Remdesivir Reduces Mortality in Hemato-Oncology Patients with COVID-19

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Introduction: Remdesivir is the first agent with proven clinical efficacy against coronavirus disease 2019 (COVID-19); however, its benefit is associated with early use, and its efficacy has been poorly studied in patients with hemato-oncological diseases, who have an increased risk of a severe course of infection. This study aimed to assess the effects of remdesivir on mortality, mechanical ventilation, and the duration of hospitalization in both the general population and in patients with hemato-oncological diseases.

Materials and Methods: Longitudinal data for 4287 patients with confirmed COVID-19 were analyzed, including a subset of 200 individuals with hemato-oncological diseases. In total, 1285 (30.0%) patients received remdesivir, while the remaining patients were treated with other methods. Survival statistics for the 14- and 30-day observation time points were calculated using non-parametric and multivariate Cox models.

Results: Mortality for the 14- and 30-day observation time points was notably lower among patients receiving remdesivir (7.2% vs 11.6%, \( p < 0.001 \) and 12.7% vs 16.0, \( p = 0.005 \), respectively); however, in multivariate models adjusted for age, sex, lung involvement, and lactate dehydrogenase and interleukin-6 levels, the administration of remdesivir did not reduce patient mortality at either the 14-day or 30-day time points. Among patients with haemato-oncological disease, significant survival benefit was observed at 14 and 30 days for patients treated with remdesivir (11.3% vs 16.7% and 24.2% vs 26.1%, respectively; \( p < 0.001 \)). A favorable effect of remdesivir was also noted for the 14-day time point in multivariate survival analysis (HR: 4.03 [95% confidence interval: 1.37–11.88]; \( p = 0.01 \)).

Conclusion: Remdesivir significantly reduced the early mortality rate in COVID-19 patients with comorbid hemato-oncological disease, which emphasizes the need to administer this agent to immunosuppressed patients.

Keywords: COVID-19, SARS-COV-2, remdesivir, mortality, hemato-oncology

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in December 2019 in Wuhan, China, with the subsequent rapid identification of pneumonia-associated coronavirus disease 2019 (COVID-19). Since then, more than 454 million cases have been reported globally, and more than 6 million people have died from the disease (1.32% mortality). In Poland, more than 5.5 million cases have been reported, with a mortality rate of 1.95%. The COVID-19 pandemic has affected almost all countries, but with divergent mortality rates across different patient populations. Severe disease risk factors include older age (> 65 or 75 years according to some studies); male sex; black race; and the presence of chronic diseases, such as kidney disease, diabetes, obesity, hypertension, and asthma. Active neoplastic disease is another risk factor for severe outcome in COVID-19 patients, as well as hematological...
malignancies and previous chemotherapy.\textsuperscript{7,8} Studies have also shown that mortality may be affected by the initiation of disease-modifying drugs, such as tocilizumab and baricitinib.\textsuperscript{9,10} Patients with immune deficiency have a significantly higher risk of a severe course of COVID-19 and, according to numerous observations, may have active replication of SARS-CoV-2 for prolonged periods. For this reason, direct antiviral therapy is important for immunodeficient individuals.\textsuperscript{11} Data thus far indicate a poorer prognosis among patients with hematological diseases, but no data on the effect of antiviral treatment in this group have been published.

Since the beginning of the pandemic, intense research has been conducted to identify effective treatments for COVID-19. The first drug with antiviral properties to be used in patients infected with SARS-CoV-2 was remdesivir (approved on 03/07/2020 by the European Commission, based on a positive opinion of the European Medicines Agency), which was repurposed from the treatment of Ebola virus disease.\textsuperscript{12} Since then, two more agents with antiviral properties have been introduced, namely, the viral RNA polymerase inhibitor, molnupiravir, and the ritonavir-boosted protease inhibitor, nirmatrelvir.\textsuperscript{13,14} The benefits of these agents are largely limited to the early stage of SARS-CoV-2 infection, during viral replication, but they have also been reported to be effective in case studies of immunodeficient patients with prolonged viral shedding.\textsuperscript{15} Low-dose steroids (mainly dexamethasone), low-molecular-weight heparin, symptomatic drugs, and oxygen therapy remain the standard of care for patients with COVID-19.\textsuperscript{16} However, COVID-19-associated mortality is largely associated with the later phase of the disease, including cytokine storm syndrome\textsuperscript{17} and immune exhaustion.

