Remdesivir during the COVID-19 Pandemic

– Analysis of the First Year of Global Spontaneous Disease-Specific Adverse Drug Reaction Reporting

Elena Rocca[1,2], Oskar Gauffin[1], Ruth Savage[1,3,4], Sara Hedfors Vidlin[1], Birgitta Grundmark[1]

1. Uppsala Monitoring Centre, Uppsala, Sweden
2. Centre for Applied Philosophy of Science, Norwegian University of Life Sciences, Ås, Norway
3. New Zealand Pharmacovigilance Centre, Division of Health Sciences, University of Otago, Dunedin, New Zealand
4. Dept of General Practice, University of Otago, Christchurch, New Zealand

VigiBase 2020

14 574 COVID-19 related ICSRs

5 299 remdesivir ICSRs

4 944 remdesivir ICSRs for analysis

355 with tocilizumab co-reported

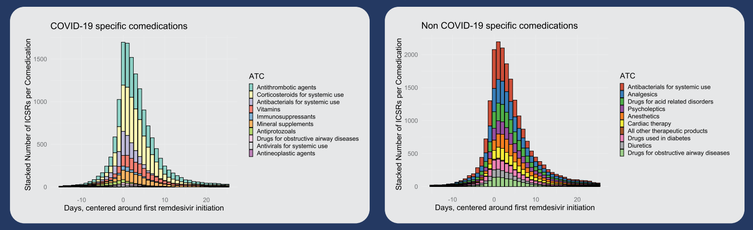
Sex distribution: ♀ 40% | ♂ 60%

Severity: Severe/ critical disease: 21%

Age distribution: Q1–Q3: **49–74 years** Median: **63 years**

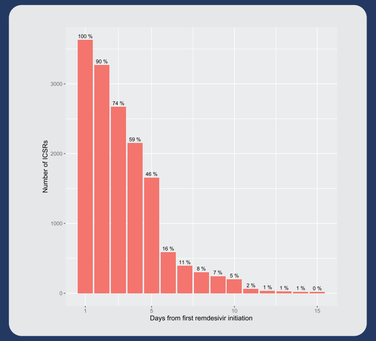
Origin:
Region of the Americas: **72%**
European Region: **15%**
South-East Asia Region: **11%**
Western Pacific Region: **1%**
Eastern Mediterranean Region: **1%**
African Region: **0%**

Co-medication pattern:



Most frequent co-reported COVID-19 specific drugs were heparins, corticosteroids and azithromycin.

Duration of treatment:



Background

Remdesivir is conditionally approved for the treatment of COVID-19 in several countries. With its poorly characterised safety profile, global monitoring of adverse drug reaction (ADR) reporting is essential.

Objectives:

Reviewing global ADR reporting for remdesivir by investigating severity of illness, co-reported COVID-19 medications, early therapy cessation and ADRs in individual case safety reports (ICSR).

Methods

All ICSRs from 2020 that included the COVID-19 indication (for any reported drug) were retrieved from the WHO global ICSR database, VigiBase, by scanning incoming ICSR indication, free text and laboratory test result fields through an in-house developed algorithm. Drugs in extracted ICSRs were classified by two independent coders as either COVID-19 specific (identified from scientific literature) or non-COVID-19 specific. Analysis of the remdesivir ICSR's demographics, co-reported drugs, therapy duration, and ADRs coded as MedDRA preferred terms (PTs), was performed. Disproportionality analysis (measured by Information Component (IC)), was performed for signal detection purposes using COVID-19 specific drugs as background to reduce confounding by the disease. Severity of COVID-19 disease was assessed based on co-reported medicines and symptoms. Among the medicines specifically targeting COVID-19, tocilizumab was chosen as a comparator for remdesivir as it had the closest proportion of ICSRs with seriously ill COVID-19 patients to remdesivir. A bar plot wasconstructed for PTs reported in at least 0.5% of the remdesivir or tocilizumab ICSRs. Disproportional PTs, marked red, were compared (rightmost figure).

Conclusion

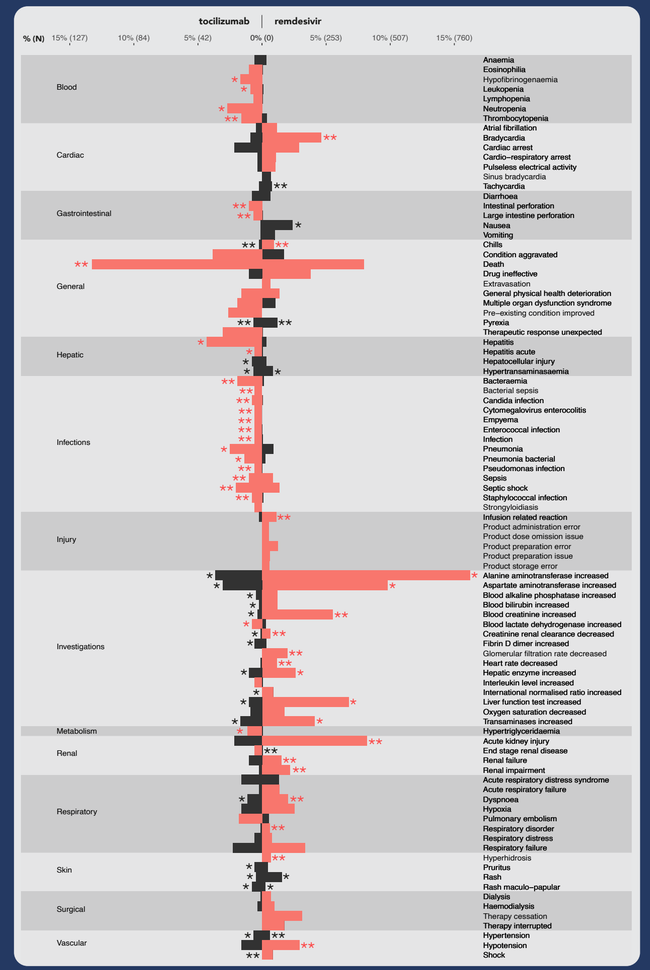
Remdesivir ICSRs show a complex pattern of care and polypharmacy making causality assessment complex. In-depth analysis of case narratives, including clinicians' safety concerns in the extensive withdrawal patterns, may aid in further evaluating disproportional ADRs such as those related to hepatic, renal and cardiac function.

Uppsala Monitoring Centre

Uppsala Monitoring Centre (UMC)
Box 1051,
SE-751 40 Uppsala,
Sweden
+46 18 65 60 60
www.who-umc.org

Results

Disproportionalities (red bars) were largely in keeping with labelled reactions (*) and showed additional potential signals that were incompletely labelled (**) or unlabelled including bradycardia and renal injury with remdesivir but not tocilizumab.



* = The PT is included as an acknowledged ADR in the EU-labelling for the related medicine.
** = The PT is included in relation to safety issues (eg warnings) in the EU- labelling for the related medicine.