprednisolone as rescue therapy after tocilizumab failure in patients with severe COVID-19 pneumonia](#Research899081)
77. [Monitoring neutrophil-to-lymphocyte ratio in patients with coronavirus disease 2019 receiving tocilizumab](#Research899086)
78. [Multifactorial expression of IL-6 with update on COVID-19 and the therapeutic strategies of its blockade (Review)](#Research899136)
79. [Multimodality treatment in immunocompromised patients with severe COVID-19: the role of IL-6 inhibitor, intravenous immunoglobulin, and haemoperfusion](#Research899110)
80. [Multistate modeling of COVID-19 patients using a large multicentric prospective cohort of critically ILL patients](#Research899181)
81. [Nomogram for prediction of fatal outcome in patients with severe COVID-19: a multicenter study](#Research899195)
82. [Observational study on off-label use of tocilizumab in patients with severe COVID-19](#Research899028)
83. [Perspectives on Targeting IL-6 as a Potential Therapeutic Strategy for COVID-19](#Research899095)
84. [Post-transplant patients with COVID-19 associated acute respiratory distress syndrome, a role for Tociluzumab: A case series](#Research899106)
85. [Posterior Reversible Encephalopathy Syndrome in a Patient With SARS-CoV-2 Infection Treated With Tocilizumab](#Research899177)
86. [Potential role of subcutaneous tocilizumab injections in patients with COVID-19 associated pneumonia](#Research899080)
87. [Predictors of Mortality Amongst Tocilizumab Administered COVID-19 Asian Indians: A Predictive Study From a Tertiary Care Centre](#Research899065)
88. [Preliminary Efficacy of Tocilizumab Treatment in The Patients With COVID-19](#Research899056)
89. [Rapid radiological improvement of COVID-19 pneumonia after treatment with tocilizumab](#Research899060)
90. [Repurposed tocilizumab in patients with severe COVID-19](#Research899180)
91. [Repurposing Antimalarials to Tackle the COVID-19 Pandemic](#Research899104)
92. [Respiratory delivery of favipiravir-tocilizumab combination through mucoadhesive protein-lipidic nanovesicles: prospective therapeutics against COVID-19](#Research899178)
93. [Risk of Hepatitis B Virus Reactivation in Rheumatoid Arthritis Patients Undergoing Tocilizumab-Containing Treatment](#Research899105)
94. [Role of IL-6 inhibitor in treatment of COVID-19-related cytokine release syndrome](#Research899068)
95. [Role of tocilizumab for concomitant systemic fungal infection in severe COVID-19 patient: Case report](#Research899168)
96. [Safety of tocilizumab in COVID-19 pregnant women and their newborn: A retrospective study](#Research899092)
97. [Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial](#Research899111)
98. [Serious adverse events with tocilizumab: Pharmacovigilance as an aid to prioritize monitoring in COVID-19](#Research899075)
99. [Single dose of subcutaneous tocilizumab in COVID-pneumonia: CT evidence of lymph nodal and parenchymal response](#Research899185)
100. [Successful treatment of severe COVID-19 pneumonia and hyperinflammatory syndrome with tocilizumab](#Research899076)
101. [The association of interleukin-6 value, interleukin inhibitors, and outcomes of patients with COVID-19 in New York City](#Research899119)
102. [The Effect of IL-6 Inhibitors on Mortality Among Hospitalized COVID-19 Patients: A Multicenter Study](#Research899173)
103. [The effect of tocilizumab on inflammatory markers in survivors and non-survivors of severe COVID-19](#Research899030)
104. [The effect of tocilizumab on mortality in hospitalized patients with COVID-19: a meta-analysis of randomized controlled trials](#Research899102)
105. [The effect of tocilizumab, anakinra, and prednisolone on antibody response to SARS-CoV-2 in patients with COVID-19: A prospective cohort study with multivariate analysis of factors affecting the antibody response](#Research899043)
106. [The Role of Convalescent Plasma and Tocilizumab in the Management of COVID-19 Infection: A Cohort of 110 Patients from a Tertiary Care Hospital in Oman](#Research899096)
107. [Therapeutic efficacy, mechanical ventilation, length of hospital stay, and mortality rate in severe COVID-19 patients treated with tocilizumab](#Research899167)
108. [Therapeutic role of tocilizumab in sars-cov-2-induced cytokine storm: Rationale and current evidence](#Research899142)
109. [Time to Reassess Tocilizumab's Role in COVID-19 Pneumonia](#Research899141)
110. [Tocilizumab : Infection and worsening of pre-existing COVID-19 symptoms following off-label treatment: case report](#Research899024)
111. [Tocilizumab administration in COVID-19 patients: Water on the fire or gasoline?](#Research899064)
112. [Tocilizumab administration in patients with SARS-CoV-2 infection: Subcutaneous injection vs intravenous infusion](#Research899169)
113. [Tocilizumab administration is associated with the reduction in biomarkers of coronavirus disease 2019 infection](#Research899091)
114. [Tocilizumab and PMX-DHP have efficacy for severe COVID-19 pneumonia](#Research899171)
115. [Tocilizumab combined with favipiravir in the treatment of COVID-19: A multicenter trial in a small sample size](#Research899197)
116. [Tocilizumab did not reduce hypoxemic respiratory failure or death in hospitalized patients with COVID-19](#Research899170)
117. [Tocilizumab efficacy in COVID-19 patients is associated with respiratory severity-based stages](#Research899029)
118. [Tocilizumab for COVID-19 Pneumonia in a Patient With Non-Small-cell Lung Cancer Treated With Chemoimmunotherapy](#Research899048)
119. [Tocilizumab for hospitalized patients with COVID-19](#Research899025)
120. [Tocilizumab for Severe Worsening COVID-19 Pneumonia: a Propensity Score Analysis](#Research899159)
121. [Tocilizumab for the Critically Ill With Severe COVID-19: A Community Hospital Case Series](#Research899125)
122. [Tocilizumab for the treatment of adult patients with severe COVID-19 pneumonia: A single-center cohort study](#Research899070)
123. [Tocilizumab for the treatment of COVID-19](#Research899069)
124. [Tocilizumab for the Treatment of COVID-19 among Hospitalized Patients: A Matched Retrospective Cohort Analysis](#Research899187)
125. [Tocilizumab for treating COVID-19: a systemic review and meta-analysis of retrospective studies](#Research899198)
126. [Tocilizumab improves survival in severe COVID-19 pneumonia with persistent hypoxia: a retrospective cohort study with follow-up from Mumbai, India](#Research899077)
127. [Tocilizumab Improves the Prognosis of COVID-19 in Patients with High IL-6](#Research899073)
128. [Tocilizumab in Coronavirus Disease 2019-Related Critical Illness: A Propensity Matched Analysis](#Research899149)
129. [Tocilizumab in Covid-19](#Research899108)
130. [Tocilizumab in COVID-19 interstitial pneumonia](#Research899145)
131. [Tocilizumab in COVID-19: Give it time!](#Research899151)
132. [Tocilizumab in COVID-19: Is the temptation worthwhile?](#Research899083)
133. [Tocilizumab in hospitalized patients with COVID-19: Clinical outcomes, inflammatory marker kinetics, and safety](#Research899088)
134. [Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia](#Research895392)
135. [Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia](#Research899157)
136. [Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial [Preprint]](#Research895384)
137. [Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia](#Research895394)
138. [Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia](#Research899118)
139. [Tocilizumab in patients infected by SARS-CoV2](#Research899165)
140. [Tocilizumab in patients with moderate or severe COVID-19: a randomized, controlled, open-label, multicenter trial](#Research899186)
141. [Tocilizumab in the Management of COVID-19: A Preliminary Report](#Research899113)
142. [Tocilizumab in the treatment of critical COVID-19 pneumonia: A retrospective cohort study of mechanically ventilated patients](#Research899071)
143. [Tocilizumab in Treatment for Patients With COVID-19](#Research899044)
144. [Tocilizumab in Treatment for Patients With COVID-19](#Research899158)
145. [Tocilizumab in Treatment for Patients With COVID-19](#Research899194)
146. [Tocilizumab plus standard care versus standard care in patients in India with moderate to severe COVID-19-associated cytokine release syndrome (COVINTOC): an open-label, multicentre, randomised, controlled, phase 3 trial](#Research899175)
147. [Tocilizumab reduces the risk of ICU admission and mortality in patients with SARS-CoV-2 infection](#Research899132)
148. [Tocilizumab treatment in critically ill patients with COVID-19: A retrospective observational study](#Research899089)
149. [Tocilizumab use in COVID-19-associated pneumonia](#Research899139)
150. [Tocilizumab use in patients with moderate to severe COVID-19: A retrospective cohort study](#Research899057)
151. [Tocilizumab versus the Covid19 tempest: All's well that ends well or much ado about nothing?](#Research899109)
152. [Tocilizumab's efficacy in patients with Coronavirus Disease 2019 (COVID-19) is determined by the presence of cytokine storm](#Research899031)
153. [Tocilizumab, Remdesivir, Favipiravir, and Dexamethasone Repurposed for COVID-19: a Comprehensive Clinical and Pharmacovigilant Reassessment](#Research899094)
154. [Tocilizumab-A beacon of hope in the management of severe COVID-19?](#Research899058)
155. [Tocilizumab-an effective therapy for severely and critically ill COVID-19 patients](#Research899046)
156. [Tocilizumab-induced cytomegalovirus colitis in a patient with COVID-19](#Research899098)
157. [Tocilizumab-induced unexpected increase of several inflammatory cytokines in critically ill COVID-19 patients](#Research899146)
158. [Tocilizumab: From Rheumatic Diseases to Covid-19](#Research899148)
159. [Treatment of COVID-19 atypical pneumonia by early Tocilizumab administration in "non-critically-ill" patients on hemodialysis](#Research899050)
160. [Treatment With Tocilizumab for Patients With COVID-19 Infections: A Case-Series Study](#Research899130)
161. [Treatment with tocilizumab or corticosteroids for COVID-19 patients with hyperinflammatory state: a multicentre cohort study (SAM-COVID-19)](#Research899154)
162. [Upregulated IL-6 Indicates a Poor COVID-19 Prognosis: A Call for Tocilizumab and Convalescent Plasma Treatment](#Research899192)
163. [Use of subcutaneous tocilizumab in patients with COVID-19 pneumonia](#Research899123)
164. [Use of tocilizumab in multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2](#Research899040)
165. [Vaccines and drugs under clinical trials for prevention and treatment of COVID-19](#Research899193)
166. [Varying illness severity in patients with myd88 deficiencyinfected with coronavirus SARS-CoV-2](#Research899121)
167. [What about tocilizumab? A retrospective study from a NYC Hospital during the COVID-19 outbreak](#Research899127)

### [D. Search History](#SearchHistory)

## A. Synopses or Summaries

#### UpToDate

**COVID-19: Management in hospitalized adults** (2021)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a8df2a861adae60b72c2db1fa2b23d0c)

Section on IL-6 pathway inhibitors (eg, tocilizumab)

## B. Systematic Reviews

#### Cochrane Database of Systematic Reviews

**Interleukin‐6 blocking agents for treating COVID‐19: a living systematic review** (2021)

Ghosn L., Chaimani A., Evrenoglou T. et al.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=9d08f7d04bada089fd398e0252119ad9)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=14cc460fd824fdf67347aaad6707be4e)

Authors' conclusions On average, tocilizumab reduces all‐cause mortality at D28 compared to standard care alone or placebo and probably results in slightly fewer serious adverse events than standard care alone or placebo. Nevertheless, tocilizumab probably results in little or no increase in the outcome clinical improvement (defined as hospital discharge or improvement measured by trialist‐defined scales) at D28. The impact of tocilizumab on other outcomes is uncertain or very uncertain. With the data available, we were not able to explore heterogeneity. Individual patient data meta‐analyses are needed to be able to identify which patients are more likely to benefit from this treatment. Evidence for an effect of sarilumab is uncertain and evidence for other anti‐IL6 agents is unavailable. Thirty‐nine RCTs of IL‐6 blocking agents with no results are currently registered, of which nine are completed and seven trials were terminated with no results available. The findings of this review will be updated as new data are made available on the COVID‐NMA platform (covid-nma.com

#### Drug Research

**Efficacy and Safety of Tocilizumab for Coronavirus Disease 2019 (Covid-19) Patients: A Systematic Review and Meta-analysis** (2021)

Hariyanto T. I., Hardyson W., Kurniawan A.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=510bd806022a4535f8784af13cc1a0c8)

Background Currently, the data regarding the effectiveness and safety of tocilizumab as treatment for COVID-19 infection is still conflicting. This study aims to give clear evidence regarding the potential benefit and safety of tocilizumab in improving the outcome of COVID-19 patients. Methods We systematically searched the PubMed and Europe PMC database using specific keywords related to our aims until November 1 <sup>st</sup>, 2020. All articles published on COVID-19 and tocilizumab were retrieved. Statistical analysis was done using Review Manager 5.4 software. Results A total of 38 studies with a total of 13 412 COVID-19 patients were included in our analysis. Our meta-analysis showed that tocilizumab treatment is associated with reduction of mortality rate from COVID-19 [OR 0.54 (95% CI 0.42-0.71), p <0.00001, I <sup>2</sup>=79%, random-effect modelling], but did not alter the severity of COVID-19 [OR 1.05 (95% CI 0.92-1.20), p =0.47, I <sup>2</sup>=84%, random-effect modelling] and length of hospital stay [Mean Difference 1.77 days (95% CI -0.61-4.14 days), p =0.15, I <sup>2</sup>=97%, random-effect modelling]. Tocilizumab also does not associated with serious adverse events compared with standard of care treatment [OR 0.91 (95% CI 0.71-1.15), p =0.42, I <sup>2</sup>=46%, random-effect modelling]. Conclusion Our study does not support the routine use of tocilizumab for COVID-19 patients. Future studies should focus more on other potential therapies for COVID-19 patients. Copyright © 2021 American Medical Association. All rights reserved.

#### Expert review of anti infective therapy

**Pharmacological interventions for COVID-19: a systematic review of observational studies and clinical trials** (2021)

Bokharee N., Khan Y. H., Khokhar A., Mallhi T. H., Alotaibi N. H., Rasheed M.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bd724c05d5703df620950be3a1a70d8c)

INTRODUCTION: Currently there is no approved therapeutic entity for coronavirus disease 2019 (COVID-19) and clinicians are primarily relying on drug repurposing. However, findings across studies are widely disparate, making it difficult to draw firm conclusions. Since clinicians need accurate evidence to treat COVID-19, this manuscript systematically analyzed the published and ongoing studies evaluating the pharmacological interventions for COVID-19. AREAS COVERED: A systematic search of observational studies and Clinical Trials on the treatment and prevention of COVID-19 was performed by using various databases from inception to December 02, 2020. EXPERT OPINION: A total of 460 studies met the inclusion criteria. Of these, 37 were research studies, 386 were ongoing trials and 37 were completed trials. Anti-virals, steroids, anti-malarial, plasma exchange and monoclonal antibodies were the most common treatment modalities used alone or in combination in these studies. However, tocilizumab, plasma exchange and steroids have shown significant improvements in patient's clinical and radiological status. Tocilizumab reported minimum hospital stay of 2 days along with maximum recovery and patient`s stability rate. Existing literature demonstrate promising results of tocilizumab, plasma exchange and steroids among COVID-19 patients. Nevertheless, these studies are accompanied by several methodological disparities which should be considered while interpreting the results.

#### Expert review of clinical immunology

**Efficacy and safety of Tocilizumab in severe and critical COVID-19: A Systematic Review and Meta-Analysis** (2021)

Rezaei Soheila, Fatemi Behzad, Karimi Majd Zahra, Minaei Hossein, Peikanpour Mohammad, Anjidani Nassim, Taheri Ali, Dastan Farzaneh, Mosaed Reza

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=65217970303ac623df4636233e7556a0)

<h4>Objectives</h4>Currently published papers and clinical guidelines regarding the effects of tocilizumab in severe and critical COVID-19 are contradictory. The aim of this meta-analysis was to combine the results of clinical studies of different designs to investigate the efficacy and safety of tocilizumab in severely-to-critically ill COVID-19 patients.<h4>Methods</h4>A systematic search was performed in PubMed, Embase, CENTRAL, ClinicalTrials.gov, Scopus, and preprint servers up to 26 December 2020. Since a substantial heterogeneity was expected, a random-effects model was applied to calculate the pooled effect size (ES) and 95% confidence interval (CI) for each study outcome.<h4>Results</h4>Forty-five comparative studies involving 13,189 patients and 28 single-arm studies involving 1,770 patients were analyzed. The risk of mortality (RR of 0.76 [95%CI 0.65 to 0.89], P < 0.01) and intubation (RR of 0.48 [95%CI 0.24 to 0.97], P = 0.04) were lower in tocilizumab patients compared with controls. We did not find any significant difference in secondary infections, length of hospital stay, hospital discharge before day 14, and ICU admission between groups.<h4>Conclusion</h4>Tocilizumab can improve clinical outcomes and reduce mortality rates in severe to critical COVID-19 patients. Large-scale randomized controlled trials are still required to improve the statistical power of meta-analysis.

#### F1000Research

**Optimal use of tocilizumab for severe and critical COVID-19: A systematic review and meta-analysis** (2021)

Nugroho C. W., Suryantoro S. D., Yuliasih Y., Rosyid A. N., Asmarawati T. P., Andrianto L., Setiawan H. W., Mahdi B. A., Windradi C., Agustin E. D., Fajar J. K.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2ad2157c16f9b7a0209cb32ceff9b6c7)

Background: Several studies have revealed the potential use of tocilizumab in treating COVID-19 since no therapy has yet been approved for COVID-19 pneumonia. Tocilizumab may provide clinical benefits for cytokine release syndrome in COVID-19 patients. Method(s): We searched for relevant studies in PubMed, Embase, Medline, and Cochrane published from March to October 2020 to evaluate optimal use and baseline criteria for administration of tocilizumab in severe and critically ill COVID-19 patients. Research involving patients with confirmed SARS-CoV-2 infection, treated with tocilizumab and compared with the standard of care (SOC) was included in this study. We conducted a systematic review to find data about the risks and benefits of tocilizumab and outcomes from different baseline criteria for administration of tocilizumab as a treatment for severe and critically ill COVID-19 patients. Result(s): A total of 26 studies, consisting of 23 retrospective studies, one prospective study, and two randomised controlled trials with 2112 patients enrolled in the tocilizumab group and 6160 patients in the SOC group, were included in this meta-analysis. Compared to the SOC, tocilizumab showed benefits for all-cause mortality events and a shorter time until death after first intervention but showed no difference in hospital length of stay. Upon subgroup analysis, tocilizumab showed fewer all-cause mortality events when CRP level >=100 mg/L, P/F ratio 200-300 mmHg, and P/F ratio <200 mmHg. However, tocilizumab showed a longer length of stay when CRP <100 mg/L than the SOC. Conclusion(s): This meta-analysis demonstrated that tocilizumab has a positive effect on all-cause mortality. It should be cautiously administrated for optimal results and tailored to the patient's eligibility criteria. Copyright © 2021 Nugroho CW et al.

#### International immunopharmacology

**The effect of tocilizumab on COVID-19 patient mortality: A systematic review and meta-analysis of randomized controlled trials** (2021)

Lin Wei-Ting, Hung Shun-Hsing, Lai Chih-Cheng, Wang Cheng-Yi, Chen Chao-Hsien

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e633622eb9fb7bb8603141f73c025515)

<h4>Objectives</h4>This systematic review and meta-analysis of randomized controlled trials (RCTs) aimed to investigate the clinical efficacy and safety of tocilizumab for treating patients with COVID-19.<h4>Methods</h4>The PubMed, Embase, Cochrane Library, Clinicaltrials.gov, WHO International Clinical Trials Registry Platform and the preprint server of medRxiv.org were searched from their inception to February 20, 2021. Only RCTs that compared the treatment efficacy and safety of tocilizumab with the placebo or the standard of care for adult patients with COVID-19 were included in this meta-analysis. The primary outcome was 28-day mortality.<h4>Results</h4>This meta-analysis included eight RCTs which enrolled a total of 6314 patients for randomization, in which 3267 and 3047 patients were assigned to the tocilizumab and control groups, respectively. The mortality at day 28 was 24.4% and 29.9% in patients in the tocilizumab and control groups, respectively, meaning there was no significant difference observed between these two groups (OR, 0.92; 95% CI, 0.66-1.28; I<sup>2</sup> = 62). This finding did not change in the subgroup analysis according to the initial use of MV or steroid while enrollment. The patients receiving tocilizumab had a lower rate of mechanical ventilation (MV) and intensive care unit (ICU) admission at day 28 compared with the control group (MV use: OR, 0.75; 95% CI, 0.62-0.90; I<sup>2</sup> = 11; ICU admission: OR, 0.51; 95% CI, 0.28-0.92; I<sup>2</sup> = 30). There were no significant differences between these two treatment groups in terms of the risk of treatment-emergent adverse events (AEs) (OR, 1.03; 95% CI, 0.71-1.49; I<sup>2</sup> = 43), serious AEs (OR, 0.86; 95% CI, 0.67-1.12; I<sup>2</sup> = 0) or infection (OR, 0.87; 95% CI, 0.63-1.20; I<sup>2</sup> = 0).<h4>Conclusions</h4>Tocilizumab does not provide a survival benefit for patients with COVID-19, but it may help reduce the risk of MV and ICU admission. In addition, tocilizumab is a safe agent to use for the treatment of COVID-19.

#### Journal of Medical Virology

**Efficacy of tocilizumab in COVID-19: A systematic review and meta-analysis** (2021)

Aziz M., Haghbin H., Abu Sitta E., Nawras Y., Fatima R., Sharma S., Lee-Smith W., Duggan J., Kammeyer J. A., Hanrahan J., Assaly R.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7fc15ed30b2e7189a6da95d046cd96e7)

The efficacy of tocilizumab (TOC), monoclonal antibody against interleukin-6 (IL-6) receptor, in patients with coronavirus disease-2019 (COVID-19) patients has led to conflicting results. We performed a systematic review and meta-analysis to compare the efficacy of addition of TOC to standard of care (SOC) versus SOC in patients with COVID-19. We performed a comprehensive literature search of PubMed, Embase, Web of Science, WHO COVID, LitCOVID, and Cochrane databases. Pooled outcomes (overall mortality, need for mechanical ventilation, intensive care unit admission, and secondary infections) were compared using DerSimonian-Laird/Random-effects approach. Risk difference (RD), confidence interval (CI), and p values were generated. A total of 23 studies with 6279 patients (1897 in TOC and 4382 in SOC group, respectively) were included. The overall mortality was lower in TOC group compared to SOC group (RD: -0.06; CI: -0.12 to -0.01; p =.03). Subgroup analysis including studies with only severe cases revealed lower mortality (RD: -0.12; CI: -0.18 to -0.06; p <.01) and need for mechanical ventilation (RD: -0.11; CI: -0.19 to -0.02; p =.01) in TOC group compared to SOC group. The addition of TOC to SOC has the potential to reduce mortality and need for mechanical ventilation in patients with severe COVID-19. Randomized controlled trials are needed to validate this. Copyright © 2020 Wiley Periodicals LLC

#### MedRxiv

**Efficacy and safety of tocilizumab in the management of COVID-19: A systematic review and meta-analysis of observational studies** (2021)

Viswanatha Gollapalle, Male C. H. Anjana, Shylaja Hanumanthappa

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0e4098b1a50e4b7742f4fbfd584797ea)

This systematic review and meta-analysis was aimed to evaluate the efficacy and safety of tocilizumab (TCZ) in treating severe coronavirus disease 2019 (COVID-19). Methods The electronic search was performed using PubMed, Scopus, CENTRAL, and Google scholar to identify the retrospective observational reports. The studies published from 01 January 2020 to 30th September 2020. Participants were hospitalized COVID-19 patients. Interventions included tocilizumab versus placebo/standard of care. The comparison will be between TCZ versus standard of care (SOC)/placebo. Inconsistency between the studies was evaluated with I 2 and quality of the evidences were evaluated by Newcastle-Ottawa scale. <h4>Results</h4> Based on the inclusion criteria there were 24 retrospective studies involving 5686 subjects were included. The outcomes of the meta-analysis have revealed that the TCZ has reduced the mortality (M-H,RE-OR −0.11(−0.18 to −0.04) 95% CI, p =0.001, I 2 =88%) and increased the incidences of super-infections (M-H, RE-OR 1.49(1.13 to 1.96) 95% CI, p=0.004, I 2 =47%). However, there is no significant difference in ICU admissions rate (M-H, RE-OR −0.06(−0.23 to 0.12), I 2 =93%), need of MV (M-H, RE-OR of 0.00(−0.06 to 0.07), I = 74%), LOS (IV −2.86(−0.91 to 3.38), I 2 =100%), LOS-ICU (IV: −3.93(−12.35 to 4.48), I 2 =100%), and incidences of pulmonary thrombosis (M-H, RE-OR 1.01 (0.45 to 2.26), I 2 =0%) compared to SOC/control. <h4>Conclusion</h4> Based on cumulative low to moderate certainty evidence shows that TCZ could reduce the risk of mortality in hospitalized patients. However, there is no statistically significant difference observed between the TCZ and SOC/control groups in other parameters.

#### Pulmonology

**Rationale and evidence on the use of tocilizumab in COVID-19: a systematic review** (2021)

Cortegiani A., Ippolito M., Greco M., Granone V., Protti A., Gregoretti C., Giarratano A., Einav S., Cecconi M.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=9f4a5c317d8ab9be6179e4b8aa23907d)

Background: Tocilizumab is an IL-6 receptor-blocking agent proposed for the treatment of severe COVID-19. The aim of this systematic review was to describe the rationale for the use of tocilizumab for the treatment of COVID-19 and to summarize the available evidence regarding its efficacy and safety. Method(s): MEDLINE, PubMed, EMBASE, pre-print repositories (bioRxiv and medRxiv) and two trial Registries were searched for studies on the use of tocilizumab in COVID-19 or SARS-CoV-2 infection, viral pneumonia, and/or sepsis until 20th June 2020. Result(s): We identified 3 indirect pre-clinical studies and 28 clinical studies including 5776 patients with COVID-19 (13 with a comparison group, 15 single-arm). To date, no randomized trials have been published. We retrieved no studies at low risk of bias. Forty-five ongoing studies were retrieved from trial registries. Conclusion(s): There is insufficient evidence regarding the clinical efficacy and safety of tocilizumab in patients with COVID-19. Its use should be considered experimental, requiring ethical approval and clinical trial oversight. Copyright © 2020 Sociedade Portuguesa de Pneumologia

#### Research Square

**Efficacy and Safety of Tocilizumab in Patients with COVID-19: A Systematic Review and Meta-Analysis** (2021)

Li Zhenlu, Che Qianqiu, Li Mao, Liu Jianping, Du Rao, Yue Chao, Zhang Ling, Li Hongwei, Zhao Liming, Hu Weiming, Lu huimin, Xiong Junjie

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ef8183eb031f423d1688a036f143f984)

<h4>Background: </h4> Tocilizumab (TCZ) is an anti-interleukin-6 antibody that has been used to treat patients with 2019 coronavirus disease (COVID-19). Numerous retrospective studies have shown beneficial treatment efficacy. Several recent randomized clinical trials have questioned the efficacy of TCZ in patients with COVID-19. Therefore, we performed an updated systematic review and meta-analysis to explore the effectiveness and safety of tocilizumab recently used for treating patients with COVID-19. <h4>Methods: </h4> Randomized clinical trials (RCTs) and comparative studies that compared the outcomes between TCZ and standard of care (SOC) were analysed. PubMed, EMBASE, and the Cochrane Library (inception to November 20, 2020) were systematically searched. Primary outcomes included mortality and the rate of requirement for mechanical ventilation (MV). In addition, several subgroup analyses stratified by disease severity, publication type and TCZ administration were performed. <h4>Results: </h4> Three RCTs, twenty-one cohort studies and nine case-control studies including 11,206 patients were finally included. The TCZ group included 2,794 patients (24.93%) and the SOC group included 8,412 patients (75.07%). The mortality rate (>14 days) of the TCZ group, 29.63% (590/1,991), was lower than the SOC group, 41.51% (2,380/5,734) (OR 0.64, 0.57 to 0.73; p <0.00001). However, no significant difference in-14-day mortality rates was observed between the two groups (13.53% vs 22.92%, p = 0.21). Meanwhile, the rate of MV was significantly decreased in the TCZ group compared with the SOC group (OR 0.42, 0.22 to 0.83; p = 0.01). According to the results of the subgroup analysis stratified by disease severity, TCZ only reduced the mortality rate for critical patients with COVID-19 compared with SOC (OR 0.60, 0.52 to 0.71; P < 0.00001), particularly for patients in the intensive care unit (ICU) or patients requiring MV. No statistically significant increase was recognized in the rates of secondary infections or thrombosis between the two groups. <h4>Conclusions: </h4> This systematic review and meta-analysis found that the addition of tocilizumab to the SOC might reduce mortality after 14 days in patients with COVID-19, particularly critical patients requiring MV. More extensive RCTs with longer follow-up periods are needed to validate these findings.

#### Systematic Reviews in Pharmacy

**Immunosuppression drugs seize the overacting immune system by preventing the cytokine storm in covid-19 symptoms** (2021)

Cioca G., Skowron L., Zak Z., Jozwiak J., Zyska A.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=677cd597f2204712382b26236f23b2b3)

The COVID-19 over-active other diseases within the human body especially respiratory system in which cytokine storm abnormally developed that results in the excessive killing of cells within the autoimmune system. To resolve this major issue, a systematic review paper is developed whose major aim is to propose such immunosuppression drugs that can easily seize the overacted immune system by blocking the cytokine storm action within human body, by systematically overview the previous scholars' articles, case reports and authentic websites based valid data. To justify this aim, different latest and authentic medicine's journals and papers are collected by posting four major keywords like "Cytokine Storm, Cytokine Storm in COVID-19 Symptoms, Immunosuppression Drugs and Immunosuppression Drugs to prevent the Cytokine storm." The major databases of this review paper are Science Direct, Wiley Online Library, Elsevier, Springer, Google Scholar, and other related ones. After collecting the random data, the proper inclusion and exclusion criteria implemented to synchronize the data into an authentic format for content analysis. According to the previous scholars' outcomes, Cyclosporine, Tocilizumab, Canakinumab, Corticosteroids are such immunosuppression drugs that play significant role in reducing the action of cytokine storm which becomes over-activated due to COVID-19 attack; also Remdesivir based immunopathology helps to reduce the auto-immune system of COVID-19 patient. But small dose of Tocilizumab and Hydroxychloroquine caused a major side effect on the COVID-19 patient. To further justify the hypothesis, rigorous studies are needed. Also, if the more searched papers considered for a review then more authentic outcomes will be generated. Copyright © 2021 EManuscript Technologies. All rights reserved.

#### Thorax

**Systematic review and meta-analysis of anakinra, sarilumab, siltuximab and tocilizumab for COVID-19** (2021)

Khan F. A., Stewart I., Fabbri L., Moss S., Robinson K., Smyth A. R., Jenkins G.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0762375e33f83a78ef80e527d6d225fd)

BACKGROUND: There is accumulating evidence for an overly activated immune response in severe COVID-19, with several studies exploring the therapeutic role of immunomodulation. Through systematic review and meta-analysis, we assess the effectiveness of specific interleukin inhibitors for the treatment of COVID-19. METHOD(S): Electronic databases were searched on 7 January 2021 to identify studies of immunomodulatory agents (anakinra, sarilumab, siltuximab and tocilizumab) for the treatment of COVID-19. The primary outcomes were severity on an Ordinal Scale measured at day 15 from intervention and days to hospital discharge. Key secondary endpoints included overall mortality. RESULT(S): 71 studies totalling 22 058 patients were included, 6 were randomised trials. Most studies explored outcomes in patients who received tocilizumab (60/71). In prospective studies, tocilizumab was associated with improved unadjusted survival (risk ratio 0.83, 95% CI 0.72 to 0.96, I2=0.0%), but conclusive benefit was not demonstrated for other outcomes. In retrospective studies, tocilizumab was associated with less severe outcomes on an Ordinal Scale (generalised OR 1.34, 95% CI 1.10 to 1.64, I2=98%) and adjusted mortality risk (HR 0.52, 95% CI 0.41 to 0.66, I2=76.6%). The mean difference in duration of hospitalisation was 0.36 days (95% CI -0.07 to 0.80, I2=93.8%). There was substantial heterogeneity in retrospective studies, and estimates should be interpreted cautiously. Other immunomodulatory agents showed similar effects to tocilizumab, but insufficient data precluded meta-analysis by agent. CONCLUSION(S): Tocilizumab was associated with a lower relative risk of mortality in prospective studies, but effects were inconclusive for other outcomes. Current evidence for the efficacy of anakinra, siltuximab or sarilumab in COVID-19 is insufficient, with further studies urgently needed for conclusive findings. PROSPERO REGISTRATION NUMBER: CRD42020176375. Copyright © Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

## C. Original Research

1. **"Tocilizumab-an option for patients with COVID-19 associated cytokine release syndrome: A single center experience", a retrospective study-original article**  
   Chachar A. Z. K. Annals of Medicine and Surgery 2021;63 (no pagination):No page numbers.