Studies of the efficacy of remdesivir have been conducted since the beginning of the pandemic, with divergent results. In the seminal Adaptive COVID-19 Treatment Trial, remdesivir was shown to be superior to placebo at shortening the time to recovery in adults hospitalized with COVID-19 and with evidence of lower respiratory tract infection.\textsuperscript{18} However, in the recent DisCoVeRy study, no clinical benefit of remdesivir was demonstrated in patients admitted to the hospital for COVID-19 and who required oxygen support and had symptoms lasting > 7 days.\textsuperscript{19} In other studies, such as NCT04292899 and EUPAS34303, remdesivir has been shown to be associated with significantly greater recovery rates (74.4% of remdesivir-treated patients vs 59.0% of non-remdesivir-treated patients at day 14) and a 62% decrease in the odds of death compared with standard-of-care treatment in patients with severe COVID-19.\textsuperscript{20} A real-world meta-analysis published by the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium in 2021 that included 96,859 COVID-19 patients, showed that the patients who benefited most from the inclusion of remdesivir were those who did not use or were not currently using low-flow oxygen delivery systems. However, there was no evidence for an effect on mortality in any of the groups studied.\textsuperscript{21}

In this study, we aimed to analyze the use of remdesivir and assess its impact on mortality, progression to invasive oxygen therapy, and duration of in-hospital treatment in a large cohort of COVID-19 patients. In this real-life study, we assessed the effectiveness of remdesivir treatment from the perspective of routine clinical care. The key analysis assessed the efficacy of remdesivir treatment among COVID-19 patients with concomitant hemato-oncological diseases. This group commonly receives immunosuppressive or long-term steroid treatment, resulting in prolonged SARS CoV-2 replication and shedding.\textsuperscript{11}

**Materials and Methods**

**Study Population**

Longitudinal data were collected from 4287 COVID-19 patients followed up at the Department of Infectious Diseases, Pomeranian Medical University, Szczecin, Poland. The study protocol was approved by the Bioethical Committee of the Pomeranian Medical University (approval KB-0012/92/2020). Study complies with the Declaration of Helsinki. Informed consent for data analysis was obtained from all participants and the data were fully anonymized before statistical analyses. Patients participating in the study were observed from March 4, 2020 to January 23, 2022 when the database was closed. The first patient in our cohort was administered remdesivir in August 2020. The observation time was counted from the date of hospital admission to the date of discharge or death, and the total in-hospital treatment time was used in the analyses. All patients analyzed in this study had mild-to-moderate (requiring oxygen support only) or severe (requiring mechanical ventilation in the intensive care unit) COVID-19-related pneumonia and presented with clinical symptoms of cough, dyspnea, and/or fever (> 38 °C) and ≤ 94% oxygen saturation at admission. In every case,
a positive polymerase chain reaction test for SARS-CoV-2 was obtained from a pharyngeal swab, and pneumonia was confirmed using chest computed tomography (CT). The decision to introduce remdesivir was made by the physician based on the guidelines and recommendations of the Polish Association of Epidemiologists and Infectiologists. Within this dataset, we separately analyzed the treatment outcomes for patients with concomitant hematological or oncological diseases based on the codes listed in the 10th revision of the International Statistical Classification of Diseases and Related Health Problems.

Clinical data, including age; sex; comorbidities based on the presence of a malignancy; treatment history; the duration of in-hospital stay; the duration of treatment in the intensive care unit; survival statistics; baseline blood oxygenation levels; chest CT scan results; and selected laboratory parameters, such as full blood count and serum procalcitonin, C-reactive protein, interleukin-6, lactate dehydrogenase, D-dimer, asparagine, alanine aminotransferase, gamma-glutamyl transpeptidase, total bilirubin, troponin, creatine kinase myocardial band, and glucose levels, were collected from the medical records. Renal creatinine levels were used to calculate glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration formula.

Parameters included in the Cox analysis were chosen according to their influence on the disease process, as determined in previous studies. The included parameters were age; sex; percentage of lung inflammation; and laboratory values, such as those related to lung involvement (interleukin-6 and lactate dehydrogenase levels). Moreover, remdesivir treatment during the therapeutic process was the main prognostic factor.

As multiple studies have evaluated the effect of remdesivir on the course of infection and analyzed its effects at different endpoints, we decided to curate the data for the two most commonly used time points, namely 14 and 30 days. To identify factors influencing the risk of mechanical ventilation, the same variables that were included in the mortality analyses were used. The patients’ characteristics according to hemato-oncological diagnoses are shown in Table 1.

Statistics
Mann–Whitney U-tests were used to compare non-parametric variables, while chi-square tests were used to compare nominal data between the analyzed groups. For normalization, the effect of the analyzed parameters on COVID-19-related mortality was censored at two time points previously associated with mortality. Furthermore, for the overall hospitalization analysis, there were no observation endpoints implemented, and therefore, the Kaplan–Meier cumulative mortality rate was calculated using statistically significant survival data identified using the Log rank test. Unadjusted and multivariate Cox proportional hazards models were used to assess the effects of the analyzed parameters on the risk of death and to calculate hazard ratios (HRs). The best fit based on Akaike’s information criterion was selected. Statistical significance was set at \( p < 0.05 \).

