

**Comparative Outcome of Covid-19 Patients with and Without Remdesivir**

<sup>1</sup>Dr. Omar Farooq, Associate Professor, Department of Medicine, Government Medical College, Srinagar

<sup>2</sup>Dr. Hafsa Haroon, Department of Medicine, Government Medical College, Srinagar

**Corresponding Author:** Dr. Omar Farooq, Associate Professor, Department of Medicine, Government Medical College, Srinagar

**Citation this Article:** Dr. Omar Farooq, Dr. Hafsa Haroon, “Comparative Outcome of Covid-19 Patients with and Without Remdesivir”, IJMSIR- December - 2020, Vol – 5, Issue - 6, P. No. 59 – 65.

**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

**Abstract**

**Background:** Covid-19 is an infection caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).<sup>[1,2]</sup> Majority of those who get infected with this particular virus experience mild to moderate respiratory illness from which they usually recover without receiving any special treatment.

A number of drugs have been tried in patients with COVID-19 including anti-viral drugs but none have been found to be efficacious.

Currently there is no specific vaccine or treatment for COVID-19.

Some studies have shown that Remdesivir shortens the disease course and speeds up recovery; some even claim it prevents the progression to more severe disease and reduces mortality to some extent.<sup>[3,4,5,18,19]</sup>

**Method:** A prospective observational comparative study of COVID-19 patients was undertaken over a period of 3 months in the Department of Medicine, Government Medical College, Srinagar. After taking consent from the patients, their detailed history, examination and investigations were done.

**Results:** Out of a total of 60 patients included in the study, 30 received “Remdesivir” and 30 did not receive

it. Otherwise, both groups received the same basic treatment. In “Non-Remdesivir group”, 25 patients survived (i.e. 83.33%) while only 20 patients of “Remdesivir group” survived (i.e. 66.66%).

**Conclusion:** Remdesivir is an antiviral ATP analogue, which is used for the therapy of severe novel coronavirus disease 2019 (COVID-19). Remdesivir intravenous therapy is given to COVID-19 patients for 5 to 10 days. The most common side effect in COVID-19 patients receiving Remdesivir is nausea.<sup>[15]</sup> Other reported side effects include elevated transaminase levels in blood (liver enzymes), and infusion related reaction.

**Keywords:** COVID-19, SARS-CoV-2, CO-RADS, RT-PCR, REMDESIVIR.

**Introduction**

Remdesivir is a broad-spectrum antiviral drug, which was approved for emergency use in COVID-19 patients in around 50 countries during the 2020 pandemic.<sup>[6]</sup> Updated WHO guidelines in November 2020 include a conditional recommendation against its use for the treatment of COVID-19.<sup>[7]</sup>

Remdesivir is a prodrug (adenosine triphosphate (ATP) analog), which delivers GS-441524 monophosphate inside the cells. Subsequent biotransformation into GS-441524 triphosphate<sup>[8,9]</sup>, a ribonucleotide analog causes inhibition of viral RNA-dependent RNA polymerase. This results in termination of RNA transcription and decreases viral RNA production.<sup>[10,11]</sup>

Remdesivir has an FDA emergency use authorization for use in COVID-19 hospitalized adult and pediatric (aged  $\geq 12$  years and weighing  $\geq 40$  kg) patients with SpO<sub>2</sub> less or equal to 94%.<sup>[12,13]</sup> A loading dose of 200mg once daily in patients weighing  $\geq 40$  kg or 5mg/kg once daily in patients 3.5 kg to less than 40 kg, followed by a maintenance dose of 100mg once daily in patients weighing  $\geq 40$  kg or 2.5 mg/kg once daily in patients 3.5 kg to less than 40 kg.