Background: The first case of Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was diagnosed in Wuhan, China in 2019. In the first half of 2020, this disease has already converted into a global pandemic. This study aimed to find that treatment of patients with COVID-19 pneumonia with Tocilizumab or steroids was associated with better outcomes. Objective(s): To analyze the effectiveness of Tocilizumab in moderate to severe Covid-19 patients based on predefined assessment criteria. Study Settings: Single-center, Fatima Memorial Hospital, Lahore. Study design: Quasi-experimental. Duration of study: From May 12, 2020 to June 12, 2020. Patients & Methods: Sample size and technique: Sample size was 93; 33 patients were kept in the experimental group, given Tocilizumab, 8 mg/kg intravenously or 162 mg subcutaneously, and the rest of the 60 patients were given corticosteroids, methylprednisolone 80 mg/day. Consecutive sampling. Failure of therapy was labeled when patients were intubated or died, and the endpoints were failure-free survival which was the primary endpoint, and overall survival secondary at the time of discharge. Result(s): A total of 93 patients were enrolled, the Tocilizumab (TCZ) group (case) and Corticosteroid (CS) group (Control). The median age was 58 years (IQR-21), 37 (39.8%) patients with diabetes mellitus, 11 (11.8%) in the TCZ group, and 26 (28%) in the CS group. On the whole, the total median hospital stay in days was 7 with IQR (4), a total of 83 (89.2%) patients recovered successfully and discharged, 27 (29%) in the TCZ group and 56 (60.2%) in the CS group. Total 10 (10.8%) patients died, out of which 6 (6.5%) belonged to the TCZ group and 4 (4.3%) belonged to the CS group The median Oxygen requirement with IQR was 8 (9) in both the groups and in total as well, p-value (0.714). Conclusion(s): Tocilizumab is a quite effective treatment option for critically sick patients of Covid-19 by reducing their oxygen requirement drastically and so the ICU stay, median hospital stay and so the mortality as well. Clinicals trials registration: UIN # NCT04730323 Copyright © 2021

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b312d0d823e9609c7a78e7246700f2f2)

1. **A Case Series of Severe Hospitalized COVID-19 Patients Treated with Tocilizumab and Glucocorticoids: A Report from Saudi Arabian Hospital**  
   AlBahrani S. Journal of epidemiology and global health. 2021;22:No page numbers.

BACKGROUND: The clinical spectrum of COVID-19 is variable and ranges from asymptomatic, mildly symptomatic, moderately severe and severe disease. A small proportion might develop severe disease and may have cytokine storm. One of the therapeutic options to treat such cases is Tocilizumab (TCZ). In this study, we present cases of severe COVID-19 treated with TCZ and glucocorticoids and discuss the treatment responses. METHOD(S): This is a retrospective observational study of severe COVID-19 cases treated with TCZ and glucocorticoids. The case series examined the characteristics and outcome of those patients. RESULT(S): This study included 40 Severe Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) confirmed patients who received TCZ and glucocorticoids. The mean age of the included patients was 57.55 (+/-Standard deviation 12.86) years. There were 34 (85%) males, 19 (47.5%) were obese (BMI >30), 13 (32.5%) over weight, and five (12.5%) normal weight. The mean days from positive SARS-CoV-2 polymerase chain reaction (PCR) test to admission was 1.641 (+/-3.2) days. Of the patients, 18 (45%) had diabetes mellitus, 14 (35%) had hypertension. The mean days from hospital admission to ICU was 1.8 (+/-2.6), 20 (50%) required mechanical ventilation, 39 (97.5%) had received prone position, seven (17.5%) had renal replacement therapy, 13 (32.5%) required inotropes, four (10%) had plasmapheresis, one (2.5%) had intravenous immunoglobulin, all patients received steroid therapy, and the majority 31 (77.5%) did not receive any anti-viral therapy. Of all the patients, six (15%) died, 28 (70%) were discharged and six (15%) were still in hospital. CONCLUSION(S): The overall mortality rate was lower than those cited in meta-analysis. As our understanding of the COVID-19 continues, the approach and therapeutics are also evolving. Copyright © 2021 The Authors. Published by Atlantis Press International B.V.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c702e8cc0932e0667fcd1947e9dae1fa)

1. **A retrospective matched cohort single-center study evaluating outcomes of COVID-19 and the impact of immunomodulation on COVID-19-related cytokine release syndrome in solid organ transplant recipients**  
   Ringer M. Transplant Infectious Disease. 2021;:No page numbers.

This retrospective matched cohort study describes 30 solid organ transplant (SOT) patients with Coronavirus Disease 2019 (COVID-19) matched 1:2 to 60 non-SOT patients (control group) based on age, body mass index (BMI), and comorbidities (hypertension and diabetes mellitus with hemoglobin A1c > 8.0%). The SOT group had a higher proportion of cardiovascular disease (P <.05). During the index hospitalization, there were no significant differences with regard to disease severity or critical care needs (mechanical intubation, vasopressors, and renal replacement therapy). At 28 days, 4 (13%) patients died in the SOT group and 8 (13%) patients died in the control group (P = 1.0). Nineteen patients received tocilizumab in the SOT group compared to 29 patients in the control group. Among these patients, interleukin-6 (IL-6) and soluble interleukin-2 receptor (sIL2R) levels increased after tocilizumab and interleukin-10 (IL-10) levels decreased after tocilizumab. Overall, SOT patients had comparable mortality to non-SOT patients, although numerically more SOT patients received tocilizumab (63% vs 48%) and steroids (37% vs 20%). Larger, multi-center studies are needed to ascertain these findings. Lastly, the complex cytokine release syndrome in COVID-19 remains an area of intense research and the analysis of key interleukin levels (IL-6, IL-10, and sIL2R) in this study contributes to the understanding of this process. Copyright © 2021 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=eb16bc2973e3e6a254caa612aade4436)

1. **Administration of tocilizumab to patients with high concentrations of IL-6 in the course of COVID-19 is associated with a better prognosis**  
   Flisiak Robert 2021;:No page numbers.

&lt;h4&gt;Summary&lt;/h4&gt; &lt;h4&gt;Background&lt;/h4&gt; Despite the direct viral activity, the pathogenesis of coronavirus disease 2019 (COVID-19) includes an overproduction of cytokines including interleukin 6 (IL-6). Therefore tocilizumab (TCZ), a monoclonal antibody against IL-6 receptors, became considered as a possible therapeutic option. &lt;h4&gt;Methods&lt;/h4&gt; Patients were selected from the SARSTer national database, which included 2332 individuals with COVID-19 and the current study included 825 adult patients with moderate to severe course. The retrospective analysis was performed in 170 patients treated with TCZ and 655 without this medication or any other anti-cytokine therapy. The end-points of treatment effectiveness were a rate of death, need for mechanical ventilation, and clinical improvement. &lt;h4&gt;Results&lt;/h4&gt; Patients treated with TCZ were balanced compared to non-TCZ regarding gender, age, BMI, and prevalence of coexisting conditions. The reduced death rate was demonstrated in patients treated with TCZ and baseline IL-6 &gt;100 pg/ml (hazard ratio [HR]: 0.27, 95% confidence interval [CI]:0.10-0.78), or those needing oxygen supplementations who worsened within 7 days of hospitalization (HR: 0.38, 95% CI:0.16-0.88). The best effectiveness of TCZ was achieved in patients with a combination of baseline IL-6&gt;100 pg/ml and either SpO2≤90% (HR for death, mechanical ventilation, and clinical improvement after 21 or 28 days: 0.07, 0.14, 5.53, 5.18 respectively) or requiring oxygen supplementation (HR for death and clinical improvement after 21 or 28 days, 0.18, 2.66, 2.85 respectively). &lt;h4&gt;Conclusions&lt;/h4&gt; Tocilizumab administered for COVID-19 in patients with a baseline concentration of IL-6&gt;100 pg/ml is associated with reduced mortality and faster clinical improvement, particularly if there is a need for oxygen supplementation due to SpO2≤90%.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=88108c1c79ec495ab835a8b049d1567a)

1. **An unfavourable outcome following switching intravenous abatacept and tocilizumab to subcutaneous forms during the COVID-19 pandemic**  
   Gupta Rishi Rheumatology (Oxford, England) 2021;60:977-979.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e1d8cb09e5e67ae65f58e5d7f0775c56)

1. **Anakinra after treatment with corticosteroids alone or with tocilizumab in patients with severe COVID-19 pneumonia and moderate hyperinflammation. A retrospective cohort study**  
   Aomar-Millan I. F. Internal and emergency medicine. 2021;05:No page numbers.

INTRODUCTION: Little evidence appears to exist for the use of anakinra, a recombinant interleukin-1 receptor antagonist, after non-response to treatment with corticosteroids alone or combined with tocilizumab in patients with severe COVID-19 pneumonia and moderate hyperinflammatory state. PATIENTS AND METHODS: A retrospective observational cohort study was carried out involving 143 patients with severe COVID-19 pneumonia and moderate hyperinflammation. They received standard therapy along with pulses of methylprednisolone (group 1) or methylprednisolone plus tocilizumab (group 2), with the possibility of receiving anakinra (group 3) according to protocol. The aim of this study was to assess the role of anakinra in the clinical course (death, admission to the intensive care ward) during the first 60 days after the first corticosteroid pulse. Clinical, laboratory, and imaging characteristics as well as infectious complications were also analyzed. RESULT(S): 74 patients (51.7%) in group 1, 59 (41.3%) patients in group 2, and 10 patients (7%) in group 3 were included. 8 patients (10.8%) in group 1 died, 6 (10.2%) in group 2, and 0 (0%) in group 3. After adjustment for age and clinical severity indices, treatment with anakinra was associated with a reduced risk of mortality (adjusted hazard ratio 0.518, 95% CI 0.265-0.910; p=0.0437). Patients in group 3 had a lower mean CD4 count after 3 days of treatment. No patients in this group presented infectious complications. CONCLUSION(S): In patients with moderate hyperinflammatory state associated with severe COVID-19 pneumonia, treatment with anakinra after non-response to corticosteroids or corticosteroids plus tocilizumab therapy may be an option for the management of these patients and may improve their prognosis.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=41805745e43f983e461ff59c2ca6902e)

1. **Anti-IL6 treatment of serious COVID-19 disease: A monocentric retrospective experience**  
   Castelnovo L. Medicine 2021;100:e23582.

ABSTRACT: COVID-19 is causing a high influx of patients suffering from serious respiratory complications leading the necessity to find effective therapies. These patients seem to present with cytokine perturbation and high levels of IL6. Tocilizumab and sarilumab could be effective in this condition.We retrospectively collected data about 112 consecutive hospitalized in a single center.Fifty (IL6 group) treated with tocilizumab (8 mg/kg intravenously [IV], 2 infusions 12 hours apart) or sarilumab 400 mg IV once and 62 treated with the standard of care but not anti-cytokine drugs (CONTROL group).To determine whether anti-IL6 drugs are effective in improving prognosis and reducing hospitalization times and mortality in COVID-19 pneumonia.To date 84% (42/50) of IL6 group patients have already been discharged and only 2/50 are still recovered and intubated in intensive care. Six/fifty patients (12%) died: 5/6 due to severe respiratory failure within a framework of severe acute respiratory distress syndrome (ARDS), 1 suffered an acute myocardial infarction, and 1 died of massive pulmonary thromboembolism. There were no adverse treatment events or infectious complications. Compared to the CONTROL group they showed a lower mortality rate (12% versus 43%), for the same number of complications and days of hospitalization.Anti-IL6 drugs seem to be effective in the treatment of medium to severe forms of COVID-19 pneumonia reducing the risk of mortality due to multi-organ failure, acting at the systemic level and reducing inflammation levels and therefore microvascular complications. However, it is essential to identify the best time for treatment, which, if delayed, is rendered useless as well as counterproductive. Further studies and ongoing clinical trials will help us to better define patients eligible as candidates for more aggressive intervention. Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ffa2132492548f271cfe2ded8e4cc908)

1. **Association between Early Treatment with Tocilizumab and Mortality among Critically Ill Patients with COVID-19**  
   Gupta S. JAMA Internal Medicine 2021;181:41-51.

Importance: Therapies that improve survival in critically ill patients with coronavirus disease 2019 (COVID-19) are needed. Tocilizumab, a monoclonal antibody against the interleukin 6 receptor, may counteract the inflammatory cytokine release syndrome in patients with severe COVID-19 illness. Objective(s): To test whether tocilizumab decreases mortality in this population. Design, Setting, and Participant(s): The data for this study were derived from a multicenter cohort study of 4485 adults with COVID-19 admitted to participating intensive care units (ICUs) at 68 hospitals across the US from March 4 to May 10, 2020. Critically ill adults with COVID-19 were categorized according to whether they received or did not receive tocilizumab in the first 2 days of admission to the ICU. Data were collected retrospectively until June 12, 2020. A Cox regression model with inverse probability weighting was used to adjust for confounding. Exposures: Treatment with tocilizumab in the first 2 days of ICU admission. Main Outcomes and Measures: Time to death, compared via hazard ratios (HRs), and 30-day mortality, compared via risk differences. Result(s): Among the 3924 patients included in the analysis (2464 male [62.8%]; median age, 62 [interquartile range {IQR}, 52-71] years), 433 (11.0%) received tocilizumab in the first 2 days of ICU admission. Patients treated with tocilizumab were younger (median age, 58 [IQR, 48-65] vs 63 [IQR, 52-72] years) and had a higher prevalence of hypoxemia on ICU admission (205 of 433 [47.3%] vs 1322 of 3491 [37.9%] with mechanical ventilation and a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen of <200 mm Hg) than patients not treated with tocilizumab. After applying inverse probability weighting, baseline and severity-of-illness characteristics were well balanced between groups. A total of 1544 patients (39.3%) died, including 125 (28.9%) treated with tocilizumab and 1419 (40.6%) not treated with tocilizumab. In the primary analysis, during a median follow-up of 27 (IQR, 14-37) days, patients treated with tocilizumab had a lower risk of death compared with those not treated with tocilizumab (HR, 0.71; 95% CI, 0.56-0.92). The estimated 30-day mortality was 27.5% (95% CI, 21.2%-33.8%) in the tocilizumab-treated patients and 37.1% (95% CI, 35.5%-38.7%) in the non-tocilizumab-treated patients (risk difference, 9.6%; 95% CI, 3.1%-16.0%). Conclusions and Relevance: Among critically ill patients with COVID-19 in this cohort study, the risk of in-hospital mortality in this study was lower in patients treated with tocilizumab in the first 2 days of ICU admission compared with patients whose treatment did not include early use of tocilizumab. However, the findings may be susceptible to unmeasured confounding, and further research from randomized clinical trials is needed.. Copyright © 2021 American Medical Association. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ec135bf2ae2674fceb9e123e9967f9b3)

1. **Benefits of early aggressive immunomodulatory therapy (tocilizumab and methylprednisolone) in COVID-19: Single center cohort study of 685 patients**  
   Luis Buzon-Martín Journal of translational autoimmunity 2021;4:100086.

&lt;h4&gt;Introduction&lt;/h4&gt;A growing evidence suggests that immune dysregulation and thrombotic phenomena are key features in the pathophysiology of COVID-19. Apart from antivirals and respiratory support, anticoagulants, corticoids and immunomodulators are increasingly being prescribed, especially for more severe cases. We describe the clinical outcome of a large cohort of patients preferentially treated with glucocorticoids and interleukin inhibitors.&lt;h4&gt;Methods&lt;/h4&gt;Single center and retrospective case series. Adult patients admitted with COVID-19 related respiratory insufficiency were included. Patients who died within 2 days after admission and those testing positive but asymptomatic were excluded. We defined two study periods: from March 3rd to March 31 st, 2020 (beginning of epidemic until peak of incidence) and April 1 st to May 7 th, 2020 (second half of epidemic). The majority of patients received respiratory support, combinations of antimicrobials, anticoagulants, corticoids and interleukin inhibitors. Antivirals were preferentially given in the first period. The clinical outcome (death and ventilator dependency) of both periods was compared.&lt;h4&gt;Results&lt;/h4&gt;From March 3 rd to May 7 th, 685 patients were included for analysis (58.4% males, mean age 68.9 years). Patients in the first period (n ​= ​408) were younger (66.6 vs 71.1 years, p ​= ​0.003), presented lower mean P a O 2/F i O2 ratio at admission (256.5 vs 270.4 ​mm Hg,p ​= ​0.0563), higher ferritin (1520 vs 1221 ​ng/ml, p ​= ​0.01), higher IL-6 (679 vs 194 ​pg/ml, p ​&lt; ​0.0001) and similar D-dimer levels (3.59 vs 3.39 ​μg/mL, p ​= ​0.65) compared to the second period (n ​= ​277). Lopinavir/ritonavir and interferon were preferentially given in the first period (23.8% and 32% vs 1.8% and 11.9%, p ​&lt; ​0.0001). Use of corticoids (88.2% vs 87.4%, p ​= ​0,74) and tocilizumab (26.29 vs 20.22% p ​= ​0.06) were similarly administered in both periods. Patients in the second period needed less mechanical ventilation (4.9% vs 16.9%, p ​&lt; ​0.0001), fewer ICU admission (6.1% vs 20.1%,p ​&lt; ​0.0001) and showed similar mortality (17.7% vs 15.4%, p ​= ​0.43). Infectious and thrombotic complications were comparable in both periods (both around 8%, with no statistical difference). Patients treated with tocilizumab (n ​= ​163) had lower mortality rate compared to those untreated under the same indication (7.9% vs 24.2%, p ​&lt; ​0.0001).&lt;h4&gt;Conclusions&lt;/h4&gt;In this large retrospective COVID-19 in-hospital cohort, lopinavir/ritonavir and interferon showed no significant impact on survival. Extensive use of corticosteroids and tocilizumab resulted in good overall outcome and showed acceptable complication rates.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0855cadf1acfe4235f2328a563953f09)

1. **Biological agents for rheumatic diseases in the outbreak of COVID-19: Friend or foe?**  
   Santos C. S. RMD Open 2021;7 (1) (no pagination):No page numbers.

Background The recent outbreak of COVID-19 has raised concerns in the rheumatology community about the management of immunosuppressed patients diagnosed with inflammatory rheumatic diseases. It is not clear whether the use of biological agents may suppose a risk or protection against SARS-CoV-2 infection; however, it has been suggested that severe respiratory forms of COVID-19 occur as a result of exacerbated inflammation status and cytokine production. This prompted the use of interleukin 6 (IL-6) (tocilizumab and sarilumab) and IL-1 inhibitors (anakinra) in severe COVID-19 disease and more recently JAK1/2 inhibitor (baricitinib). Therefore, patients with rheumatic diseases provide a great opportunity to learn about the use of biological agents as protective drugs against SARS-CoV-2. Objectives To estimate COVID-19 infection rate in patients treated with biological disease-modifying antirheumatic drugs (bDMARDs) for inflammatory rheumatic diseases (RMD), determine the influence of biological agents treatment as risk or protective factors and study the prognosis of patients with rheumatic diseases receiving biological agents compared to the general population in a third-level hospital setting in Leon, Spain. Methods We performed a retrospective observational study including patients seen at our rheumatology department who received bDMARDs for rheumatic diseases between December 1st 2019 and December 1st 2020, and analysed COVID-19 infection rate. All patients who attended our rheumatology outpatient clinic with diagnosis of inflammatory rheumatic disease receiving treatment with biological agents were included. Main variable was the hospital admission related to COVID-19. The covariates were age, sex, comorbidities, biological agent, duration of treatment, mean dose of glucocorticoids and need for intensive care unit. We performed an univariate and multivariate logistic regression models to assess risk factors of COVID-19 infection. Results There were a total of 4464 patients with COVID-19 requiring hospitalisation. 40 patients out of a total of 820 patients with rheumatic diseases (4.8%) receiving bDMARDs contracted COVID-19 and 4 required hospital care. Crude incidence rate of COVID-19 requiring hospital care among the general population was 3.6%, and it was 0.89% among the group with underlying rheumatic diseases. 90% of patients receiving bDMARDS with COVID-19 did not require hospitalisation. Out of the 4464 patients, 869 patients died, 2 of which received treatment with biological agents. Patients with rheumatic diseases who tested positive for COVID-19 were older (female: median age 60.8 IQR 46-74; male: median age 61.9 IQR 52-70.3) than those who were negative for COVID-19 (female: median age 58.3 IQR 48-69; male: median age 56.2 IQR 47-66), more likely to have hypertension (45% vs 26%, OR 2.25 (CI 1.18-4.27),p 0.02), cardiovascular disease (23 % vs 9.6%, OR 2.73 (1.25-5.95), p 0.02), be smokers (13% vs 4.6%, OR 2.95 (CI 1.09-7.98), p 0.04), receiving treatment with rituximab (20% vs 8%, 2.28 (CI 1.24-6.32), p 0.02) and a higher dose of glucocorticoids (OR 2.5 (1.3-10.33, p 0.02) and were less likely to be receiving treatment with IL-6 inhibitors (2.5% vs 14%, OR 0.16, (CI 0.10-0.97, p 0.03). When exploring the effect of the rest of the therapies between groups (affected patients vs unaffected), we found no significant differences in bDMARD proportions. IL-1 inhibitors, IL-6 inhibitors, JAK inhibitors and belimumab-treated patients showed the lowest incidence of COVID-19 among adult patients with rheumatic diseases. We found no differences in sex or rheumatological disease between patients who tested positive for COVID-19 and patients who tested negative. Conclusions Overall, the use of biological disease-modifying antirheumatic drugs (bDMARDs) does not associate with severe manifestations of COVID-19. Patients with rheumatic disease diagnosed with COVID-19 were more likely to be receiving a higher dose of glucocorticoids and treatment with rituximab. IL-6 inhibitors may have a protective effect. Copyright © Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e5907f49dca68356f14b2d991906717c)

1. **Characteristics of the First 102 Severe COVID-19 Cases Treated With Convalescent Plasma or Tocilizumab or Both in Al-Nahdha Hospital, Oman**  
   Al Harthi Saud Health services research and managerial epidemiology 2021;8:2333392820986639.

&lt;h4&gt;Background&lt;/h4&gt;In the absence of an effective vaccine, the coronavirus disease (COVID-19) continues to cause more deaths. Evidence on the effectiveness of various COVID-19 management plans is inconclusive. This paper describes the characteristics of the first 102 severe COVID-19 in-patients treated with Convalescent Plasma (CP) therapy or Tocilizumab or both at Al-Nahdha hospital in Muscat, Oman. Additionally, differences in requiring critical care were explored across the treatment groups.&lt;h4&gt;Methods&lt;/h4&gt;Data of all the positive cases in Al-Nahdha hospital were retrieved from the electronic health information system retrospectively from April 1st to July 31st 2020. The required information was recorded in a bespoke sheet and exported to SPSS for further analysis. The primary outcome was defined as improved (discharged home) vs worsening (requiring critical care).&lt;h4&gt;Results&lt;/h4&gt;Out of the 102 severe cases of COVID-19 admissions, 20.6%, 59.8% and 20.6% received CP, Tocilizumab and both respectively. In average, CP was introduced at day 3.7(4.8) whereas Tocilizumab at day 7.8(5.1) from admission. The between-group differences in the proportion of patient who improved vs worsened were not significant (&lt;i&gt;P&lt;/i&gt; = 0.7). However, the within-group difference in the proportion of patient who improved vs worsened was significant in the Tocilizumab treatment group (&lt;i&gt;P&lt;/i&gt; = 0.03). All socio-demographics were not significantly different across the treatment groups. Most improvements in the studies parameters [CBC (total WBC, Lymph and neutrophil counts), oxygen and immune response "cytokine storm" parameters] post-treatment was attributed to the use of Tocilizumab. There was a statistically significant difference in the mean hospital stay between the improved and worsened cases across all treatment categories [at the population level: 8.2(5.0) improved vs 4.7(3.7) worsened-&lt;i&gt;P&lt;/i&gt; &lt; 0.001].&lt;h4&gt;Conclusions&lt;/h4&gt;Results from this study provided baseline information about the characteristics of confirmed COVID-19 cases in Al-Nahdha hospital who received CP, Tocilizumab or both. Results obtained seems to be promising in preventing critical care, especially for Tocilizumab. However, further randomized studies are needed.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e9f4a6a0118b3a2883681f02814a8011)

1. **Clinical course of severe COVID19 treated with tocilizumab and antivirals post-allogeneic stem cell transplant with extensive chronic GVHD**  
   Mirgh Sumeet Transplant infectious disease : an official journal of the Transplantation Society 2021;:e13576.

Recipients of allogeneic hematopoietic stem cell transplantation (allo-HSCT) are an immunocompromised group who are likely to develop severe complications and mortality because of coronavirus disease 2019 (COVID-19). We report here a 61-year-old male patient of primary myelofibrosis who underwent an allo-HSCT 6 years earlier, had chronic graft-versus-host disease (cGVHD) involving the liver, lung, eyes, and skin, (with recurrent episodes of pulmonary infections) who developed severe COVID-19. The patient was treated with tocilizumab, and a combination of lopinavir/ritonavir, ribavirin, interferon-β1b. He was discharged after 31 days with full recovery. Tocilizumab, a humanized monoclonal antibody against IL6, has been shown to benefit respiratory manifestations in severe COVID19. However, this is first report, to our knowledge, of its use and benefit in a post HSCT recipient.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=892795db3ea35bacfb1c2a1aa0629e51)

1. **Clinical course of severe patients with COVID-19 treated with tocilizumab: report from a cohort study in Spain**  
   Chamorro-de-Vega E. Expert Review of Clinical Pharmacology 2021;14:249-260.

Background: We report the long-term outcomes, changes in laboratory parameters, the incidence of secondary nosocomial infections and treatment cost of a Spanish cohort of patients with severe COVID-19 that received tocilizumab (TCZ). Method(s): Retrospective cohort of PCR confirmed adult patients who received TCZ from March 1 to 24, 2020 in a tertiary hospital was analyzed. Patients were followed up until 10 May 2020. Result(s): We included 162 patients (median age 64 years; 70.4% male). At time of TCZ administration, 48.1% of patients were on invasive mechanical ventilation (IMV). Over a median follow-up of 53 days, 46.9% of patients were discharge in good conditions and 19.8% were still hospitalized. The overall mortality was 33.3%, being higher in patients on IMV than those who did not (46.2% vs 26.7%, P < 0.001). A significant improvement in the lymphocyte count, C-reactive protein, lactate dehydrogenase, and D-dimer was observed. Overall, 43.2% patients presented nosocomial infections, causing death in 8%. Infections were more prevalent in ICU units (63.0% vs 17.1%, P < 0.001). The total cost of TCZ was 371,784. Conclusion(s): Among the patients who used TCZ, one third died, regardless the improvement in some inflammatory biomarkers. The incidence of secondary nosocomial infections was high. Copyright © 2021 Informa UK Limited, trading as Taylor & Francis Group.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ecc73905758530b05fcb1b3609a403f1)

1. **Combination of Tocilizumab and Steroids to Improve Mortality in Patients with Severe COVID-19 Infection: A Spanish, Multicenter, Cohort Study**  
   Ruiz-Antoran B. Infectious Diseases and Therapy 2021;10:347-362.

Background: We aimed to determine the impact of tocilizumab use on severe COVID-19 (coronavirus disease 19) pneumonia mortality. Method(s): We performed a multicentre retrospective cohort study in 18 tertiary hospitals in Spain from March to April 2020. Consecutive patients admitted with severe COVID-19 treated with tocilizumab were compared to patients not treated with tocilizumab, adjusting by inverse probability of the treatment weights (IPTW). Tocilizumab's effect in patients receiving steroids during the 48 h following inclusion was analysed. Result(s): During the study period, 506 patients with severe COVID-19 fulfilled the inclusion criteria. Among them, 268 were treated with tocilizumab and 238 patients were not. Median time to tocilizumab treatment from onset of symptoms was 11 days [interquartile range (IQR) 8-14]. Global mortality was 23.7%. Mortality was lower in patients treated with tocilizumab than in controls: 16.8% versus 31.5%, hazard ratio (HR) 0.514 [95% confidence interval (95% CI) 0.355-0.744], p < 0.001; weighted HR 0.741 (95% CI 0.619-0.887), p = 0.001. Tocilizumab treatment reduced mortality by 14.7% relative to no tocilizumab treatment [relative risk reduction (RRR) 46.7%]. We calculated a number necessary to treat of 7. Among patients treated with steroids, mortality was lower in those treated with tocilizumab than in those treated with steroids alone [10.9% versus 40.2%, HR 0.511 (95% CI 0.352-0.741), p = 0.036; weighted HR 0.6 (95% CI 0.449-0.804), p < 0.001] (interaction p = 0.094). Conclusion(s): These results show that survival of patients with severe COVID-19 is higher in those treated with tocilizumab than in those not treated and that tocilizumab's effect adds to that of steroids administered to non-intubated patients with COVID-19 during the first 48 h of presenting with respiratory failure despite oxygen therapy. Randomised controlled studies are needed to confirm these results. Trial registration: European Union electronic Register of Post-Authorization Studies (EU PAS Register) identifier, EUPAS34415 Copyright © 2020, The Author(s).

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=69f671b91bf989af08bc0d3d5ce3ca78)

1. **Combination therapy of Tocilizumab and steroid for management of COVID-19 associated cytokine release syndrome: A single center experience from Pune, Western India**  
   Dravid Ameet 2021;:No page numbers.

&lt;h4&gt;Background&lt;/h4&gt; Cytokine release syndrome (CRS) or cytokine storm is thought to be the cause of inflammatory lung damage, worsening pneumonia and death in patients with COVID-19. Steroids (Methylprednisolone or Dexamethasone) and Tocilizumab (TCZ), an interleukin-6 receptor antagonist, are approved for the treatment of CRS in India. The aim of this study was to evaluate the efficacy and safety of combination therapy of TCZ and steroids in COVID-19 associated CRS. &lt;h4&gt;Methods&lt;/h4&gt; This retrospective cohort study was conducted at a tertiary level private hospital in Pune, India between 2 nd April and 2 nd November 2020. All patients administered TCZ and steroids for treatment of CRS were included. The primary endpoint was incidence of all-cause mortality. Secondary outcomes studied were need for mechanical ventilation and incidence of infectious complications. Baseline and time-dependent risk factors significantly associated with death were identified by Relative risk estimation. &lt;h4&gt;Results&lt;/h4&gt; Out of 2831 admitted patients, 515 (24.3% females) were administered TCZ and steroids. Median age of the cohort was 57 (IQR: 46.5, 66) years. Almost 72 % patients had preexisting co-morbidities. Median time to TCZ administration since onset of symptoms was 9 days (IQR: 7, 11). 63% patients needed intensive care unit (ICU) admission. Mechanical ventilation was required in 242 (47%) patients. Of these, 44.2% (107/242) recovered and were weaned off the ventilator. There were 135 deaths (26.2%), while 380 patients (73.8%) had clinical improvement. Infectious complications like hospital acquired pneumonia, bloodstream bacterial and fungal infections were observed in 2.13 %, 2.13 % and 0.06 % patients respectively. Age ≥ 60 years (p=0.014), presence of co-morbidities like hypertension (p = 0.011), IL-6 ≥ 100 pg/ml (p = 0.002), D-dimer ≥ 1000 ng/ml (p &lt; 0.0001), CT severity index ≥ 18 (p &lt; 0.0001) and systemic complications like lung fibrosis (p = 0.019), cardiac arrhythmia (p &lt; 0.0001), hypotension (p &lt; 0.0001) and encephalopathy (p &lt; 0.0001) were associated with increased risk of death. &lt;h4&gt;Conclusions&lt;/h4&gt; Combination therapy of TCZ and Steroids is likely to be safe and effective in the management of COVID-19 associated cytokine release syndrome. Efficacy of this anti-inflammatory combination therapy needs to be validated in randomized controlled clinical trials.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b9765a49b06c26b011e011f4a4d23784)

1. **Combination therapy with tocilizumab and corticosteroids for aged patients with severe COVID-19 pneumonia: A single-center retrospective study**  
   Lopez-Medrano F. International Journal of Infectious Diseases 2021;105:487-494.

Background: The role of combination immunomodulatory therapy with systemic corticosteroids and tocilizumab (TCZ) for aged patients with COVID-19-associated cytokine release syndrome remains unclear. Method(s): A retrospective single-center study was conducted on consecutive patients aged >=65 years who developed severe COVID-19 between 03 March and 01 May 2020 and were treated with corticosteroids at various doses (methylprednisolone 0.5 mg/kg/12 h to 250 mg/24 h), either alone (CS group) or associated with intravenous tocilizumab (400-600 mg, one to three doses) (CS-TCZ group). The primary outcome was all-cause mortality by day +14, whereas secondary outcomes included mortality by day +28 and clinical improvement (discharge and/or a >=2 point decrease on a 6-point ordinal scale) by day +14. Propensity score (PS)-based adjustment and inverse probability of treatment weights (IPTW) were applied. Result(s): Totals of 181 and 80 patients were included in the CS and CS-TCZ groups, respectively. All-cause 14-day mortality was lower in the CS-TCZ group, both in the PS-adjusted (hazard ratio [HR]: 0.34; 95% confidence interval [CI]: 0.17-0.68; P = 0.002) and IPTW-weighted models (odds ratio [OR]: 0.38; 95% CI: 0.21-0.68; P = 0.001). This protective effect was also observed for 28-day mortality (PS-adjusted HR: 0.38; 95% CI: 0.21-0.72; P = 0.003). Clinical improvement by day +14 was higher in the CS-TCZ group with IPTW analysis only (OR: 2.26; 95% CI: 1.49-3.41; P < 0.001). The occurrence of secondary infection was similar between both groups. Conclusion(s): The combination of corticosteroids and TCZ was associated with better outcomes among patients aged >=65 years with severe COVID-19. Copyright © 2021 The Authors

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=edb046baf1dcc65ac6b246da6f36d879)

1. **Comparative Survival Analysis of Immunomodulatory Therapy for Coronavirus Disease 2019 Cytokine Storm**  
   Narain S. Chest 2021;159:933-948.