Results
General Population of SARS-COV-2-Infected Individuals
Patient Characteristics by Remdesivir Use
The study group had more men than women (n = 2405; 56.1%) and had a median age of 67 years (interquartile range [IQR]: 55–75 years). Patients who received remdesivir were significantly younger, with a median age of 63 (IQR: 51–72) years, compared to those who did not receive remdesivir, who had a median age of 68 (IQR: 57–77) years (\( p < 0.001 \)). Differences in sex distribution were observed, with male patients being more commonly treated with remdesivir (\( p = 0.003 \)). In general, inflammatory parameters were less pronounced in the remdesivir group, but lung involvement was similar between patients receiving and not receiving remdesivir (Table 2). Mortality rates were 16.7% (718 patients) in the total study population, 14.7% (189 patients) in the remdesivir group, and 17.6% (529 patients) in the non-remdesivir group; \( p = 0.02 \).

Effect on Remdesivir Treatment on Mortality, Time to Mechanical Ventilation, and Duration of in-Hospital Treatment
At the 14-day observation time point, 93 (7.2%) patients who received remdesivir had died, compared to 347 (11.6%) who did not receive remdesivir (\( p < 0.001 \)). In addition, the mortality rate was notably lower at the 30-day observation
time point in the remdesivir group (n = 163; 12.7%). than the non-remdesivir group (n = 481, 16.0%; p = 0.005).
However, in multivariate Cox hazard analysis adjusted for age, sex, lung involvement and lactate dehydrogenase and interleukin-6 levels, it was found that the administration of remdesivir had no effect on the mortality of SARS-COV-2-infected individuals at 14 days, with an HR of 1.18 (95% CI: 0.93–1.49, p = 0.2), and 30 days, with an HR of 1.06 (95% CI: 0.88–1.28, p = 0.5). For patients who did not receive remdesivir, the factors influencing mortality for both time points were older age and higher interleukin-6 and lactate dehydrogenase levels. A higher percentage of lung involvement was important at the 30-day time point (Table 3).

Additionally, multivariate Cox models were used to analyze the risk of mechanical ventilation. The model adjusting for age, sex, percentage of lung involvement and interleukin-6 and lactate dehydrogenase levels indicated no difference in the risk of mechanical ventilation between SARS-COV-2-positive patients treated with or without remdesivir (HR: 0.88 [95% CI: 0.68–1.15], p = 0.36). Mechanical ventilation was required in 120 (9.3%) patients treated with remdesivir and 139 (4.6%) patients not treated with remdesivir. The only variable significantly associated with the risk of mechanical ventilation was a higher lactate dehydrogenase level (Table 4). Furthermore, there was no association between remdesivir treatment and the duration of in-hospital treatment (remdesivir group, median time: 11.7 [IQR: 8.5–16.8] days vs non-remdesivir group, median time: 12.0 [IQR: 8.1–16.8]; p = 0.61).

**Table 1** Patients’ Characteristics Based on Their ICD-10 Diagnosis

| Number of Patients | Disease Based on the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) |
|--------------------|------------------------------------------------------------------------------------------------------------------|
| 24 (10.8%)         | Leukemia (myeloid, lymphoid)                                                                                       |
| 8 (3.6%)           | Lymphomas (Hodgkin’s, non-Hodgkin’s, follicular, non-follicular, and mature T/natural killer cell lymphomas)        |
| 5 (2.2%)           | Multiple myeloma                                                                                                   |
| 8 (3.6%)           | Malignant neoplasm of the nervous system                                                                           |
| 14 (6.3%)          | Malignant neoplasm of the genitourinary system                                                                    |
| 8 (3.6%)           | Malignant neoplasm of the breast                                                                                   |
| 5 (2.2%)           | Malignant neoplasm of the skin, bones, or other connective or soft tissue                                         |
| 22 (9.9%)          | Malignant neoplasm of the respiratory tract                                                                         |
| 12 (5.4%)          | Malignant neoplasm of the parenchymal organs of the abdominal cavity (liver, pancreas, or other)                    |
| 19 (8.5%)          | Malignant neoplasm of the digestive tract                                                                          |
| 3 (1.3%)           | Sarcoïdosis                                                                                                        |
| 4 (1.8%)           | Myelodysplastic syndromes                                                                                           |
| 3 (1.3%)           | Immunodeficiency associated with different factors                                                                  |
| 1 (0.4%)           | Diseases of the spleen                                                                                              |
| 1 (0.4%)           | Agranulocytosis                                                                                                    |
| 19 (8.5%)          | Neoplasm of uncertain or unknown type                                                                               |
| 4 (1.8%)           | Two or more neoplasms                                                                                              |
| 61 (27.6%)         | Other hematological diseases                                                                                       |

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Hemato-Oncology Population of SARS-COV-2 Infected Individuals
Patient Characteristics

