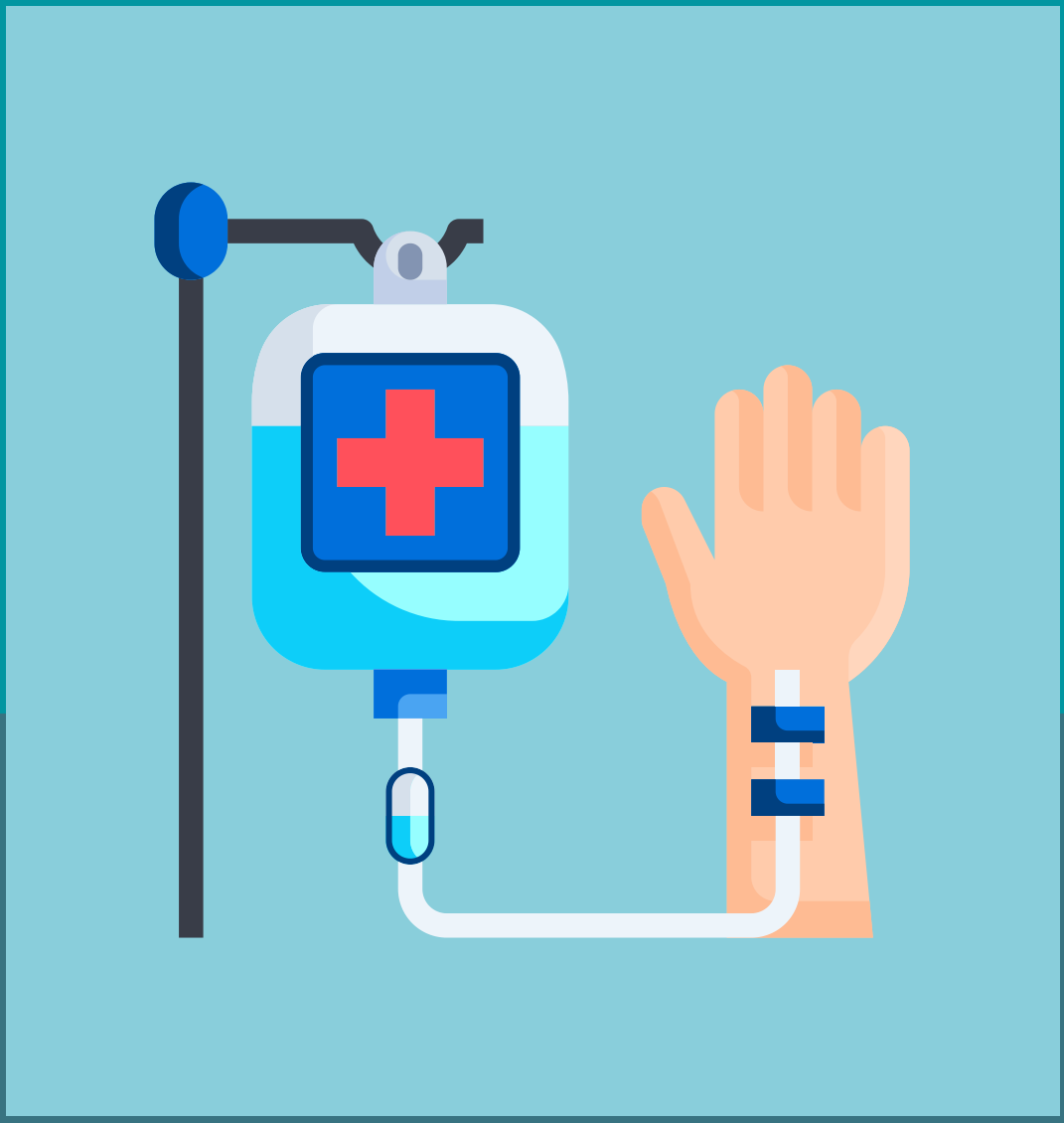
UNDERSTANDING REMDESIVIR



What You and Your Healthcare Provider Should Know

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The History of Remdesivir

Remdesivir (Rem-des-siv-ir) or Veklury is an antiviral drug originally intended for treating Hepatitis C. During the pandemic, this drug was approved for emergency use to treat COVID-19 patients. However, data is showing more and more signals of organ damage.

THE FACTS

- Remdesivir was originally intended to treat Hepatitis C.
- It was used for treatment during the Ebola epidemic because of successful preclinical trial data.
- However, studies conducted between 2014-2016 and 2018-2019 showed it was less effective and had significant safety signals, such as cardiac complications and death.
- The table below compares the data between deaths from Remdesivir and the monoclonal antibody that was studied in this trial.

Table 2. Comparison of Death at 28 Days According to Treatment Group.