Background: Cytokine storm is a marker of coronavirus disease 2019 (COVID-19) illness severity and increased mortality. Immunomodulatory treatments have been repurposed to improve mortality outcomes. Research Question: Do immunomodulatory therapies improve survival in patients with COVID-19 cytokine storm (CCS)? Study Design and Methods: We conducted a retrospective analysis of electronic health records across the Northwell Health system. COVID-19 patients hospitalized between March 1, 2020, and April 24, 2020, were included. CCS was defined by inflammatory markers: ferritin, > 700 ng/mL; C-reactive protein (CRP), > 30 mg/dL; or lactate dehydrogenase (LDH), > 300 U/L. Patients were subdivided into six groups: no immunomodulatory treatment (standard of care) and five groups that received either corticosteroids, anti-IL-6 antibody (tocilizumab), or anti-IL-1 therapy (anakinra) alone or in combination with corticosteroids. The primary outcome was hospital mortality. Result(s): Five thousand seven hundred seventy-six patients met the inclusion criteria. The most common comorbidities were hypertension (44%-59%), diabetes (32%-46%), and cardiovascular disease (5%-14%). Patients most frequently met criteria with high LDH (76.2%) alone or in combination, followed by ferritin (63.2%) and CRP (8.4%). More than 80% of patients showed an elevated D-dimer. Patients treated with corticosteroids and tocilizumab combination showed lower mortality compared with patients receiving standard-of-care (SoC) treatment (hazard ratio [HR], 0.44; 95% CI, 0.35-0.55; P < .0001) and with patients treated with corticosteroids alone (HR, 0.66; 95% CI, 0.53-0.83; P = .004) or in combination with anakinra (HR, 0.64; 95% CI, 0.50-0.81; P = .003). Corticosteroids when administered alone (HR, 0.66; 95% CI, 0.57-0.76; P < .0001) or in combination with tocilizumab (HR, 0.43; 95% CI, 0.35-0.55; P < .0001) or anakinra (HR, 0.68; 95% CI, 0.57-0.81; P < .0001) improved hospital survival compared with SoC treatment. Interpretation(s): The combination of corticosteroids with tocilizumab showed superior survival outcome when compared with SoC treatment as well as treatment with corticosteroids alone or in combination with anakinra. Furthermore, corticosteroid use either alone or in combination with tocilizumab or anakinra was associated with reduced hospital mortality for patients with CCS compared with patients receiving SoC treatment. Copyright © 2020 American College of Chest Physicians

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1a5dc03ea42d5ae4612f56de89be46ad)

1. **Compassionate use of tocilizumab in severe SARS-CoV2 pneumonia**  
   Gorgolas Hernandez-Mora M. International Journal of Infectious Diseases 2021;102:303-309.

Introduction: Tocilizumab (TCZ) is an interleukin-6 receptor antagonist, which has been used for the treatment of severe SARS-CoV-2 pneumonia (SSP), which aims to ameliorate the cytokine release syndrome (CRS) induced acute respiratory distress syndrome (ARDS). However, there are no consistent data about who might benefit most from it. Method(s): We administered TCZ on a compassionate-use basis to patients with SSP who were hospitalized (excluding intensive care and intubated cases) and who required oxygen support to have a saturation >93%. The primary endpoint was intubation or death after 24 h of its administration. Patients received at least one dose of 400 mg intravenous TCZ from March 8, 2020 to April 20, 2020. Result(s): A total of 207 patients were studied and 186 analyzed. The mean age was 65 years and 68% were male patients. A coexisting condition was present in 68% of cases. Prognostic factors of death were older age, higher IL-6, D-dimer and high-sensitivity C-reactive protein (HSCRP), lower total lymphocytes, and severe disease that requires additional oxygen support. The primary endpoint (intubation or death) was significantly worst (37% vs 13%, p < 0.001) in those receiving the drug when the oxygen support was high (FiO2 >0.5%). Conclusion(s): TCZ is well tolerated in patients with SSP, but it has a limited effect on the evolution of cases with high oxygen support needs. Copyright © 2020 The Authors

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=974b8b1fe60a02d0cf17b490c3aaab14)

1. **Corrigendum to: Outcomes in patients with severe COVID-19 disease treated with tocilizumab: a case-controlled study**  
   Rojas-Marte G. QJM : monthly journal of the Association of Physicians. 2021;14:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5324c0bb95c34c78dc833e8383ef3916)

1. **Corticosteroids and tocilizumab reduce in-hospital mortality in severe COVID-19 pneumonia: a retrospective study in a Spanish hospital**  
   Van den Eynde E. Infectious Diseases 2021;53:291-302.

Background: There is an urgent need to reduce mortality of COVID-19. We examined if corticosteroids and tocilizumab reduce risk for death in patients with severe pneumonia caused by SARS-CoV-2. Method(s): A retrospective cohort study was performed in a single university hospital. All adult patients admitted with confirmed severe COVID-19 pneumonia from 9 March to 9 April 2020 were included. Severe pneumonia was defined as multi-lobar or bilateral pneumonia and a ratio of oxygen saturation by pulse oximetry to the fraction of inspired oxygen (SpFi)<315. All patients received antiviral and antibiotic treatment. From March 26, patients also received immunomodulatory treatment with corticosteroids (methylprednisolone 250 mg/day for 3 days), or tocilizumab or both. In-hospital mortality in the entire cohort and in a 1:1 matched cohort sub-analysis was evaluated. Result(s): 255 patients were included, 118 received only antiviral and antibiotic treatment while 137, admitted after March 26, also received immunomodulators. In-hospital mortality of patients on immunomodulatory treatment was significantly lower than in those without [47/137(34.3%) vs. 69/118(58.5%), (p <.001)]. The risk of death was 0.44 (CI, 0.26-0.76) in patients receiving corticosteroids alone and 0.292 (CI, 0.18-0.47) in those treated with corticosteroids and tocilizumab. In the sub-analysis with 202 matched patients, the risk of death was 0.356 (CI 0.179-0.707) in patients receiving corticosteroids alone and 0.233 (0.124-0.436) in those treated with the combination. Conclusion(s): Combined treatment with corticosteroids and tocilizumab reduced mortality with about 25% in patients with severe COVID-19 pneumonia. Corticosteroids alone also resulted in lower in-hospital mortality rate compared to patients receiving only antiviral and antibiotic treatment. Corticosteroids alone or combined with tocilizumab may be considered in patients with severe COVID-19 pneumonia. Copyright © 2021 Society for Scandinavian Journal of Infectious Diseases.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=62b6c71dceef7a24191a49c8988ebead)

1. **COVID-19 and IL-6: Why vitamin D (probably) helps but tocilizumab might not**  
   Silberstein M. European Journal of Pharmacology 2021;899 (no pagination):No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ef52431611d41d274fca5337d162b2a3)

1. **Covid-19 controversies: the tocilizumab chapter**  
   McCreary Erin K. BMJ (Clinical research ed.) 2021;372:n244.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=3ea3ea995468605c2e63ba60f082242f)

1. **COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network**  
   Buetti N. Intensive Care Medicine 2021;47:180-187.

Purpose: The primary objective of this study was to investigate the risk of ICU bloodstream infection (BSI) in critically ill COVID-19 patients compared to non-COVID-19 patients. Subsequently, we performed secondary analyses in order to explain the observed results. Method(s): We conducted a matched case-cohort study, based on prospectively collected data from a large ICU cohort in France. Critically ill COVID-19 patients were matched with similar non-COVID-19 patients. ICU-BSI was defined by an infection onset occurring > 48 h after ICU admission. We estimated the effect of COVID-19 on the probability to develop an ICU-BSI using proportional subdistribution hazards models. Result(s): We identified 321 COVID-19 patients and 1029 eligible controls in 6 ICUs. Finally, 235 COVID-19 patients were matched with 235 non-COVID-19 patients. We observed 43 ICU-BSIs, 35 (14.9%) in the COVID-19 group and 8 (3.4%) in the non-COVID-19 group (p <= 0.0001), respectively. ICU-BSIs of COVID-19 patients were more frequently of unknown source (47.4%). COVID-19 patients had an increased probability to develop ICU-BSI, especially after 7 days of ICU admission. Using proportional subdistribution hazards models, COVID-19 increased the daily risk to develop ICU-BSI (sHR 4.50, 95% CI 1.82-11.16, p = 0.0012). Among COVID-19 patients (n = 235), a significantly increased risk for ICU-BSI was detected in patients who received tocilizumab or anakinra (sHR 3.20, 95% CI 1.31-7.81, p = 0.011) but not corticosteroids. Conclusion(s): Using prospectively collected multicentric data, we showed that the ICU-BSI risk was higher for COVID-19 than non-COVID-19 critically ill patients after seven days of ICU stay. Clinicians should be particularly careful on late ICU-BSIs in COVID-19 patients. Tocilizumab or anakinra may increase the ICU-BSI risk. Copyright © 2021, Springer-Verlag GmbH Germany, part of Springer Nature.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=246cc87fd0c83539fc1aa7c1effd8b42)

1. **COVID-19 treatment options: a difficult journey between failed attempts and experimental drugs**  
   Bartoli A. Internal and emergency medicine 2021;16:281-308.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b94ece181380d18540af47e3ec211720)

1. **Covid-19: Arthritis drug tocilizumab reduces deaths in hospitalised patients, study shows**  
   Wise Jacqui BMJ (Clinical research ed.) 2021;372:n433.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2845a1f2fad8a6a0b00c107bb84dc3c0)

1. **COVID-19: Still a place for tocilizumab?**  
   Richier Q. Revue de Medecine Interne 2021;42:73-78.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a537eb379b7dbc02b671c5a46d53f8ae)

1. **COVIDOSE: A Phase II Clinical Trial of Low-Dose Tocilizumab in the Treatment of Noncritical COVID-19 Pneumonia**  
   Strohbehn G. W. Clinical Pharmacology and Therapeutics 2021;109:688-696.

Interleukin-6 (IL-6)-mediated hyperinflammation may contribute to the mortality of coronavirus disease 2019 (COVID-19). The IL-6 receptor-blocking monoclonal antibody tocilizumab has been repurposed for COVID-19, but prospective trials and dose-finding studies in COVID-19 have not yet fully reported. We conducted a single-arm phase II trial of low-dose tocilizumab in nonintubated hospitalized adult patients with COVID-19, radiographic pulmonary infiltrate, fever, and C-reactive protein (CRP) >= 40 mg/L. We hypothesized that doses significantly lower than the emerging standards of 400 mg or 8 mg/kg would resolve clinical and laboratory indicators of hyperinflammation. A dose range from 40 to 200 mg was evaluated, with allowance for one repeat dose at 24 to 48 hours. The primary objective was to assess the relationship of dose to fever resolution and CRP response. Thirty-two patients received low-dose tocilizumab, with the majority experiencing fever resolution (75%) and CRP decline consistent with IL-6 pathway abrogation (86%) in the 24-48 hours following drug administration. There was no evidence of a relationship between dose and fever resolution or CRP decline over the dose range of 40-200 mg. Within the 28-day follow-up, 5 (16%) patients died. For patients who recovered, median time to clinical recovery was 3 days (interquartile range, 2-5). Clinically presumed and/or cultured bacterial superinfections were reported in 5 (16%) patients. Low-dose tocilizumab was associated with rapid improvement in clinical and laboratory measures of hyperinflammation in hospitalized patients with COVID-19. Results of this trial provide rationale for a randomized, controlled trial of low-dose tocilizumab in COVID-19. Copyright © 2020 The Authors. Clinical Pharmacology & Therapeutics © 2020 American Society for Clinical Pharmacology and Therapeutics

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c69443ab454de95addaa592e64dfd157)

1. **Cytokine Profiles Before and After Immune Modulation in Hospitalized Patients with COVID-19**  
   Azmy V. Journal of Clinical Immunology. 2021;:No page numbers.

We describe the cytokine profiles of a large cohort of hospitalized patients with moderate to critical COVID-19, focusing on IL-6, sIL2R, and IL-10 levels before and after receiving immune modulating therapies, namely, tocilizumab and glucocorticoids. We also discuss the possible roles of sIL2R and IL-10 as markers of ongoing immune dysregulation after IL-6 inhibition. We performed a retrospective chart review of adult patients admitted to a tertiary care center with moderate to critical SARS-CoV-2 infection. Disease severity was based on maximum oxygen requirement during hospital stay to maintain SpO2 > 93% (moderate, 0-3 L NC; severe, 4-6 L NC or non-rebreather; critical, HFNC, NIPPV, or MV). All patients were treated using the institution's treatment algorithm, which included consideration of tocilizumab for severe and critical disease. The most common cytokine elevations among all patients included IL-6, sIL2R, IFN-gamma, and IL-10; patients who received tocilizumab had higher incidence of IL-6 and sIL2R elevations. Pre-tocilizumab IL-6 levels increased with disease severity (p =.0151). Both IL-6 and sIL2R levels significantly increased after administration of tocilizumab in all severity groups; IL-10 levels decreased in severe (p =.0203), but not moderate or critical, patients after they received tocilizumab. Cluster analysis revealed association between higher admission IL-6, sIL2R, and CRP levels and disease severity. Mean IL-6, sIL2R, and D-dimer were associated with mortality, and tocilizumab-treated patients with elevated IL-6, IL-10, and D-dimer were more likely to also receive glucocorticoids. Accessible clinical cytokine panels may be useful for monitoring response to treatment in COVID-19. The increase in sIL2R post-tocilizumab, despite administration of glucocorticoids, may indicate the need for combination therapy in order to modulate more than one hyperinflammatory pathway in COVID-19. We also discuss the role of cytokines as potential biomarkers for use of adjunct glucocorticoid therapy. Copyright © 2021, The Author(s), under exclusive licence to Springer Science+Business Media, LLC part of Springer Nature.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0f4118f8f78fbe5cbcaec90b58f13a89)

1. **Decreased serum levels of the inflammaging marker miR-146a are associated with non-clinical response to tocilizumab in COVID-19 patients**  
   Sabbatinelli J. Mechanisms of Ageing and Development 2021;193 (no pagination):No page numbers.

Current COVID-19 pandemic poses an unprecedented threat to global health and healthcare systems. The most amount of the death toll is accounted by old people affected by age-related diseases that develop a hyper-inflammatory syndrome. In this regard, we hypothesized that COVID-19 severity may be linked to inflammaging. Here, we examined 30 serum samples from patients enrolled in the clinical trial NCT04315480 assessing the clinical response to a single-dose intravenous infusion of the anti-IL-6 receptor drug Tocilizumab (TCZ) in COVID-19 patients with multifocal interstitial pneumonia. In these serum samples, as well as in 29 age- and gender-matched healthy control subjects, we assessed a set of microRNAs that regulate inflammaging, i.e. miR-146a-5p, miR-21-5p, and miR-126-3p, which were quantified by RT-PCR and Droplet Digital PCR. We showed that COVID-19 patients who did not respond to TCZ have lower serum levels of miR-146a-5p after the treatment (p = 0.007). Among non-responders, those with the lowest serum levels of miR-146a-5p experienced the most adverse outcome (p = 0.008). Our data show that a blood-based biomarker, such as miR-146a-5p, can provide clues about the molecular link between inflammaging and COVID-19 clinical course, thus allowing to better understand the use of biologic drug armory against this worldwide health threat. Copyright © 2020 Elsevier B.V.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ccab29678e7a239bed8fa5158fc853e8)

1. **Development and validation of a prediction model for tocilizumab failure in hospitalized patients with SARS-CoV-2 infection**  
   Mussini C. PLoS ONE 2021;16 (2 February) (no pagination):No page numbers.

Background The aim of this secondary analysis of the TESEO cohort is to identify, early in the course of treatment with tocilizumab, factors associated with the risk of progressing to mechanical ventilation and death and develop a risk score to estimate the risk of this outcome according to patients' profile. Methods Patients with COVID-19 severe pneumonia receiving standard of care + tocilizumab who were alive and free from mechanical ventilation at day 6 after treatment initiation were included in this retrospective, multicenter cohort study. Multivariable logistic regression models were built to identify predictors of mechanical ventilation or death by day-28 from treatment initiation and beta-coefficients were used to develop a risk score. Secondary outcome was mortality. Patients with the same inclusion criteria as the derivation cohort from 3 independent hospitals were used as validation cohort. Results 266 patients treated with tocilizumab were included. By day 28 of hospital follow-up post treatment initiation, 40 (15%) underwent mechanical ventilation or died [26 (10%)]. At multivariable analysis, sex, day-4 PaO<inf>2</inf>/FiO<inf>2</inf> ratio, platelets and CRP were independently associated with the risk of developing the study outcomes and were used to generate the proposed risk score. The accuracy of the score in AUC was 0.80 and 0.70 in internal validation and test for the composite endpoint and 0.92 and 0.69 for death, respectively. Conclusions Our score could assist clinicians in identifying, early after tocilizumab administration, patients who are likely to progress to mechanical ventilation or death, so that they could be selected for eventual rescue therapies. Copyright © 2021 Mussini et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=869ac5d9fb1aeedbc2ab5233b9262695)

1. **Does timing matter on tocilizumab administration? Clinical, analytical and radiological outcomes in COVID-19**  
   Moreno Diaz R. European Journal of Hospital Pharmacy 2021;(no pagination):No page numbers.

Introduction: While there are no pharmacological treatments with proven efficacy for coronavirus disease 2019 (COVID-19), tocilizumab has emerged as a candidate therapy. Some aspects of this therapy are still unknown, including the optimal timing of administration. Objective(s): This observational study aimed to compare the 90-day mortality in two cohorts of patients when the drug was administered within the first 10 days from onset of symptoms or after day 11. Method(s): Patients hospitalised with severe COVID-19 pneumonia who had received tocilizumab were divided into two groups according to when the medication was administered. The primary outcome was 90-day mortality. Secondary outcomes were 30-day mortality, clinical improvement on a 6-item scale by day 6, biomarker improvement by day 6, radiological image improvement by day 10 and SaO2 quotient by day 6. The results in the two groups were compared. Additionally, adverse events relating to tocilizumab were recorded. Result(s): A total of 112 patients were analysed. Both groups were epidemiologically comparable. The results obtained in the primary efficacy variable of the study (90-day mortality) showed a statistically significant difference in the subgroups according to the time of administration of tocilizumab (18.6% vs 5.0%, p=0.048). There was clinical improvement in 24.1% of patients at 6 days, with similar behaviour in both subgroups. No statistically significant differences were found in the percentage of patients who achieved radiological improvement at 10 days or in the other inflammatory parameters, with the exception of significant reductions in lactate dehydrogenase and C-reactive protein. Administration of tocilizumab was not associated with relevant adverse events. Conclusion(s): To our knowledge, this is the first report of data regarding the timing of administration of tocilizumab in patients with COVID-19 pneumonia. A strategy involving tocilizumab administration after 10 days from onset of symptoms may decrease mortality. Further randomised controlled trials are needed to confirm this emerging hypothesis. Copyright © European Association of Hospital Pharmacists 2021. No commercial re-use. See rights and permissions. Published by BMJ.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ffc03460e07849c45215fc25d05f209b)

1. **Dynamic changes in serum IL-6, IL-8, and IL-10 predict the outcome of ICU patients with severe COVID-19**  
   Li J. Annals of palliative medicine. 2021;08:No page numbers.

BACKGROUND: Biomarkers to prognosticate the outcomes and guide the treatment of patients with severe coronavirus disease 2019 (COVID-19) are currently required. We aimed to investigate whether the dynamic variation of cytokines was associated with the survival of patients admitted to the intensive care unit (ICU). METHOD(S): A retrospective study was performed on 40 patients with COVID-19 admitted to the ICU in Wuhan, China. Demographic, clinical, and laboratory variables were collected, and serum cytokines were kinetically assessed. A multivariable-adjusted generalized linear regression model was used to analyze the differences in serum cytokine levels between survivors and non-survivors. RESULT(S): Among the 40 patients included, we found a positive correlation between multiple cytokines. Serum levels of interleukin (IL)-6, IL-10, and tumor necrosis factor alpha (TNFalpha) in non-survivors were consistently elevated compared to those in the survivors. Kinetic variations in IL-6, IL-8, and IL-10 were associated with a fatal outcome in patients with severe COVID-19, independent of sex, age, absolute lymphocyte count, direct bilirubin, hypertension, chronic obstructive pulmonary disease, and cancer as well as the use of glucocorticoids and tocilizumab. CONCLUSION(S): Dynamic changes in serum IL-6, IL-8, and IL-10 levels were associated with survival in patients in the ICU, and could serve as a predictive biomarker to determine the therapeutic options for patients with severe COVID-19.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=739d2a9960f0fa3bf0d9094c3c8f5109)

1. **Early clinical outcomes with tocilizumab for severe COVID-19: a two-centre retrospective study**  
   Smoke S. M. International Journal of Antimicrobial Agents 2021;57 (2) (no pagination):No page numbers.

Severe COVID-19 (coronavirus disease 2019) is associated with elevated inflammatory markers, consistent with cytokine release syndrome (CRS). Tocilizumab is an interleukin-6 (IL-6) inhibitor effective in treating CRS secondary to chimeric antigen receptor T-cell (CAR T-cell) therapy. The efficacy of tocilizumab in treating COVID-19 is unknown. This was a retrospective cohort study conducted at two hospitals in northern New Jersey (USA). All patients treated with tocilizumab for confirmed or suspected COVID-19 between 10 March 2020 and 9 April 2020 at the study sites were included. The primary endpoint was clinical improvement on Day 7 after treatment as assessed by respiratory status. Univariate analysis compared data between those who improved and those who did not. A total of 45 severe and critically ill patients treated with tocilizumab for COVID-19 were evaluated. Of the 45 patients, 11 (24.4%), 22 (48.9%) and 12 (26.7%) patients improved, had no change or worsened by Day 7 after treatment, respectively. Lower white blood cell count and lactate dehydrogenase at the time of drug administration as well as shorter time from supplemental oxygen initiation to dosing were significantly associated with clinical improvement in the univariate analysis. In conclusion, tocilizumab administration was associated with a low rate of clinical improvement within 7 days in this cohort of severe and critically ill patients with COVID-19. Copyright © 2020 Elsevier Ltd

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b0051320a987e45a4da914afa8923de6)

1. **Early Tocilizumab Dosing Is Associated With Improved Survival in Critically Ill Patients Infected With Severe Acute Respiratory Syndrome Coronavirus-2**  
   Petrak Russell M. Critical care explorations 2021;3:e0395.

To identify the most efficacious timing for tocilizumab administration in critically ill patients infected with severe acute respiratory syndrome coronavirus-2.&lt;h4&gt;Design&lt;/h4&gt;Observational multicenter cohort study.&lt;h4&gt;Setting&lt;/h4&gt;A total of 23 acute care hospitals in four states.&lt;h4&gt;Patients&lt;/h4&gt;One-hundred eighteen patients admitted between March 13, 2020, and April 16, 2020. Eighty-one patients received tocilizumab, and 37 were untreated and served as a control group.&lt;h4&gt;Measurements and main results&lt;/h4&gt;The main outcome was mortality and was analyzed by timing of tocilizumab dosing. Early dosing was defined as a tocilizumab dose administered prior to or within 1 day of intubation. Late dosing was defined as a dose administered greater than 1 day after intubation. A control group that was treated only with standard of care, and without tocilizumab, was used for comparison. Early tocilizumab therapy was associated with a statistically significant decrease in mortality as compared to patients who were untreated (&lt;i&gt;p&lt;/i&gt; = 0.003). Dosing tocilizumab late was associated with an increased mortality compared with the untreated group (&lt;i&gt;p&lt;/i&gt; = 0.006).&lt;h4&gt;Conclusions&lt;/h4&gt;Early tocilizumab administration was associated with decreased mortality in critically ill severe acute respiratory syndrome coronavirus-2 patients, but a potential detriment was suggested by dosing later in a patient's course.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8b1919ab1752811cfc2246cf9412e2ed)

1. **Early use of tocilizumab in the prevention of adult respiratory failure in SARS-CoV-2 infections and the utilization of interleukin-6 levels in the management**  
   Antony S. J. Journal of Medical Virology 2021;93:491-498.

Respiratory failure in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection appears related to cytokine release syndrome that often results in mechanical ventilation (MV). We investigated the role of tocilizumab (TCZ) on interleukin-6 (IL-6) trends and MV in patients with SARS-CoV-2. In this longitudinal observational study, 112 patients were evaluated from 1 February to 31 May 2020. TCZ was administered followed by methylprednisolone to patients with >3L oxygen requirement and pneumonia severity index score <=130 with computed tomography scan changes. IL-6, C-reactive protein (CRP), ferritin, lactate dehydrogenase (LDH), D-dimer, and procalcitonin were monitored on days 0, 3, and 6 of therapy. Statistical analyses were performed with significance <=0.05. Eighty out of 112 SARS-CoV-2-positive patients (45 males, 56.96%; 34 females, 43.04%) were included in this study. Seven patients expired (8.75%) and nine patients required MV (11.25%). Median IL-6 levels pre-administration of TCZ was 342.50 (78.25-666.25) pg/mL compared with post-administration on day 3 (563; 162-783) pg/mL (P <.00001). On day 6, the median dropped to 545 (333.50-678.50) pg/mL compared with day 3 (P =.709). CRP, ferritin, LDH, and D-dimer levels were reduced after TCZ therapy. Early use of TCZ may reduce the need for MV and decrease CRP, ferritin, LDH, and D-dimer levels. The sequential use of methylprednisolone for 72 hours seems to potentiate the effect and prolong the suppression of the cytokine storm. IL-6 levels may be helpful as a prognostic tool. Copyright © 2020 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=356f96f5555cc381480d6ae439103a54)

1. **Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: Randomised controlled trial**  
   Veiga V. C. The BMJ 2021;372 (no pagination):No page numbers.

AbstractObjective To determine whether tocilizumab improves clinical outcomes for patients with severe or critical coronavirus disease 2019 (covid-19). Design Randomised, open label trial. Setting Nine hospitals in Brazil, 8 May to 17 July 2020. Participants Adults with confirmed covid-19 who were receiving supplemental oxygen or mechanical ventilation and had abnormal levels of at least two serum biomarkers (C reactive protein, D dimer, lactate dehydrogenase, or ferritin). The data monitoring committee recommended stopping the trial early, after 129 patients had been enrolled, because of an increased number of deaths at 15 days in the tocilizumab group. Interventions Tocilizumab (single intravenous infusion of 8 mg/kg) plus standard care (n=65) versus standard care alone (n=64). Main outcome measure The primary outcome, clinical status measured at 15 days using a seven level ordinal scale, was analysed as a composite of death or mechanical ventilation because the assumption of odds proportionality was not met. Results A total of 129 patients were enrolled (mean age 57 (SD 14) years; 68% men) and all completed follow-up. All patients in the tocilizumab group and two in the standard care group received tocilizumab. 18 of 65 (28%) patients in the tocilizumab group and 13 of 64 (20%) in the standard care group were receiving mechanical ventilation or died at day 15 (odds ratio 1.54, 95% confidence interval 0.66 to 3.66; P=0.32). Death at 15 days occurred in 11 (17%) patients in the tocilizumab group compared with 2 (3%) in the standard care group (odds ratio 6.42, 95% confidence interval 1.59 to 43.2). Adverse events were reported in 29 of 67 (43%) patients who received tocilizumab and 21 of 62 (34%) who did not receive tocilizumab. Conclusions In patients with severe or critical covid-19, tocilizumab plus standard care was not superior to standard care alone in improving clinical outcomes at 15 days, and it might increase mortality. Trial registration ClinicalTrials.gov NCT04403685. Copyright © 2021 BMJ Publishing Group. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=53ebbf2c7cf31d5b136c46294b8ba8a6)

1. **Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized with COVID-19 Pneumonia: A Randomized Clinical Trial**  
   Salvarani C. JAMA Internal Medicine 2021;181:24-31.

Importance: The coronavirus disease 2019 (COVID-19) pandemic is threatening billions of people worldwide. Tocilizumab has shown promising results in retrospective studies in patients with COVID-19 pneumonia with a good safety profile. Objective(s): To evaluate the effect of early tocilizumab administration vs standard therapy in preventing clinical worsening in patients hospitalized with COVID-19 pneumonia. Design, Setting, and Participant(s): Prospective, open-label, randomized clinical trial that randomized patients hospitalized between March 31 and June 11, 2020, with COVID-19 pneumonia to receive tocilizumab or standard of care in 24 hospitals in Italy. Cases of COVID-19 were confirmed by polymerase chain reaction method with nasopharyngeal swab. Eligibility criteria included COVID-19 pneumonia documented by radiologic imaging, partial pressure of arterial oxygen to fraction of inspired oxygen (Pao<inf>2</inf>/Fio<inf>2</inf>) ratio between 200 and 300 mm Hg, and an inflammatory phenotype defined by fever and elevated C-reactive protein. Intervention(s): Patients in the experimental arm received intravenous tocilizumab within 8 hours from randomization (8 mg/kg up to a maximum of 800 mg), followed by a second dose after 12 hours. Patients in the control arm received supportive care following the protocols of each clinical center until clinical worsening and then could receive tocilizumab as a rescue therapy. Main Outcome and Measures: The primary composite outcome was defined as entry into the intensive care unit with invasive mechanical ventilation, death from all causes, or clinical aggravation documented by the finding of a Pao<inf>2</inf>/Fio<inf>2</inf>ratio less than 150 mm Hg, whichever came first. Result(s): A total of 126 patients were randomized (60 to the tocilizumab group; 66 to the control group). The median (interquartile range) age was 60.0 (53.0-72.0) years, and the majority of patients were male (77 of 126, 61.1%). Three patients withdrew from the study, leaving 123 patients available for the intention-to-treat analyses. Seventeen patients of 60 (28.3%) in the tocilizumab arm and 17 of 63 (27.0%) in the standard care group showed clinical worsening within 14 days since randomization (rate ratio, 1.05; 95% CI, 0.59-1.86). Two patients in the experimental group and 1 in the control group died before 30 days from randomization, and 6 and 5 patients were intubated in the 2 groups, respectively. The trial was prematurely interrupted after an interim analysis for futility. Conclusions and Relevance: In this randomized clinical trial of hospitalized adult patients with COVID-19 pneumonia and Pao<inf>2</inf>/Fio<inf>2</inf>ratio between 200 and 300 mm Hg who received tocilizumab, no benefit on disease progression was observed compared with standard care. Further blinded, placebo-controlled randomized clinical trials are needed to confirm the results and to evaluate possible applications of tocilizumab in different stages of the disease. Trial Registration: ClinicalTrials.gov Identifier: NCT04346355; EudraCT Identifier: 2020-001386-37. Copyright © 2021 American Medical Association. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=beeba8e4d875ff4ec674cdbf12df3f52)

1. **Effect of Tocilizumab vs Usual Care in Adults Hospitalized with COVID-19 and Moderate or Severe Pneumonia: A Randomized Clinical Trial**  
   Hermine O. JAMA Internal Medicine 2021;181:32-40.

Importance: Severe pneumonia with hyperinflammation and elevated interleukin-6 is a common presentation of coronavirus disease 2019 (COVID-19). Objective(s): To determine whether tocilizumab (TCZ) improves outcomes of patients hospitalized with moderate-to-severe COVID-19 pneumonia. Design, Setting, and Particpants: This cohort-embedded, investigator-initiated, multicenter, open-label, bayesian randomized clinical trial investigating patients with COVID-19 and moderate or severe pneumonia requiring at least 3 L/min of oxygen but without ventilation or admission to the intensive care unit was conducted between March 31, 2020, to April 18, 2020, with follow-up through 28 days. Patients were recruited from 9 university hospitals in France. Analyses were performed on an intention-to-treat basis with no correction for multiplicity for secondary outcomes. Intervention(s): Patients were randomly assigned to receive TCZ, 8 mg/kg, intravenously plus usual care on day 1 and on day 3 if clinically indicated (TCZ group) or to receive usual care alone (UC group). Usual care included antibiotic agents, antiviral agents, corticosteroids, vasopressor support, and anticoagulants. Main Outcomes and Measures: Primary outcomes were scores higher than 5 on the World Health Organization 10-point Clinical Progression Scale (WHO-CPS) on day 4 and survival without need of ventilation (including noninvasive ventilation) at day 14. Secondary outcomes were clinical status assessed with the WHO-CPS scores at day 7 and day 14, overall survival, time to discharge, time to oxygen supply independency, biological factors such as C-reactive protein level, and adverse events. Result(s): Of 131 patients, 64 patients were randomly assigned to the TCZ group and 67 to UC group; 1 patient in the TCZ group withdrew consent and was not included in the analysis. Of the 130 patients, 42 were women (32%), and median (interquartile range) age was 64 (57.1-74.3) years. In the TCZ group, 12 patients had a WHO-CPS score greater than 5 at day 4 vs 19 in the UC group (median posterior absolute risk difference [ARD] -9.0%; 90% credible interval [CrI], -21.0 to 3.1), with a posterior probability of negative ARD of 89.0% not achieving the 95% predefined efficacy threshold. At day 14, 12% (95% CI -28% to 4%) fewer patients needed noninvasive ventilation (NIV) or mechanical ventilation (MV) or died in the TCZ group than in the UC group (24% vs 36%, median posterior hazard ratio [HR] 0.58; 90% CrI, 0.33-1.00), with a posterior probability of HR less than 1 of 95.0%, achieving the predefined efficacy threshold. The HR for MV or death was 0.58 (90% CrI, 0.30 to 1.09). At day 28, 7 patients had died in the TCZ group and 8 in the UC group (adjusted HR, 0.92; 95% CI 0.33-2.53). Serious adverse events occurred in 20 (32%) patients in the TCZ group and 29 (43%) in the UC group (P =.21). Conclusions and Relevance: In this randomized clinical trial of patients with COVID-19 and pneumonia requiring oxygen support but not admitted to the intensive care unit, TCZ did not reduce WHO-CPS scores lower than 5 at day 4 but might have reduced the risk of NIV, MV, or death by day 14. No difference on day 28 mortality was found. Further studies are necessary for confirming these preliminary results. Trial Registration: ClinicalTrials.gov Identifier: NCT04331808. Copyright © 2021 American Medical Association. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=9077ad059b5a5ebde5c5e2a275c38eff)

1. **Effective treatment with Tocilizumab in a COVID-19 patient on maintenance hemodialysis: A case report**  
   Nourié Nicole CEN case reports 2021;:No page numbers.