The characteristics of hemato-oncology patients were similar to those of the overall group, with a similar sex and age distribution (110 [55.0%] men; median age of 69 years [IQR: 61–75]). Patients who received remdesivir in this group were also significantly younger, with a median age of 65.5 (IQR: 58–74), than patients who did not receive remdesivir, who had a median age of 70 (IQR: 63–76 years ($p = 0.05$). Key differences in the laboratory parameters for the

### Table 2 Comparison of the Analyzed Cohorts in the General Database

| Parameter                           | Remdesivir Group, Median (IQR) | Number of Patients | Non-Remdesivir Group, Median (IQR) | Number of Patients | $p$ value |
|-------------------------------------|---------------------------------|--------------------|------------------------------------|--------------------|-----------|
| Age (years)                         | 63 (51–72)                      | 1270               | 68 (57–77)                         | 2959               | < 0.001   |
| Gender                              |                                 |                    |                                    |                    |           |
| Female (519; 40.4%)                 | 1284                            | 136 (4.9–27.7)     | 3002                               | 0.003              |
| Male (765; 59.6%)                   |                                 |                    |                                    |                    |           |
| Percentage of lung involvement      | 13.7 (5.7–25.8)                 | 1285               | 13.6 (4.9–27.7)                    | 3002               | 0.56      |
| WBC ($\times 10^3/\mu L$)           | 5.7 (4.4–7.5)                   | 1285               | 7.1 (5.3–9.5)                      | 2996               | < 0.001   |
| NEU ($\times 10^3/\mu L$)           | 4 (2.9–5.8)                     | 1284               | 5.2 (3.5–7.4)                      | 2995               | < 0.001   |
| LYM ($\times 10^3/\mu L$)           | 0.9 (0.7–1.3)                   | 1283               | 1.1 (0.7–1.5)                      | 2995               | < 0.001   |
| RBC ($\times 10^6/\mu L$)           | 4.7 (4.3–5.1)                   | 1285               | 4.6 (4.1–5)                        | 2996               | < 0.001   |
| HGB (g/dL)                          | 14.1 (12.9–15)                  | 1285               | 13.6 (12.2–14.8)                   | 2996               | < 0.001   |
| HCT (%)                             | 41 (37.8–43.6)                  | 1285               | 39.7 (36.1–42.9)                   | 2996               | < 0.001   |
| PLT ($\times 10^5/\mu L$)           | 185 (148–229)                   | 1285               | 220 (167.5–286)                    | 2996               | < 0.001   |
| PCT (ng/mL)                         | 0.1 (0.1–0.2)                   | 1269               | 0.1 (0.1–0.3)                      | 2907               | < 0.001   |
| CRP (mg/L)                          | 57.8 (24.9–113.8)               | 1285               | 64.8 (24.3–126.1)                  | 2999               | 0.07      |
| IL-6 (pg/mL)                        | 48.3 (23.2–90.9)                | 1283               | 43.6 (18.3–94.4)                   | 2964               | 0.02      |
| LDH (U/L)                           | 337 (258–454)                   | 1232               | 329 (246–456)                      | 2852               | 0.29      |
| D-dimer (µg/L)                      | 508 (292.5–961.8)               | 1284               | 714 (359–1758)                     | 2913               | < 0.001   |
| eGFR CKD-EPI (mL/min/1.73 m²)       | 78.3 (57.7–96.5)                | 1268               | 74 (48.8–94.8)                     | 2955               | < 0.001   |
| AST (U/L)                           | 40 (29–60)                      | 1236               | 38 (18–58)                         | 2885               | 0.002     |
| ALT (U/L)                           | 31 (22–48)                      | 1235               | 31 (20–49)                         | 2888               | 0.1       |
| Serum glucose (mg/dL)               | 116 (103–141)                   | 1215               | 118 (103–147)                      | 2804               | 0.04      |
| CK-MB (ng/mL)                       | 1.4 (0.9–2.5)                   | 1242               | 1.7 (1–3.1)                        | 2851               | < 0.001   |
| Troponin (ng/L)                     | 11.2 (6.4–20.2)                 | 1221               | 15.3 (8.3–32.6)                    | 2780               | < 0.001   |
| GGTP (U/L)                          | 45 (26–79)                      | 1200               | 45 (26–87)                         | 2703               | 0.59      |
| Total bilirubin (mg/dL)             | 0.4 (0.3–0.6)                   | 1190               | 0.5 (0.3–0.7)                      | 2667               | < 0.001   |

