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THE DRUG IS USE IN THE TREATMENT OF PNEUMONIA IN COVID 19: REMDESIVIR

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ABSTRACT

A prospective (compassionate) open-label study of remdesivir conducted from 23 February to 20 March 2020 at the Luigi Sacco Hospital in Milan, Italy, in patients aged 18 years and older with SARS-CoV-2 pneumonia. Patient enrolled. If you are on a ventilator, have an oxygen saturation in the air of 94% or less, or have a national early warning level 2 of 4 or more. The primary endpoint was change in clinical status based on a 7-point ordinal scale (1 = not hospitalized, resumed normal activities, 7 = death). From 23 February 2020 to 20 March 2020, of her 35 patients who were hospitalized, 18 were in the intensive care unit (ICU) and 17 were in the infectious disease ward (IDW). His 10-day treatment with remdesivir was completed by 22 patients (63%) and discontinued by 13 patients, of whom 8 (22.8%) of him discontinued treatment due to adverse events. Median follow-up was 39 days. On day 28, 14 (82.3%) patients were discharged from the IDW, 2 were still hospitalized, 1 (5.9%) died, and 6 (33.3%) were discharged from the ICU. 8 (44.4%) patients died and 3 (16.7%) died. %) were still on a ventilator, and one (5.6%) improved but was still hospitalized. Hypertransaminasemia and acute renal failure were the most frequently observed serious adverse events (42.8% and 22%).

KEYWORDS: Remdesivir, COVID-19, SARS-CoV-2, Hypertransaminasemia, Pneumonia.

1. INTRODUCTION

SARS-CoV-2 is spread from person to person by droplet transmission or direct contact, with a median incubation period of 5.1 days and a basic reproduction number of 2.24 to 3.58. The clinical spectrum of COVID-19 ranges from mild illness (i.e., pneumonia or absence of mild pneumonia) in approximately 80% of cases to acute respiratory disease syndrome (ARDS) requiring critical care. To life-threatening pneumonia. 6% required. The fatality rate (CFR)

varies, with reported estimates appearing to range from 1% to 7%, but this should be more accurate once research studies reveal the number of people infected.

Given the severity of pneumonia caused by SARS-CoV-2 and the expected high CFR, it is imperative to find an effective treatment, as supportive care and supplemental oxygen are not always sufficient. Remdesivir, a nucleoside prodrug believed to act by inhibiting viral RNA transcription, has shown in vitro antiviral activity against bat coronaviruses and SARS-CoV-2, and has demonstrated antiviral activity against SARS-CoV deployed in the United States. -2 It has been shown to be safe in patients with pneumonia.

This study was developed in connection with the emergency caused by the COVID-19 pandemic in Lombardy, Italy, which began on February 20, 2020. On February 21, pharmaceutical company Gilead Sciences will make compassionate use for individual patients severely affected by SARS-CoV-2 pneumonia and admitted to Luigi Sacco Hospital in Milan, Italy. Approved a request to donate remdesivir for A report containing clinical information and laboratory test results for all eligible patients requiring supplemental oxygen was submitted to Gilead for approval. Program enrollment March 2020 as it plans to initiate a randomized, controlled, double-blind clinical trial evaluating the efficacy and safety of remdesivir in hospitalized patients with mild to moderate respiratory illness due to COVID-19 Ended on the 20th. Pending the results of this study, we report the results of his 35 patients who received compassionate treatment with remdesivir during the first days of his SARS-CoV-2 epidemic in Italy.

2. Patients and Treatment schedule

If a male or non-pregnant patient has confirmed SARS-CoV-2 infection with a positive airway reverse transcriptase polymerase chain reaction (RT-PCR) test, a respiratory tract sample is obtained, and pneumonia is confirmed, the patient will be considered humane. Were eligible for treatment with remdesivir for therapeutic use. Patients who are mechanically ventilated, have room oxygen saturation (SaO2) <94%, or have a National Early Warning Score (NEWS)2 ≥4 on chest radiograph or computed tomography (CT) scan. Aspartate aminotransferase levels were >5x the upper limit of normal, and creatinine clearance was <30 mL/min.

Emergency approval for each eligible patient was obtained from the Ethics Committee and submitted to Gilead along with the patient's medical history. Written informed consent

was obtained from all patients except those undergoing invasive mechanical ventilation to which the principle of urgency was applied.