Coronavirus disease 2019 (COVID-19) is a rapidly spreading infective disease caused by the severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2). The management of this disease remains a challenge particularly in certain subgroups of patients such in hemodialysis patients who have higher exposure rates due to the nature of their in-hospital care, and higher mortality due to their burden of comorbidities. We report a case of a 52-year-old patient with Von Hippel Lindau syndrome and end-stage renal disease on hemodialysis who contracted COVID-19 infection. Despite the patient's rapidly deteriorating clinical status he was successfully treated with Tocilizumab, after which he showed rapid improvement in his clinical, biological and radiological parameters. Although few studies were available regarding the use of Tocilizumab in the dialysis population, its use proved to be effective and well tolerated in our patient.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d3d53f825434de93f8b5d88e46f3a874)

1. **Effectiveness and safety of intravenous tocilizumab to treat COVID-19-associated hyperinflammatory syndrome: Covizumab-6 observational cohort**  
   Corominas H. Clinical Immunology 2021;223 (no pagination):No page numbers.

Although the starting event in COVID-19 is a viral infection some patients present with an over-exuberant inflammatory response, leading to acute lung injury (ALI) and adult respiratory distress syndrome (ARDS). Since IL-6 plays a critical role in the inflammatory response, we assessed the efficacy and safety of tocilizumab (TCZ) in this single-centre, observational study in all Covid-19 in-patient with a proven SARS-CoV-2 rapidly progressing infection to prevent ALI and ARDS. 104 patients with COVID-19 treated with TCZ had a lower mortality rate (5.8%) compared with the regional mortality rate (11%), hospitalized patient's mortality (10%), and slightly lower than hospitalized patients treated with our standard of care alone (6%). We found that TCZ rapidly decreased acute phase reactants, ferritin and liver release of proteins. D-Dimer decreased slowly. We did not observe specific safety concerns. Early administration of IL6-R antagonists in COVID-19 patients with impending hyperinflammatory response, may be safe and effective treatment to prevent, ICU admission and further complications. Copyright © 2020 Elsevier Inc.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f87ed4516c8e364323ce312e91e0a33d)

1. **Effectiveness of anakinra for tocilizumab-refractory severe COVID-19: A single-centre retrospective comparative study**  
   de la Calle C. International Journal of Infectious Diseases 2021;105:319-325.

Objectives: A subgroup of patients with SARS-CoV-2 infection was thought to have developed cytokine release syndrome and were treated with tocilizumab; however, a significant percentage of patients evolved. This study aimed to determine the usefulness of anakinra as a rescue treatment for patients with tocilizumab-refractory COVID-19 disease. Method(s): A prospective cohort of patients with COVID-19 pneumonia who received anakinra as salvage therapy after failure of tocilizumab were compared (1:1) with selected controls in a historical cohort of patients treated with tocilizumab. Cases and controls were matched by age, comorbidities, pulse oximetry oxygen saturation to fraction of inspired oxygen (SpO2/FiO2) ratio at baseline, and time elapsed since the initiation of treatment with tocilizumab. The primary outcome was the improvement in clinical status measured by a 6-point ordinal scale, from baseline to day 21. Result(s): The study included 20 cases and 20 controls (mean age 65.3 +/- 12.8 years, 65% males). No differences were found in the clinical improvement rates at 7, 14 and 21 days of follow-up. The in-hospital mortality rate for patients receiving anakinra was 55% vs. 45% in the control group (P = 0.527). Conclusion(s): Treatment with anakinra was not useful in improving the prognosis of patients with tocilizumab-refractory severe COVID-19. Copyright © 2021 The Authors

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=15879ef2a576b63af84fdf4912277b28)

1. **Effects of tocilizumab on mortality in hospitalized patients with COVID-19: a multicentre cohort study**  
   Martinez-Sanz J. Clinical Microbiology and Infection 2021;27:238-243.

Objectives: Tocilizumab has been proposed as a candidate therapy for patients with severe coronavirus disease 2019 (COVID-19), especially among those with higher systemic inflammation. We investigated the association between receipt of tocilizumab and mortality in a large cohort of hospitalized patients. Method(s): In this cohort study of patients hospitalized with COVID-19 in Spain, the primary outcome was time to death and the secondary outcome time to intensive care unit (ICU) admission or death. We used inverse probability weighting to fit marginal structural models adjusted for time-varying covariates to determine the causal relationship between receipt of tocilizumab and outcome. Result(s): Data from 1229 patients were analysed, with 261 patients (61 deaths) in the tocilizumab group and 969 patients (120 deaths) in the control group. In the adjusted marginal structural models, a significant interaction between receipt of tocilizumab and high C-reactive protein (CRP) levels was detected. Tocilizumab was associated with decreased risk of death (adjusted hazard ratio 0.34, 95% confidence interval 0.16-0.72, p 0.005) and ICU admission or death (adjusted hazard ratio 0.39, 95% confidence interval 0.19-0.80, p 0.011) among patients with baseline CRP >150 mg/L but not among those with CRP <=150 mg/L. Exploratory subgroup analyses yielded point estimates that were consistent with these findings. Conclusion(s): In this large observational study, tocilizumab was associated with a lower risk of death or ICU admission or death in patients with higher CRP levels. While the results of ongoing clinical trials of tocilizumab in patients with COVID-19 will be important to establish its safety and efficacy, our findings have implications for the design of future clinical trials. Copyright © 2020 European Society of Clinical Microbiology and Infectious Diseases

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=54dbdc3faa18e8f8800b32b77881ccd7)

1. **Effects of tocilizumab versus hemoadsorption combined with tocilizumab in patients with SARS-CoV-2 pneumonia: Preliminary results**  
   Berlot G. International Journal of Artificial Organs. 2021;:No page numbers.

Objective: To assess the variations of Interleukin-6 (IL-6) in patients with SARS-CoV-2 infection treated with Tocilizumab (TCZ) alone or in association with hemoadsorption (HA). Design(s): Retrospective. Setting(s): An Intensive Care Unit (ICU) admitting mechanically ventilated patients with SARS-CoV-2 pneumonia. Patient(s): Four adult patients. Intervention(s): We compared the blood values of IL-6, C-reactive protein (CRP) and of other biochemical variables including the PaO<inf>2</inf>/FiO<inf>2</inf> in two patients who received TCZ alone and in other 2 in whom it was associated with the HA (TCZ-HA) due to the presence of impending or established organ failures other than the lung. All variables were measured before, during and after the treatment. Main Result(s): In all patients, the IL-6 increased during the treatment; after its termination, its values sharply decreased only in those treated also with HA; conversely, the CRP decreased in all patients; the PaO<inf>2</inf>/FiO<inf>2</inf> increased in three patients and remained stable in the remaining one. Both the TCZ and the HA were well tolerated; all patients were weaned from the mechanical ventilation and discharged from the hospital. Limitation(s): Although the limited number of patients does not allow to draw firm conclusions, the increase of the IL-6 of can be ascribed to its displacement from cellular and soluble receptors, whereas its decrease is likely due to the scavenging effect exerted by the HA. Although the association TCZ-HA could be valuable in the treatment of the Cytokine Release Storm (CRS) associated with the SARS-CoV-2, the HA could be more effective as it neutralizes a wider panel of inflammatory mediators. Copyright © The Author(s) 2021.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cbbc06adade781aee0bf7bbce9565859)

1. **Experience of using tocilizumab for treatment in Indonesian patients with severe COVID-19**  
   Widysanto A. Cytokine 2021;138 (no pagination):No page numbers.

COVID-19 is a public health emergency of international concern with millions confirmed cases globally including in Indonesia with more than two hundred thousand confirmed cases to date COVID-19. (1) COVID-19 has wide clinical manifestation ranging from asymptomatic, acute respiratory illness, respiratory failure that necessitates mechanical ventilation and support in an ICU, to MODS. (2) Several comorbidities have been demonstrated to be associated with the development of severe outcomes from COVID-19 infection, such as hypertension, diabetes, cardiovascular disease, dyslipidemia, thyroid disease, and pulmonary disease. (3)-(5) Severe COVID-19 is associated with increased plasma concentrations of IL-6, resulting in cytokine storm. (6) Tocilizumab, an interleukin-6 inhibitor, might alleviates the cytokine storm, prevents significant lungs and organs damage, thus improving clinical outcomes. (7) Therefore, tocilizumab, might be one of the promising therapies for severe COVID-19. (8) However there were limited studies regarding the efficacy in COVID-19 patients, especially with control group. We would like to report our experience in using tocilizumab as treatment in severe COVID-19 patients in Indonesia, which is the first in Indonesia to the best of our knowledge. Copyright © 2020 Elsevier Ltd

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=274e4e3f37e753264def42cc41440155)

1. **Feasibility of tocilizumab in ICU patients with COVID-19**  
   Issa N. Journal of Medical Virology 2021;93:46-47.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=671fadb7d6b42624f4814a20d03ff82e)

1. **Fighting the storm: could novel anti-TNFα and anti-IL-6 C. sativa cultivars tame cytokine storm in COVID-19?**  
   Kovalchuk Anna Aging 2021;13:1571-1590.

The main aspects of severe COVID-19 disease pathogenesis include hyper-induction of proinflammatory cytokines, also known as 'cytokine storm', that precedes acute respiratory distress syndrome (ARDS) and often leads to death. COVID-19 patients often suffer from lung fibrosis, a serious and untreatable condition. There remains no effective treatment for these complications. Out of all cytokines, TNFα and IL-6 play crucial roles in cytokine storm pathogenesis and are likely responsible for the escalation in disease severity. These cytokines also partake in the molecular pathogenesis of fibrosis. Therefore, new approaches are urgently needed, that can efficiently and swiftly downregulate TNFα, IL-6, and the inflammatory cytokine cascade, in order to curb inflammation and prevent fibrosis, and lead to disease remission. &lt;i&gt;Cannabis sativa&lt;/i&gt; has been proposed to modulate gene expression and inflammation and is under investigation for several potential therapeutic applications against autoinflammatory diseases and cancer. Here, we hypothesized that the extracts of novel &lt;i&gt;C. sativa&lt;/i&gt; cultivars may be used to downregulate the expression of pro-inflammatory cytokines and pathways involved in inflammation and fibrosis. Initially, to analyze the anti-inflammatory effects of novel &lt;i&gt;C. sativa&lt;/i&gt; cultivars, we used a well-established full thickness human 3D skin artificial EpiDermFTTM tissue model, whereby tissues were exposed to UV to induce inflammation and then treated with extracts of seven new cannabis cultivars. We noted that out of seven studied extracts of novel &lt;i&gt;C. sativa&lt;/i&gt; cultivars, three (#4, #8 and #14) were the most effective, causing profound and concerted down-regulation of COX2, TNFα, IL-6, CCL2, and other cytokines and pathways related to inflammation and fibrosis. These data were further confirmed in the WI-38 lung fibroblast cell line model. Most importantly, one of the tested extracts had no effect at all, and one exerted effect that may be deleterious, signifying that careful cannabis cultivar selection must be based on thorough pre-clinical studies. The observed pronounced inhibition of TNFα and IL-6 is the most important finding, because these molecules are currently considered to be the main targets in COVID-19 cytokine storm and ARDS pathogenesis. Novel anti-TNFα and anti-IL-6 cannabis extracts can be useful additions to the current anti-inflammatory regimens to treat COVID-19, as well as various rheumatological diseases and conditions, and 'inflammaging' - the inflammatory underpinning of aging and frailty.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f325062b38d2eb58a3b42f8fee5f1d42)

1. **Genetically proxied interleukin-6 receptor inhibition: Opposing associations with COVID-19 and pneumonia**  
   Larsson S. C. European Respiratory Journal 2021;57 (1) (no pagination):No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b34ca0397db496b7584165f83b5218d4)

1. **Glucocorticoids alone versus tocilizumab alone or glucocorticoids plus tocilizumab in patients with severe SARS-CoV-2 pneumonia and mild inflammation**  
   Aomar-Millán Ismael Francisco Medicina clinica 2021;:No page numbers.

&lt;h4&gt;Aim&lt;/h4&gt;To assess clinical outcomes according to the immunosuppressive treatment administered to patients with severe SARS-CoV-2 pneumonia and moderate inflammation.&lt;h4&gt;Methods&lt;/h4&gt;A retrospective observational cohort study involving 142 patients with severe COVID-19 pneumonia and moderate inflammation divided into three treatment groups (pulses of methylprednisolone alone [groupI], tocilizumab alone [groupII] and methylprednisolone plus tocilizumab [groupIII]). The aim was to assess intergroups differences in the clinical course with a 60-day follow-up and related analytical factors.&lt;h4&gt;Results&lt;/h4&gt;14 patients (9,8%) died: 8 (10%) in groupI and 6 (9,5%) in groupsII andIII. 15 (10,6%) were admitted to ICU: 2 (2,5%) from groupI, 4 (28,5%) from groupII and 9 (18,4%) from groupIII. The mean hospital stay was longer in groupII and clinical outcome was not associated with treatment.&lt;h4&gt;Conclusions&lt;/h4&gt;Tocilizumab seems to be not associated with better clinical outcomes and should be reserved for clinical trial scenario, since its widespread use may result in higher rate of ICU admission and longer mean hospital stay without differences in mortality rate and potentially adverse events.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=99138ba62a20ae0246fcc2b80e47b2c8)

1. **High expression of ace2 in the human lung leads to the release of il6 by suppressing cellular immunity: Il6 plays a key role in covid-19**  
   Bao Z. European Review for Medical and Pharmacological Sciences 2021;25:527-540.

OBJECTIVE: The pathogenesis of coronavirus disease 2019 (COVID-19) remains clear, and no effective treatment exists. SARSCoV-2 is the virus that causes COVID-19 and uses ACE2 as a cell receptor to invade human cells. Therefore, ACE2 is a key factor to analyze the SARS-CoV-2 infection mechanism. MATERIALS AND METHODS: We included 9,783 sequencing results of different organs, analyzed the effects of different ACE2 expression patterns in organs and immune regulation. RESULT(S): We found that ACE2 expression was significantly increased in the lungs and digestive tract. The cellular immunity of individuals with elevated ACE2 expression is activated, whereas humoral immunity is dampened, leading to the release of many inflammatory factors dominated by IL6. Furthermore, by studying the sequencing results of SARS-CoV-2-infected and uninfected cells, IL6 was found to be an indicator of a significant increase in the number of infected cells. However, although patients with high expression of ACE2 will release many inflammatory factors dominated by IL6, cellular immunity in the colorectum is significantly activated. This effect may explain why individuals with SARS-CoV-2 infection have severe lung symptoms and digestion issues, which are important causes of milder symptoms. CONCLUSION(S): This finding indicates that ACE2 and IL6 inhibitors have important value in COVID-19. Copyright © 2021 Verduci Editore s.r.l. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cbd2541ee5815d5ee2ffe5f25e3dfd05)

1. **Host-directed therapies for COVID-19**  
   Maeurer M. Current opinion in pulmonary medicine. 2021;23:No page numbers.

PURPOSE OF REVIEW: Severe acute respiratory syndrome coronavirus-2-induced hyperinflammation is a major cause of death or end-organ dysfunction in COVID-19 patients. We review adjunct host-directed therapies (HDTs) for COVID-19 management. RECENT FINDINGS: The use of umbilical cord-derived mesenchymal stem cells as HDT for COVID-19 has been shown to be safe in phase 1 and 2 trials. Trials of anti-interleukin-6 receptor antibodies show promising mortality benefit in hospitalized COVID-19 patients. Repurposed drugs and monoclonal antibodies targeting specific cytokines acting on different aspects of the pro- and anti-inflammatory cascades are under evaluation. SUMMARY: A range of HDTs shows promise for reducing mortality and improving long term disability in patients with severe COVID-19, and require evaluation in randomized, controlled trials. Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e8ea98cd1bbc482bc97b16a25f321081)

1. **IL-6 blockade for COVID-19: a global scientific call to arms**  
   Murthy Srinivas The Lancet. Respiratory medicine 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=03085dbc67cfc6d5c039534c476d0b92)

1. **IL-6 inhibition in the treatment of COVID-19: a meta-analysis and meta-regression**  
   Tharmarajah E. The Journal of infection. 2021;18:No page numbers.

OBJECTIVES: Multiple RCTs of interkeukin-6 (IL-6) inhibitors in COVID-19 have been published, with conflicting conclusions. We performed a meta-analysis to assess the impact of IL-6 inhibition on mortality from COVID-19, utilising meta-regression to explore differences in study results. METHOD(S): Systematic database searches were performed to identify RCTs comparing IL-6 inhibitors (tocilizumab and sarilumab) to placebo or standard of care in adults with COVID-19. Meta-analysis was used to estimate the relative risk of mortality at 28 days between arms, expressed as a risk ratio. Within-study mortality rates were compared, and meta-regression was used to investigate treatment effect modification. RESULT(S): Data from nine RCTs were included. The combined mortality rate across studies was 19% (95% CI: 18, 20%), ranging from 2% to 31%. The overall risk ratio for 28-day mortality was 0.90 (95% CI: 0.81, 0.99), in favour of benefit for IL-6 inhibition over placebo or standard of care, with low treatment effect heterogeneity: I2 0% (95% CI: 0, 53%). Meta-regression showed no evidence of treatment effect modification by patient characteristics. Trial-specific mortality rates were explained by known patient-level predictors of COVID-19 outcome (male sex, CRP, hypertension), and country-level COVID-19 incidence. CONCLUSION(S): IL-6 inhibition is associated with clinically meaningful improvements in outcomes for patients admitted with COVID-19. Long-term benefits of IL-6 inhibition, its effectiveness across healthcare systems, and implications for differing standards of care are currently unknown. Copyright © 2021 The Authors. Published by Elsevier Ltd.. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c1e6cb5b21377d76517e9771b8226ac7)

1. **IL-6 modulation for COVID-19: the right patients at the right time?**  
   Ascierto Paolo Antonio Journal for immunotherapy of cancer 2021;9:No page numbers.

The ongoing pandemic caused by the novel coronavirus SARS-CoV-2 has disrupted the global economy and strained healthcare systems to their limits. After the virus first emerged in late 2019, the first intervention that demonstrated significant reductions in mortality for severe COVID-19 in large-scale trials was corticosteroids. Additional options that may reduce the burden on the healthcare system by reducing the number of patients requiring intensive care unit support are desperately needed, yet no therapy has conclusively established benefit in randomized studies for the management of moderate or mild cases of disease. Severe COVID-19 disease is characterized by a respiratory distress syndrome accompanied by elevated levels of several systemic cytokines, in a profile that shares several features with known inflammatory pathologies such as hemophagocytic lymphohistiocytosis and cytokine release syndrome secondary to chimeric antigen receptor (CAR) T cell therapy. Based on these observations, modulation of inflammatory cytokines, particularly interleukin (IL)-6, was proposed as a strategy to mitigate severe disease. Despite encouraging recoveries with anti-IL-6 agents, especially tocilizumab from single-arm studies, early randomized trials returned mixed results in terms of clinical benefit with these interventions. Later, larger trials such as RECOVERY and REMAP-CAP, however, are establishing anti-IL-6 in combination with steroids as a potential option for hypoxic patients with evidence of hyperinflammation. We propose that a positive feedback loop primarily mediated by macrophages and monocytes initiates the inflammatory cascade in severe COVID-19, and thus optimal benefit with anti-IL-6 therapies may require intervention during a finite window of opportunity at the outset of hyperinflammation but before fulminant disease causes irreversible tissue damage-as defined clinically by C reactive protein levels higher than 75 mg/L.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=04836eb16a8d9329e6d23d142fe9f54b)

1. **IL-6 serum levels predict severity and response to tocilizumab in COVID-19: An observational study**  
   Galvan-Roman J. M. Journal of Allergy and Clinical Immunology 2021;147:72-80.e8.

Background: Patients with coronavirus disaese 2019 (COVID-19) can develop a cytokine release syndrome that eventually leads to acute respiratory distress syndrome requiring invasive mechanical ventilation (IMV). Because IL-6 is a relevant cytokine in acute respiratory distress syndrome, the blockade of its receptor with tocilizumab (TCZ) could reduce mortality and/or morbidity in severe COVID-19. Objective(s): We sought to determine whether baseline IL-6 serum levels can predict the need for IMV and the response to TCZ. Method(s): A retrospective observational study was performed in hospitalized patients diagnosed with COVID-19. Clinical information and laboratory findings, including IL-6 levels, were collected approximately 3 and 9 days after admission to be matched with preadministration and postadministration of TCZ. Multivariable logistic and linear regressions and survival analysis were performed depending on outcomes: need for IMV, evolution of arterial oxygen tension/fraction of inspired oxygen ratio, or mortality. Result(s): One hundred forty-six patients were studied, predominantly males (66%); median age was 63 years. Forty-four patients (30%) required IMV, and 58 patients (40%) received treatment with TCZ. IL-6 levels greater than 30 pg/mL was the best predictor for IMV (odds ratio, 7.1; P < .001). Early administration of TCZ was associated with improvement in oxygenation (arterial oxygen tension/fraction of inspired oxygen ratio) in patients with high IL-6 (P = .048). Patients with high IL-6 not treated with TCZ showed high mortality (hazard ratio, 4.6; P = .003), as well as those with low IL-6 treated with TCZ (hazard ratio, 3.6; P = .016). No relevant serious adverse events were observed in TCZ-treated patients. Conclusion(s): Baseline IL-6 greater than 30 pg/mL predicts IMV requirement in patients with COVID-19 and contributes to establish an adequate indication for TCZ administration. Copyright © 2020 American Academy of Allergy, Asthma & Immunology

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5c08f3c4df446d9e000e694b3cb99379)

1. **Immediate amelioration of severe respiratory distress in sjogren's syndrome with covid-19 treated with a single dose of off-label tocilizumab**  
   Kataoka H. Internal Medicine 2021;60:639-643.

The coronavirus disease 2019 (COVID-19) pandemic has become an urgent global health issue. An older age and underlying conditions, such as diabetes, have been reported as risk factors, but whether or not autoimmune diseases increase the risk remains unknown. An 85-year-old man with Sjogren's syndrome developed a severe COVID-19 infection that required oxygen supplementation. After discussing the goals of care with him and his wife, off-label tocilizumab was given concomitantly, resulting in a rapid improvement in his symptoms and respiratory failure. This patient represents a supplementary case confirming the efficacy and safety of tocilizumab for COVID-19 in elderly patients with autoimmune diseases. Copyright © 2021 Japanese Society of Internal Medicine. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4fcb2b9cea94f510eb0246a250114878)

1. **Immunomodulation for the management of severe SARS-CoV2 infections. State of the art and review of the literature**  
   Bacca E. Biochemical and Biophysical Research Communications 2021;538:151-155.

This Mini Review of the literature aimed to assess the role of tocilizumab for the treatment of severe coronavirus disease 2019 (COVID-19). Based on the available scientific evidence, it is not clear to date what is the best therapeutic strategy for the treatment of COVID-19. Since SARS-CoV-2 infection stimulates a vigorous proinflammatory response and may cause the so-called "cytokine storm", immunomodulator drugs have been investigated as potential treatment for severe COVID-19 pneumonia. Among immunomodulators, tocilizumab, a recombinant humanized monoclonal antibody directed against IL-6 receptor, seems to be promising. An increasing number of clinical trials are exploring the role of tocilizumab in COVID-19, focusing on outcomes like mortality, risk of intensive care unit admission and the need for mechanical ventilation. At the moment, there is no conclusive evidence that tocilizumab would be proper outright in all patients with COVID-19 pneumonia, but some studies suggest that its use may be beneficial in selected categories of patients. Copyright © 2020 Elsevier Inc.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ebdeb073abc064056f66e9082f40c0cd)

1. **Impact of Interleukin-6 Receptor Blockade With Tocilizumab on Cardiac Injury in Patients With COVID-19: A Retrospective Cohort Study**  
   Weber Brittany N. Open forum infectious diseases 2021;8:ofab012.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1e089abafe47c6e5cb3b51c1b7ecddf9)

1. **Influence of Cytokine Release Syndrome in Severe COVID-19 Patients Treated With Tocilizumab Over the Quantiferon TB Gold Plus Results**  
   Sanchez-Martinez F. Archivos de bronconeumologia. 2021;13:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5e86dfb9bd552b43dc8e575c8cb1462c)

1. **Insights from compassionate use of tocilizumab for COVID-19 to inform appropriate design of randomised controlled trials**  
   Baker E. H. British Journal of Clinical Pharmacology 2021;87:1584-1586.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cb992fd1420149c72314afc2bb0de1ca)

1. **Interleukin-1 and interleukin-6 inhibition compared with standard management in patients with COVID-19 and hyperinflammation: a cohort study**  
   Cavalli G. The Lancet Rheumatology. 2021;:No page numbers.

Background: Patients with severe COVID-19 develop a life-threatening hyperinflammatory response to the virus. Interleukin (IL)-1 or IL-6 inhibitors have been used to treat this patient population, but the comparative effectiveness of these different strategies remains undetermined. We aimed to compare IL-1 and IL-6 inhibition in patients admitted to hospital with COVID-19, respiratory insufficiency, and hyperinflammation. Method(s): This cohort study included patients admitted to San Raffaele Hospital (Milan, Italy) with COVID-19, respiratory insufficiency, defined as a ratio of the partial pressure of oxygen to the fraction of inspired oxygen of 300 mm Hg or less, and hyperinflammation, defined as serum C-reactive protein concentration of 100 mg/L or more or ferritin concentration of 900 ng/mL or more. The primary endpoint was survival, and the secondary endpoint was a composite of death or mechanical ventilation (adverse clinical outcome). Multivariable Cox regression analysis was used to compare clinical outcomes of patients receiving IL-1 inhibition (anakinra) or IL-6 inhibition (tocilizumab or sarilumab) with those of patients who did not receive interleukin inhibitors, after accounting for baseline differences. All patients received standard care. Interaction tests were used to assess the probability of survival according to C-reactive protein or lactate dehydrogenase concentrations. Finding(s): Of 392 patients included between Feb 25 and May 20, 2020, 275 did not receive interleukin inhibitors, 62 received the IL-1 inhibitor anakinra, and 55 received an IL-6 inhibitor (29 received tocilizumab and 26 received sarilumab). In the multivariable analysis, compared with patients who did not receive interleukin inhibitors, patients treated with IL-1 inhibition had a significantly reduced mortality risk (hazard ratio [HR] 0.450, 95% CI 0.204-0.990, p=0.047), but those treated with IL-6 inhibition did not (0.900, 0.412-1.966; p=0.79). In the multivariable analysis, there was no difference in adverse clinical outcome risk in patients treated with IL-1 inhibition (HR 0.866, 95% CI 0.482-1.553; p=0.63) or IL-6 inhibition (0.882, 0.452-1.722; p=0.71) relative to patients who did not receive interleukin inhibitors. For increasing C-reactive protein concentrations, patients treated with IL-6 inhibition had a significantly reduced risk of mortality (HR 0.990, 95% CI 0.981-0.999; p=0.031) and adverse clinical outcome (0.987, 0.979-0.995; p=0.0021) compared with patients who did not receive interleukin inhibitors. For decreasing concentrations of serum lactate dehydrogenase, patients treated with an IL-1 inhibitor and patients treated with IL-6 inhibitors had a reduced risk of mortality; increasing concentrations of lactate dehydrogenase in patients receiving either interleukin inhibitor were associated with an increased risk of mortality (HR 1.009, 95% CI 1.003-1.014, p=0.0011 for IL-1 inhibitors and 1.006, 1.001-1.011, p=0.028 for IL-6 inhibitors) and adverse clinical outcome (1.006, 1.002-1.010, p=0.0031 for IL-1 inhibitors and 1.005, 1.001-1.010, p=0.016 for IL-6 inhibitors) compared with patients who did not receive interleukin inhibitors. Interpretation(s): IL-1 inhibition, but not IL-6 inhibition, was associated with a significant reduction of mortality in patients admitted to hospital with COVID-19, respiratory insufficiency, and hyperinflammation. IL-6 inhibition was effective in a subgroup of patients with markedly high C-reactive protein concentrations, whereas both IL-1 and IL-6 inhibition were effective in patients with low lactate dehydrogenase concentrations. Funding(s): None. Copyright © 2021 Elsevier Ltd

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5576663cb9f4d99f63d253e398290a87)

1. **Interleukin-6 Antagonists: Lessons From Cytokine Release Syndrome to the Therapeutic Application in Severe COVID-19 Infection**  
   Meanwatthana J. Journal of Pharmacy Practice. 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1af23250d3ad775ffcd37e35b05c7024)

1. **Interleukin-6 blockade with tocilizumab in COVID-19: Does it live up to its hype?**  
   Kow C. S. Pulmonology 2021;27:86-87.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4633389a923e04382488563b691eddcd)

1. **Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19**   
   Gordon AC New England Journal of Medicine 2021;(25 Feb):https://doi.org/10.1056/nejmoa2100433.

Results: Both tocilizumab and sarilumab met the predefined criteria for efficacy. At that time, 353 patients had been assigned to tocilizumab, 48 to sarilumab, and 402 to control. The median number of organ support-free days was 10 (interquartile range, -1 to 16) in the tocilizumab group, 11 (interquartile range, 0 to 16) in the sarilumab group, and 0 (interquartile range, -1 to 15) in the control group. The median adjusted cumulative odds ratios were 1.64 (95% credible interval, 1.25 to 2.14) for tocilizumab and 1.76 (95% credible interval, 1.17 to 2.91) for sarilumab as compared with control, yielding posterior probabilities of superiority to control of more than 99.9% and of 99.5%, respectively. An analysis of 90-day survival showed improved survival in the pooled interleukin-6 receptor antagonist groups, yielding a hazard ratio for the comparison with the control group of 1.61 (95% credible interval, 1.25 to 2.08) and a posterior probability of superiority of more than 99.9%. All secondary analyses supported efficacy of these interleukin-6 receptor antagonists. Conclusions: In critically ill patients with Covid-19 receiving organ support in ICUs, treatment with the interleukin-6 receptor antagonists tocilizumab and sarilumab improved outcomes, including survival.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f3fe3a8216db2a90e3c6b1005c02ab82)

1. **Interleukin-6 receptor blockade with subcutaneous tocilizumab improves coagulation activity in patients with COVID-19**  
   Di Nisio M. European Journal of Internal Medicine 2021;83:34-38.

Background: Many COVID-19 patients develop a hyperinflammatory response which activates blood coagulation and may contribute to the occurrence of thromboembolic complications. Blockade of interleukin-6, a key cytokine in COVID-19 pathogenesis, may improve the hypercoagulable state induced by inflammation. The aim of this study was to evaluate the effects of subcutaneous tocilizumab, a recombinant humanized monoclonal antibody against the interleukin-6 receptor on coagulation parameters. Method(s): Hospitalized adult patients with laboratory-confirmed moderate to critical COVID-19 pneumonia and hyperinflammation, who received a single 324 mg subcutaneous dose of tocilizumab on top of standard of care were enrolled in this analysis. Coagulation parameters were measured before tocilizumab and at day 1, 3, and 7 after treatment. All patients were followed-up for 35 days after admission or until death. Result(s): 70 patients (mean age 60 years, interquartile range 52-75) were included. Treatment with tocilizumab was associated with a reduction in D-dimer levels (-56%; 95% confidence interval [CI], -68% to -44%), fibrinogen (-48%; 95%CI, -60% to -35%), C-reactive protein (-93%; 95%CI, -99% to -87%), prothrombin time (-4%; 95%CI,-9% to 0.8%), and activated thromboplastin time (-4%; 95%CI,-8.7% to 0.8%), and an increase in platelet count (34%; 95%CI, 23% to 45%). These changes occurred already one day after treatment with sustained reductions throughout day 7. The improvement in coagulation was consistently observed in patients receiving prophylactic or therapeutic dose anticoagulants, and was paralleled by a rapid improvement in respiratory function. Conclusion(s): Subcutaneous tocilizumab was associated with significant improvement of blood coagulation parameters independently of thromboprophylaxis dose. Copyright © 2020

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=97934e28c828be7f0d0f3aec354ac880)

1. **Interleukin-6 receptor blockade with subcutaneous tocilizumab in severe COVID-19 pneumonia and hyperinflammation: a case-control study**  
   Potere N. Annals of the Rheumatic Diseases 2021;80:271-272.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6160ad6b8f3ba908c7ba0ddfbb53dd7d)

1. **Interleukin-6 Receptor Inhibition in Covid-19 - Cooling the Inflammatory Soup**  
   Rubin E. J. The New England journal of medicine. 2021;25:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=555e446bd9cf7bb21c22c0b4f4805931)

1. **Interleukin-6 signaling blockade treatment for cytokine release syndrome in COVID-19 (Review)**  
   Chen J. J. Experimental and Therapeutic Medicine 2021;21:1-6.

A severe immune response in patients with coro- navirus disease 2019 (COVID-19) can cause a potentially lethal unconstrained inflammatory cytokine storm, known as cytokine release syndrome (CRS). The present study provides an overview of the biology underlying CRS and how targeted inhibition of interleukin (IL)-6 signaling may improve outcomes and the survival of patients suffering from COVID-19. Preliminary clinical results have indicated that antagonism of the IL-6 receptor (IL-6R), including with the FDA-approved humanized monoclonal antibody tocili- zumab, can improve the outcomes of patients with severe or critical COVID-19 while maintaining a good safety profile. The available clinical data support the expansion of clinical trials using IL-6R targeting inhibitors for severe and critical COVID-19 treatment. Copyright © 2021 Spandidos Publications. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=48bb5470732bc079e90665bff805b46d)

1. **Interleukin-6: From arthritis to CAR-T cell therapy and COVID-19**  
   Kishimoto T. International immunology. 2021;14:No page numbers.