Abbreviations: WBC, white blood cells; NELI, neutrophils; LYM, lymphocytes; RBC, red blood cells; HGB, hemoglobin; HCT, hematocrit; PLT, platelets; PCT, procalcitonin; CRP, C-reactive protein; IL-6, interleukin-6; LDH, lactate dehydrogenase; eGFR CKD-EPI, glomerular filtration rate calculated using the Chronic Kidney Disease Epidemiology Collaboration formula; AST, asparagine aminotransferase; ALT, alanine aminotransferase; CK-MB, creatine kinase myocardial band; GGTP, gamma-glutamyl transpeptidase; IQR, interquartile range.
| Effect                        | 14-Day Time Point | 30-day time point |
|-------------------------------|-------------------|------------------|
| **Median (IQR) for Patients Who Died** | **Median (IQR) for Patients Who Survived** | **p value (Mann Whitney-U)** |
| Age                           | 78.0 (IQR: 69.0–86.0) | 65.0 (IQR: 54.0–73.0) | < 0.001 |
| Age                           | 80.0 (IQR: 68.0–84.0) | 65.0 (IQR: 53.0–73.0) | < 0.001 |
| Percent of lung involvement   | 33.7 (IQR: 16.4–51.5) | 12.4 (IQR: 4.7–24.7) | < 0.001 |
| Percent of lung involvement   | 32.7 (IQR: 15.9–51.5) | 11.7 (IQR: 4.5–23.4) | < 0.001 |
| Interleukin-6 level           | 107.5 (IQR: 49.7–213.0) pg/mL | 40.9 (IQR: 18.5–83.3) pg/mL | < 0.001 |
| Interleukin-6 level           | 102.0 (IQR: 48.7–187.0) pg/mL | 39.2 (IQR: 17.9–79.3) pg/mL | < 0.001 |
| Lactate dehydrogenase level   | 477.5 (IQR: 332–604) U/L | 322.0 (IQR: 244–433) U/L | < 0.001 |
| Lactate dehydrogenase level   | 464.0 (IQR: 327.0–599.0) U/L | 318.0 (IQR: 241.0–425.0) U/L | 0.005 |
| Gender                        | 1.23              | 0.89             | 1.49   |
| Gender                        | 1.24              | 0.89             | 1.49   |

**Abbreviations:** CI, confidence interval; IQR, interquartile range.
remdesivir group were lower neutrophil and platelet counts and D-dimer levels, but there were no notable differences in inflammatory parameters (Table 5). The mortality rates were 30.5% (61 patients) in the total group, 8.5% (17 patients) in the remdesivir group, and 22.0% (44 patients) in the non-remdesivir group ($p = 0.53$).

**Effect on Mortality, Risk of Mechanical Ventilation, and In-Hospital Treatment Duration**

For both observed time points, more patients died in the group without remdesivir usage. At the 14-day time point, 7 (11.3%) patients in the remdesivir group died compared to 23 (16.7%) in the non-remdesivir group ($p = 0.32$). At the 30-day time point, 15 (24.2%) patients in the remdesivir group died compared to 36 (26.1%) in the non-remdesivir group ($p = 0.78$).

In the multivariate Cox hazard analysis, administration of remdesivir was found to significantly reduce mortality in SARS-COV-2-infected patients during the 14-day observation period (HR: 4.03 [95% CI: 1.37–11.88]; $p = 0.01$; Figure 1). This effect was not observed at the 30-day time point (HR: 1.44 [95% CI: 0.75–2.75]; Table 6).

When the risk of mechanical ventilation was analyzed using multivariate models, two clinical factors remained significant. Younger patients (HR: 0.8 [95% CI: 0.7–1.0], $p = 0.006$) and women had a higher risk of mechanical ventilation (HR: 18.8 [95% CI: 2.1–165.2], $p = 0.008$). There were six women (6.7%) and 12 men (10.9%) who required mechanical ventilation. However, remdesivir treatment did not affect the time to mechanical ventilation (HR: 1.9 [95% CI: 0.5–6.7], $p = 0.28$). Other factors affecting the need for mechanical ventilation were a higher percentage of lung inflammation and higher interleukin-6 levels (Table 7).

**Discussion**

This study assessed the effect of remdesivir treatment on the severity of infection, mortality rate, and the risk of mechanical ventilation in COVID-19 patients. The analysis included a large group of more than 4,000 patients treated in a single center in Poland. This cohort was larger than the cohorts analyzed in other single-center studies and in many multicenter studies. It was almost 2.5 times larger than the largest Polish cohort, SARSTer and almost 3.5 times larger than the Canadian-wide CATCO cohort. The data analyzed in this study account for more than 4% of all analyzed data in the largest cohort assessed to date.