The duration of treatment varies from 5 to 10 days.<sup>[14]</sup> It is infused over a period ranging from 30 minutes to 2 hours.<sup>[14]</sup>

Those patients who do not need invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO) should be treated for 5 days (loading dose on day 1 included) and up to 10 days if condition does not improve.<sup>[14]</sup> Patients who require invasive mechanical ventilation or ECMO should be treated for a period of 10 days.<sup>[14]</sup>

Clinical trials used a regimen with a loading dose of 200mg once daily on the first day, followed by maintenance dose of 100mg once daily for another 9 days.

Early data suggests that some patients may benefit from only 5 days of treatment.

Remdesivir injection may cause serious reactions during and after the infusion of the medication, which may include the following:

chills or shivering; nausea; vomiting; sweating; dizziness upon standing up; rash; wheezing or shortness of breath; abnormally fast or slow heartbeat; or swelling of the face, throat, tongue, lips, or eyes.<sup>[13]</sup>

The most common side effect reported from studies of Remdesivir for COVID-19 is nausea.<sup>[15]</sup> Others may include liver inflammation with raised transaminases in the blood; gastrointestinal distress: respiratory failure and organ impairment, including low albumin, low potassium, low count of red blood cells, low count of platelets and yellow discoloration of skin.<sup>[16,17]</sup>

Many studies have showed that antiviral therapy with remdesivir is beneficial to COVID-19 patients. Patients who received remdesivir were quicker to recover and the therapy prevented progression to more severe disease.<sup>[5]</sup> Those treated with remdesivir were less likely to need high levels of respiratory support. Some studies claim remdesivir therapy showed significant improved mortality rates.<sup>[18,19]</sup>

Studies are underway to evaluate remdesivir in combination with other therapies.

### **Materials and Methods**

A prospective observational comparative study of COVID-19 was conducted over a period of 3 months in the Department of Medicine, Government Medical College, Srinagar.

After obtaining written informed consent and ethical clearance from institutional ethics committee, patients who tested positive for COVID-19 were analyzed.

### **Inclusion Criteria**

All age groups with COVID-19 irrespective of sex and ethnicity were included in the study.

### **Exclusion Criteria**

Those who had other respiratory illnesses not caused by COVID-19 virus were excluded from the study.

For each positive case, a detailed history was obtained followed by thorough physical examination. Relevant investigations such as Chest X-ray and Computed Tomography were obtained in addition to complete blood counts, kidney function tests, liver function tests and serum electrolytes. In few patients who were critical, biomarkers like serum ferritin, CRP, IL-6, LDH and D-Dimer were also measured.

COVID-19 was diagnosed as a respiratory illness in a setting of appropriate clinical syndrome, positive real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay and/or radiological tests.

All 60 patients received the following treatment:

- Oxygen therapy
- Intravenous antibiotics (Ceftriaxone/Piperacillin-Tazobactam/Meropenem/Vancomycin)
- Intravenous steroids (Dexamethasone)
- Subcutaneous anticoagulants (Enoxaparin/Unfractionated Heparin)
- Oral antibiotics (Azithromycin and/or Doxycycline)
- Oral or intravenous antipyretic (Paracetamol)
- Oral multivitamin supplements (mainly Vitamin C and Zinc)
- Oral Ivermectin

Half of the total (i.e. 30 patients) were given remdesivir therapy in addition to the above treatment. Remdesivir was given for a period of 5 or 10 days depending on the severity of their illness and oxygen requirement. A loading dose of 200mg in 200ml normal saline was given intravenously once daily on the first day, followed by maintenance doses of 100mg in 100ml normal saline for the next 5 or 10 days. The infusion was given over a period of 1 to 2 hours.

The other 30 patients did not receive remdesivir because of the following reasons:

- Allergy to remdesivir
- Estimated glomerular filtration rate (eGFR) less than 30ml/min or requiring dialysis
- Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) greater than 5 times the upper limit of normal
- Pregnancy or breastfeeding
- Consent to start the therapy not given

### Results

A total of 60 patients who tested positive for COVID-19 were included in the study.

Most of the patients belonged to the age group of 40-60, which constituted 28 patients (46.66%).