Blockade of interleukin (IL)-6 function by an anti-IL-6 receptor (IL-6R) antibody (tocilizumab, trade name Actemra) has been shown to be effective for the treatment of chronic autoimmune inflammatory diseases including rheumatoid arthritis. Interestingly, treatment with tocilizumab has also been found to alleviate the cytokine storm induced by chimeric antigen receptor (CAR)-T cell therapy. Patients with serious cases of coronavirus disease 2019 (COVID-19) exhibit cytokine release syndrome (CRS), which suggested that tocilizumab might be an effective therapeutic for serious cases of COVID-19. In the first part of this short review, the therapeutic effect of tocilizumab for the disease induced by IL-6 overproduction is described. CRS induced by CAR-T cell therapy and COVID-19 is then discussed. Copyright © The Japanese Society for Immunology. 2021. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ea1c106ff679028bd8fc94192bb01c56)

1. **Intestinal perforation in patient with COVID-19 infection treated with tocilizumab and corticosteroids. Report of a clinical case☆ Perforación intestinal en paciente COVID-19 en tratamiento con tocilizumab y corticoides. A propósito de un caso**  
   Gonzálvez Guardiola Paula Cirugia Espan~ola 2021;99:156-157.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a3ecf796d12ff8c7bf8b591e389b39b3)

1. **Invasive pulmonary aspergillosis after treatment with tocilizumab in a patient with COVID-19 ARDS: a case report**  
   Witting C. Diagnostic Microbiology and Infectious Disease 2021;99 (4) (no pagination):No page numbers.

Tocilizumab, an interleukin-6 receptor antagonist, has been used to treat critically ill patients with coronavirus disease-2019. We present the case of a previously immunocompetent man with coronavirus disease-2019 who developed invasive pulmonary aspergillosis after treatment with tocilizumab, illustrating the importance of considering opportunistic infections when providing immune modulating therapy. Copyright © 2020 Elsevier Inc.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f5e07e4e4e84abae3f4b2f1f9bc7b07a)

1. **Investigation of the disease process and drug combinations in patients with suspected/confirmed Covid-19 using favipiravir**  
   Oruc M. A. International journal of clinical practice 2021;:e14167.

AIMS: It is aimed to investigate the disease processes and drug combinations in patients who received favipiravir treatment. METHOD(S): This cross-sectional, analytical and retrospective study included all patients aged >=18 years (n = 502) who were hospitalised in Samsun, Turkey for COVID-19 and were given favipiravir from the date between 25 March, 2020- 3 June, 2020. RESULT(S): In total, 58.6% (n = 294) of the patients were male and 24.5% (n=123) were between the ages of 71 and 80 years. During the first case process, the mortality rate was 19.9%, whereas the rate of those who were discharged as is/followed up at home for 14 days was 37.3%. During the second case process, the mortality rate was 6.2%, and the rate of those who were discharged as is/followed up at home for 14 days was 65.6%. The mean length of hospital stay was 10.61 +/- 8.17 days for the first and 7.97 +/- 4.16 days for the second hospitalisation, this difference was significant. Mortality risk of those who used Tocilizumab or vitamin C beside Favipiravir was higher than those who did not. The length of hospital stay was higher in patients using tocilizumab than in those who did not (p < 0.001). CONCLUSION(S): Administration of favipiravir later in the course of the disease makes it difficult to achieve the true efficacy expected from the drug and also makes it difficult for other combination drugs to contribute to survival. Favipiravir may also be effective in case of recurrence. Copyright This article is protected by copyright. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0c0fdb9c40b2e96d1c613f8d315822c3)

1. **Is There Still a Place for Tocilizumab in Coronavirus Disease 2019?**  
   Klopfenstein Timothée Open forum infectious diseases 2021;8:ofab013.

In this article, we sought to summarize the available evidence of tocilizumab as a treatment for coronavirus disease 2019. Recent tocilizumab randomized trials have not shown clear evidence of efficacy, especially on mortality, in contrast to observational studies. These clinical trials focus on a heterogeneous population of patients (clinical severity and inflammatory stage), and this is possibly one of the reasons that explain heterogeneity of results. However, these same trials have shown some evidence that tocilizumab may reduce intensive care unit admissions and/or mechanical ventilation incidence, which are huge challenges in the severe acute respiratory syndrome coronavirus 2 pandemic. Future clinical trials with primary endpoint built on this assumption are needed (1) to confirm whether tocilizumab reduces mechanical ventilation requirement and (2) to describe the right patient population and optimal timing for tocilizumab administration. Finding the optimal timing for tocilizumab administration and the group of patients who are susceptible to having the greatest benefit are probably the main challenge.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=57d6686cd28adadbf0ffec8653944d91)

1. **Late onset infectious complications and safety of tocilizumab in the management of COVID-19**  
   Pettit N. N. Journal of Medical Virology 2021;93:1459-1464.

Background: Tocilizumab (TCZ) has been used in the management of COVID-19-related cytokine release syndrome (CRS). Concerns exist regarding the risk of infections and drug-related toxicities. We sought to evaluate the incidence of these TCZ complications among COVID-19 patients. Method(s): All adult inpatients with COVID-19 between 1 March and 25 April 2020 that received TCZ were included. We compared the rate of late-onset infections (>48 hours following admission) to a control group matched according to intensive care unit admission and mechanical ventilation requirement. Post-TCZ toxicities evaluated included: elevated liver function tests (LFTs), GI perforation, diverticulitis, neutropenia, hypertension, allergic reactions, and infusion-related reactions. Result(s): Seventy-four patients were included in each group. Seventeen infections in the TCZ group (23%) and 6 (8%) infections in the control group occurred >48 hours after admission (P =.013). Most infections were bacterial with pneumonia being the most common manifestation. Among patients receiving TCZ, LFT elevations were observed in 51%, neutropenia in 1.4%, and hypertension in 8%. The mortality rate among those that received TCZ was greater than the control (39% versus 23%, P =.03). Conclusion(s): Late onset infections were significantly more common among those receiving TCZ. Combining infections and TCZ-related toxicities, 61% of patients had a possible post-TCZ complication. While awaiting clinical trial results to establish the efficacy of TCZ for COVID-19 related CRS, the potential for infections and TCZ related toxicities should be carefully weighed when considering use. Copyright © 2020 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d8439352c97eb7edd25f3d1ff876bb96)

1. **Matched cohort study on the efficacy of tocilizumab in patients with COVID-19**  
   Rodriguez-Molinero A. One Health 2021;12 (no pagination):No page numbers.

Background: Tocilizumab has been proposed as a treatment for the new disease COVID-19, however, there is not enough scientific evidence to support this treatment. The objective of this study is to analyze whether the use of tocilizumab is associated with respiratory improvement and a shorter time to discharge in patients with COVID-19 and lung involvement. Method(s): Observational study on a cohort of 418 patients, admitted to three county hospitals in Catalonia (Spain). Patients admitted consecutively were included and followed until discharge or up to 30 days of admission. A sub-cohort of patients treated with tocilizumab and a sub-cohort of control patients were identified, matched by a large number of risk factors and clinical variables. Sub-cohorts were also matched by the number of other treatments for COVID-19 that patients received. Increment in SAFI (inspired oxygen fraction / saturation) 48 h after the start of treatment, and time to discharge, were the primary outcomes. Mortality, which was a secondary outcome, was analyzed in the total cohort, by using logistic regression models, adjusted by confounders. Result(s): There were 96 patients treated with tocilizumab. Of them, 22 patients could be matched with an equivalent number of control patients. The increment in SAFI from baseline to 48 h of treatment, was not significantly different between groups (tocilizumab: -0.04; control: 0.09; p = 0.636). Also, no difference in time to discharge was found between the two sub-cohorts (logrank test: p = 0.472). The logistic regression models, did not show an effect of tocilizumab on mortality (OR 0.99; p = 0.990). Conclusion(s): We did not find a clinical benefit associated with the use tocilizumab, in terms of respiratory function at 48 h of treatment, or time to discharge. Copyright © 2021 The Authors

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c2f853bb3d05ef16afa4f8557d74cdf4)

1. **Metabolomic/lipidomic profiling of COVID-19 and individual response to tocilizumab**  
   Meoni G. PLoS Pathogens 2021;17 (2) (no pagination):No page numbers.

The current pandemic emergence of novel coronavirus disease (COVID-19) poses a relevant threat to global health. SARS-CoV-2 infection is characterized by a wide range of clinical manifestations, ranging from absence of symptoms to severe forms that need intensive care treatment. Here, plasma-EDTA samples of 30 patients compared with age- and sexmatched controls were analyzed via untargeted nuclear magnetic resonance (NMR)-based metabolomics and lipidomics. With the same approach, the effect of tocilizumab administration was evaluated in a subset of patients. Despite the heterogeneity of the clinical symptoms, COVID-19 patients are characterized by common plasma metabolomic and lipidomic signatures (91.7% and 87.5% accuracy, respectively, when compared to controls). Tocilizumab treatment resulted in at least partial reversion of the metabolic alterations due to SARS-CoV-2 infection. In conclusion, NMR-based metabolomic and lipidomic profiling provides novel insights into the pathophysiological mechanism of human response to SARSCoV- 2 infection and to monitor treatment outcomes. Copyright: Copyright © 2021 Meoni et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ae5bbe17d92d72af5545e63d2632b8c2)

1. **Methylprednisolone as rescue therapy after tocilizumab failure in patients with severe COVID-19 pneumonia**  
   Guaraldi Giovanni Clinical and experimental rheumatology 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=3dd36937cb83340f4810840d64dd7a1a)

1. **Monitoring neutrophil-to-lymphocyte ratio in patients with coronavirus disease 2019 receiving tocilizumab**  
   Hartog N. L. Annals of Allergy, Asthma and Immunology 2021;126:306-308.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1cacbda2d6bfba25ed2bec55b0641771)

1. **Multifactorial expression of IL-6 with update on COVID-19 and the therapeutic strategies of its blockade (Review)**  
   Niculet Elena Experimental and therapeutic medicine 2021;21:263.

Interleukin 6 (IL-6), a cytokine produced by various cells of the human body (macrophages, lymphocytes, astrocytes, ischemic myocytes, endothelial cells) has both pro-inflammatory and anti-inflammatory properties, being a key component in regulating various physiologic and pathological processes. The structure of this molecule and the receptor system it possesses are important due to the different activities that IL-6 can exert; through trans-signaling pro-inflammatory activities are mediated, while through classic signaling, IL-6 is responsible for anti-inflammatory and regenerative activities. IL-6 signaling is involved in coronary artery disease and the global COVID-19 pandemic. This proatherogenic cytokine reaches elevated serum levels in the cytokine storm generated by SARS-CoV-2, and is also associated with smoking or obesity-classic cardiovascular risk factors which promote inflammatory states. IL-6 levels are proportionally correlated with dyslipidemia, hypertension and glucose dysregulation, and they are associated with poor outcomes in patients with unstable angina or acute myocardial infarction. IL-6 targeting for treatment development (not only) in cardiovascular disease and COVID-19 is still a matter of ongoing research, although tocilizumab has proven to be effective in reducing the proatherogenic effects of IL-6 and is suggested to improve COVID-19 patient survival.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=50b7a4746dcb2ca7a9f43b8ed4c823cc)

1. **Multimodality treatment in immunocompromised patients with severe COVID-19: the role of IL-6 inhibitor, intravenous immunoglobulin, and haemoperfusion**  
   Leelayuwatanakul N. Respirology Case Reports 2021;9 (4) (no pagination):No page numbers.

Cytokine release syndrome (CRS) is known to be associated with severe coronavirus disease 2019 (COVID-19). Multiple anti-inflammatory therapies such as tocilizumab, corticosteroids, intravenous immunoglobulin (IVIG), and haemoadsorption or haemoperfusion have been used to combat this life-threatening condition. However, immunocompromised hosts are often omitted from research studies, and knowledge on the clinical efficacy of these therapies in immunocompromised patients is therefore limited. We report two cases of immunocompromised patients with severe COVID-19-related CRS requiring mechanical ventilation who were treated with multimodality treatment consisting of tocilizumab, IVIG, and haemoperfusion. Within 48 h, both patients showed clinical improvement with PaO<inf>2</inf>:FiO<inf>2</inf> ratio and haemodynamic stability. Both survived to discharge. There were no adverse events following these therapies. In conclusion, combined therapeutic modalities, possibly tailored to individual inflammatory profiles, are promising treatment for severe COVID-19 infection in the immunocompromised host. Timely administration of adjunctive therapies that alleviate overwhelming inflammation may provide the best outcome. Copyright © 2021 The Authors. Respirology Case Reports published by John Wiley & Sons Australia, Ltd on behalf of The Asian Pacific Society of Respirology.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=dd143f9b22c6078c1066aef0f5b42f26)

1. **Multistate modeling of COVID-19 patients using a large multicentric prospective cohort of critically ILL patients**  
   Ursino M. Journal of Clinical Medicine 2021;10:1-13.

The mortality of COVID-19 patients in the intensive care unit (ICU) is influenced by their state at admission. We aimed to model COVID-19 acute respiratory distress syndrome state transitions from ICU admission to day 60 outcome and to evaluate possible prognostic factors. We analyzed a prospective French database that includes critically ill COVID-19 patients. A six-state multistate model was built and 17 transitions were analyzed either using a non-parametric approach or a Cox proportional hazard model. Corticosteroids and IL-antagonists (tocilizumab and anakinra) effects were evaluated using G-computation. We included 382 patients in the analysis: 243 patients were admitted to the ICU with non-invasive ventilation, 116 with invasive mechanical ventilation, and 23 with extracorporeal membrane oxygenation. The predicted 60-day mortality was 25.9% (95% CI: 21.8%-30.0%), 44.7% (95% CI: 48.8%-50.6%), and 59.2% (95% CI: 49.4%-69.0%) for a patient admitted in these three states, respectively. Corticosteroids decreased the risk of being invasively ventilated (hazard ratio (HR) 0.59, 95% CI: 0.39-0.90) and IL-antagonists increased the probability of being successfully extubated (HR 1.8, 95% CI: 1.02-3.17). Antiviral drugs did not impact any transition. In conclusion, we observed that the day-60 outcome in COVID-19 patients is highly dependent on the first ventilation state upon ICU admission. Moreover, we illustrated that corticosteroid and IL-antagonists may influence the intubation duration. Copyright © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a09fa255c2c885664fd7b7f3d9798dae)

1. **Nomogram for prediction of fatal outcome in patients with severe COVID-19: a multicenter study**  
   Yang Y. Military Medical Research 2021;8 (1) (no pagination):No page numbers.

Background: To develop an effective model of predicting fatal outcomes in the severe coronavirus disease 2019 (COVID-19) patients. Method(s): Between February 20, 2020 and April 4, 2020, consecutive confirmed 2541 COVID-19 patients from three designated hospitals were enrolled in this study. All patients received chest computed tomography (CT) and serological examinations at admission. Laboratory tests included routine blood tests, liver function, renal function, coagulation profile, C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), and arterial blood gas. The SaO<inf>2</inf> was measured using pulse oxygen saturation in room air at resting status. Independent high-risk factors associated with death were analyzed using Cox proportional hazard model. A prognostic nomogram was constructed to predict the survival of severe COVID-19 patients. Result(s): There were 124 severe patients in the training cohort, and there were 71 and 76 severe patients in the two independent validation cohorts, respectively. Multivariate Cox analysis indicated that age >= 70 years (HR = 1.184, 95% CI 1.061-1.321), panting (breathing rate >= 30/min) (HR = 3.300, 95% CI 2.509-6.286), lymphocyte count < 1.0 x 10<sup>9</sup>/L (HR = 2.283, 95% CI 1.779-3.267), and interleukin-6 (IL-6) > 10 pg/ml (HR = 3.029, 95% CI 1.567-7.116) were independent high-risk factors associated with fatal outcome. We developed the nomogram for identifying survival of severe COVID-19 patients in the training cohort (AUC = 0.900, 95% CI 0.841-0.960, sensitivity 95.5%, specificity 77.5%); in validation cohort 1 (AUC = 0.811, 95% CI 0.763-0.961, sensitivity 77.3%, specificity 73.5%); in validation cohort 2 (AUC = 0.862, 95% CI 0.698-0.924, sensitivity 92.9%, specificity 64.5%). The calibration curve for probability of death indicated a good consistence between prediction by the nomogram and the actual observation. The prognosis of severe COVID-19 patients with high levels of IL-6 receiving tocilizumab were better than that of those patients without tocilizumab both in the training and validation cohorts, but without difference (P = 0.105 for training cohort, P = 0.133 for validation cohort 1, and P = 0.210 for validation cohort 2). Conclusion(s): This nomogram could help clinicians to identify severe patients who have high risk of death, and to develop more appropriate treatment strategies to reduce the mortality of severe patients. Tocilizumab may improve the prognosis of severe COVID-19 patients with high levels of IL-6. Copyright © 2021, The Author(s).

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=fd3ca10a3a258d2eb217c1d5cf22cb12)

1. **Observational study on off-label use of tocilizumab in patients with severe COVID-19**  
   Albertini L. European Journal of Hospital Pharmacy 2021;28:22-27.

Background In December 2019 a novel coronavirus designated SARS-CoV-2 was identified, and the disease COVID-19 has caused many deaths. SARS-CoV-2 infection has been associated with the development of cytokine storm (including interleukin 6 (IL-6)), which can cause lung damage and lack of oxygen. Tocilizumab (TCZ) inhibits ligand binding to the IL-6 receptor and may be a potential treatment for the hyperinflammation symptoms of COVID-19. However, data regarding the efficacy of TCZ in COVID-19 are lacking. The rapid spread of the pandemic in France, especially in the Paris region, constrained us to the off-label use of TCZ in patients with severe clinical conditions. Methods A single-centre observational cohort study of 44 patients infected with COVID-19 was carried out between 6 April and 21 April 2020 in Groupe Hospitalier Intercommunal Le Raincy-Montfermeil (GHILRM). Twenty-two patients diagnosed with COVID-19 were treated with TCZ and were compared with 22 patients not treated with TCZ matched for age, gender and length of hospital stay for COVID-19. Respiratory rate and oxygen supplementation as well as laboratory parameters (such as C-reactive protein (CRP), aspartate aminotransferase and alanine aminotransferase) were collected at baseline and during 14 days of follow-up. Our primary objective was to assess the efficacy of TCZ on respiratory clinical conditions. Findings The average respiratory rate was lower in the TCZ group than in the control group (21.5 vs 25.5 breaths/min at day 14, 95% CI-7.5 to-0.4; p=0.03). Treated patients tended to be intubated less during the course of the disease (2/22 vs 6/22, 95% CI-0.4 to 0.1; p=0.12). In each group, 10 patients no longer required oxygen therapy. We found a significant decrease in CRP in treated patients on day 7 (p=0.04). TCZ caused cytolysis in more than half (14/22) of the patients but without clinical impact. Interpretation There was a significant difference in the respiratory rate on day 14 of follow-up, with a greater decrease observed in the treated group. Fewer patients required mechanical ventilation in the TCZ group, especially among patients with more extensive CT lung damage, than in the control group. The same number of patients were weaned off oxygen on day 14 in the two groups, while the patients in the TCZ group had more severe impairment at inclusion. We consider that TCZ showed significant control of the biological inflammatory syndrome, suggesting that it may limit the effect of the cytokine storm. Our study seems to indicate the efficacy of TCZ, particularly in patients with severe initial pulmonary impairment. Selecting the best candidates and the best timing for TCZ therapy needs to be determined in randomised clinical trials. Copyright ©

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f6924b81c1ad7aa3497b285de64fb744)

1. **Perspectives on Targeting IL-6 as a Potential Therapeutic Strategy for COVID-19**  
   Khaedir Yordan Journal of interferon &amp; cytokine research : the official journal of the International Society for Interferon and Cytokine Research 2021;41:37-43.

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been a major threat to global public health. In Indonesia, the cases have rapidly increased, and the case fatality rate remains high. With COVID-19, most of the deaths have been caused by acute respiratory distress syndrome and dysregulation of the immune response. A lung biopsy from a patient with COVID-19 showed inflammatory cellular infiltration with diffuse alveolar damage. Massive pulmonary destruction has also been reported as a result of highly increased levels of proinflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), IL-1β, interferon-γ (IFN-γ), induced protein 10 (IP-10), and monocyte chemoattractant protein-1 (MCP-1). IL-6 is an inflammatory cytokine produced by various cell types, including immune cells and nonleukocytes, such as endothelial cells, fibroblasts, epithelial cells, type II pneumocytes, and certain tumor cells. Several studies have shown that IL-6 contributes to the severity and mortality of COVID-19. In this review, we would like to explore the immune response in COVID-19 and the role of IL-6 in the immunopathogenesis of COVID-19.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6d369e2200b2e270dfdb1a7ec07cc84c)

1. **Post-transplant patients with COVID-19 associated acute respiratory distress syndrome, a role for Tociluzumab: A case series**  
   Ladna M. Respiratory Medicine Case Reports 2021;32 (no pagination):No page numbers.

COVID-19 is the disease caused by SARS-CoV-2 that portends both a relatively high mortality rate as well as high rate of intensive care admission amongst all age groups; however effective therapy remains poorly characterized. Post-transplant patients are especially high risk and underrepresented in the literature. In these patients, cytokine release may play a significant role in the development of acute respiratory distress syndrome, raising the hypothesis that interleukin-6 inhibitors such as tocilizumab may be of benefit. Here, we describe two high-risk post-transplant patients who were treated with single-dose tocilizumab after intubation for moderate acute respiratory distress syndrome secondary to confirmed COVID-19 infection. Both patients recovered rapidly and were successfully extubated and discharged from the hospital without need for supplemental oxygen shortly thereafter, and their clinical improvement correlated with response in interleukin-6 levels. Tocilizumab appears to hold promise for critically ill COVID-19 patients who require mechanical ventilation when given shortly after intubation. Copyright © 2020

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e43f6a7d86356f55bab8dad4232342e8)

1. **Posterior Reversible Encephalopathy Syndrome in a Patient With SARS-CoV-2 Infection Treated With Tocilizumab**  
   Talluri Krishna Cureus 2021;13:e13475.

As the world has struggled to adapt to the coronavirus disease (COVID-19) pandemic, new evidence has emerged suggesting that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may manifest with a wide variety of neurologic symptoms. We present the case of a 70-year-old patient hospitalized for COVID-19 related pneumonia who was treated with off-label interleukin (IL)-6 inhibitor tocilizumab and eventually developed prolonged delirium. MRI findings were consistent with posterior reversible encephalopathy syndrome (PRES). PRES was felt to be from SARS-CoV-2 infection, tocilizumab, or a combination. The patient received symptomatic treatment without success. These findings are consistent with few other recent reports, which have chronicled PRES findings in patients with SARS-CoV-2 infections. However, this is only the second example of PRES in a COVID-19 patient treated with tocilizumab. While cases of PRES have been noted to occur with other infectious diseases, clinicians should be aware of the association with SARS-CoV-2 infection and tocilizumab therapy, particularly when considering tocilizumab treatment outside its approved indication. Future research efforts are needed to establish evidence-based guidelines for the management of these patients.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0ddb3b5af4d84bf675c4d4b55c60202e)

1. **Potential role of subcutaneous tocilizumab injections in patients with COVID-19 associated pneumonia**  
   Greco G. Journal of Medical Virology 2021;93:686-688.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=346888b977e3c29f190dafc6d1043651)

1. **Predictors of Mortality Amongst Tocilizumab Administered COVID-19 Asian Indians: A Predictive Study From a Tertiary Care Centre**  
   Desai Hardik D. Cureus 2021;13:e13116.

Introduction Hyper-cytokinemia is a dreaded complication of severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) infection and an important predictor of mortality in coronavirus disease 2019 (COVID-19). The current evidence at best is still ambiguous for use of tocilizumab in cytokine storm in COVID-19. Moreover, the factors that are associated with beneficial response from tocilizumab are unknown in COVID-19. We aimed to study the clinical outcomes especially mortality vis-à-vis clinical and laboratory characteristics of patients administered tocilizumab and identify predictors of mortality benefits amongst deceased vs recovered COVID-19 patients. Methods The present study is a retrospective observation of the demographic, clinical, and biological data of all the consecutive patients treated with tocilizumab for COVID-19 pneumonia at the COVID tertiary care centre from July 2020 to October 2020 at Ahmedabad, India. We compared the deceased group with those who recovered/discharged and evaluated patient-level demographics, clinical attributes, and laboratory investigations available to identify subgroups in whom tocilizumab reduced mortality. Results Of the 112 patients included, the mean (SD) age was 56.84 ± 13.56 years and 80 (71.4%) were male. There were 97 (86.6%) patients in the survivors and 15 (13.39%) in the deceased group. Deceased were older than the recovered group (mean: 66.14, SD: 14.41 vs mean: 55.36, SD: 12.98; p=0.04). Hypertension (33.03%) was the commonest comorbidity observed. Mortality was significantly higher in patients with cancer and type-2 diabetes (p=0.05 and p=0.01, respectively). Level of D-dimer and lactate dehydrogenase (LDH) showed trends towards significance as a predictor of mortality (p=0.07 and p=0.08, respectively) not reaching significance. D-dimer level &gt; 5,000 nanograms per millilitre (ng/mL) was the significant predictor of subsequent deaths (p&lt;0.0001). Fourteen patients reported adverse events of tocilizumab. Patients who developed in-hospital complications (such as septic or vasodilatory shock and/or sepsis, acute kidney injury, multiorgan dysfunction) had significantly higher mortality (p&lt;0.0001, p=0.009, and p=0.03, respectively). Conclusion Tocilizumab might be more beneficial in younger patients without sepsis/ septic shock, acute kidney injury, multiorgan dysfunction, and who were non-ventilated. The predictors of mortality amongst Asian Indians treated with tocilizumab were older patients, the presence of type-2 diabetes, cancer, in-hospital complication (such as acute kidney injury, sepsis/septic shock, multiorgan dysfunction), higher D-dimer &gt; 5,000 ng/mL. A larger study with pre-defined inclusion cut-offs of these variables may aid in defining patient's characteristics of Asian Indians who may benefit from tocilizumab in COVID-19.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=18ee7adc4b29d525fd66fdcb2d069ca9)

1. **Preliminary Efficacy of Tocilizumab Treatment in The Patients With COVID-19**  
   Chen Yu 2021;:No page numbers.

&lt;h4&gt;Background: &lt;/h4&gt; Interleukin-6 (IL-6) was considered to be with the severity and mortality in COVID-19 patients, which implies a potential therapeutic target for treatment. We aimed to evaluate the safety and initial efficacy of Tocilizumab treatment for COVID-19 patients. &lt;h4&gt;Methods: &lt;/h4&gt; In the retrospective study, sixty-one patients with COVID-19 with the mean age of 69 were enrolled from Feb 27 to Mar 14, 2020 in Wuhan Huoshenshan Hospital. Twenty-nine of them received one dose (400 mg) of add-on Tocilizumab treatment as the treated group and remaining 32 cases served as control group. The clinical manifestations and laboratory examinations were compared between the two groups. &lt;h4&gt;Results: &lt;/h4&gt;: The average duration of symptoms to admission was 28.2 days. Compared with the cases in control group, the treated cases exhibited a significant increase of serum IL-6 on the seventh day since Tocilizumab injection, however, there were no differences in whole blood white cell count, circulating lymphocyte count, serum C-reactive protein, and respiratory parameters or other clinical manifestations between the treated and control groups. There were no adverse events associated with Tocilizumab treatment in the treated COVID-19 patients. &lt;h4&gt;Conclusions: &lt;/h4&gt; In the elder moderate and severe patients with COVID-19, one dose of Tocilizumab treatment was safe but no clinical benefit was observed on the seventh day in this study. Trial registration: Chinese Clinical Trail Registry, ChiCTR2000033705. Registered June 10, 2020 - Retrospectively registered, http://www.chictr.org.cn/showprojen.aspx?proj=54989.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c33257071b559e50a78d430236cfed91)

1. **Rapid radiological improvement of COVID-19 pneumonia after treatment with tocilizumab**  
   Comel A. C. Infection 2021;49:195-196.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=850ce5d11b0313ecef671a06d6a4dfa4)

1. **Repurposed tocilizumab in patients with severe COVID-19**  
   Tian J. Journal of Immunology 2021;206:599-606.

The coronavirus disease 2019 (COVID-19) has caused a global pandemic, resulting in considerable morbidity and mortality. Tocilizumab, an inhibitor of IL-6, has been widely repurposed as a treatment of severely ill patients without robust evidence supporting its use. In this study, we aimed to systematically describe the effectiveness of treatment and prevention of the cytokine storms in COVID-19 patients with tocilizumab. In this multicentered retrospective and observational cohort study, 65 patients with COVID-19 receiving tocilizumab and 130 not receiving tocilizumab were propensity score matched at a ratio of 2:1 based on age, sex, and comorbidities from January 20, 2020 to March 18, 2020 in Wuhan, China. After adjusting for confounding, the detected risk for in-hospital death was lower in the tocilizumab group versus nontocilizumab group (hazard ratio = 0.47; 95% confidence interval = 0.25-0.90; p = 0.023). Moreover, use of tocilizumab was associated with a lower risk of acute respiratory distress syndrome (odds ratio = 0.23; 95% confidence interval = 0.11-0.45; p < 0.0001). Furthermore, patients had heightened inflammation and more dysregulated immune cells before treatment, which might aggravate disease progression. After tocilizumab administration, abnormally elevated IL-6, C-reactive protein, fibrinogen, and activated partial thromboplastin time decreased. Tocilizumab may be of value in prolonging survival in patients with severe COVID-19, which provided a novel strategy for COVID-19-induced cytokine release syndrome. Our findings could inform bedside decisions until data from randomized, controlled clinical trials become available. Copyright © 2021 by The American Association of Immunologists, Inc.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=efab55e3a2152bc39d9cfe80ed18eb6b)

1. **Repurposing Antimalarials to Tackle the COVID-19 Pandemic**  
   Krishna S. Trends in Parasitology 2021;37:8-11.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=072eef1f1dc91a2a080ce8f368daca31)

1. **Respiratory delivery of favipiravir-tocilizumab combination through mucoadhesive protein-lipidic nanovesicles: prospective therapeutics against COVID-19**  
   Thakur V. VirusDisease. 2021;:No page numbers.

Coronavirus disease 19 (COVID-19) is the prime global health concern of the year 2020. Infecting more than 112 million individuals so far, this pandemic has already reported more than 2.4 million deaths around the world. With such high infectivity and mortality, effective treatment intervention is the need of the hour. The integration of medical science with nanotechnology may solve the current problem by exploring collective benefits. In this manuscript, we theoretically proposed the duo-combination of an approved antiviral i.e. favipiravir along with an immunomodulator i.e. tocilizumab loaded in protein-lipid nanovesicles as an effective anti-COVID-19 therapeutic. This proposed nanomedicine delivered through the respiratory mode may enhance the effectiveness of the antiviral and help in restricting the virus and associated complications, utilizing both anti-viral activity and immunomodulation in COVID-19 patients. This proposed nanomedicine could be an effective treatment modality for the severe acute respiratory syndrome- coronavirus-2 (SARS-CoV-2) infected patients. Copyright © 2021, Indian Virological Society.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=115fe7ef8c104e34de82e24257090c3f)

1. **Risk of Hepatitis B Virus Reactivation in Rheumatoid Arthritis Patients Undergoing Tocilizumab-Containing Treatment**  
   Kuo M. H. Digestive Diseases and Sciences. 2021;:No page numbers.

Background and Aim: To investigate the risk of hepatitis B virus reactivation in patients undergoing long-term tocilizumab therapy for rheumatoid arthritis. Method(s): From January 2011 through August 2019, a total of 97 patients were enrolled in this retrospective study. Clinical data, comedications, and the occurrence of HBV reactivation were recorded. Result(s): Seven patients were HBsAg+ (7.2%), 64 were HBsAg-/HBcAb+ (65.9%), and 26 were HBsAg-/HBcAb- (26.8%). The median disease follow-up time was 9 years. TCZ was administered for a median of 29 months. Four patients (4.1%) experienced HBV reactivation after tocilizumab therapy. Of the 7 HBsAg+ patients, 4 received antiviral prophylaxis and had no HBV reactivation; the remaining 3 patients did not receive antiviral prophylaxis, and all 3 (100%) experienced HBV reactivation and hepatitis flare-up. Hyperbilirubinemia occurred in 2 of these 3 patients, with mild prothrombin time prolongation in one. After salvage entecavir treatment, all patients had a favorable outcome. Of the 64 HBsAg-/HBcAb+ patients, only one became positive for serum HBV DNA (2.5 x 10<sup>7</sup> IU/mL) after 18 months of tocilizumab treatment (1.6%; 1/64). This patient was immediately treated with entecavir, which prevented hepatitis flare-up. Conclusion(s): Tocilizumab is widely used in treating rheumatoid arthritis and has the potential to reduce the mortality rate among severe COVID-19 patients. However, HBV reactivation needs to be considered. HBsAg+ patients have a high risk of HBV reactivation, which could be prevented by antiviral prophylaxis. Although the risk of reactivation is low in HBsAg-/HBcAb+ patients, strict monitoring is necessary. Copyright © 2021, Springer Science+Business Media, LLC, part of Springer Nature.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=756e235bbed8a7b5b23c24aec253b85c)

1. **Role of IL-6 inhibitor in treatment of COVID-19-related cytokine release syndrome**  
   Du P. International Journal of Medical Sciences 2021;18:1356-1362.