No overall positive effect of remdesivir treatment was demonstrated in this large cohort of hospitalized patients. However, in the group of patients with hemato-oncological comorbidity, a significant reduction in mortality was
demonstrated, with a four-fold lower risk of death than patients who did not receive remdesivir during the 14-day observation period. Patients who did not receive remdesivir were admitted to the hospital when the drug was not yet available, or were not eligible to receive it according to Polish recommendations (due to either contraindications or because they were already past the replication phase of infection). At the time of writing this manuscript, no other studies

| Parameter                          | Patients Who Received Remdesivir, Median (IQR) | Number of Patients | Patients Who did not Receive Remdesivir, Median (IQR) | Number of Patients | p value |
|------------------------------------|-----------------------------------------------|--------------------|--------------------------------------------------------|--------------------|---------|
| Age (years)                        | 65.5 (58–74)                                  | 62                 | 70 (63–76)                                             | 138                | 0.05    |
| Gender                             | Female (33; 53.2%)                             | 62                 | Female (57; 41.3%)                                     | 138                | 0.1     |
| Percentage of lung involvement     | 19.6 (5.3–26.1)                                | 62                 | 9.5 (2.1–29.3)                                         | 138                | 0.24    |
| WBC (×10³/µL)                      | 6.4 (3.3–10.9)                                 | 62                 | 7.9 (5.1–11.6)                                         | 137                | 0.054   |
| NEU (×10³/µL)                      | 4.6 (2–7.6)                                    | 62                 | 5.7 (3.5–8.1)                                          | 137                | 0.04    |
| LYM (×10³/µL)                      | 0.8 (0.5–1.5)                                  | 61                 | 0.9 (0.5–1.4)                                          | 137                | 0.85    |
| RBC (×10⁹/µL)                      | 4.2 (3.4–4.6)                                  | 62                 | 3.9 (3.1–4.5)                                          | 137                | 0.22    |
| HGB (g/dL)                         | 11.9 (9.7–13.8)                                | 62                 | 11.4 (9.1–13.1)                                        | 137                | 0.14    |
| HCT (%)                            | 35.3 (29.1–40.2)                               | 62                 | 33.9 (28.1–38.2)                                       | 137                | 0.22    |
| PLT (×10³/µL)                      | 161.5 (103–203)                                | 62                 | 212 (137–293)                                          | 137                | < 0.001 |
| PCT (ng/mL)                        | 0.1 (0.1–0.3)                                  | 62                 | 0.2 (0.1–0.5)                                          | 135                | 0.25    |
| CRP (mg/L)                         | 57.9 (17.5–144.1)                              | 62                 | 73.8 (22–147.8)                                        | 138                | 0.41    |
| IL-6 (pg/mL)                       | 45.2 (18.6–119)                                | 62                 | 46.3 (18.5–113)                                        | 136                | 0.77    |
| LDH (U/L)                          | 367 (276–515)                                  | 61                 | 315 (229–504)                                          | 131                | 0.14    |
| D-dimer (µg/l)                     | 792.5 (466–1632.1)                             | 62                 | 1308 (529.4–3512)                                     | 134                | 0.02    |
| eGFR CKD-EPI (mL/min/1.73 m²)      | 71.7 (50.2–95.2)                               | 62                 | 74.2 (45.3–93.2)                                       | 136                | 0.6     |
| AST (U/L)                          | 38 (27–62)                                     | 61                 | 31 (24–58)                                             | 131                | 0.23    |
| ALT (U/L)                          | 36 (24–56)                                     | 61                 | 27 (16–42)                                             | 131                | 0.02    |
| Serum glucose (mg/dL)              | 116 (104–145)                                  | 57                 | 114.5 (94–139)                                         | 126                | 0.63    |
| CK-MB (ng/mL)                      | 1.3 (0.8–1.9)                                  | 58                 | 2 (1.3–3.7)                                            | 123                | 0.001   |
| Troponin (ng/L)                    | 15 (7.9–25.3)                                  | 59                 | 23.5 (13.6–49.4)                                       | 121                | 0.001   |
| GGTP (U/L)                         | 66 (35–88)                                     | 59                 | 55 (27–145)                                            | 120                | 0.77    |
| Total bilirubin (mg/dL)            | 0.5 (0.3–0.7)                                  | 59                 | 0.4 (0.3–0.6)                                          | 126                | 0.6     |

Abbreviations: WBC, white blood cells; NEU, neutrophils; LYM, lymphocytes; RBC, red blood cells; HGB, hemoglobin; HCT, hematocrit; PLT, platelets; PCT, procalcitonin; CRP, C-reactive protein; IL-6, interleukin-6; LDH, lactate dehydrogenase; eGFR, CKD-EPI, glomerular filtration rate calculated using the Chronic Kidney Disease Epidemiology Collaboration formula; AST, asparagine aminotransferase; ALT, alanine aminotransferase; CK-MB, creatine kinase myocardial band; GGTP, gamma-glutamyl transpeptidase; IQR, interquartile range.
were found assessing the effect of remdesivir specifically in a group of hemato-oncological patients, which indicates the novelty of this real-life observational dataset.