Table 1: Age Distribution

| Age Group (Years) | Frequency | Percentage |
|-------------------|-----------|------------|
| 20-40             | 7         | 11.6       |
| 40-60             | 28        | 46.66      |
| >60               | 25        | 41.66      |

Out of 60 patients, 32 were males (53.33%) and 28 were females (46.66%).

Table 2: Sex Distribution

| Sex Category | Frequency | Percentage |
|--------------|-----------|------------|
| Male         | 32        | 53.33      |
| Female       | 28        | 46.66      |

Out of 60 patients, 30 received “Remdesivir” and 30 did not receive remdesivir. Other than remdesivir, both groups received the same basic treatment.

Table 3: Outcome of the Two Groups

In “Remdesivir group” which included a total of 30 patients, 20 patients survived (66.66%) and 10 died (33.33%).

While in “Non-Remdesivir group” which also included 30 patients, 25 patients survived (83.33%) and 5 died (16.66%).

|                                       | Survived    | Died       |
|---------------------------------------|-------------|------------|
| Remdesivir Group<br>(30 Patients)     | 20 (66.66%) | 10(33.33%) |
| Non-Remdesivir<br>Group (30 Patients) | 25(83.33%)  | 5 (16.66%) |

Table 4: Remdesivir Group

In patients who received remdesivir therapy, 50% got symptom relief and 53.33% showed marked improvement in their oxygen saturation during their hospital admission. 43.33% showed significant improvement in performing their basic day-to-day activities.

| Parameters (Improved) | Frequency | Percentage |
|-----------------------|-----------|------------|
| Symptom Relief        | 15        | 50         |
| O2 Saturation         | 16        | 53.33      |
| Daily Activities      | 13        | 43.33      |

Table 5: Non-Remdesivir Group

In patients who did not receive remdesivir therapy, 53.33% got symptom relief and 56.66% showed marked improvement in their oxygen saturation during the hospital admission. 63.33% showed significant improvement in performing their basic day-to-day activities.

| Parameters (Improved) | Frequency | Percentage |
|-----------------------|-----------|------------|
| Symptom Relief        | 16        | 53.33      |
| O2 Saturation         | 17        | 56.66      |
| Daily Activities      | 19        | 63.33      |

### Discussion

The current study was conducted to draw comparison between treatment of COVID-19 with and without “Remdesivir”.

Many studies previously conducted claim that the treatment with remdesivir decreases the recovery period significantly and also reduces the overall progression to

severe disease.<sup>[3,4,5]</sup> Few studies claim that remdesivir therapy also reduces the mortality rates.<sup>[18,19]</sup>

In our hospital based observational study, 60 patients were included irrespective of age, gender and ethnicity. It was found that 28 subjects belonged to the age group of 40-60 years, which constituted 46.66% of the total subjects. 25 others belonged to >60 age group and the rest 7 belonged to the age group 20-40 years. The mean age of presentation was 45.6 years.

Increasing age was seen to be associated with more severe illness as compared to the younger age group.

Among these 60 subjects, 32 belonged to male sex category (53.33%) and 28 belonged to female sex category (46.66%).

30 patients received remdesivir in addition to the other basic medication. In this group of patients, 20 patients survived accounting for 66.66% and only 10 died (i.e. 33.33%).

Among those who survived, 15 patients (i.e. 50%) got symptom relief during their hospital stay. Oxygen saturation markedly improved in 16 patients accounting for exactly 53.33%. 13 patients (43.33%) experienced marked improvement in their ability to perform daily activities sooner as compared to those not receiving remdesivir.

All the patients who survived in this group had faster recovery as compared to the non remdesivir group. The recovery period was cut short by about 5 to 10 days. Moreover, it was seen that remdesivir when started early in the disease course prevented the overall progression to severe disease in many patients.