Cytokine release syndrome (CRS) may be the key factor in the pathology of severe coronavirus disease 2019 (COVID-19). As a major driver in triggering CRS in patients with COVID-19, interleukin-6 (IL-6) appears to be a promising target for therapeutics. The results of inhibiting both trans- and classicalsignaling with marketed IL-6 inhibitors (tocilizumab, siltuximab and sarilumab) in severe COVID-19 patients are effective based on several small studies and case reports thus far. In this review, we described the evidence of the IL-6 response in patients with COVID-19, clarified the pathogenesis of the role of IL-6-mediated CRS in severe COVID-19, and highlighted the rationale for the use of anti-IL-6 agents and key information regarding the potential features of these IL-6 inhibitors in COVID-19 patients. Copyright © The author(s).

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8ff285873e66ed0897498dabc6c6d702)

1. **Role of tocilizumab for concomitant systemic fungal infection in severe COVID-19 patient: Case report**  
   Sari Anggraini Permata Medicine 2021;100:e25173.

&lt;h4&gt;Rationale&lt;/h4&gt;Bacterial and fungal infections in Coronavirus Disease-19 (COVID-19) patients have been inadequately investigated and reported thus far. The safety profile of tocilizumab (TCZ) administration in candidemia patient still debatable.&lt;h4&gt;Patient concerns&lt;/h4&gt;A 54 year-old woman presenting with weakness on the left side of her body was diagnosed with COVID-19. After 7 days of admission, her condition worsened and developed respiratory distress and was having respiratory distress despite standard treatment.&lt;h4&gt;Diagnoses&lt;/h4&gt;Acute respiratory distress syndrome (ARDS) in COVID 19 was diagnoses based on real time-PCR swab, deterioration of PaO2/FiO2 and increased of acute phase reactants.&lt;h4&gt;Interventions&lt;/h4&gt;Anti Interleukin-6 (IL-6) was considered to tackle her inflammatory condition. Prior to TCZ administration, blood culture was performed and the result came with Candida tropicalis in the absence of bacterial growth.&lt;h4&gt;Outcomes&lt;/h4&gt;No major complications associated with intravenous antifungal or TCZ occurred. After 40 days of hospitalization, the patient's clinical condition improved and was finally discharged.&lt;h4&gt;Lessons&lt;/h4&gt;This case underscores the safety profile of giving TCZ in candidemia as a secondary infection in severe COVID-19 patient.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d42204ccb42f336f71b71f23ef0e69dd)

1. **Safety of tocilizumab in COVID-19 pregnant women and their newborn: A retrospective study**  
   Jimenez-Lozano I. Journal of Clinical Pharmacy and Therapeutics. 2021;:No page numbers.

What is known and objective: Tocilizumab is an IL-6 receptor inhibitor agent which has been proposed as a candidate to stop the inflammatory phase of infection by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). However, safety data of tocilizumab in pregnant women and their newborn are scarce. We aimed to describe maternal and neonatal safety outcomes associated with tocilizumab treatment in pregnant women with severe COVID-19. Method(s): This is a retrospective study of severe COVID-19 pregnant women, treated with tocilizumab in two Spanish hospitals between 1 March and 31 April 2020. Demographics, medical history, clinical and radiologic findings, treatment information and laboratory data of mothers and their newborns were collected from electronic medical records. Results and discussion: A total of 12 pregnant women were identified to have received tocilizumab during pregnancy in the two hospitals. Median gestational age at admission was 27.7 weeks (interquartile range, 18.0-36.4). Most of them received lopinavir/ritonavir, azithromycin and hydroxychloroquine, two patients received corticosteroids and one received interferon beta 1B. All 12 pregnancies resulted in live births. Somatometric values were normal for all newborns, and evolution at 14 and 28 days was favourable for all of them. Hepatotoxicity was observed in 2 patients, which improved or resolved at discharge. Cytomegalovirus reactivation was detected in another patient who had also received corticosteroids for 15 days, causing a congenital infection in her newborn. Both hepatotoxicity and viral reactivation adverse events were classified as possibly related to tocilizumab administration according to Naranjo's causality algorithm. What is new and conclusions: It does not appear that tocilizumab has detrimental effects for the mother and newborn. Close monitoring of infections should be considered, especially if other immunosuppressive agents are used. Copyright © 2021 John Wiley & Sons Ltd

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7f4f18a741b5a489528d6a3237b37f13)

1. **Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial**  
   Lescure F. X. The Lancet. Respiratory medicine. 2021;04:No page numbers.

BACKGROUND: Elevated proinflammatory cytokines are associated with greater COVID-19 severity. We aimed to assess safety and efficacy of sarilumab, an interleukin-6 receptor inhibitor, in patients with severe (requiring supplemental oxygen by nasal cannula or face mask) or critical (requiring greater supplemental oxygen, mechanical ventilation, or extracorporeal support) COVID-19. METHOD(S): We did a 60-day, randomised, double-blind, placebo-controlled, multinational phase 3 trial at 45 hospitals in Argentina, Brazil, Canada, Chile, France, Germany, Israel, Italy, Japan, Russia, and Spain. We included adults (>=18 years) admitted to hospital with laboratory-confirmed SARS-CoV-2 infection and pneumonia, who required oxygen supplementation or intensive care. Patients were randomly assigned (2:2:1 with permuted blocks of five) to receive intravenous sarilumab 400 mg, sarilumab 200 mg, or placebo. Patients, care providers, outcome assessors, and investigators remained masked to assigned intervention throughout the course of the study. The primary endpoint was time to clinical improvement of two or more points (seven point scale ranging from 1 [death] to 7 [discharged from hospital]) in the modified intention-to-treat population. The key secondary endpoint was proportion of patients alive at day 29. Safety outcomes included adverse events and laboratory assessments. This study is registered with ClinicalTrials.gov, NCT04327388; EudraCT, 2020-001162-12; and WHO, U1111-1249-6021. FINDINGS: Between March 28 and July 3, 2020, of 431 patients who were screened, 420 patients were randomly assigned and 416 received placebo (n=84 [20%]), sarilumab 200 mg (n=159 [38%]), or sarilumab 400 mg (n=173 [42%]). At day 29, no significant differences were seen in median time to an improvement of two or more points between placebo (12.0 days [95% CI 9.0 to 15.0]) and sarilumab 200 mg (10.0 days [9.0 to 12.0]; hazard ratio [HR] 1.03 [95% CI 0.75 to 1.40]; log-rank p=0.96) or sarilumab 400 mg (10.0 days [9.0 to 13.0]; HR 1.14 [95% CI 0.84 to 1.54]; log-rank p=0.34), or in proportions of patients alive (77 [92%] of 84 patients in the placebo group; 143 [90%] of 159 patients in the sarilumab 200 mg group; difference -1.7 [-9.3 to 5.8]; p=0.63 vs placebo; and 159 [92%] of 173 patients in the sarilumab 400 mg group; difference 0.2 [-6.9 to 7.4]; p=0.85 vs placebo). At day 29, there were numerical, non-significant survival differences between sarilumab 400 mg (88%) and placebo (79%; difference +8.9% [95% CI -7.7 to 25.5]; p=0.25) for patients who had critical disease. No unexpected safety signals were seen. The rates of treatment-emergent adverse events were 65% (55 of 84) in the placebo group, 65% (103 of 159) in the sarilumab 200 mg group, and 70% (121 of 173) in the sarilumab 400 mg group, and of those leading to death 11% (nine of 84) were in the placebo group, 11% (17 of 159) were in the sarilumab 200 mg group, and 10% (18 of 173) were in the sarilumab 400 mg group. INTERPRETATION: This trial did not show efficacy of sarilumab in patients admitted to hospital with COVID-19 and receiving supplemental oxygen. Adequately powered trials of targeted immunomodulatory therapies assessing survival as a primary endpoint are suggested in patients with critical COVID-19. FUNDING: Sanofi and Regeneron Pharmaceuticals. Copyright © 2021 Elsevier Ltd. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c892b31b8370b1161ebc76dd547998a4)

1. **Serious adverse events with tocilizumab: Pharmacovigilance as an aid to prioritize monitoring in COVID-19**  
   Gatti M. British Journal of Clinical Pharmacology 2021;87:1533-1540.

Given its approval for the treatment of cytokine release syndrome, tocilizumab is under investigation in severe coronavirus disease-2019. To characterize serious adverse events (AEs) with tocilizumab, we queried the worldwide FDA Adverse Event Reporting System and performed disproportionality analysis, selecting only designated medical events (DMEs) where tocilizumab was reported as suspect, with a focus on hepatic reactions. The reporting odds ratios (RORs) were calculated, deemed significant by a lower limit of the 95% confidence interval (LL 95% CI) > 1. A total of 2,433 reports of DMEs were recorded with tocilizumab, mainly in rheumatic diseases. Statistically significant RORs emerged for 13 DMEs, with drug-induced liver injury (n = 91; LL 95% CI 3.07), pancreatitis (151; 1.41), and pulmonary fibrosis (222; 7.21) as unpredictable AEs. A total of 174 cases of liver-related DMEs were retrieved (proportion of deaths = 18.4%), with median onset of 27.5 days. These serious unpredictable reactions occurring in chronic real-world tocilizumab use may support patient care and monitoring of ongoing clinical trials. Copyright © 2020 The British Pharmacological Society

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=50e8be6842be7b258a3197eaa9a79c24)

1. **Single dose of subcutaneous tocilizumab in COVID-pneumonia: CT evidence of lymph nodal and parenchymal response**  
   Vizzuso A. Journal of Medical Virology 2021;93:599-600.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=689d9a3de771ed041d4f9dc49afad227)

1. **Successful treatment of severe COVID-19 pneumonia and hyperinflammatory syndrome with tocilizumab**  
   Gentile Giorgio BMJ case reports 2021;14:No page numbers.

As of 28 October 2020, there are over 44 000 000 confirmed COVID-19 infections and over 1 000 000 deaths worldwide, including 945 367 infections and 45 765 deaths in the UK. Acute respiratory distress syndrome occurs in 50% of patients with secondary haemophagocytic lymphohistiocytosis, a hyperinflammatory syndrome characterised by a surge of cytokines, including interleukin 6 (IL-6). Here we describe the case of the first patient with severe COVID-19 pneumonia successfully treated with tocilizumab, a humanised monoclonal antibody against the IL-6 receptor, in the UK. Early treatment (after 7-10 days from the onset of symptoms) with tocilizumab could (1) reduce the risk of requiring non-invasive or invasive ventilation; (2) offer a chance of survival to people who are not fit for escalation or have refused to be ventilated; and (3) potentially increase the chance of survival in some patients who are already ventilated but fail to improve with supportive treatment.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c38b1eaa2e62bf75f050938b2d8af67d)

1. **The association of interleukin-6 value, interleukin inhibitors, and outcomes of patients with COVID-19 in New York City**  
   Maeda T. Journal of Medical Virology 2021;93:463-471.

Since cytokine release syndrome with elevation of interleukin-6 (IL-6) is considered to be associated with severe cases of coronavirus disease 2019 (COVID-19); IL-6 inhibitors, such as tocilizumab, are expected to be effective for its treatment. This was a retrospective study using a consecutive cohort of 224 patients hospitalized with COVID-19 in March 2020. Patients were divided into those admitted to the intensive care unit (ICU group) and those not (no ICU group), and clinical data including usage of tocilizumab were compared. Correlation between IL-6 value at admission and at peak, and tocilizumab use, as well as clinical outcomes were also investigated. The ICU group had higher rates of pre-existing comorbidities such as hypertension, diabetes, and coronary disease, and higher IL-6 than no ICU group (all P <.05). Age, peak IL-6, and peak d-dimer were significant predictors of in-hospital mortality (1.05 [1.01-1.09], P =.012; 1.001 [1.000-1.002], P =.002; 1.10 [1.03-1.18], P =.008). Receiver operating characteristics curve showed higher predictability of in-hospital mortality with IL-6 at peak than others (area under curve; IL-6 at peak: 0.875 [0.87-0.942], IL-6 at admission: 0.794 [0.699-0.889], d-dimer at peak 0.787 [0.690-0.883], d-dimer at admission 0.726 [0.625-0.827]). Incidence of fungal infections was significantly higher in patients who were given tocilizumab than those who were not (13.0% vs 1.1%, P <.001). Notably, tocilizumab did not affect in-hospital mortality after adjustment including IL-6 (odds ratio [95% confidential interval]: 1.00 [0.27-3.72, P =.998]). Age, peak IL-6, and peak d-dimer levels were significant predictors of in-hospital mortality. Tocilizumab did not decrease in-hospital mortality in our cohort. Copyright © 2020 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=feab75ad649aeebc1f66d29da044f1b4)

1. **The Effect of IL-6 Inhibitors on Mortality Among Hospitalized COVID-19 Patients: A Multicenter Study**  
   Sinha P. The Journal of infectious diseases 2021;223:581-588.

BACKGROUND: The effectiveness of interleukin-6 inhibitors (IL-6i) in ameliorating coronavirus disease 2019 (COVID-19) remains uncertain. METHOD(S): We analyzed data for patients aged >=18 years admitted with a positive severe acute respiratory syndrome coronavirus 2 polymerase chain reaction test at 4 safety-net hospital systems with diverse populations and high rates of medical comorbidities in 3 US regions. We used inverse probability of treatment weighting via machine learning for confounding adjustment by demographics, comorbidities, and disease severity markers. We estimated the average treatment effect, the odds of IL-6i effect on in-hospital mortality from COVID-19, using a logistic marginal structural model. RESULT(S): Of 516 patients, 104 (20.1%) received IL-6i. Estimate of the average treatment effect adjusted for confounders suggested a 37% reduction in odds of in-hospital mortality in those who received IL-6i compared with those who did not, although the confidence interval included the null value of 1 (odds ratio = 0.63; 95% confidence interval, .29-1.38). A sensitivity analysis suggested that potential unmeasured confounding would require a minimum odds ratio of 2.55 to nullify our estimated IL-6i effect size. CONCLUSION(S): Despite low precision, our findings suggested a relatively large effect size of IL-6i in reducing the odds of COVID-19-related in-hospital mortality. Copyright © The Author(s) 2020. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=feeb28460c2f2eb6ab0af42f91fadb67)

1. **The effect of tocilizumab on inflammatory markers in survivors and non-survivors of severe COVID-19**  
   Amin S. Journal of the College of Physicians and Surgeons Pakistan 2021;31:S7-S10.

Objective: To determine the effects of tocilizumab (TCZ) on inflammatory markers, laboratory indices; and short-term outcome in patients with severe COVID-19. Study Design: Cross-sectional analytical study. Place and Duration of the Study: Hayatabad Medical Complex, Peshawar, Pakistan from 10<sup>th</sup> June till 31<sup>st</sup> August 2020. Methodology: Fifty-four patients with severe COVID-19 fulfilled the inclusion criteria and were included. All patients had received TCZ (4 mg/kg) in addition to standard treatment. Serum C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer levels, full blood count, and liver function tests (LFTs) were checked before and 24 hours after receiving TCZ. Short-term outcome, defined as survival at day 28, was determined from hospital record/telephonic contact. Paired t-test was employed to assess the statistical significance of mean differences between the pre- and post-TCZ variables, considering a p-value of <0.05 as significant. Result(s): Overall, the mean pre- and post-TCZ CRP was 18.7 +/- 10.7 and 10.2 +/- 8.6 mg/dl (p <0.001). It was 18.0 +/- 10.3 and 10.3 +/- 8.8 mg/dl (p=0.003) in survivors; and 19.4 +/- 11.4 and 10.2 +/- 8.7 mg/dl (p=0.005) in non-survivors, respectively. Overall, mean D-dimer level decreased from 12.5 +/- 23 to 10.3 +/- 12.2 microg/ml following TCZ (p=0.643); it decreased from 15.8 +/- 29.8 to 11.4 +/- 10.6 microg/ml (p=0.612) in survivors; and 9.0 +/- 12.8 to 9.2 +/- 14.1 microg/ml (p=0.961) in non-survivors, respectively. There were no significant differences in the pre- and post-TCZ LDH levels overall and between the groups. The 28-day mortality was 46.3%. Conclusion(s): Tocilizumab results in a significant reduction in CRP, while mean change in LDH and D-dimers was not substantial. The mean change in inflammatory markers did not predict survival. Copyright © 2021 College of Physicians and Surgeons Pakistan. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c424de18df38d46aeb4b5536f6e37a6f)

1. **The effect of tocilizumab on mortality in hospitalized patients with COVID-19: a meta-analysis of randomized controlled trials**  
   Kow C. S. European Journal of Clinical Pharmacology. 2021;:No page numbers.

Objective: We aimed to perform a meta-analysis of randomized controlled trials (RCTs) to summarize the overall effect of tocilizumab on the risk of mortality among patients with coronavirus disease 2019 (COVID-19). Method(s): We systematically searched PubMed, Cochrane Central Register of Controlled Trials, Google Scholar, and medRxiv (preprint repository) databases (up to 7 January 2021). Pooled effect sizes with 95% confidence interval (CI) were generated using random-effects and inverse variance heterogeneity models. The risk of bias of the included RCTs was appraised using version 2 of the Cochrane risk-of-bias tool for randomized trials. Result(s): Six RCTs were included: two trials with an overall low risk of bias and four trials had some concerns regarding the overall risk of bias. Our meta-analysis did not find significant mortality benefits with the use of tocilizumab among patients with COVID-19 relative to non-use of tocilizumab (pooled hazard ratio = 0.83; 95% CI 0.66-1.05, n = 2,057). Interestingly, the estimated effect of tocilizumab on the composite endpoint of requirement for mechanical ventilation and/or all-cause mortality indicated clinical benefits, with some evidence against our model hypothesis of no significant effect at the current sample size (pooled hazard ratio = 0.62; 95% CI 0.42-0.91, n = 749). Conclusion(s): Despite no clear mortality benefits in hospitalized patients with COVID-19, tocilizumab appears to reduce the likelihood of progression to mechanical ventilation. Copyright © 2021, The Author(s), under exclusive licence to Springer-Verlag GmbH, DE part of Springer Nature.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e5f8670370a5dc95af875094c39a28bb)

1. **The effect of tocilizumab, anakinra, and prednisolone on antibody response to SARS-CoV-2 in patients with COVID-19: A prospective cohort study with multivariate analysis of factors affecting the antibody response**  
   Basaran S. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2021;15:No page numbers.

OBJECTIVES: Disease severity, previous medications, immunosuppresive agents could affect the antibody response against SARS-CoV-2. We aimed to analyze variables affecting the humoral response to SARS-CoV-2. METHOD(S): In this prospective cohort study, we included adult patients who recovered from COVID-19 and were admitted to COVID-19 follow-up unit. We defined 8 patient groups in accordance with the results of thorax CT, SARS-CoV-2 PCR test, and tocilizumab or anakinra use during active disease. Anti-S IgG antibodies were determined by ELISA in serum samples. Anti-S positive and negative cases were compared. RESULT(S): A total of 518 patients were included in the study. SARS-CoV-2 IgG antibodies were positive in 82.8% of patients. SARS-CoV-2 PCR positivity, extent of lung involvement on CT, and time to antibody testing were independently associated with antibody positivity. Tocilizumab, anakinra or prednisolone use was not a factor affecting the antibody response. The rate of antibody response and sample/CO values among antibody positive patients showed a linear relationship with the extent of lung involvement on CT. CONCLUSION(S): The use of tocilizumab, anakinra, and prednisolone for COVID-19 did not affect the antibody response against SARS-CoV-2. The main driver of antibody response among patients with COVID-19 was the extent of pulmonary involvement on CT. Copyright © 2021. Published by Elsevier Ltd.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4960b81e449005a71e3af417407bf159)

1. **The Role of Convalescent Plasma and Tocilizumab in the Management of COVID-19 Infection: A Cohort of 110 Patients from a Tertiary Care Hospital in Oman**  
   Khamis F. Journal of epidemiology and global health. 2021;07:No page numbers.

AIM: As Coronavirus Disease-2019 (COVID-19) pandemic continues to evolve, the search for safe and effective therapeutic interventions remain essential. METHOD(S): We conducted a retrospective cohort study on patients hospitalized with laboratory confirmed severe acute respiratory syndrome coronavirus-2 infection, comparing standard of care along with Convalescent Plasma with or without Tocilizumab (CP vs. CPT). RESULT(S): A total of 110 patients were enrolled with an overall mean age of 50 +/- 16 years. Patients on CPT were more likely to have had acute respiratory distress syndrome (77% vs. 42%; p < 0.001), sepsis (9.7% vs. 0; p = 0.036), chest X-ray abnormealities (71% vs. 44%; p = 0.004), intensive care unit admission (84% vs. 56%; p = 0.001) as well as being on mechanical ventilation (79% vs. 48%; p = 0.001). After CPT treatment, all measured inflammatory markers, except interleukine-6, showed an overall steady decline over time (all p-values <0.05) and the ventilatory parameters showed significant improvement of PaO2/FiO2 ratio from 127 to 188 within 7 days (p < 0.001). Additionally, 52% (32/62) of the patients had favorable outcome, either as improvement of ventilatory parameters or extubation within 14 days of hospitalization. However, mortality rate in those on CPT was higher than those who received CP alone (24% vs. 8.3%; p = 0.041). CONCLUSION(S): In patients with severe COVID-19 infection, using tocilizumab with convalescent plasma is associated with improvement in inflammatory and ventilatory parameters but no effect on mortality. These findings require validation from randomized clinical trials. Copyright © 2020 The Authors. Published by Atlantis Press International B.V.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6d1e60afd93aa3c610539decef8bc96b)

1. **Therapeutic efficacy, mechanical ventilation, length of hospital stay, and mortality rate in severe COVID-19 patients treated with tocilizumab**  
   Sarhan R. M. International Journal of Clinical Practice. 2021;:No page numbers.

Background: The treatment of severe cases of COVID-19 disease remains a dilemma so far, because there is no approved therapy for it. This study aimed to estimate the therapeutic efficacy of tocilizumab and its role in reducing the need for mechanical ventilation, length of hospital stay, mortality rate for these cases. Method(s): The study included 25 adult patients with confirmed severe COVID-19 infection. Treatment of all patients followed Egyptian Ministry of Health COVID-19 protocol in addition to tocilizumab IV (400-800 mg) as a single dose and then the dose was repeated after at least 12 hours and up to 24 hours from the previous dose. All laboratory and clinical parameters were assessed before and within 24 hours after tocilizumab administration. Result(s): After receiving TCZ, all patients showed significantly lower median IL 6, LDH, CRP, ferritin, TLC at P <.001, and D-Dimer at P =.223 than their baseline levels. Also, the number of patients who required mechanical ventilation decreased from 11 to 8. Only five patients died after TCZ treatment. A moderate correlation was found between therapeutic failure and death outcomes and mechanical ventilation need at baseline. The median days of hospitalisation (IQR) were 10 (6-16). Conclusion(s): Tocilizumab treatment in patients with severe COVID-19 is safe and has significant therapeutic effects and a significant role in the improvement of all laboratory parameters. Also TCZ plays a significant role in the reduction of the length of stay in hospital and ICU, need for mechanical ventilation, and mortality rate.What's known IL-6 plays the main role in the acute respiratory distress syndrome (ARDS) associated with severe COVID-19 infection. Consequently, serum IL-6 can be considered as an important target in therapeutic management of severe COVID-19 patients. What's new Prospective study, carried on 25 adult patients with confirmed severe COVID-19 infection using tocilizumab, showed significant improvement in their case. Tocilizumab, as an IL-6 inhibitor, not only lowered IL-6 level put also showed a significant reduction on median LDH, CRP, ferritin, TLC at P <.001 and D-Dimer at P =.223 than their baseline levels. Improvement of all laboratory parameters using TCZ was reflected in the reduction of the length of stay in hospital and ICU, need for mechanical ventilation and mortality rate. Copyright © 2021 John Wiley & Sons Ltd

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6da343a233993b17b957be295bae1847)

1. **Therapeutic role of tocilizumab in sars-cov-2-induced cytokine storm: Rationale and current evidence**  
   Pelaia C. International Journal of Molecular Sciences 2021;22:1-16.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b6cef5b7d65a6b618b6e7c3ba570f92c)

1. **Time to Reassess Tocilizumab's Role in COVID-19 Pneumonia**  
   Parr J. B. JAMA Internal Medicine 2021;181:12-15.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e80e272594f35639dc2a5b80fd90cb6a)

1. **Tocilizumab : Infection and worsening of pre-existing COVID-19 symptoms following off-label treatment: case report**  
   Anon. Reactions Weekly 2021;1841:227-227.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a610eef47913aab9ff9957a64a6ee048)

1. **Tocilizumab administration in COVID-19 patients: Water on the fire or gasoline?**  
   Deana C. Medical Mycology Case Reports 2021;31:32-34.

Tocilizumab is widely being used to treat COVID-19. Although reducing systemic inflammation, it also increases the risk for secondary infections as a result of the immunosuppression produced. We report the case of a 69-year-old patient admitted to the ICU with severe respiratory distress caused by COVID-19 pneumonia who developed pulmonary aspergillosis. On the basis of these findings, we suggest early testing for pulmonary aspergillosis in COVID-19 patients treated with tocilizumab. Copyright © 2021 The Authors

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=599e395643d7dfc3d0e2168738dd3d36)

1. **Tocilizumab administration in patients with SARS-CoV-2 infection: Subcutaneous injection vs intravenous infusion**  
   Shabani M. Journal of Medical Virology 2021;93:69-70.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6c665ee29e3a8e079aba068120da493e)

1. **Tocilizumab administration is associated with the reduction in biomarkers of coronavirus disease 2019 infection**  
   Ivan Hariyanto T. Journal of Medical Virology 2021;93:1832-1836.

Coronavirus disease 2019 (COVID-19) has caused a significant impact on all aspects of life, with the number of death cases still increasing. Therefore, identification of potential treatment for reducing the severity of the disease is important. Currently, the data regarding the effectiveness of tocilizumab as treatment agents for COVID-19 infection is still conflicting. This study aims to give clear evidence regarding the potential benefit of tocilizumab in reducing the biomarkers of COVID-19 infection. We systematically searched the PubMed Central database using specific keywords related to our aims until July 24th, 2020. All articles published on COVID-19 and tocilizumab were retrieved. A total of 9 studies with a total of 577 patients were included in our analysis. Our meta-analysis showed that tocilizumab treatment is associated with reduction of C-reactive protein (mean difference [MD]: -106.69 mg/L [95% confidence interval [CI]: -146.90, -66.49 mg/L], p <.00001; I<sup>2</sup> = 98%, random-effect modeling), d-dimer (MD: -3.06 mg/L [95% CI: -5.81, -0.31 mg/L], p =.03; I<sup>2</sup> = 98%, random-effect modeling), Ferritin (MD: -532.80 ng/ml [95% CI: -810.93, -254.67 ng/ml], p =.0002; I<sup>2</sup> = 25%, random-effect modeling), procalcitonin (MD: -0.67 ng/ml [95% CI: -1.13, -0.22 ng/ml], p =.004; I<sup>2</sup> = 92%, random-effect modeling], and increment in the levels of lymphocyte count (MD: 0.36 x 10<sup>3</sup>/mul [95% CI: 0.18, 0.54 x 10<sup>3</sup>/mul], p <.0001; I<sup>2</sup> = 88%, random-effect modeling). Administration of tocilizumab is effective in reducing the biomarkers of the COVID-19 infection. Copyright © 2020 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e24a925f317d73a8e1fca2b6ee354ae5)

1. **Tocilizumab and PMX-DHP have efficacy for severe COVID-19 pneumonia**  
   Shinomiya S. SAGE Open Medical Case Reports 2021;9:No page numbers.

In coronavirus disease 2019 pneumonia, a cytokine storm resulting from an excessive inflammatory response to the viral infection is thought to play a role in the exacerbation of the pneumonia and its prognosis. Favipiravir and ciclesonide are not effective in the inhibition of the cytokine storm. In this case report, we describe the experience of tocilizumab administration and polymyxin B immobilized fiber direct hemoperfusion in severe coronavirus disease 2019 pneumonia patient. A 52-year-old man presented with fever and dyspnea and was diagnosed with coronavirus disease 2019 pneumonia based on a polymerase chain reaction test. Mechanical ventilation and favipiravir administration were started for respiratory failure. However, favipiravir could not be continued due to hepatic dysfunction. Consequently, tocilizumab was administered, and continuous hemodiafiltration and endotoxin adsorption therapy (polymyxin B immobilized fiber direct hemoperfusion) were performed for acute renal failure. C-reactive protein decreased from 44 to 3.52 mg/dL, and the patient's respiratory status improved over time, enabling mechanical ventilation to be withdrawn. This case indicates that adding polymyxin B immobilized fiber direct hemoperfusion to tocilizumab administration may further increase efficacy in coronavirus disease 2019 treatment; however, more case-control studies are needed. Copyright © The Author(s) 2021.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b7303553dd18ffb70fc88649778a9cf0)

1. **Tocilizumab combined with favipiravir in the treatment of COVID-19: A multicenter trial in a small sample size**  
   Zhao H. Biomedicine and Pharmacotherapy 2021;133 (no pagination):No page numbers.

Background: Since December 2019, COVID-19 has spread to almost every corner of the world. In theory, tocilizumab and favipiravir are considered to be reliable drugs for the treatment of COVID-19 with elevated IL-6. We aimed to assess the efficacy and safety of tocilizumab combined with favipiravir in patients with COVID-19. Method(s): This was a multicenter trial in adults with COVID-19. Patients were randomly assigned (3:1:1) to a 14-day combination of favipiravir combined with tocilizumab (combination group), favipiravir, and tocilizumab. The primary outcome was the cumulative lung lesion remission rate (lung CT examination indicated absorption of lung inflammation). Result(s): Between Feb 2 and March 15, 2020, 26 patients were recruited; 14 were randomly assigned to the combination group, 7 were assigned to the favipiravir group and 5 were assigned to the tocilizumab group. The cumulative lung lesion remission rate at day 14 was significantly higher in combination group as compared with favipiravir group (P = 0.019, HR 2.66 95 % CI [1.08-6.53]). And there was also a significant difference between tocilizumab and favipivavir (P = 0.034, HR 3.16, 95 % CI 0.62-16.10). In addition, there was no significant difference between the combination group and the tocilizumab group (P = 0.575, HR 1.28 95 %CI 0.39-4.23). Furthermore, combined therapy can also significantly relieve clinical symptoms and help blood routine to return to normal. No serious adverse events were reported. Conclusion(s): Tocilizumab combined with or without favipiravir can effectively improve the pulmonary inflammation of COVID-19 patients and inhibit the deterioration of the disease. Copyright © 2020

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=921d6b042a81d795437d10fee12f41c5)

1. **Tocilizumab did not reduce hypoxemic respiratory failure or death in hospitalized patients with COVID-19**  
   Sharif S. Annals of internal medicine 2021;174:JC16.

SOURCE CITATION: Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of tocilizumab in patients hospitalized with Covid-19. N Engl J Med. 2020;383:2333-44. 33085857.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f338c44ca467db5c41dfe873c98b3b2d)

1. **Tocilizumab efficacy in COVID-19 patients is associated with respiratory severity-based stages**  
   Alvarez-Mon Melchor 2021;:No page numbers.

&lt;h4&gt;ABSTRACT&lt;/h4&gt; &lt;h4&gt;Background&lt;/h4&gt; Tocilizumab treatment is investigated, and effectiveness in ICU-admitted COVID-19 patients has been reported. Although controversy exists regarding the efficacy of tocilizumab treatment, it has been suggested that tocilizumab might show positive results depending on patient severity status. We examined an association between tocilizumab and distinct disease severity stages. &lt;h4&gt;Methods and Findings&lt;/h4&gt; From March 3 to March 23 2020, 494 consecutively admitted COVID-19 patients received tocilizumab or standard treatment alone. Data were obtained retrospectively. Clinical respiratory severity (CRS) stages were defined by patient oxygenation status and were also associated to scores of WHO clinical progression scale. We categorized patients in three stages, mild/moderate CRS1 (FiSpO 2 &lt;0.35; WHO score 5), moderate/severe CRS2 (FiO 2 =0.5/high flow mask; WHO score 6) and severe/critical CRS3 (FiO 2 &lt;80%/high flow/prone position or mechanical ventilation; score&gt;6). The primary outcome was the composite of death or ICU admission in patients of stages CRS1, CRS2, and CRS3, as well as in total patients. We also addressed mortality alone in total patients. Kaplan-Maier curves, Cox proportional regression and inverse probability weighting marginal structural models were used. We conducted the study from March 3 to April 7 2020 with broad-ranged severity patients; 167 tocilizumab-treated and 327 untreated. CRS1 patients showed no apparent benefit after treatment, while the risk of the primary outcome was greatly reduced in CRS2 treated participants ((HR=0.22; 95% CI (0.16-0.44)). Moreover, tocilizumab treatment was associated with significantly decreased CRS2 patient proportion that reached the outcome compared to non-treated controls (27.8.0% vs. 65.4%; p&lt;0.001). Severe/critical CRS3 patients, also showed benefit after treatment (HR=0.38; 95% CI (0.16-90)), although not as robust as was that of CRS2 treated individuals. Tocilizumab was associated with reduced outcome risk in total patients (HR=0.42; 95% CI (0.26-0.66)) after CRS adjustment, but not if CRS classification was not accounted as confounding factor (HR=1.19; 95% CI (0.84-1.69)). The outcome of mortality alone upon tocilizumab treatment was significant (HR=0.58; 95% CI (0.35-0.96)) after accounting for CRS classification. &lt;h4&gt;Conclusions&lt;/h4&gt; Tocilizumab treatment is associated with reduced COVID-19 escalation in CRS2 patients, suggesting efficacy in moderate/severe non-ICU-admitted patients. CRS classification could represent an essential confounding factor in evaluating tocilizumab in studies of broad-ranged severity patients.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0c314c551c45e382e4279d059f7ee9d7)

1. **Tocilizumab for COVID-19 Pneumonia in a Patient With Non-Small-cell Lung Cancer Treated With Chemoimmunotherapy**  
   Bonomi M. Clinical Lung Cancer 2021;22:e67-e69.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=10059ab17c707b68b4ff4d8b1881418b)

1. **Tocilizumab for hospitalized patients with COVID-19**  
   Afra Kevin CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=366df9a705bef406ffe38050e7ff807c)

1. **Tocilizumab for Severe Worsening COVID-19 Pneumonia: a Propensity Score Analysis**  
   Roumier M. Journal of Clinical Immunology 2021;41:303-314.