Other groups of patients who showed a beneficial effect of remdesivir on survival were patients with atrial fibrillation.\textsuperscript{31} However, in some cases, for example in patients with sepsis, the implementation of remdesivir may not have a beneficial therapeutic effect.\textsuperscript{32}

In previous studies, the effect of remdesivir on patient survival has varied depending on the analyses performed. However, similar to our findings, the large CHARGE meta-analysis found no effect of remdesivir on mortality.\textsuperscript{21} However, in that analysis, hemato-oncological patients were not specifically analyzed. Most studies have shown no effect of remdesivir on the requirement for mechanical ventilation. We also found no effect of remdesivir treatment on the risk of progression to more severe stages of disease requiring mechanical ventilation.\textsuperscript{33} Consensus regarding the observation time for remdesivir-dependent survival is not easy to find, and many studies have analyzed multiple endpoints, including 10, 14, 15, 28, or 29 days.\textsuperscript{18,21,29} In this study, we chose 14 and 28 days as the time points for in-hospital observation.

The current study showed associations between an array of laboratory and clinical variables and the severity of the course of SARS-COV-2 infection, including links between the levels of C-reactive protein, interleukin 6, and lactate dehydrogenase levels and glomerular filtration and COVID-19-related mortality. These data are similar to those from previously published studies.\textsuperscript{25,26,34} The severity of lung tissue involvement was also associated with the severity of infection and increased mortality, which is consistent with the results of previous studies.\textsuperscript{34}
| 14-Day Time Point | Effect                  | \(p\) value (Cox Hazard) | Hazard Ratio | 95% CI, Lower | 95% CI, Upper | Median (IQR) for Patients Who Died | Median (IQR) For Patients Who Survived | \(p\) value (Mann Whitney-U) |
|------------------|------------------------|--------------------------|--------------|---------------|--------------|----------------------------------|---------------------------------------|-------------------------------|
| Age              | 0.03                   | 1.047                    | 1.004        | 1.094         | 73.5 (68.0–81.0) | 68.0 (59.5–75.0) | 0.009                          |
| Percentage of lung involvement | < 0.001 | 1.027 | 1.011 | 1.044 | 32.5 (IQR: 9.1–56.3) | 9.8 (IQR: 2.3–25.5) | 0.01                           |
| Interleukin-6 level | < 0.001 | 1.005 | 1.003 | 1.007 | 168.0 (IQR: 54.9–525.0) pg/mL | 37.2 (IQR: 17.9–92.4) pg/mL | < 0.001                       |
| Lactate dehydrogenase level | 0.01 | 1.0013 | 1.0003 | 1.0023 | 502.5 (IQR: 327.0–658.0) U/L | 311.0 (IQR: 239.0–478.0) U/L | < 0.001                       |
| Gender           | Male                   | 0.09                     | 0.46         | 0.19          | 1.13         |                                  |                                      |                               |
| Remdesivir       | No                     | 0.01                     | 4.03         | 1.37          | 11.88        |                                  |                                      |                               |

| 30-day time point | Effect                  | \(p\) value (Cox Hazard) | Hazard Ratio | 95% CI, Lower | 95% CI, Upper | Median (IQR) for Patients Who Died | Median (IQR) For Patients Who Survived | \(p\) value (Mann Whitney-U) |
|-------------------|------------------------|--------------------------|--------------|---------------|--------------|----------------------------------|---------------------------------------|-------------------------------|
| Age               | 0.1                    | 1.027                    | 0.995        | 1.06          | 70.0 (65.0–76.0) | 69.0 (60.0–75.0) | 0.2                           |
| Percent of lung involvement | < 0.001 | 1.027 | 1.015 | 1.039 | 35.6 (IQR: 9.1–56.4) | 9.1 (IQR:1.7–23.4) | < 0.001                       |
| Interleukin-6 level | < 0.001 | 1.0025 | 1.0012 | 1.0038 | 111.5 (IQR: 39.1–251.0) pg/mL | 34.6 (17.2–87.7) pg/mL | 0.002                         |
| Lactate dehydrogenase level | 0.2 | 1.0007 | 0.9997 | 1.0016 | 454.0 (323.0–641.0) U/L | 295.0 (233.0–443.0) U/L | < 0.001                       |
| Gender            | Male                   | 0.5                     | 0.81         | 0.42          | 1.54         |                                  |                                      |                               |
| Remdesivir        | No                     | 0.3                     | 1.44         | 0.75          | 2.75         |                                  |                                      |                               |

**Abbreviations:** CI, confidence interval; IQR, interquartile range.
In the analyzed cohort, only lactate dehydrogenase levels were significantly associated with the requirement for mechanical ventilation in COVID-19 patients, which is consistent with previous data on the effects of selected laboratory parameters on the severity of infection.\textsuperscript{25,26} The aforementioned reports regarding the effect of remdesivir treatment on mortality and mechanical ventilation are very ambiguous, while large meta-analyses have often indicated either a complete lack of an effect of remdesivir on the aforementioned parameters or shown discrepancies in the results.\textsuperscript{21,33}