The other 30 patients who received all the basic treatment but did not receive remdesivir had a survival of 83.33% (25 in number). Only 5 patients (i.e. 16.66%) in this group died. Among those who survived, 16 patients got symptom relief (53.33%). 17

patients (i.e. 56.66%) had significant improvement in their oxygen saturation during their hospital stay. Precisely 63.33% (19 patients) of those who survived in this group had marked improvement in performing basic day-to-day activities. The recovery period in this group was a bit longer as compared to those who received remdesivir therapy as a part of their treatment. But the mortality rate was less in the non remdesivir group as compared to its counterpart.

### Conclusion

COVID-19 infection usually resolves spontaneously without any special treatment in most patients except those who are immune-compromised or with underlying co-morbidities such as diabetes, cardiovascular disease, chronic lung disease, etc.

Remdesivir is an antiviral drug, which has been used for treating COVID-19 patients in many countries. Intravenous remdesivir therapy is given for 5 or 10 days depending on the patient's condition. As per our study, it has shown significant improvement in symptom relief, oxygen saturation and daily activities of those who survive after the therapy. Moreover, it roughly cuts down the recovery period by 5 to 10 days compared to those who do not receive it.

But as compared to those who do not receive remdesivir therapy, the mortality rate remains on the higher side. This study helped us to compare treatment options with or without remdesivir.

More studies need to be conducted to understand the benefits/or adverse effects of remdesivir therapy in COVID-19 patients.

### References

1. Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, et al. (March 2020). "The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it

SARS-CoV-2". *Nature Microbiology*. 5 (4): 536–544. doi:10.1038/s41564-020-0695-z. PMC 7095448. PMID 32123347.

2. ^ "Coronavirus disease named Covid-19". BBC News Online. 11 February 2020. Archived from the original on 15 February 2020. Retrieved 15 February 2020.
3. Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. Spinner CD, Gottlieb RL, Criner GJ, Arribas López JR, Cattelan AM, Soriano Viladomiu A, Ogbuagu O, Malhotra P, Mullane KM, Castagna A, Chai LYA, Roestenberg M, Tsang OTY, Bernasconi E, Le Turnier P, Chang SC, SenGupta D, Hyland RH, Osinusi AO, Cao H, Blair C, Wang H, Gaggar A, Brainard DM, McPhail MJ, Bhagani S, Ahn MY, Sanyal AJ, Huhn G, Marty FM; GS-US-540-5774 Investigators. *JAMA*. 2020 Sep 15;324(11):1048-1057. doi: 10.1001/jama.2020.16349. PMID: 32821939
4. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, Fu S, Gao L, Cheng Z, Lu Q, Hu Y, Luo G, Wang K, Lu Y, Li H, Wang S, Ruan S, Yang C, Mei C, Wang Y, Ding D, Wu F, Tang X, Ye X, Ye Y, Liu B, Yang J, Yin W, Wang A, Fan G, Zhou F, Liu Z, Gu X, Xu J, Shang L, Zhang Y, Cao L, Guo T, Wan Y, Qin H, Jiang Y, Jaki T, Hayden FG, Horby PW, Cao B, Wang C. *Lancet*. 2020 May 16;395(10236):1569-1578. doi: 10.1016/S0140-6736(20)31022-9. Epub 2020 Apr 29. PMID: 32423584
5. **Remdesivir** for the Treatment of Covid-19 - Final Report. Beigel JH, Tomashek KM, Dodd LE,