Patients were prospectively enrolled in the remdesivir treatment program between 23 February 2020 and 20 March 2020 (Figure. 1). The dosing regimen was a 200 mg i.v. loading dose on day 1 followed by 100 mg/day i.v. Patients were able to continue existing therapy, including hydroxychloroquine (HCQ), but had to discontinue lopinavir/ritonavir (LPV/r) recommended by Gilead.

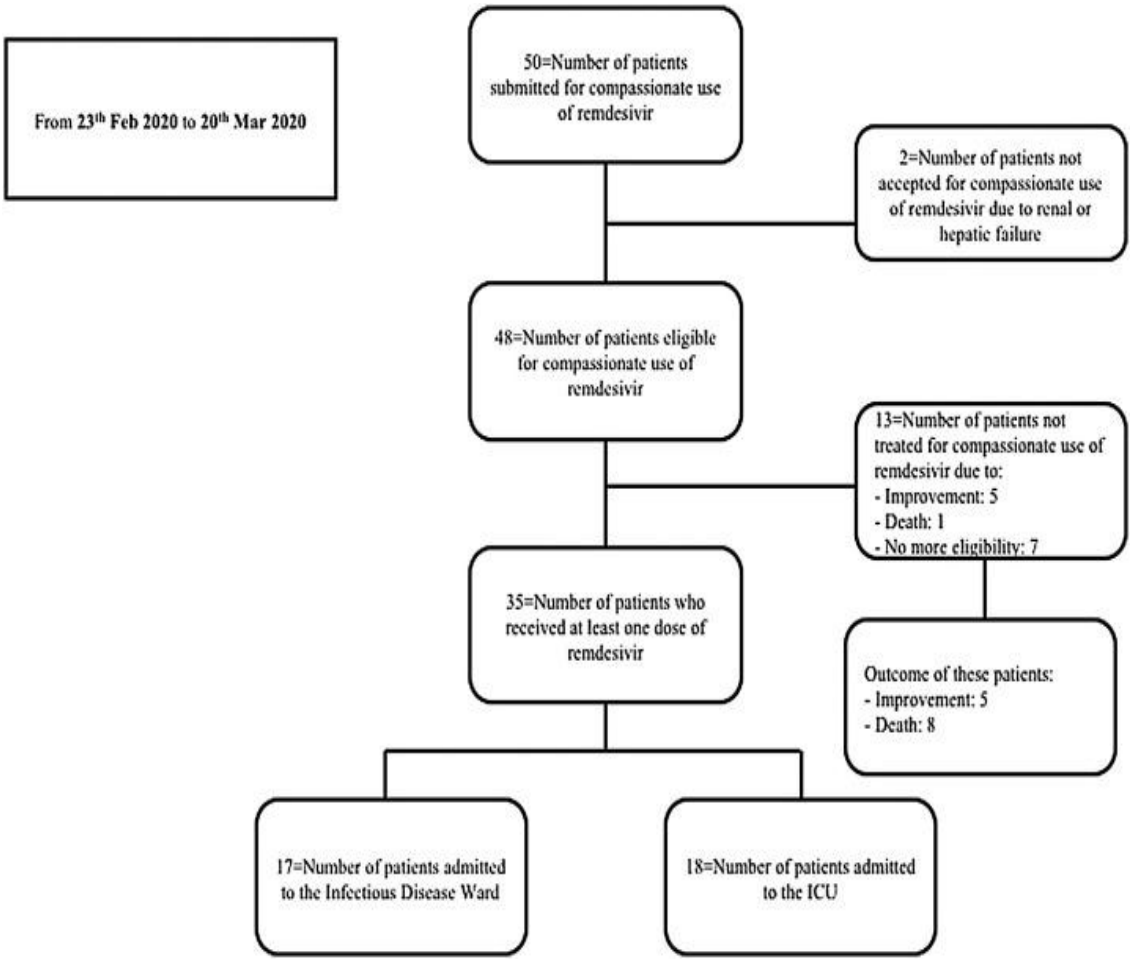

Figure 1: Remdesivir treatment program between 23 February 2020 and 20 March 2020.

The clinical and laboratory data of all of the patients who received at least one dose of remdesivir were collected on a daily basis from the date of enrolment to the date of discharge, death or censoring (20 April 2020) (Figure. 2).

