CoLab Network

Summary Report

Remdesivir for the Treatment of COVID-19 in the Inpatient Setting

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Executive Summary

The objective of the rapid systematic review was to synthesize the current evidence on remdesivir for hospitalized adults and adolescents (inpatients). Remdesivir is likely safe and may be effective in reducing the need for mechanical ventilation in inpatients. The studies demonstrating these findings (7 randomized controlled trials [RCTs]) lack clinical evidence for some of the key populations of interest, and they have varying definitions of the clinical end points. The generalizability of these findings may be affected by the difference in vaccination status among participants, the dominant COVID-19 variant during the study periods, and the comparability of the standard of care across studies.

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 tocilizumab (Actemra).

Policy Issue

Gathering evidence on the safety and efficacy of remdesivir 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 in Canada and countries with similar health care systems and economies to Canada on remdesivir for inpatients, updating an existing CADTH evidence review that was conducted in February 2021.

Policy Questions

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

Results

Selection of Studies

Researchers used a rapid systematic review approach to identify RCTs that met the inclusion criteria. Six unique studies and 1 platform trial across 18 publications were included in the final analysis, with 4 studies involving patients that were part of the large platform trial known as the WHO Solidarity trial. The WHO Solidarity trial was analyzed separately.

Randomized Controlled Trials

> The studies were conducted before the emergence of the Omicron and Delta variants and before widespread vaccination. This may not fit well with the vaccination status of the current population in Canada.

Efficacy

Findings from 6 RCTs suggest that, when compared to standard of care, remdesivir **significantly reduces**:

- the need for mechanical ventilation (pooled results from 3 studies)
- the need for intubation (only reported in 1 study).

Findings from 6 RCTs suggest that, when compared to standard of care, remdesivir **does not** significantly:

- reduce intensive care unit (ICU) admissions
- reduce length of ICU stay
- increase time to ventilation.

Remdesivir's impact on the other outcomes of interest (length of hospitalization, time to clinical improvement, and progression to high-flow oxygen) was inconsistent.

Safety

The pooled results from 6 RCTs suggest that remdesivir significantly reduces the risk of death compared to standard therapy. However, alone, each individual RCT showed no significant difference. The reduction seen in the pooled results is likely considered clinically important.

The incidence of serious adverse events and grade 3 or 4 adverse events did not differ between remdesivir and standard therapy. There are insufficient data to draw any conclusions on withdrawals due to adverse events and specific serious adverse events, including acute kidney injury, acute liver injury, and thrombocytopenia.

Risk of Bias

These 6 RCTs were assessed at a low risk of bias for 3 of 7 bias domains. For 5 RCTs, there is an unclear risk of bias for blinding of participants and personnel because they are open-label RCTs.

WHO Solidarity Trial

Researchers excluded the WHO Solidarity trial from the main analysis, reporting on it individually. The trial included 405 hospitals across 30 countries, with 4,169 patients randomized to the remdesivir treatment group. It is estimated that less than 40% of the included patients were from a setting where the health care system and/or economy are similar to Canada.

Efficacy

Like the main analysis, the trial found that remdesivir reduces the need for mechanical ventilation compared to standard of care. However, the significance was marginal.

Safety

Unlike the main analysis, the trial found no significant difference in the risk of death between remdesivir and standard of care.

Risk of Bias

The trial is at low risk of bias for 4 of 7 bias domains. It has a high risk of bias in selective outcome reporting, and the risk of bias for the other 2 domains is unclear.

Studies Assessing Specific Populations

Only 1 study reported on underserved or equity-deserving groups in a subgroup analysis. Researchers were unable to perform their own subgroup analysis because of insufficient data.

Limitations

There are 2 main limitations to the studies included in the systematic review. The studies lack clinical evidence for some of the key populations of interest, and they have varying definitions of the clinical end points.

Implications for Policy-Making

Remdesivir is likely safe and may be effective in reducing the need for mechanical ventilation in inpatients with COVID-19 infection, but further evidence is needed.

There are also concerning characteristics impacting generalizability, including:

- the difference in vaccination status
- the dominant COVID-19 variant during study periods
- the comparability of the standard of care.

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

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This work was supported by CADTH and its Post-Market Drug Evaluation Program, through funding provided by Health Canada.

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.