CoLab Network

Summary Report

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

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Executive Summary

The objective of the rapid systematic review was to evaluate the efficacy, effectiveness, and safety of remdesivir for the treatment of nonhospitalized adults (outpatients). Findings from 1 randomized controlled trial (RCT) and 9 comparative observational studies are limited because of small sample sizes, uncontrolled underlying factors that could distort the relationship between remdesivir and comparators, and conflicting results. Firm conclusions cannot be made, and further evidence is needed.

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 post-market drug evidence on the safety, efficacy, and effectiveness 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 evaluate the efficacy, effectiveness, and safety of remdesivir for the treatment of COVID-19 in outpatients from settings within the health care systems in Canada or from countries with economies similar to Canada.

Policy Questions

1. What is the efficacy, effectiveness, and safety of remdesivir in nonhospitalized patients with COVID-19?
2. Which nonhospitalized patients are most likely to benefit from treatment with remdesivir?

Results

Selection of Studies

Researchers used a rapid systematic review approach to identify RCTs and comparative observational studies that met the inclusion criteria. The final analysis included 10 unique studies across 12 publications: 1 RCT and 9 comparative observational studies.

All 10 studies included nonhospitalized patients with mild to moderate COVID-19 infection and 1 or more risk factors for severe disease, who were at approximately 7 days after their first symptoms.

Randomized Controlled Trial

Patients who were vaccinated were excluded from the trial. The study was also conducted before the emergence of Omicron and Delta variants and subvariants.

Efficacy

Findings from the RCT suggest that, when compared to placebo, remdesivir reduces the risk of COVID-19—related hospitalization.

This risk reduction is notable in males and those aged 60 years or older. However, these results should be interpreted with caution because of the small sample size of the study.

The RCT was funded by Gilead Sciences, the manufacturer of remdesivir. Overall, the RCT is at low risk of bias, with unclear bias in sequence generation and allocation.

Comparative Observational Studies

All the observational studies provided real-world evidence of early remdesivir treatment in the Omicron era, with variable percentages of patients with COVID-19 vaccination.

Effectiveness (Remdesivir vs. No Treatment)

Findings from observational studies suggest that, when compared to no treatment, remdesivir **may reduce**:

- hospitalizations (protective effect seen in 2 of 3 studies)
- emergency department visits (only reported in 1 study)
- the need for supplemental oxygen (protective effect seen in 1 study)
- COVID-19 aftereffects (only reported in 1 study).

Findings from observational studies suggest that, when compared to no treatment, remdesivir **does not reduce**:

- length of hospitalization (reported in 2 studies)
- number of ICU admissions (reported in 3 studies).

Results should be interpreted with caution because of the limitations in the observational data and the lack of adjustment for underlying factors.

Effectiveness (Remdesivir vs. Molnupiravir or Nirmatrelvir-Ritonavir)

Findings from observational studies suggest molnupiravir and nirmatrelvir-ritonavir are more effective than remdesivir at reducing:

- the rate of COVID-19–related hospitalization (effect seen after combining the risks from the 2 studies)
- persistent symptoms (only reported in 1 study).

Remdesivir is comparable to other antivirals for symptom rebound.

Results should be interpreted with caution because of the limitations in the observational data and the lack of adjustment for underlying factors.

Effectiveness (Remdesivir vs. Inhaled Glucocorticoids or Budesonide)

Researchers did not identify any studies in the literature that compared remdesivir with inhaled glucocorticoids or budesonide.

Safety

The results from 3 observational studies suggest that remdesivir does not lower the risk of all-cause or COVID-19–related deaths compared with no treatment. The

results from 3 observational studies suggest that remdesivir is comparable to other antivirals in reducing COVID-19–related deaths. The studies did not account for underlying factors.

Serious adverse events and drug discontinuation were uncommon in the studies that reported these safety outcomes. Acute liver injury outcomes were only reported in 1 study, and no injuries were noted for those treated with remdesivir.

Risk of Bias

The risk of bias across the observational studies ranged from serious to critical. The studies failed to account for underlying factors, which may distort the relationship between remdesivir and comparators.

Studies Assessing Specific Populations

Analysis for subgroups of interest was not feasible because of insufficient data. Only 1 study presented results for specific subgroups for age, sex and gender, and race and ethnicity.

Limitations

There are 2 main limitations to the studies included in the systematic review. The studies in the systematic review lack clinical evidence for some of the key populations of interest and have varying definitions of the clinical end points. The comparative observational studies are limited because of uncontrolled underlying factors that may distort the relationship between remdesivir and comparators.

Implications for Policy-Making

Study findings are limited because of small sample sizes, uncontrolled underlying factors, and conflicting results. Firm conclusions cannot be made, and further evidence is needed.

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

Canada's Drug and Health Technology Agency

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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.