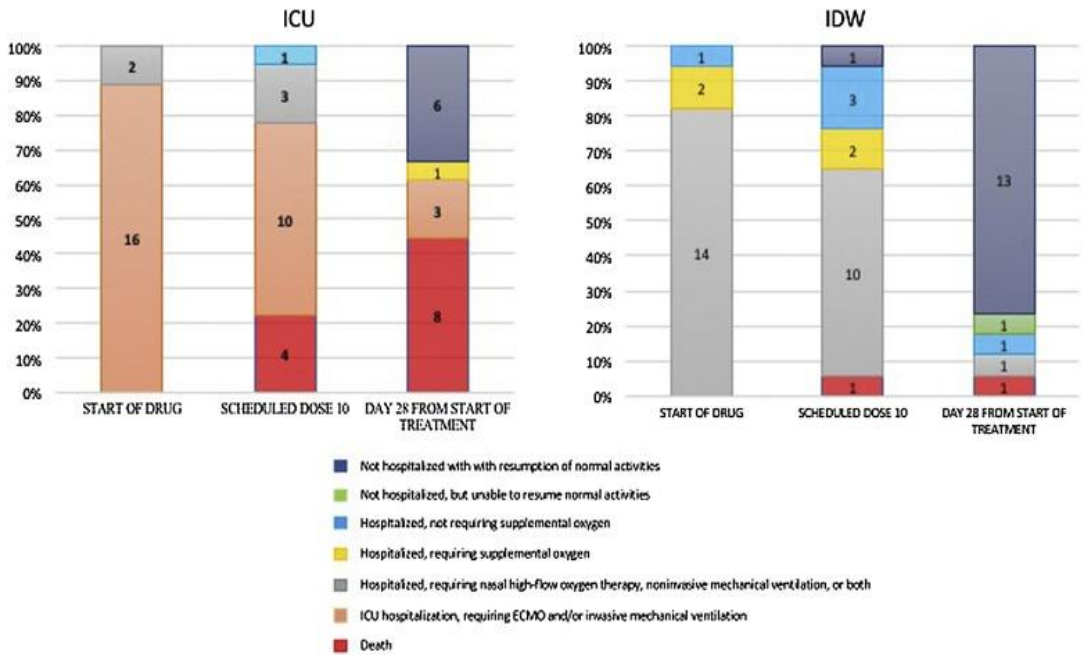

Figure 2: Clinical outcomes based on the 7-category ordinal scale endpoints.

In a subset of patients, semi-quantitative RT-PCR testing of nasopharyngeal swabs was performed at baseline and during remdesivir treatment using the ELITe InGenius® automated system and the GeneFinder™ COVID-19 Plus RealAmp Kit (ELITechGroup, France) it was done. Reaction mixtures were prepared manually according to the manufacturer's instructions, loaded onto the system along with other reagents, and RNA was extracted from 200 µl samples and eluted in 100 µl. The final reaction volume consisted of 5 µl RNA and 15 µl reagent mix. The RT-PCR profile was 50 °C for 20 min, 95 °C for 5 min and 45 cycles of 95 °C for 15 sec and 58 °C for 60 sec according to the manufacturer's instructions. Three target genes, RNA-dependent RNA polymerase (RdRP), nucleocapsid protein (N), and envelope membrane protein (E), were simultaneously amplified and tested. Viral load was measured as cycle threshold (Ct).

3. RESULTS

Between February 23 and March 20, 2020, 50 consecutive patients (fully representative of all hospitalized COVID-19 patients in Italy) were informed about the compassionate use of remdesivir. evaluated and 48 were considered for treatment. Thirteen patients did not start the drug for the reasons shown in Figure 1. The remaining 35 of her received at least one dose of her and were evaluated for outcomes of interest. Thirty-one of these patients had previously been on her LPV/r + HCQ for a median of 5 days, but all discontinued her LPV/r at study entry.

Eighteen patients were started on remdesivir in the ICU and 17 patients were started on remdesivir in the Infectious Diseases Unit (IDW).