- Mehta AK, Zingman BS, Kalil AC, Hohmann E, Chu HY, Luetkemeyer A, Kline S, Lopez de Castilla D, Finberg RW, Dierberg K, Tapson V, Hsieh L, Patterson TF, Paredes R, Sweeney DA, Short WR, Touloumi G, Lye DC, Ohmagari N, Oh MD, Ruiz-Palacios GM, Benfield T, Fätkenheuer G, Kortepeter MG, Atmar RL, Creech CB, Lundgren J, Babiker AG, Pett S, Neaton JD, Burgess TH, Bonnett T, Green M, Makowski M, Osinusi A, Nayak S, Lane HC; ACTT-1 Study Group Members. *N Engl J Med.* 2020 Nov 5;383(19):1813-1826. doi: 10.1056/NEJMoa2007764. Epub 2020 Oct 8. PMID: 32445440
6. "U.S. Food and Drug Administration Approves Gilead's Antiviral Veklury (remdesivir) for Treatment of COVID-19". Gilead Sciences, Inc. 22 October 2020. Retrieved 23 October 2020.
7. World Health Organization (2020). Therapeutics and COVID-19: living guideline, 20 November 2020. World Health Organization (WHO) (Report). hdl:10665/336729. WHO/2019-nCov/remdesivir/2020.1.
8. Sheahan TP, Sims AC, Graham RL, Menachery VD, Galinski LE, Case JB, et al. (June 2017). "Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses". *Science Translational Medicine.* **9** (396):eaal3653. doi:10.1126/scitranslmed.aal3653. PMC 5567817. PMID 28659436.
9. Gordon CJ, Tchesnokov EP, Woolner E, Perry JK, Feng JY, Porter DP, Götte M (May 2020). "Remdesivir is a direct-acting antiviral that inhibits RNA-dependent RNA polymerase from severe acute respiratory syndrome coronavirus 2 with high potency". *The Journal of Biological Chemistry.* **295**(20): 6785–6797. doi:10.1074/jbc.RA120.013679. PMC 7242698. PMID 32284326
10. Cho A, Saunders OL, Butler T, Zhang L, Xu J, Vela JE, et al. (April 2012). "Synthesis and antiviral activity of a series of 1'-substituted 4-aza-7,9-dideazaadenosine C-nucleosides". *Bioorganic & Medicinal Chemistry Letters.* **22** (8): 2705–7. doi:10.1016/j.bmcl.2012.02.105. PMC 7126871. PMID 22446091.
11. Ferner RE, Aronson JK (April 2020). "Remdesivir in covid-19". *BMJ.* **369**: m1610. doi:10.1136/bmj.m1610. PMID 32321732.
12. "Coronavirus (COVID-19) Update: FDA Issues Emergency Use Authorization for Potential COVID-19 Treatment" (Press release). U.S. Food and Drug Administration (FDA). 1 May 2020. Retrieved 1 May 2020.
13. "Frequently Asked Questions on the Emergency Use Authorization for Remdesivir for Certain Hospitalized COVID-19 Patients" (PDF). U.S. Food and Drug Administration (FDA). 1 May 2020. Retrieved 1 May 2020.
14. "Remdesivir". *Drugs.com.* 20 April 2020. Retrieved 30 April 2020.
15. "Veklury EPAR". *European Medicines Agency(EMA).* 23 June 2020. Retrieved 6 July 2020.
16. Mehta N, Mazer-Amirshahi M, Alkindi N, Pourmand A (July 2020). "Pharmacotherapy in COVID-19; A narrative review for emergency providers". *The American Journal of Emergency Medicine.* **38** (7):14881493. doi:10.1016/j.ajem.2020.04.035. eISSN 07356757. PMC 7158837. PMID 32336586.

17. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, et al. (May 2020). "Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial". *Lancet*. **395** (10236): 1569–1578. doi:10.1016/S0140-6736(20)31022-9. PMC 7190303. PMID 32423584.
18. Remdesivir: A potential game-changer or just a myth? A systematic review and meta-analysis. Shrestha DB, Budhathoki P, Syed NI, Rawal E, Raut S, Khadka S. *Life Sci*. 2020 Oct 26:118663.

doi: 10.1016/j.lfs.2020.118663. Online ahead of print. PMID: 33121991

**Remdesivir** for Adults With COVID-19 : A Living Systematic Review for an American College of Physicians Practice Points. Wilt TJ, Kaka AS, MacDonald R, Greer N, Obley A, Duan-Porter W. *Ann Intern Med*. 2020 Oct 5:M20-5752. doi: 10.7326/M20-5752. Online ahead of print. PMID: 33017170