Background: High levels of serum interleukin-6 (IL-6) correlate with disease severity in COVID-19. We hypothesized that tocilizumab (a recombinant humanized anti-IL-6 receptor) could improve outcomes in selected patients with severe worsening COVID-19 pneumonia and high inflammatory parameters. Method(s): The TOCICOVID study included a prospective cohort of patients aged 16-80 years with severe (requiring > 6 L/min of oxygen therapy to obtain Sp02 > 94%) rapidly deteriorating (increase by >= 3 L/min of oxygen flow within the previous 12 h) COVID-19 pneumonia with >= 5 days of symptoms and C-reactive protein levels > 40 mg/L. They entered a compassionate use program of treatment with intravenous tocilizumab (8 mg/kg with a maximum of 800 mg per infusion; and if needed a second infusion 24 to 72 h later). A control group was retrospectively selected with the same inclusion criteria. Outcomes were assessed at D28 using inverse probability of treatment weighted (IPTW) methodology. Result(s): Among the 96 patients included (81% male, mean (SD) age: 60 (12.5) years), underlying conditions, baseline disease severity, and concomitant medications were broadly similar between the tocilizumab (n = 49) and the control (n = 47) groups. In the IPTW analysis, treatment with tocilizumab was associated with a reduced need for overall ventilatory support (49 vs. 89%, wHR: 0.39 [0.25-0.56]; p < 0.001). Albeit lacking statistical significance, there was a substantial trend towards a reduction of mechanical ventilation (31% vs. 45%; wHR: 0.58 [0.36-0.94]; p = 0.026). However, tocilizumab did not improve overall survival (wHR = 0.68 [0.31-1.748], p = 0.338). Among the 85 (89%) patients still alive at D28, patients treated with tocilizumab had a higher rate of oxygen withdrawal (82% vs. 73.5%, wHR = 1.66 [1.17-2.37], p = 0.005), with a shorter delay before being weaned of oxygen therapy (mean 11 vs. 16 days; p < 0.001). At D28, the rate of patients discharged from hospital was higher in the tocilizumab group (70% vs. 40%, wHR = 1.82 [1.22-2.75]; p = 0.003). The levels of CRP and fibrinogen post therapy (p < 0.001 for both variables) were significantly lower in the tocilizumab group (interaction test, mixed model). Rates of neutropenia (35% vs. 0%; p < 0.001) were higher in the tocilizumab group, yet rates of infections (22% vs. 38%, p = 0.089) including ventilator-acquired pneumonia (8% vs. 26%, p = 0.022) were higher in the control group. Conclusion(s): These data could be helpful for the design of future trials aiming to counter COVID-19-induced inflammation, especially before patients require admission to the intensive care unit. Copyright © 2020, Springer Science+Business Media, LLC, part of Springer Nature.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=80c9221265c547e665956d5c54b101b0)

1. **Tocilizumab for the Critically Ill With Severe COVID-19: A Community Hospital Case Series**  
   McKenzie M. G. Journal of Pharmacy Practice. 2021;:No page numbers.

Objective: To evaluate the use of tocilizumab in a community hospital setting for critically ill patients with severe COVID-19. Design(s): A retrospective case series Setting: Five community hospitals within 1 urban health system Patients: Adult patients whom received tocilizumab between March 27th, 2020 to April 30th, 2020 for severe COVID-19. Intervention(s): None. Measurements and Main Results: Sixteen patients in total were evaluated from the 5 community hospitals. The mean (+/- SD) age of the patients was 53.9 +/- 9.2 years, 56% were men, and the most common comorbidities present on admission were hypertension (31%) and diabetes mellitus (25%). All patients received at least 1 other treatment modality for COVID-19 (steroids, hydroxychloroquine, or convaslescent plasma). Additionally, all patients on admission to intensive care units had severe COVID-19 with 56% requiring mechanical ventilation with a pre-tocilizumab median (IQR) Pao<inf>2</inf>: Fio<inf>2</inf> of 84 (69 - 108.6), 19% requiring vasopressor support, and inflammatory markers (CRP, LDH, ferritin, and IL-6) were elevated. The median (IQR) tocilizumab dose was 400 mg (400-600) which correlated with a weight-based mean (+/- SD) dose of 5.4 mg/kg +/- 1.3. Of the 16 patients that received tocilizumab, 8 (50%) were discharged home, 7 (44%) died, and 1 (6%) was still hospitalized at the end of data collection. Patients who died were more likely to be older 62 +/- 2 years, female (57%), had a higher rate of mechanical ventilation (86%) and vasopressors (43%) use at baseline, and had a higher median (IQR) IL-6 level prior to tocilizumab administration 550 pg/mL (IQR 83-1924). There were no reported adverse drug reactions reported after the administration of tocilizumab for any patient. Conclusion(s): Our findings do not support the effectiveness of tocilizumab in treatment of severe COVID-19 infection in critically ill patients. Copyright © The Author(s) 2021.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c6bd5716be7f433d1623a17d61a73209)

1. **Tocilizumab for the treatment of adult patients with severe COVID-19 pneumonia: A single-center cohort study**  
   Fernandez-Ruiz M. Journal of Medical Virology 2021;93:831-842.

Coronavirus disease 2019 (COVID-19) can lead to a massive cytokine release. The use of the anti-interleukin-6 receptor monoclonal antibody tocilizumab (TCZ) has been proposed in this hyperinflammatory phase, although supporting evidence is limited. We retrospectively analyzed 88 consecutive patients with COVID-19 pneumonia that received at least one dose of intravenous TCZ in our institution between 16 and 27 March 2020. Clinical status from day 0 (first TCZ dose) through day 14 was assessed by a 6-point ordinal scale. The primary outcome was clinical improvement (hospital discharge and/or a decrease of >=2 points on the 6-point scale) by day 7. Secondary outcomes included clinical improvement by day 14 and dynamics of vital signs and laboratory values. Rates of clinical improvement by days 7 and 14 were 44.3% (39/88) and 73.9% (65/88). Previous or concomitant receipt of subcutaneous interferon-beta (adjusted odds ratio [aOR]: 0.23; 95% confidence interval [CI]: 0.06-0.94; P =.041) and serum lactate dehydrogenase more than 450 U/L at day 0 (aOR: 0.25; 95% CI: 0.06-0.99; P =.048) were negatively associated with clinical improvement by day 7. All-cause mortality was 6.8% (6/88). Body temperature and respiratory and cardiac rates significantly decreased by day 1 compared to day 0. Lymphocyte count and pulse oximetry oxygen saturation/FiO<inf>2</inf> ratio increased by days 3 and 5, whereas C-reactive protein levels dropped by day 2. There were no TCZ-attributable adverse events. In this observational single-center study, TCZ appeared to be useful and safe as immunomodulatory therapy for severe COVID-19 pneumonia. Copyright © 2020 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=db1e2fff38006226186677441d3eb4e0)

1. **Tocilizumab for the treatment of COVID-19**  
   Fernandez-Ruiz M. Expert opinion on biological therapy 2021;:1-4.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=64081e0f720180ea1f148ebb6134f04d)

1. **Tocilizumab for the Treatment of COVID-19 among Hospitalized Patients: A Matched Retrospective Cohort Analysis**  
   Wang K. Open Forum Infectious Diseases 2021;8 (1) (no pagination):No page numbers.

Background: There is currently no single treatment that mitigates all harms caused by severe acute respiratory syndrome coronavirus 2 infection. Tocilizumab, an interleukin-6 antagonist, may have a role as an adjunctive immune-modulating therapy. Method(s): This was an observational retrospective study of hospitalized adult patients with confirmed coronavirus disease 2019 (COVID-19). The intervention group comprised patients who received tocilizumab; the comparator arm was drawn from patients who did not receive tocilizumab. The primary outcome was all-cause mortality censored at 28 days; secondary outcomes were all-cause mortality at discharge, time to clinical improvement, and rates of secondary infections. Marginal structural Cox models via inverse probability treatment weights were applied to estimate the effect of tocilizumab. A time-dependent propensity score-matching method was used to generate a 1:1 match for tocilizumab recipients; infectious diseases experts then manually reviewed these matched charts to identify secondary infections. Result(s): This analysis included 90 tocilizumab recipients and 1669 controls. Under the marginal structural Cox model, tocilizumab was associated with a 62% reduced hazard of death (adjusted hazard ratio [aHR], 0.38; 95% CI, 0.21 to 0.70) and no change in time to clinical improvement (aHR, 1.13; 95% CI, 0.68 to 1.87). The 1:1 matched data set also showed a lower mortality rate (27.8% vs 34.4%) and reduced hazards of death (aHR, 0.47; 95% CI, 0.25 to 0.88). Elevated inflammatory markers were associated with reduced hazards of death among tocilizumab recipients compared with controls. Secondary infection rates were similar between the 2 groups. Conclusion(s): Tocilizumab may provide benefit in a subgroup of patients hospitalized with COVID-19 who have elevated biomarkers of hyperinflammation, without increasing the risk of secondary infection. Copyright © 2020 The Author(s) 2020. Published by Oxford University Press on behalf of Infectious Diseases Society of America.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b84bb8dbb4f00bcce4139d4029d70d85)

1. **Tocilizumab for treating COVID-19: a systemic review and meta-analysis of retrospective studies**  
   Zhao M. European Journal of Clinical Pharmacology 2021;77:311-319.

Objectives: COVID-19 has become a global epidemic, and effective therapies have not been discovered up to now. We conducted this study to explore the effectiveness and safety of tocilizumab recently used for treating COVID-19. Method(s): A comprehensive search was conducted (up to September 27, 2020), and 19 eligible records were identified according to the inclusion and exclusion criteria. The data of the studies were extracted by 2 independent reviewers and were analyzed to evaluate the safety and availability of tocilizumab for treating COVID-19. Result(s): Thirteen retrospective case-control studies (n = 2285 patients) and 6 retrospective single-armed studies (n = 208) were retrieved in this study. In the comparison of tocilizumab treatment group (TCZ) and standard treatment group (ST), significant associations with a lower risk of admission to ICU, use of ventilation, and mortality (OR, 95% CI: 0.53, 0.26~1.09; 0.66, 0.46~0.94; 0.44, 0.36~0.55) were found in the tocilizumab treatment group. What is more, patients treated with tocilizumab had better clinical improvement compared with the patients treated with ST (OR, 1.24; 95% CI, 0.96~1.62). After taking tocilizumab, the patients had lower C-reactive protein (CRP), white blood cell count (WBC), aspartate aminotransferase (AST) (WMD, 95% CI: - 99.66, - 156.24~- 43.09; - 0.95, - 1.8~- 0.11; - 12.58, - 18.88~-6.29) but higher troponin (WMD, 7.61; 95% CI, 3.06~12.15) than before. In addition, tocilizumab did not have significant influence on patients' neutrophil count (Neut), lymphocyte count (Lymp), platelet count (Plt), alanine aminotransferase (ALT), and creatine (WMD, 95% CI: - 0.29, - 2.91~2.33; 0.42, - 0.23~1.07; 5.2, - 2.85~13.25; 22.49, - 2.73~47.7; - 44.78, - 93.37~3.81). Conclusion(s): Tocilizumab may have potential effectiveness to treat COVID-19 according to the results of this study. However, more large-scale studies are needed for more accurate conclusions. Copyright © 2020, Springer-Verlag GmbH Germany, part of Springer Nature.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4173d565f232d0f41f02683dd74aee6e)

1. **Tocilizumab improves survival in severe COVID-19 pneumonia with persistent hypoxia: a retrospective cohort study with follow-up from Mumbai, India**  
   Gokhale Y. BMC Infectious Diseases 2021;21 (1) (no pagination):No page numbers.

Background: Cytokine storm triggered by Severe Coronavirus Disease 2019 (COVID-19) is associated with high mortality. With high Interleukin -6 (IL-6) levels reported in COVID-19 related deaths in China, IL-6 is considered to be the key player in COVID-19 cytokine storm. Tocilizumab, a monoclonal antibody against IL-6 receptor, is used on compassionate grounds for treatment of COVID-19 cytokine storm. The aim of this study was to assess effect of tocilizumab on mortality due to COVID-19 cytokine storm. Method(s): This retrospective, observational study included patients of severe COVID-19 pneumonia with persistent hypoxia (defined as saturation 94% or less on supplemental Oxygen of 15 L per minute through non-rebreathing mask or PaO2/FiO2 ratio of less than 200) who were admitted to a tertiary care center in Mumbai, India, between 31st March to 5th July 2020. In addition to standard care, single Inj. Tocilizumab 400 mg was given intravenously to 151 consecutive COVID-19 patients with persistent hypoxia, from 13th May to 5th July 2020. These 151 patients were retrospectively analysed and compared with historic controls, ie consecutive COVID-19 patients with persistent hypoxia, defined as stated above (N = 118, from our first COVID-19 admission on 31st March to 12th May 2020 i.e., till tocilizumab was available in hospital). Univariate and multivariate Cox regression analysis was performed for identifying predictors of survival. Statistical analysis was performed using IBM SPSS version 26. Result(s): Out of 269 (151 in tocilizumab group and 118 historic controls) patients studied from 31st March to 5th July 2020, median survival in the tocilizumab group was significantly longer than in the control group; 18 days (95% CI, 11.3 to 24.7) versus 9 days (95% CI, 5.7 to 12.3); log rank p 0.007. On multivariate Cox regression analysis, independent predictors of survival were use of tocilizumab (HR 0.621, 95% CI 0.427-0.903, P 0.013) and higher oxygen saturation. Conclusion(s): Tocilizumab may improve survival in severe COVID-19 pneumonia with persistent hypoxia. Randomised controlled trials on use of tocilizumab as rescue therapy in patients of severe COVID-19 pneumonia with hypoxia (PaO2/FiO2 less than 200) due to hyperinflammatory state, are warranted. Copyright © 2021, The Author(s).

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=023d717164d51207b5909db48020f82c)

1. **Tocilizumab Improves the Prognosis of COVID-19 in Patients with High IL-6**  
   Flisiak Robert 2021;:No page numbers.

Background: Despite direct viral effect, the pathogenesis of coronavirus disease 2019 (COVID-19) includes an overproduction of cytokines including interleukin 6 (IL-6). Therefore tocilizumab (TCZ), a monoclonal antibody against IL-6 receptors, became considered as a possible therapeutic option. Methods: Patients were selected from the SARSTer national database, which included 2332 individuals with COVID-19 and the current study included 825 adult patients with moderate to severe course. The retrospective analysis was performed in 170 patients treated with TCZ and 655 without this medication or any other anti-cytokine therapy. The end-points of treatment effectiveness were a rate of death, need for mechanical ventilation, and clinical improvement. Results: Patients treated with TCZ were balanced compared to non-TCZ regarding gender, age, BMI, and prevalence of coexisting conditions. Significant effect of TCZ on death was demonstrated in patients with baseline IL-6 &amp;amp;gt;100 pg/ml (hazard ratio [HR]: 0.27, 95% confidence interval [CI]:0.10-0.78), or those needing oxygen supplementations who worsened within 7 days of hospitalization (HR: 0.38, 95% CI:0.16-0.88). The best effectiveness of TCZ was achieved in patients with a combination of baseline IL-6&amp;amp;gt;100 pg/ml and either SpO&amp;lt;sub&amp;gt;2&amp;lt;/sub&amp;gt; &amp;le;90% (HR for death, mechanical ventilation and clinical improvement after 21 or 28 days: 0.07, 0.14, 5.53, 5.18 respectively) or requiring oxygen supplementation (HR for death and clinical improvement after 21 or 28 days, 0.18, 2.66, 2.85 respectively). Conclusions: Tocilizumab administration in COVID-19 reduces mortality and speed up clinical improvement in patients with a baseline concentration of IL-6&amp;amp;gt;100 pg/ml, particularly if they need oxygen supplementation due to SpO&amp;lt;sub&amp;gt;2&amp;lt;/sub&amp;gt; &amp;le;90%. Funding Statement: The study was supported by the Polish Association of Epidemiologists and Infectiologists and Medical Research Agency. Declaration of Interests: RF reports grants from Abbvie, Gilead, Merck, personal fees from Gilead, Abbvie, Merck, Roche, and non-financial support from Abbvie, Gilead, and Merck outside the submitted work. DZM, PP reports personal fees from Gilead and Abbvie, outside the submitted work. JJ reports personal fees from Gilead, Abbvie, Bausch Health, Merck, Promed, Roche, and non-financial support from Abbvie, Gilead, and Merck outside the submitted work. KS reports personal fees from Gilead, Abbvie, Merck, outside the submitted work KT reports personal fees from Gilead, Abbvie, Merck, Promed, Roche, and non-financial support from Abbvie, Gilead, and Merck outside the submitted work. JK reports personal fees from Gilead, Merck, ViiV, Janssen outside the submitted work. IML reports personal fees from Gilead, Abbvie and Pfizer ABK, JP, BB, KK, MP, AP, DK, MTZ, CI, MRog, MRor declare no competing interests. Ethics Approval Statement: The study received the approval of the Ethics Committee of the Medical University of Białystok.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4c1364527a4aaa9e1554fe2a854e8b00)

1. **Tocilizumab in Coronavirus Disease 2019-Related Critical Illness: A Propensity Matched Analysis**  
   Rajendram Prabalini Critical care explorations 2021;3:e0327.

The primary objective was to evaluate ICU mortality at 28 days in patients with severe hypoxemic respiratory failure due to coronavirus disease 2019 infection who received tocilizumab. The secondary objectives were to evaluate ICU-, hospital-, mechanical ventilation-, and vasopressor-free days at day 28 and development of secondary infections.&lt;h4&gt;Design&lt;/h4&gt;Retrospective, observational, multicenter, cohort study between March 15, 2020, and May 31, 2020. Using propensity score matching based on ICU admission source, C-reactive protein, Sequential Organ Failure Assessment score, vasopressor use, age, race, weight, and mechanical ventilation, patients who received tocilizumab were matched to patients who did not receive tocilizumab.&lt;h4&gt;Setting&lt;/h4&gt;Ten hospitals within the Cleveland Clinic Enterprise.&lt;h4&gt;Patients&lt;/h4&gt;Adult patients admitted to a medical, surgical, neurosciences, or mixed ICU with severe acute respiratory syndrome coronavirus 2 infection.&lt;h4&gt;Interventions&lt;/h4&gt;None.&lt;h4&gt;Measurements and main results&lt;/h4&gt;Four-hundred forty-four patients were included: 342 patients (77%) did not receive tocilizumab and 102 patients (23%) received tocilizumab. Of those, 82 patients in each arm were matched. Before matching, patients who received tocilizumab had higher Sequential Organ Failure Assessment scores (6.1 ± 3.4 vs 4.7 ± 3.6), higher C-reactive protein (21.0 ± 10.2 vs 13.7 ± 9.6 mg/dL), higher frequency of intubation, vasopressor requirement, and paralytics. After matching, characteristics were more balanced and over 85% of patients required mechanical ventilation. ICU mortality was lower in tocilizumab group (23.2% vs 37.8%; risk difference, -15%; 95% CI, -29% to -1%), with more ICU-, hospital-, and vasoactive-free days at day 28 compared with those who did not receive tocilizumab. There was no difference in mechanical ventilation-free days at day 28 or development of secondary infections.&lt;h4&gt;Conclusions&lt;/h4&gt;Tocilizumab use was associated with a significant decrease in ICU mortality in critically ill coronavirus disease 2019 patients with severe hypoxemic respiratory failure. Future randomized controlled trials limited to tocilizumab administration in critically ill coronavirus disease 2019 patients, with severe hypoxemic respiratory failure, are needed to support these findings.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=356379a4e54b437b571c83d944529bce)

1. **Tocilizumab in Covid-19**  
   Leaf D. E. New England Journal of Medicine 2021;384:86-87.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4dad20c4803e441363029fe46e4bfc8a)

1. **Tocilizumab in COVID-19 interstitial pneumonia**  
   Pomponio G. Journal of Internal Medicine. 2021;:No page numbers.

Background: Published reports on tocilizumab in COVID-19 pneumonitis show conflicting results due to weak designs or heterogeneity in critical methodological issues. Method(s): This open-label trial, structured according to Simon's optimal design, aims to identify factors predicting which patients could benefit from anti-IL6 strategies and to enhance the design of unequivocal and reliable future randomized trials. A total of 46 patients with COVID-19 pneumonia needing of oxygen therapy to maintain SO2 > 93% and with recent worsening of lung function received a single infusion of tocilizumab. Clinical and biological markers were measured to test their predictive values. Primary end point was early and sustained clinical response. Result(s): Twenty-one patients fulfilled pre-defined response criteria. Lower levels of IL-6 at 24 h after tocilizumab infusion (P = 0.049) and higher baseline values of PaO2/FiO2 (P = 0.008) predicted a favourable response. Conclusion(s): Objective clinical response rate overcame the pre-defined threshold of 30%. Efficacy of tocilizumab to improve respiratory function in patients selected according to our inclusion criteria warrants investigations in randomized trials. Copyright © 2020 The Association for the Publication of the Journal of Internal Medicine

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=485219984fe8c76f27ff6e2923fa2ba5)

1. **Tocilizumab in COVID-19: Give it time!**  
   Richier Q. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2021;30:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bf238133669cfef6615de0d290551c4f)

1. **Tocilizumab in COVID-19: Is the temptation worthwhile?**  
   Gupta S. Indian Journal of Critical Care Medicine 2021;25:247-248.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=20105f7adf3009ae1e364e38451854a0)

1. **Tocilizumab in hospitalized patients with COVID-19: Clinical outcomes, inflammatory marker kinetics, and safety**  
   Hill J. A. Journal of Medical Virology 2021;93:2270-2280.

Coronavirus disease 2019 (COVID-19) due to infection with severe acute respiratory syndrome coronavirus 2 causes substantial morbidity. Tocilizumab, an interleukin-6 receptor antagonist, might improve outcomes by mitigating inflammation. We conducted a retrospective study of patients admitted to the University of Washington Hospital system with COVID-19 and requiring supplemental oxygen. Outcomes included clinical improvement, defined as a two-point reduction in severity on a six-point ordinal scale or discharge, and mortality within 28 days. We used Cox proportional-hazards models with propensity score inverse probability weighting to compare outcomes in patients who did and did not receive tocilizumab. We evaluated 43 patients who received tocilizumab and 45 who did not. Patients receiving tocilizumab were younger with fewer comorbidities but higher baseline oxygen requirements. Tocilizumab treatment was associated with reduced C-reactive protein, fibrinogen, and temperature, but there were no meaningful differences in time to clinical improvement (adjusted hazard ratio [aHR], 0.92; 95% confidence interval [CI], 0.38-2.22) or mortality (aHR, 0.57; 95% CI, 0.21-1.52). A numerically higher proportion of tocilizumab-treated patients had subsequent infections, transaminitis, and cytopenias. Tocilizumab did not improve outcomes in hospitalized patients with COVID-19. However, this study was not powered to detect small differences, and there remains the possibility for a survival benefit. Copyright © 2020 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=fbdd3d2b5c95fb863e02c497a7d26a77)

1. **Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia**   
   Rosas IO New England Journal of Medicine 2021;(25 Feb):https://doi.org/10.1056/nejmoa2028700.

Results: Of the 452 patients who underwent randomization, 438 (294 in the tocilizumab group and 144 in the placebo group) were included in the primary and secondary analyses. The median value for clinical status on the ordinal scale at day 28 was 1.0 (95% confidence interval [CI], 1.0 to 1.0) in the tocilizumab group and 2.0 (non-ICU hospitalization without supplemental oxygen) (95% CI, 1.0 to 4.0) in the placebo group (between-group difference, -1.0; 95% CI, -2.5 to 0; P = 0.31 by the van Elteren test). In the safety population, serious adverse events occurred in 103 of 295 patients (34.9%) in the tocilizumab group and in 55 of 143 patients (38.5%) in the placebo group. Mortality at day 28 was 19.7% in the tocilizumab group and 19.4% in the placebo group (weighted difference, 0.3 percentage points (95% CI, -7.6 to 8.2; nominal P = 0.94). Conclusions: In this randomized trial involving hospitalized patients with severe Covid-19 pneumonia, the use of tocilizumab did not result in significantly better clinical status or lower mortality than placebo at 28 days.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4f253e1aa34c77950c7f97d50a9d2286)

1. **Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia**  
   Rosas Ivan O. The New England journal of medicine 2021;:No page numbers.

&lt;h4&gt;Background&lt;/h4&gt;Coronavirus disease 2019 (Covid-19) is associated with immune dysregulation and hyperinflammation, including elevated interleukin-6 levels. The use of tocilizumab, a monoclonal antibody against the interleukin-6 receptor, has resulted in better outcomes in patients with severe Covid-19 pneumonia in case reports and retrospective observational cohort studies. Data are needed from randomized, placebo-controlled trials.&lt;h4&gt;Methods&lt;/h4&gt;In this phase 3 trial, we randomly assigned patients who were hospitalized with severe Covid-19 pneumonia in a 2:1 ratio receive a single intravenous infusion of tocilizumab (at a dose of 8 mg per kilogram of body weight) or placebo. Approximately one quarter of the participants received a second dose of tocilizumab or placebo 8 to 24 hours after the first dose. The primary outcome was clinical status at day 28 on an ordinal scale ranging from 1 (discharged or ready for discharge) to 7 (death) in the modified intention-to-treat population, which included all the patients who had received at least one dose of tocilizumab or placebo.&lt;h4&gt;Results&lt;/h4&gt;Of the 452 patients who underwent randomization, 438 (294 in the tocilizumab group and 144 in the placebo group) were included in the primary and secondary analyses. The median value for clinical status on the ordinal scale at day 28 was 1.0 (95% confidence interval [CI], 1.0 to 1.0) in the tocilizumab group and 2.0 (non-ICU hospitalization without supplemental oxygen) (95% CI, 1.0 to 4.0) in the placebo group (between-group difference, -1.0; 95% CI, -2.5 to 0; P = 0.31 by the van Elteren test). In the safety population, serious adverse events occurred in 103 of 295 patients (34.9%) in the tocilizumab group and in 55 of 143 patients (38.5%) in the placebo group. Mortality at day 28 was 19.7% in the tocilizumab group and 19.4% in the placebo group (weighted difference, 0.3 percentage points (95% CI, -7.6 to 8.2; nominal P = 0.94).&lt;h4&gt;Conclusions&lt;/h4&gt;In this randomized trial involving hospitalized patients with severe Covid-19 pneumonia, the use of tocilizumab did not result in significantly better clinical status or lower mortality than placebo at 28 days. (Funded by F. Hoffmann-La Roche and the Department of Health and Human Services; COVACTA ClinicalTrials.gov number, NCT04320615.).

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8d0c8e0039dc8cc144be45faad0f11f0)

1. **Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial [Preprint]**  
   Horby P. W. and Landray M.J. medRxiv 2021;:https://doi.org/10.1101/2021.02.11.21249258.

Findings: Between 23 April 2020 and 24 January 2021, 4116 adults were included in the assessment of tocilizumab, including 562 (14%) patients receiving invasive mechanical ventilation, 1686 (41%) receiving non-invasive respiratory support, and 1868 (45%) receiving no respiratory support other than oxygen. Median CRP was 143 [IQR 107-204] mg/L and 3385 (82%) patients were receiving systemic corticosteroids at randomisation. Overall, 596 (29%) of the 2022 patients allocated tocilizumab and 694 (33%) of the 2094 patients allocated to usual care died within 28 days (rate ratio 0·86; 95% confidence interval [CI] 0·77-0·96; p=0·007). Consistent results were seen in all pre-specified subgroups of patients. In particular, a clear mortality benefit was seen in those receiving systemic corticosteroids. Patients allocated to tocilizumab were more likely to be discharged from hospital alive within 28 days (54% vs. 47%; rate ratio 1·22; 95% CI 1·12-1·34; p<0·0001). Among those not receiving invasive mechanical ventilation at baseline, patients allocated tocilizumab were less likely to reach the composite endpoint of invasive mechanical ventilation or death (33% vs. 38%; risk ratio 0·85; 95% CI 0·78-0·93; p=0·0005).

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=662e274cd7049345cf31bd5949437f95)

1. **Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia**  
   Salama C. New England Journal of Medicine 2021;384(1):20-30.

Results: A total of 389 patients underwent randomization, and the modified intention-to-treat population included 249 patients in the tocilizumab group and 128 patients in the placebo group; 56.0% were Hispanic or Latino, 14.9% were Black, 12.7% were American Indian or Alaska Native, 12.7% were non-Hispanic White, and 3.7% were of other or unknown race or ethnic group. The cumulative percentage of patients who had received mechanical ventilation or who had died by day 28 was 12.0% (95% confidence interval [CI], 8.5 to 16.9) in the tocilizumab group and 19.3% (95% CI, 13.3 to 27.4) in the placebo group (hazard ratio for mechanical ventilation or death, 0.56; 95% CI, 0.33 to 0.97; P = 0.04 by the log-rank test). Clinical failure as assessed in a time-to-event analysis favored tocilizumab over placebo (hazard ratio, 0.55; 95% CI, 0.33 to 0.93). Death from any cause by day 28 occurred in 10.4% of the patients in the tocilizumab group and 8.6% of those in the placebo group (weighted difference, 2.0 percentage points; 95% CI, -﻿5.2 to 7.8). In the safety population, serious adverse events occurred in 38 of 250 patients (15.2%) in the tocilizumab group and 25 of 127 patients (19.7%) in the placebo group. Conclusions: In hospitalized patients with Covid-19 pneumonia who were not receiving mechanical ventilation, tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival. No new safety signals were identified. See additional correspondence about this research here: https://www.nejm.org/doi/10.1056/NEJMc2100217?url\_ver=Z39.88-2003&rfr\_id=ori%3Arid%3Acrossref.org&rfr\_dat=cr\_pub++0pubmed

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=dfb0f657fe42e47ecdc264f7a37e92b2)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=717f2538c067e72e5be1e064c12466ab)

1. **Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia**  
   Lundh Andreas The New England journal of medicine 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7d6e0815876a2b2a1cabdb9fdbd2cd4a)

1. **Tocilizumab in patients infected by SARS-CoV2**  
   Sancho M. Medicina Clinica. 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=3bfa12c54d537efac362792b60df88f7)

1. **Tocilizumab in patients with moderate or severe COVID-19: a randomized, controlled, open-label, multicenter trial**  
   Wang D. Frontiers of medicine. 2021;09:No page numbers.

Tocilizumab has been reported to attenuate the "cytokine storm" in COVID-19 patients. We attempted to verify the effectiveness and safety of tocilizumab therapy in COVID-19 and identify patients most likely to benefit from this treatment. We conducted a randomized, controlled, open-label multicenter trial among COVID-19 patients. The patients were randomly assigned in a 1:1 ratio to receive either tocilizumab in addition to standard care or standard care alone. The cure rate, changes of oxygen saturation and interference, and inflammation biomarkers were observed. Thirty-three patients were randomized to the tocilizumab group, and 32 patients to the control group. The cure rate in the tocilizumab group was higher than that in the control group, but the difference was not statistically significant (94.12% vs. 87.10%, rate difference 95% CI-7.19%-21.23%, P = 0.4133). The improvement in hypoxia for the tocilizumab group was higher from day 4 onward and statistically significant from day 12 (P = 0.0359). In moderate disease patients with bilateral pulmonary lesions, the hypoxia ameliorated earlier after tocilizumab treatment, and less patients (1/12, 8.33%) needed an increase of inhaled oxygen concentration compared with the controls (4/6, 66.67%; rate difference 95% CI-99.17% to-17.50%, P = 0.0217). No severe adverse events occurred. More mild temporary adverse events were recorded in tocilizumab recipients (20/34, 58.82%) than the controls (4/31, 12.90%). Tocilizumab can improve hypoxia without unacceptable side effect profile and significant influences on the time virus load becomes negative. For patients with bilateral pulmonary lesions and elevated IL-6 levels, tocilizumab could be recommended to improve outcome.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ef6b63c0cbe6e7d563792b06c0bb99e6)

1. **Tocilizumab in the Management of COVID-19: A Preliminary Report**  
   Li M. American Journal of the Medical Sciences 2021;361:208-215.