Table 1 presents the main baseline characteristics of ICU and IDW patients who were predominantly male (77.8% and 70.6%) and had a mean age of 60.5 years (IQR 49.25-63.75) and 64 years, respectively). The median time from onset of symptoms to hospitalization was 7 days in both groups, and the median time from hospitalization to initiation of remdesivir treatment in his ICU was shorter than his IDW patients (4 days, IQR 3.0 -5.0 vs. 5). day to day)., IQR 4–6). The median Charlson comorbidity index was 2 in the ICU group and 2 in the IDW group, with hypertension being the most common comorbidity in both groups (27.8% and 41.2%).

Table 1: Baseline Demographic and Clinical characteristics of the patients.

Characteristic	Total (n = 35)	ICU patients (n = 18)	IDW patients (n = 17)
Age (years), median (IQR)	63.0 (51.0−69.0)	60.5 (49.2−63.7)	64.0 (51.0−75.0)
Males, n (%)	26 (74.3)	14 (77.8)	12 (70.6)
Time from onset of symptoms to hospitalisation (days), median (IQR)	7.0 (5.0−10.0)	7.0 (6.0−10.0)	7.0 (5.0−9.0)
Median time from hospitalisation to start of remdesivir (days), median (IQR)	4.0 (3.0−5.0)	4.0 (3.0−5.0)	5.0 (4.0−6.0)
Charlson Comorbidity Index, median (IQR)	2.0 (1.0−3.0)	2.0 (1.0−2.0)	2.0 (1.0−3.0)
Co-existing conditions, n (%)			
- Diabetes	3 (8.6)	3 (16.7)	–
- Hypertension	12 (34.3)	5 (27.8)	7 (41.2)
- Cancer	1 (2.9)	1 (5.6)	–
- Obesity	3 (8.6)	2 (11.1)	1 (5.9)
FiO_2, median (IQR)	0.6 (0.50−0.80)	0.7 (0.52−0.80)	0.6 (0.40−0.60)
PaO_2/FiO_2 ratio, median (IQR)	129.5 (110.2−161.0)	133.0 (115−171)	124 (106.7−139.5)
NEWS2, median (IQR)	5.5 (4.0−6.7)	6.0 (5.0−87)	4.0 (3.0−6.0)
Body temperature (°C), median (IQR)	37.0 (36.0−37.9)	37.0 (36.0−37.6)	37.0 (36.0−38.5)
WBC (10^9/L), median (IQR)	7.2 (5.9−9.1)	7.6 (6.5−9.5)	6.6 (5.8−7.7)
Lymphocytes (10^9/L), median (IQR)	0.67 (0.5−1.2)	0.62 (0.45−0.98)	0.89 (0.57−1.18)
Platelets (10^9/L), median (IQR)	249 (194.0−316.0)	252 (216.0−303.0)	249(191.0−313.0)
Prothrombin (INR), median (IQR)	1.40 (1.19−1.54)	1.40 (1.21−1.55)	1.38 (1.19−1.53)
D-dimer (μg/L), median (IQR)	4011	5632	1306

	(1406−14400)	(2509−12977)	(646−13992)
Alanine aminotransferase (U/L), median (IQR)	43 (20.0−57.5)	48.5 (18.7−62.7)	34.0 (20−50)
Lactate dehydrogenase (U/L), median (IQR)	492 (364−587)	559 (445−672)	399 (352−475)
C-reactive protein (mg/L), median (IQR)	106.0 (54.5−262)	177.0 (57−311)	106 (55−185)
Serum creatinine (mg/dL), median (IQR)	1.01 (0.68−1.24)	0.95 (0.64−1.48)	1.01 (0.82−1.16)

Intensive care unit, intensive care unit; IDW, infectious disease station; IQR, quartile. FiO2, fraction of inspired oxygen. PaO2, partial pressure of oxygen, NEWS2, national early warning score 2. WBC, white blood cells; 22 (63%) completed planned treatment with remdesivir, 13 (9 in ICU, 4 in IDW) had toxicity (n = 8, 22.8%), death (n=4). , 11.4%) and early discharge (n=1, 2.9%).

CONCLUSION

In conclusion, remdesivir treatment may have a beneficial effect on SARS CoV-2 pneumonia, especially in the case of non-critically ill patients. Our decision to administer it for compassionate use was triggered by a state of emergency, but randomised controlled trials are now needed to determine the safety and efficacy of remdesivir and any other investigational agent in the treatment of patients with SARS CoV-2 infection.

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