A significant reduction in mortality was observed in hemato-oncology patients who received remdesivir. These patients, according to the guidelines of the Polish Society of Epidemiologists and Doctors of Infectious Diseases, received remdesivir for a maximum of 10 days, whereas the general population receive remdesivir initially for 5 days, and then for 3 days if pneumonia is not observed. It has been shown that patients with immunodeficiency may harbor actively replicating SARS-CoV-2 virions for a long time, in some cases up to approximately 3 months.\textsuperscript{35,36} These patients are particularly susceptible to severe courses of infection, including acute respiratory distress syndrome.\textsuperscript{15,37,38}

No data on mortality or mechanical ventilation risk in hemato-oncological patients were found from other cohorts. The effect of remdesivir on mortality in the general population is uncertain. While some studies have shown that it is effective at reducing mortality,\textsuperscript{39} most of the data do not support its effect.\textsuperscript{33,40} Moreover, there is a lack of data on the efficacy of remdesivir in hemato-oncology patients.

In addition to the aforementioned associations, a significant increase in both mortality and the risk of mechanical ventilation was demonstrated in women compared to men in the hemato-oncology patient group. These findings have not been confirmed in previous studies, which have shown an increased risk of severe infection in men, related to the influence of androgens on the severity of SARS-CoV-2 infection.\textsuperscript{41,42} Other analyzes have shown an adverse effect of female sex in younger COVID-19 patients,\textsuperscript{43} therefore, these sex-specific differences may be due to local group characteristics.

Remdesivir seems to be effective in selected groups of patients, especially those with immunodeficiency, who are prone to prolonged viral shedding and severe disease. Meta-analyses in most cases have not confirmed the effects of remdesivir on the course of infection. Some have reported faster recovery in patients treated with remdesivir, but most have shown no effect on mortality.

### Table 7

| Effect                          | $p$ value (Multivariant Cox Hazard) | Hazard Ratio | 95% CI, Lower | 95% CI, Upper | Median (IQR) for Patients Requiring Mechanical Ventilation | Median (IQR) for Patients Who Survived | $p$ value (U-Mann Whitney) |
|--------------------------------|-------------------------------------|--------------|---------------|---------------|----------------------------------------------------------|----------------------------------------|--------------------------|
| Age                            | 0.01                                | 0.84         | 0.74          | 0.95          | 63.0 (IQR: 57.0–69.0)                                     | 70.0 (IQR: 63.0–76.0)                  | 0.007                    |
| Percentage of lung involvement | 0.04                                | 1.03         | 1.0           | 1.07          | 48.0 (IQR: 21.5–59.7)                                     | 9.7 (IQR: 2.2–26.5)                   | < 0.001                  |
| Interleukin-6 level            | 0.01                                | 1.005        | 1.001         | 1.01          | 111.0 (IQR: 39.0–252.0) pg/mL                             | 42.6 (IQR: 18.6–99.6) pg/mL            | 0.02                     |
| Lactate dehydrogenase level    | 0.6                                 | 1.001        | 0.997         | 1.006         | 477.0 (IQR: 360.0–584.0) U/L                              | 310.0 (IQR: 235.0–497.0) U/L           | 0.001                    |
| Gender                         | Female                              | 0.01         | 18.8          | 2.14          | 165.2                                                    |                                        |                          |
| Remdesivir                     | Yes                                 | 0.3          | 0.53          | 0.15          | 1.84                                                     |                                        |                          |

**Abbreviations:** CI, confidence interval; IQR, interquartile range.
Conclusions
Remdesivir significantly reduced the mortality rate in immunodeficient patients and significantly improved their prognosis, it may also have a beneficial effect when analyzing the general population. Further analyses of hemato-oncology patients and other patients with immune deficiencies are required, as these patients often require several lines of antireplication and anti-inflammatory treatment. Immunodeficient patients often require a very individualized approach, and after the end of the COVID-19 pandemic, they may be the group that continues to be most affected by this disease.

Study Limitations
This study has several limitations that should be noted. First, the cohort analyzed in this study was 100% Caucasian. Therefore, the study findings may not be applicable to other ethnic groups. Second, not all factors were collected for evaluation at baseline, as the type of tests performed depended on the decision of the attending physician and this may have affected their availability for statistical analysis. Third, this was a retrospective study in which all patients admitted to the study center were assessed. The decision to initiate treatment with remdesivir and other therapies, including anti-inflammatory and maintenance treatments, was entirely up to the treating physician of the patient. Moreover, the Polish Society of Epidemiologists and Doctors of Infectious Diseases guidelines were followed, and these guidelines changed during the pandemic. However, the study cohort included more than 4000 patients, and therefore, any missing data should not have greatly affected the overall results of the statistical analyses. As in other retrospective studies, this analysis assessed remdesivir in the context of standard care and different comorbidities and patient burdens. Such a broad analysis should adequately show the observed real-life dependencies.

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Disclosure
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