Importance: Pneumonia due to COVID-19 can lead to respiratory failure and death due to the development of the acute respiratory distress syndrome. Tocilizumab, a monoclonal antibody targeting the interleukin-6 receptor, is being administered off-label to some patients with COVID-19, and although early small studies suggested a benefit, there are no conclusive data proving its usefulness. Objective(s): To evaluate outcomes in hospitalized patients with COVID-19 with or without treatment with Tocilizumab. Design, setting, participants: Retrospective study of 1938 patients with confirmed COVID-19 pneumonia admitted to hospitals within the Jefferson Health system in Philadelphia, Pennsylvania, between March 25, 2020 and June 17, 2020, of which 307 received Tocilizumab. Exposures: Confirmed COVID-19 pneumonia. Main Outcomes and Measures: Outcomes data related to length of stay, admission to intensive care unit (ICU), requirement of mechanical ventilation, and mortality were collected and analyzed. Result(s): The average age was 65.2, with 47% women; 36.4% were African-American. The average length of stay was 22 days with 26.3% of patients requiring admission to the ICU and 14.9% requiring mechanical ventilation. The overall mortality was 15.3%. Older age, admission to an ICU, and requirement for mechanical ventilation were associated with higher mortality. Treatment with Tocilizumab was also associated with higher mortality, which was mainly observed in subjects not requiring care in an ICU with estimated odds ratio (OR) of 2.9 (p = 0.0004). Tocilizumab treatment was also associated with higher likelihood of admission to an ICU (OR = 4.8, p < 0.0001), progression to requiring mechanical ventilation (OR = 6.6, p < 0.0001), and increased length of stay (OR = 16.2, p < 0.0001). Conclusion and relevance: Our retrospective analysis revealed an association between Tocilizumab administration and increased mortality, ICU admission, mechanical ventilation, and length of stay in subjects with COVID-19. Prospective trials are needed to evaluate the true effect of Tocilizumab in this condition. Copyright © 2020 Southern Society for Clinical Investigation

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bd2d9e966dffaf081319c89136c2510f)

1. **Tocilizumab in the treatment of critical COVID-19 pneumonia: A retrospective cohort study of mechanically ventilated patients**  
   Fisher M. J. International Journal of Infectious Diseases 2021;103:536-539.

Objectives: The purpose of this study is to evaluate clinical outcomes in patients with critical COVID-19 pneumonia requiring invasive mechanical ventilation who were treated with tocilizumab Design: Single-center retrospective cohort study Setting: Stony Brook University Hospital, a 600-bed academic tertiary medical center in Suffolk County, New York Participants: Consecutive patients with COVID-19 confirmed by nasopharyngeal polymerase chain reaction (PCR) who were admitted to Stony Brook University Hospital between March 10 and April 2 2020 and required mechanical ventilation in any intensive care unit during their hospitalization Exposure: Treatment with tocilizumab while intubated Main Outcome: Overall mortality 30 days from the date of intubation Results: Forty-five patients received tocilizumab compared to seventy controls. Baseline demographic characteristics, inflammatory markers, treatment with corticosteroids, and sequential organ failure assessment (SOFA) scores were similar between the two cohorts. Patients who received tocilizumab had significantly lower Charlson co-morbidity index (2.0 vs 3.0,P = 0.01) than controls. There was a trend towards younger mean age in the tocilizumab exposed group (56.2 vs 60.6; P = 0.09). In logistic regression analysis there was no reduction in mortality associated with receipt of tocilizumab (odds ratio (OR) 1.04; 95% CI, 0.27-3.75). There was no observed increased risk of secondary infection in patients given tocilizumab (28.9 vs 25.7; OR 1.17; 95% CI, 0.51-2.71). Conclusion(s): When controlling for age, severity of illness, and co-morbidities, tocilizumab was not associated with reduction in mortality in this retrospective cohort study of mechanically ventilated patients with COVID-19 pneumonia. Further studies are needed to determine the role of tocilizumab in the treatment of COVID-19. Copyright © 2020 The Authors

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=224909ddf6ac73c1b9bfe01634f03eef)

1. **Tocilizumab in Treatment for Patients With COVID-19**  
   Bell Lucy C. K. JAMA internal medicine 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4fcfe75e901504667d881f45964ea99a)

1. **Tocilizumab in Treatment for Patients With COVID-19**  
   Rossi Jean-François JAMA internal medicine 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d4e55a3aed803004fb138090cc9df4c6)

1. **Tocilizumab in Treatment for Patients With COVID-19**  
   Yang Chengliang JAMA internal medicine 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bf188bb34c5d30b7dbf1702551c3159b)

1. **Tocilizumab plus standard care versus standard care in patients in India with moderate to severe COVID-19-associated cytokine release syndrome (COVINTOC): an open-label, multicentre, randomised, controlled, phase 3 trial**  
   Soin A. S. The Lancet. Respiratory medicine. 2021;04:No page numbers.

BACKGROUND: Global randomised controlled trials of the anti-IL-6 receptor antibody tocilizumab in patients admitted to hospital with COVID-19 have shown conflicting results but potential decreases in time to discharge and burden on intensive care. Tocilizumab reduced progression to mechanical ventilation and death in a trial population enriched for racial and ethnic minorities. We aimed to investigate whether tocilizumab treatment could prevent COVID-19 progression in the first multicentre randomised controlled trial of tocilizumab done entirely in a lower-middle-income country. METHOD(S): COVINTOC is an open-label, multicentre, randomised, controlled, phase 3 trial done at 12 public and private hospitals across India. Adults (aged >=18 years) admitted to hospital with moderate to severe COVID-19 (Indian Ministry of Health grading) confirmed by positive SARS-CoV-2 PCR result were randomly assigned (1:1 block randomisation) to receive tocilizumab 6 mg/kg plus standard care (the tocilizumab group) or standard care alone (the standard care group). The primary endpoint was progression of COVID-19 (from moderate to severe or from severe to death) up to day 14 in the modified intention-to-treat population of all participants who had at least one post-baseline assessment for the primary endpoint. Safety was assessed in all randomly assigned patients. The trial is completed and registered with the Clinical Trials Registry India (CTRI/2020/05/025369). FINDINGS: 180 patients were recruited between May 30, 2020, and Aug 31, 2020, and randomly assigned to the tocilizumab group (n=90) or the standard care group (n=90). One patient randomly assigned to the standard care group inadvertently received tocilizumab at baseline and was included in the tocilizumab group for all analyses. One patient randomly assigned to the standard care group withdrew consent after the baseline visit and did not receive any study medication and was not included in the modified intention-to-treat population but was still included in safety analyses. 75 (82%) of 91 in the tocilizumab group and 68 (76%) of 89 in the standard care group completed 28 days of follow-up. Progression of COVID-19 up to day 14 occurred in eight (9%) of 91 patients in the tocilizumab group and 11 (13%) of 88 in the standard care group (difference -3.71 [95% CI -18.23 to 11.19]; p=0.42). 33 (36%) of 91 patients in the tocilizumab group and 22 (25%) of 89 patients in the standard care group had adverse events; 18 (20%) and 15 (17%) had serious adverse events. The most common adverse event was acute respiratory distress syndrome, reported in seven (8%) patients in each group. Grade 3 adverse events were reported in two (2%) patients in the tocilizumab group and five (6%) patients in the standard care group. There were no grade 4 adverse events. Serious adverse events were reported in 18 (20%) patients in the tocilizumab group and 15 (17%) in the standard care group; 13 (14%) and 15 (17%) patients died during the study. INTERPRETATION: Routine use of tocilizumab in patients admitted to hospital with moderate to severe COVID-19 is not supported. However, post-hoc evidence from this study suggests tocilizumab might still be effective in patients with severe COVID-19 and so should be investigated further in future studies. FUNDING: Medanta Institute of Education and Research, Roche India, Cipla India, and Action COVID-19 India. Copyright © 2021 Elsevier Ltd. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=eb6091dc733cadae6dbd4504698805ec)

1. **Tocilizumab reduces the risk of ICU admission and mortality in patients with SARS-CoV-2 infection**  
   Moreno-García E. Revista espanola de quimioterapia : publicacion oficial de la Sociedad Espanola de Quimioterapia 2021;:No page numbers.

&lt;h4&gt;Objective&lt;/h4&gt;In some patients the immune response triggered by SARS-CoV-2 is unbalanced, presenting an acute respiratory distress syndrome which in many cases requires intensive care unit (ICU) admission. The limitation of ICU beds has been one of the major burdens in the management around the world; therefore, clinical strategies to avoid ICU admission are needed. We aimed to describe the influence of tocilizumab on the need of transfer to ICU or death in non-critically ill patients.&lt;h4&gt;Methods&lt;/h4&gt;A retrospective study of 171 patients with SARS-CoV-2 infection that did not qualify as requiring transfer to ICU during the first 24h after admission to a conventional ward, were included. The criteria to receive tocilizumab was radiological impairment, oxygen demand or an increasing of inflammatory parameters, however, the ultimate decision was left to the attending physician judgement. The primary outcome was the need of ICU admission or death whichever came first.&lt;h4&gt;Results&lt;/h4&gt;A total of 77 patients received tocilizumab and 94 did not. The tocilizumab group had less ICU admissions (10.3% vs. 27.6%, P=0.005) and need of invasive ventilation (0 vs 13.8%, P=0.001). In the multivariable analysis, tocilizumab remained as a protective variable (OR: 0.03, CI 95%: 0.007-0.1, P=0.0001) of ICU admission or death.&lt;h4&gt;Conclusions&lt;/h4&gt;Tocilizumab in early stages of the inflammatory flare could reduce an important number of ICU admissions and mechanical ventilation. The mortality rate of 10.3% among patients receiving tocilizumab appears to be lower than other reports. This is a non-randomized study and the results should be interpreted with caution.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=136df6a8bca11fe90419a8a82941d2fa)

1. **Tocilizumab treatment in critically ill patients with COVID-19: A retrospective observational study**  
   Huang E. International Journal of Infectious Diseases 2021;105:245-251.

Objective: Elevated levels of pro-inflammatory cytokines are observed in severe COVID-19 infections, and cytokine storm is associated with disease severity. Tocilizumab, an interleukin-6 receptor antagonist, is used to treat chimeric antigen receptor T cell-induced cytokine release syndrome and may attenuate the dysregulated immune response in COVID-19. We compared outcomes among tocilizumab-treated and non-tocilizumab-treated critically ill COVID-19 patients. Design, setting, and participants: This was a retrospective observational study conducted at a tertiary referral center investigating all patients admitted to the intensive care unit for COVID-19 who had a disposition from the hospital because of death or hospital discharge between March 1 and May 18, 2020 (n = 96). The percentages of death and secondary infections were compared between patients treated with tocilizumab (n = 55) and those who were not (n = 41). Measurements and Main Results: More tocilizumab-treated patients required mechanical ventilation (44/55, 80%) compared to non-treated patients (15/41, 37%; P < 0.001). Of 55 patients treated with tocilizumab, 32 (58%) were on mechanical ventilation at the time of administration, and 12 (22%) progressed to mechanical ventilation after treatment. Of patients treated with tocilizumab requiring mechanical ventilation, 30/44 (68%) were intubated within 1 day of administration. Fewer deaths were observed among tocilizumab-treated patients, both in the overall population (15% vs 37%; P = 0.02) and among the subgroup of patients requiring mechanical ventilation (14% vs 60%; P = 0.001). Secondary infections were not different between the 2 groups (tocilizumab: 31%, non-tocilizumab: 17%; P = 0.16) and were predominantly related to invasive devices, such as urinary and central venous catheters. Conclusion(s): Tocilizumab treatment was associated with fewer deaths compared to non-treatment despite predominantly being used in patients with more advanced respiratory disease. Copyright © 2021 The Authors

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=c2c7b4f56b6a1f1ccfd68e34fbe3d4a1)

1. **Tocilizumab use in COVID-19-associated pneumonia**  
   Okoh A. K. Journal of Medical Virology 2021;93:1023-1028.

Background: We sought to evaluate the effect of tocilizumab (TCB), a recombinant humanized monoclonal antibody against soluble interleukin-6 receptors, in patients hospitalized for coronavirus disease 2019 (COVID-19). Method(s): We included all patients with laboratory-confirmed COVID-19 who had completed hospitalization between March 10, 2020 and April 10, 2020 with follow-up through April 20, 2020. Patients who received TCB in addition to standard of care within 48 h of admission were matched in a 1:2 fashion to a similar cohort who received standard of care alone. Clinical outcomes were compared between matched groups. The primary outcome was de-escalation in oxygen therapy. Secondary outcomes were in-hospital death, septic shock, and acute kidney injury (AKI) requiring hemodialysis. Result(s): Out of 77 patients who received TCB in addition to standard of care, 34% (n = 26) received TCB within 48 h of admission. One-to-two propensity matching identified 20 versus 40 patients in the TCB and no-TCB treatment arms. In the TCB group, an improvement in oxygenation was observed in 80% (n = 16) of the patients by 7 days post TCB administration. After matching, there was no difference in clinical outcomes between TCB and no-TCB patients. In-hospital death: 10% versus 8%; p =.823, septic shock: 10% versus 11%, p =.912, AKI requiring hemodialysis (10% vs. 13%; p =.734). Conclusion(s): Early treatment with TCB in patients admitted for COVID-19 led to an improvement in their oxygen status during hospitalization. This change however did not translate into improved survival when compared to a matched cohort with a similar clinical profile. Copyright © 2020 Wiley Periodicals LLC

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e110509923c9037594b23b6207c751e2)

1. **Tocilizumab use in patients with moderate to severe COVID-19: A retrospective cohort study**  
   Chilimuri S. Journal of Clinical Pharmacy and Therapeutics 2021;46:440-446.

What is known and objective: The coronavirus disease 2019 (COVID-19) associated cytokine activation can lead to a rapid progression into respiratory failure, shock and multiorgan failure. Interleukin-6 (IL-6) is a pro-inflammatory cytokine that likely contributes to the pathogenesis of cytokine release syndrome. It is hypothesized that modulating IL-6 levels or its effects with tocilizumab, a recombinant humanized anti-IL-6 receptor monoclonal antibody, may alter the course of disease. Method(s): We examined the association between tocilizumab use and intubation or death at a community hospital in New York City. Data were obtained regarding consecutive patients hospitalized with COVID-19. The primary end point was a composite of intubation or death in a time-to-event analysis. We compared outcomes in patients who received tocilizumab with those in patients who did not, using a multivariable Cox model with inverse probability weighting according to the propensity score. Results and Discussion: In this single-centre retrospective cohort study involving 1225 hospitalized patients with SARS-CoV-2 infection, the probability to respiratory failure, which was measured as intubation or death, was less frequent in patients who received tocilizumab. What is new and conclusion: Tocilizumab and other IL-6 receptor monoclonal antibodies may evolve as a viable option in treating patients with moderate and severe COVID-19. Copyright © 2020 John Wiley & Sons Ltd

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d758b43d0a9f566cb02ec9ef17f739cd)

1. **Tocilizumab versus the Covid19 tempest: All's well that ends well or much ado about nothing?**  
   Lee T. C. Clinical Microbiology and Infection 2021;27:158-159.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d90544d1ed48a5ac6c430235f22f5d2d)

1. **Tocilizumab's efficacy in patients with Coronavirus Disease 2019 (COVID-19) is determined by the presence of cytokine storm**  
   Andrianopoulos I. Journal of Medical Virology 2021;93:120-121.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=15424188d8b02cb9e8fc196c846e5e7a)

1. **Tocilizumab, Remdesivir, Favipiravir, and Dexamethasone Repurposed for COVID-19: a Comprehensive Clinical and Pharmacovigilant Reassessment**  
   Kelleni Mina T. SN comprehensive clinical medicine 2021;:1-5.

In this manuscript, we discuss the expectations versus the real-world results of four repurposed COVID-19 drugs: tocilizumab, remdesivir, favipiravir, and dexamethasone from a clinical and pharmacovigilant point of view. We suggest that though the results of two-phase III double-blind clinical trials have been less than expected, tocilizumab has a real remaining potential to treat selected critical cases of COVID-19 beyond clinical trials until more data are revealed. On the contrary, remdesivir, though its FDA approval, and favipiravir are least likely to benefit COVID-19 patients. Moreover, we recommend that the RECOVERY dexamethasone should only be considered for critical hospitalized COVID-19 patients and we urge physicians in developing countries to avoid using it in mild-moderate COVID-19 cases. Finally, we recommend considering a personalized risk-benefit ratio before a decision is made using any of these drugs.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1d3a3ac930ccb4117acc60839e9670a7)

1. **Tocilizumab-A beacon of hope in the management of severe COVID-19?**  
   Christou S. Journal of Medical Virology 2021;93:675-677.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=46023f08c292aadce372e5cf110949dd)

1. **Tocilizumab-an effective therapy for severely and critically ill COVID-19 patients**  
   Bhandari S. Indian Journal of Critical Care Medicine 2021;25:260-266.

Background: Tocilizumab (TCZ), a monoclonal antibody against the most prevalent cytokine interleukin-6 (IL-6), is an emerging therapeutic option for COVID-19 infections. The present study was undertaken to assess the therapeutic response of TCZ therapy in severely or critically ill COVID-19 patients and its role as an effective modality of management. Method(s): The present retrospective observational study included 30 admitted severely or critically ill COVID-19 patients, treated with TCZ therapy on behalf of raised IL-6 levels. The patient's data concerning medical history, clinical manifestation, arterial blood gas analysis, mode of oxygenation, radiological imaging, and outcome were extracted from their medical records and compared pre- and post-TCZ infusion. Result(s): All patients of the study group had symptomatic presentations with a mean PaO<inf>2</inf>/FiO<inf>2</inf> (PF) ratio of 205.41 before TCZ infusion. All patients had a raised IL-6 level (mean value 206.56 pg/mL) that was extremely elevated in 90% of patients. Infusion of TCZ dramatically reduced mean body temperature (100.78-99.32degreeF) and the requirement for supplemental oxygen (68-48%) and improved mean SpO<inf>2</inf> (86-89%) and mean PF ratio (208-240) within 24 hours. Three patients on noninvasive ventilation were weaned off after TCZ infusion. Serum levels of IL-6 were raised initially but declined within 3 to 5 days of post-TCZ infusion. Conclusion(s): TCZ appears to be an effective therapeutic option in severely or critically ill COVID-19 patients with raised IL-6 levels. TCZ immediately improves the clinical status of patients by a probable mechanism of inhibition of cytokine storm and reduces COVID-19-related mortalities. Copyright © Jaypee Brothers Medical Publishers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=fd3b435bf795d6dbbfe437e006735b49)

1. **Tocilizumab-induced cytomegalovirus colitis in a patient with COVID-19**  
   Khatib M. Y. Clinical Case Reports 2021;9:148-152.

The authors urge clinicians to observe for early signs of CMV reactivation in patients presenting with gastrointestinal bleeding and intestinal perforation after receiving tocilizumab or other immunosuppressive therapy as a treatment for COVID 19. Early recognition of CMV infection and treatment will prevent life-threatening bleeding and mortality. Copyright © 2020 The Authors. Clinical Case Reports published by John Wiley & Sons Ltd.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=258aec85f8c47cd6b329253378ab1553)

1. **Tocilizumab-induced unexpected increase of several inflammatory cytokines in critically ill COVID-19 patients**  
   Ponthieux Fanny 2021;:No page numbers.

Early evidence during the COVID-19 pandemic indicated high levels of IL-6 in patients with severe COVID-19. This led to the off-label use of tocilizumab (TCZ) during the first wave of the pandemic.We aimed to monitor IL-6 and several inflammatory cytokines in critically ill COVID-19 patients receiving off-label TCZ. Fifteen critically ill SARS-CoV-2 PCR confirmed cases were enrolled and serum samples were collected during 8 days, before and following administration of a single dose of TCZ. In parallel, a control group consisting of 8 non-treated COVID-19 patients not receiving TCZ was established. Serum profile of 12 cytokines (IL-1β, -2, -4, -6, -8, -10, -12, -13, -17, -18, TNF-α and INF-γ) and of IL-6R were assessed in these two groups. Although the increased IL-6 concentrations after TCZ infusion were expected, we observed an unexpected increase in IL-1β, -2, -4, -10, -12p70, -18 and IL-6R levels in the treated patients with maximal values reached 2 to 4 days after TCZ. In contrast, no change in cytokine levels was observed in the control group. There was no significant difference in cytokine levels between survivors (TCZ/S) or non-survivors (TCZ/D). This observation suggests that some inflammatory pathways escape IL-6R blockade leading to an increase in several pro-inflammatory cytokines. Our findings could highlight an anti-inflammatory role of IL-6 and may explain why TCZ has failed to improve survival in critically ill COVID-19 patients when given alone.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5f512fd9b2b3b279fb6d50d51aa560fd)

1. **Tocilizumab: From Rheumatic Diseases to Covid-19**  
   Raiteri A. Current pharmaceutical design. 2021;11:No page numbers.

Tocilizumab is a humanised interleukin-6 receptor-inhibiting monoclonal antibody that is currently approved for the treatment of rheumatoid arthritis and other immune-related conditions. Recently, tocilizumab has been investigated as a possible treatment for severe coronavirus-induced disease 2019 (COVID-19). Despite the lack of direct antiviral effects, tocilizumab could reduce the immune-induced organ damage caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) infection. Until recently, most reports on tocilizumab for COVID-19 included a limited number of patients, preventing an overall evaluation of its efficacy and safety for this specific condition. Therefore, we reviewed the literature regarding the physiopathological rationale of tocilizumab for COVID-19 and its outcomes. We searched the MEDLINE database with the string "(SARS-CoV-2 OR coronavirus OR COVID-19 OR MERS-cov OR SARS-cov) AND (IL-6 OR interleukin 6 OR tocilizumab)". While the scientific rationale supporting tocilizumab for COVID-19 is solid, the evidence regarding the outcomes remains controversial. Available data and results from ongoing trials will provide useful information in the event of new COVID-19 outbreaks or future pandemics from different coronaviruses. Copyright© Bentham Science Publishers; For any queries, please email at epub@benthamscience.net.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5a660277fc99564e6afb265ce6fa3f40)

1. **Treatment of COVID-19 atypical pneumonia by early Tocilizumab administration in "non-critically-ill" patients on hemodialysis**  
   Castellano G. Journal of Nephrology 2021;34:259-262.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ee3d6feaccaa80a8f92cfefc86b7350e)

1. **Treatment With Tocilizumab for Patients With COVID-19 Infections: A Case-Series Study**  
   Mo Y. Journal of Clinical Pharmacology 2021;61:406-411.

Tocilizumab (TCZ), a humanized monoclonal antibody targeting the interleukin-6 receptor, holds the potential for treating coronavirus disease 2019 (COVID-19) patients, particularly those at high risk of cytokine storm syndrome. However, data regarding the clinical impact of treatment with TCZ in patients with COVID-19 are limited. This study was conducted to evaluate the safety and effectiveness of TCZ as an adjunct therapy for the treatment of severe COVID-19 infection. This was a retrospective observational chart review of confirmed COVID-19 patients who received TCZ, along with other COVID-19 therapies. The outcomes of interest included changes in vital signs such as temperature and laboratory biomarkers, duration of mechanical ventilation, adverse events possibly associated with TCZ, and intensive care unit and hospital lengths of stay. This study included 38 patients with an average age of 63 years (IQR, 48-70 years). The average dose of TCZ given was 519 +/- 61 mg. Median C-reactive protein significantly decreased following TCZ administration (189.9 vs 54.8 mg/L, P =.003). Nineteen of all febrile patients before the initiation of TCZ (73%) became fever free on the fourth day of TCZ treatment. Following TCZ treatment, 11 patients developed infections because of multidrug-resistant bacteria, and elevated liver transaminases were observed in 6 patients. The preliminary findings of this study suggested TCZ appeared to ameliorate COVID-19-related cytokine storm syndrome. However, large randomized, controlled trials are needed to investigate whether treatment with TCZ is associated with better outcomes in COVID-19. Copyright © 2020, The American College of Clinical Pharmacology

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a739c023f1318ea3df5b4cef8db42e52)

1. **Treatment with tocilizumab or corticosteroids for COVID-19 patients with hyperinflammatory state: a multicentre cohort study (SAM-COVID-19)**  
   Rodriguez-Bano J. Clinical Microbiology and Infection 2021;27:244-252.

Objectives: The objective of this study was to estimate the association between tocilizumab or corticosteroids and the risk of intubation or death in patients with coronavirus disease 19 (COVID-19) with a hyperinflammatory state according to clinical and laboratory parameters. Method(s): A cohort study was performed in 60 Spanish hospitals including 778 patients with COVID-19 and clinical and laboratory data indicative of a hyperinflammatory state. Treatment was mainly with tocilizumab, an intermediate-high dose of corticosteroids (IHDC), a pulse dose of corticosteroids (PDC), combination therapy, or no treatment. Primary outcome was intubation or death; follow-up was 21 days. Propensity score-adjusted estimations using Cox regression (logistic regression if needed) were calculated. Propensity scores were used as confounders, matching variables and for the inverse probability of treatment weights (IPTWs). Result(s): In all, 88, 117, 78 and 151 patients treated with tocilizumab, IHDC, PDC, and combination therapy, respectively, were compared with 344 untreated patients. The primary endpoint occurred in 10 (11.4%), 27 (23.1%), 12 (15.4%), 40 (25.6%) and 69 (21.1%), respectively. The IPTW-based hazard ratios (odds ratio for combination therapy) for the primary endpoint were 0.32 (95%CI 0.22-0.47; p < 0.001) for tocilizumab, 0.82 (0.71-1.30; p 0.82) for IHDC, 0.61 (0.43-0.86; p 0.006) for PDC, and 1.17 (0.86-1.58; p 0.30) for combination therapy. Other applications of the propensity score provided similar results, but were not significant for PDC. Tocilizumab was also associated with lower hazard of death alone in IPTW analysis (0.07; 0.02-0.17; p < 0.001). Conclusion(s): Tocilizumab might be useful in COVID-19 patients with a hyperinflammatory state and should be prioritized for randomized trials in this situation. Copyright © 2020 The Author(s)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cd4cba6f4fb955241a70f7136f29042b)

1. **Upregulated IL-6 Indicates a Poor COVID-19 Prognosis: A Call for Tocilizumab and Convalescent Plasma Treatment**  
   Wu J. Frontiers in Immunology 2021;12 (no pagination):No page numbers.

A comprehensive understanding of the dynamic changes in interleukin-6 (IL-6) levels is essential for monitoring and treating patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2). By analyzing the correlations between IL-6 levels and health conditions, underlying diseases, several key laboratory detection indices, and the prognosis of 1,473 patients with the coronavirus disease 2019 (COVID-19), the role of IL-6 during SARS-CoV-2 infection was demonstrated. Our results indicated that IL-6 levels were closely related to age, sex, body temperature, oxygen saturation (SpO<inf>2</inf>) of blood, and underlying diseases. As a stable indicator, the changes in IL-6 levels could indicate the inflammatory conditions during a viral infection. Two specific treatments, namely, tocilizumab and convalescent plasma therapy (CPT), decreased the level of IL-6 and relieved inflammation. CPT has an important role in the therapy for patients with critical COVID-19. We also found that patients with IL-6 levels, which were 30-fold higher than the normal level, had a poor prognosis compared to patients with lower levels of IL-6. © Copyright © 2021 Wu, Shen, Han, Qiao, Dai, He, Pang, Zhao, Luo, Guo, Yang, Wu, Jiang, Zhang, Zhang, Li, Li and Xia.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2469086ab76ee404535c044d8093d4f1)

1. **Use of subcutaneous tocilizumab in patients with COVID-19 pneumonia**  
   Mazzitelli M. Journal of Medical Virology 2021;93:32-34.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=49ea610e3a322e9d915f53498b734e62)

1. **Use of tocilizumab in multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2**  
   Banday A. Z. The Journal of Pediatrics 2021;228:315.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=477c998b92d2002692726e3731202cfc)

1. **Vaccines and drugs under clinical trials for prevention and treatment of COVID-19**  
   Yadav U. C. S. VirusDisease. 2021;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=dd6ef5f42acf772e0d111ce47641ea1e)

1. **Varying illness severity in patients with myd88 deficiencyinfected with coronavirus SARS-CoV-2**  
   Mahmood H. Z. Pediatrics 2021;147 (3):453-454.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=90df556cabf9c23b291ca47f9d86195d)

1. **What about tocilizumab? A retrospective study from a NYC Hospital during the COVID-19 outbreak**  
   Mehta Monica PloS one 2021;16:e0249349.

&lt;h4&gt;Background&lt;/h4&gt;Tocilizumab, an interleukin-6 receptor blocker, has been used in the inflammatory phase of COVID-19, but its impact independent of corticosteroids remains unclear in patients with severe disease.&lt;h4&gt;Methods&lt;/h4&gt;In this retrospective analysis of patients with COVID-19 admitted between March 2 and April 14, 2020 to a large academic medical center in New York City, we describe outcomes associated with tocilizumab 400 mg (without methylprednisolone) compared to a propensity-matched control. The primary endpoints were change in a 7-point ordinal scale of oxygenation and ventilator free survival, both at days 14 and 28. Secondary endpoints include incidence of bacterial superinfections and gastrointestinal perforation. Primary outcomes were evaluated using t-test.&lt;h4&gt;Results&lt;/h4&gt;We identified 33 patients who received tocilizumab and matched 74 controls based on demographics and health measures upon admission. After adjusting for illness severity and baseline ordinal scale, we failed to find evidence of an improvement in hypoxemia based on an ordinal scale at hospital day 14 in the tocilizumab group (OR 2.2; 95% CI, 0.7-6.5; p = 0.157) or day 28 (OR 1.1; 95% CI, 0.4-3.6; p = 0.82). There also was no evidence of an improvement in ventilator-free survival at day 14 (OR 0.8; 95% CI, 0.18-3.5; p = 0.75) or day 28 (OR 1.1; 95% CI, 0.1-1.8; p = 0.23). There was no increase in secondary bacterial infection rates in the tocilizumab group compared to controls (OR 0.37; 95% CI, 0.09-1.53; p = 0.168).&lt;h4&gt;Conclusions&lt;/h4&gt;There was no evidence to support an improvement in hypoxemia or ventilator-free survival with use of tocilizumab 400 mg in the absence of corticosteroids. No increase in secondary bacterial infections was observed in the group receiving tocilizumab.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cc0444ca931e1f4b67cfd61fee3dab3f)

### Opening Internet Links

The links to internet sites in this document are 'live' and can be opened by holding down the CTRL key on your keyboard while clicking on the web address with your mouse

### Full text papers

Links are given to full text resources where available. For some of the papers, you will need an **NHS OpenAthens Account**. If you do not have an account you can [register online](https://openathens.nice.org.uk/).

You can then access the papers by simply entering your username and password. If you do not have easy access to the internet to gain access, please let us know and we can download the papers for you.

### Guidance on searching within online documents

Links are provided to the full text of each document. Relevant extracts have been copied and pasted into these results. Rather than browse through lengthy documents, you can search for specific words as follows:

**Portable Document Format / pdf / Adobe**  
Click on the Search button (illustrated with binoculars). This will open up a search window. Type in the term you need to find and links to all of the references to that term within the document will be displayed in the window. You can jump to each reference by clicking it.

**Word documents**  
Select Edit from the menu, the Find and type in your term in the search box which is presented. The search function will locate the first use of the term in the document. By pressing 'next' you will jump to further references.

## D. Search History

|  | **Source** | **Criteria** | **Results** |
| --- | --- | --- | --- |
| 1. | EMBASE | ((corona\* or corono\*) adj1 (virus\* or viral\* or virinae\*)).ab,kw,ti. | 2572 |
| 2. | EMBASE | (coronavirus\* or coronovirus\* or coronavirinae\* or CoV).ab,kw,ti. | 77629 |
| 3. | EMBASE | ("2019-nCoV\*" or 2019nCoV\* or "19-nCoV\*" or 19nCoV\* or nCoV2019\* or "nCoV-2019\*" or nCoV19\* or "nCoV-19\*" or "COVID-19\*" or COVID19\* or "COVID-2019\*" or COVID2019\* or "HCoV-19\*" or HCoV19\* or "HCoV-2019\*" or HCoV2019\* or "2019 novel\*" or Ncov\* or "n-cov" or "SARS-CoV-2\*" or "SARSCoV-2\*" or "SARSCoV2\*" or "SARS-CoV2\*" or SARSCov19\* or "SARS-Cov19\*" or "SARSCov-19\*" or "SARS-Cov-19\*" or SARSCov2019\* or "SARS-Cov2019\*" or "SARSCov-2019\*" or "SARS-Cov-2019\*" or SARS2\* or "SARS-2\*" or SARScoronavirus2\* or "SARS-coronavirus-2\*" or "SARScoronavirus 2\*" or "SARS coronavirus2\*" or SARScoronovirus2\* or "SARS-coronovirus-2\*" or "SARScoronovirus 2\*" or "SARS coronovirus2\*" or covid).ab,kw,ti. | 113184 |
| 4. | EMBASE | exp Coronavirinae/ | 33615 |
| 5. | EMBASE | exp Coronavirus infection/dr, dt [Drug Resistance, Drug Therapy] | 5357 |
| 6. | EMBASE | 1 or 2 or 3 or 4 or 5 | 138522 |
| 7. | EMBASE | tocilizumab.ab,ti. | 9131 |
| 8. | EMBASE | sarilumab.ab,ti. | 447 |
| 9. | EMBASE | exp \*sarilumab/ | 313 |
| 10. | EMBASE | (("interleukin 6" or "interleukin-6" or IL6) adj2 inhibit\*).ab,ti. | 1214 |
| 11. | EMBASE | ("anti-interleukin-6" or "anti interleukin 6" or "anti-IL6" or "anti IL6").ab,ti. | 1124 |
| 12. | EMBASE | exp \*tocilizumab/ | 4258 |
| 13. | EMBASE | 7 or 8 or 9 or 10 or 11 or 12 | 11106 |
| 14. | EMBASE | 6 and 13 | 1090 |
| 15. | EMBASE | limit 14 to (english language and yr="2021 - 2022") | 277 |

**Disclaimer**  
We hope that you find the evidence search service useful. Whilst care has been taken in the selection of the materials included in this evidence search, the Library and Knowledge Service is not responsible for the content or the accuracy of the enclosed research information. Accordingly, whilst every endeavour has been undertaken to execute a comprehensive search of the literature, the Library and Knowledge Service is not and will not be held responsible or liable for any omissions to pertinent research information not included as part of the results of the enclosed evidence search. Users are welcome to discuss the evidence search findings with the librarian responsible for executing the search. We welcome suggestions on additional search strategies / use of other information resources for further exploration. You must not use the results of this search for commercial purposes. Any usage or reproduction of the search output should acknowledge the Library and Knowledge Service that produced it.