CoLab Network

Summary Report

Tocilizumab for the Treatment of Hospitalized Patients With COVID-19

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Executive Summary

The objective of the rapid systematic review was to synthesize the current evidence on tocilizumab (TCZ) for hospitalized patients. TCZ is likely safe and may be efficacious in reducing the length of hospitalization and the progression to the combined end point of mechanical ventilation or death. The studies demonstrating these findings (12 randomized controlled trials [RCTs]) lack similarity in their study populations, treatment characteristics, and usual care used among trial sites. Administration of TCZ and a patient population matching the characteristics of those in the RECOVERY and REMAP-CAP (2 of the largest and best-run) trials may yield the best outcomes. Evidence is lacking for patients with a compromised immune system, comorbidities, and concomitant bacterial infections.

Background

Several drug treatments for the management of COVID-19 are approved for use in Canada. Currently, the federal government, through the Public Health Agency of Canada, is responsible for overseeing the procurement and allocation of these drugs to ensure their availability for federal, provincial, and territorial health care systems. The following drugs, which are in high demand, are currently funded by the Public Health Agency of Canada: nirmatrelvir-ritonavir (Paxlovid), remdesivir (Veklury), and TCZ (Actemra).

Policy Issue

Gathering evidence on the safety and efficacy of TCZ is needed to help inform future decisions about its procurement, allocation, and equitable distribution within Canadian health care systems.

Objective

The objective of the rapid systematic review was to synthesize the current evidence on TCZ for hospitalized patients, updating an existing CADTH evidence review that was conducted in March 2021.

Policy Questions

1. What new evidence on the efficacy and safety of TCZ is available since the publication of the CADTH report?
2. Which patients are most likely to benefit from treatment with TCZ?

Results

Selection of Studies

Researchers used a rapid systematic review approach to identify RCTs and controlled clinical trials that met the inclusion criteria. Twelve RCT studies are included in the final analysis, 7 of which were included in the initial CADTH report done in March 2021.

Randomized Controlled Trials

Efficacy

The findings from the 12 RCTs suggest that TCZ may be efficacious in reducing the following when compared to placebo or standard therapy:

- the length of hospitalization
- progression to the combined end point of mechanical ventilation or death.

The other outcomes of interest (clinical status, improvement, or failure; hospital discharge; ICU admission, discharge, and duration; incidence of invasive mechanical ventilation and discontinuation of ventilation or supplementary oxygen; and duration of ventilation or supplementary oxygen) remain inconclusive.

Notably, TCZ appears to be more efficacious than usual care and there are indications of clinically positive outcomes. However, there were some inconsistencies, and patient sample sizes were too small to draw firm conclusions.

Safety

The safety of TCZ is variable in terms of death and the occurrence of serious adverse events. Few studies reported on safety outcomes, and their patient sample sizes were too small to draw firm conclusions.

Risk of Bias

These 12 studies were assessed at an overall low risk of bias. There was some lack of clarity across a few of the bias domains.

Studies Assessing Specific Populations

The analysis shows little to no evidence on the impact of TCZ in patients who are immunocompromised, have comorbidities, or have concomitant bacterial infections.

Target Population

Administration of TCZ in a patient population matching the characteristics of those in the RECOVERY and REMAP-CAP (2 of the largest and strongest) trials may yield the best outcomes. The use of TCZ in these trials can be applied to develop practice standards that align with current clinical recommendations.

Table 1

Summary of RECOVERY and REMAP-CAP Studies

Study	Patient characteristics	Methods	Treatment	Other therapies
RECOVERY	Hospitalized patients with clinically suspected or confirmed COVID-19 infection Hypoxia and systemic inflammation	TCZ given within 24 hours of recruitment Additional dose 12 to 24 hours if no improvement	TCZ dose stratified by weight (8 mg to 800 mg by 4 weight categories)	Treatment in combination with a systemic corticosteroid
REMAP-CAP	Critically ill hospitalized patients with clinically suspected or confirmed COVID-19 infection	TCZ given within 24 hours of ICU admission Additional dose 12 to 24 hours later at the discretion of a clinician	TCZ: 8 mg/kg (maximum 800 mg)	Treatment in combination with glucocorticoids

Limitations

There are important limitations to the studies included in the systematic review. The studies lacked similarity in their study populations and treatment characteristics (e.g., COVID-19 severity, medication taken in addition to the study treatments, and time of medication administration relating to the clinical course of infection), and usual care was not standardized across the studies.

Implications for Policy-Making

TCZ is likely safe and efficacious in some hospitalized patients with COVID-19. Patients with similar characteristics as those included in the RECOVERY and REMAP-CAP trials would likely benefit the most.

The included studies are overall methodologically strong, but further evidence is required to draw more concrete conclusions, especially among some important subpopulations.

For more information on CoLab and its work visit the **CoLab website**.

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About CADTH: CADTH is a not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

About CoLab: CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with CADTH's Post-Market Drug Evaluation Program to produce credible and timely evidence on post-market drug safety and effectiveness.