Population	ZMapp	Remdesivir	Difference, Remdesivir vs. ZMapp	MAb114	Difference, MAb114 vs. ZMapp	REGN-EB3	ZMapp Subgroup	Difference, REGN-EB3 vs. ZMapp Subgroup
	no. of deaths/ total no. (%)	*no. of deaths/ total no. (%)*	*percentage points (95% CI)*	*no. of deaths/ total no. (%)*	*percentage points (95% CI)*	*no. of deaths/ total no. (%)*	*no. of deaths/ total no. (%)*	*percentage points (95% CI)*
Overall	84/169 (49.7)	93/175 (53.1)	3.4 (−7.2 to 14.0)	61/174 (35.1)	−14.6 (−25.2 to −1.7)*	52/155 (33.5)	79/154 (51.3)	−17.8 (−28.9 to −2.9)*
Patients with high viral load†	60/71 (84.5)	64/75 (85.3)	0.8 (−15.3 to 17.2)	51/73 (69.9)	−14.6 (−33.0 to −0.5)	42/66 (63.6)	56/65 (86.2)	−22.5 (−41.8 to −5.1)
Patients with low viral load†	24/98 (24.5)	29/100 (29.0)	4.5 (−9.1 to 19.1)	10/101 (9.9)	−14.6 (−32.4 to −2.6)	10/89 (11.2)	23/89 (25.8)	−14.6 (−32.6 to −2.3)

* The result is significant according to the interim stopping boundary of P<0.035 for the MAb114 group and P<0.028 for the REGN-EB3 group.
† Patients with a high viral load had an EBOV nucleoprotein Ct value of 22.0 or less. Patients with a low viral load had an EBOV nucleoprotein Ct value of more than 22.0. The total number is the total number of patients in this category for each group.

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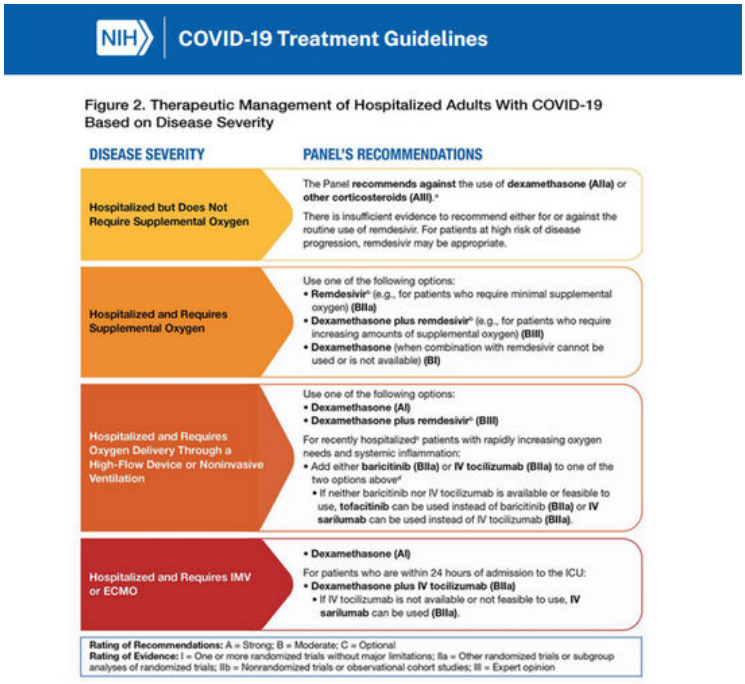
THE FACTS

- Before the COVID-19 pandemic, the safety data was not well known, but the decision was made to use this drug for treatment for COVID-19 under an Emergency Use Authorization.
- In November 2020, the WHO recommended against the use of Remdesivir for the treatment of COVID-19, based on the lack of positive evidence to support the treatment.
- The NIH has it listed on its COVID-19 Treatment Guidelines.



NIH | COVID-19 Treatment Guidelines

Figure 2. Therapeutic Management of Hospitalized Adults With COVID-19 Based on Disease Severity

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or **other corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use one of the following options: • **Remdesivir**[c] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone plus remdesivir**[b] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)** • **Dexamethasone** (when combination with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone (AI)** • **Dexamethasone plus remdesivir**[b] **(BIII)** For recently hospitalized[d] patients with rapidly increasing oxygen needs and systemic inflammation: • Add either **baricitinib (BIIa)** or **IV tocilizumab (BIIa)** to one of the two options above[e] • If neither baricitinib nor IV tocilizumab is available or feasible to use, **tofacitinib** can be used instead of baricitinib **(BIIa)** or **IV sarilumab** can be used instead of IV tocilizumab **(BIIa)**.
Hospitalized and Requires IMV or ECMO	• **Dexamethasone (AI)** For patients who are within 24 hours of admission to the ICU: • **Dexamethasone plus IV tocilizumab (BIIa)** • If IV tocilizumab is not available or not feasible to use, **IV sarilumab** can be used **(BIIa)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

THE FACTS

- In April 2022, Remdesivir was approved for use in children for the treatment of COVID-19 based on a Gilead-funded study. Gilead is the pharmaceutical company that makes Remdesivir.
- In August 2023, the FDA approved the use of Remdesivir for the treatment of COVID-19 in patients who have liver disease.
- This fact sheet discusses the side effects and contraindications for Remdesivir.

VigiAccess™ Uppsala Monitoring Centre | WHO Collaborating Centre for International Drug Monitoring

Medicine	Year started reporting	Deaths	Adverse events
Ivermectin	1992	18	4 669
Remdesivir	2020	582	8 057
Tocilizumab	2005	786	47 345
COVID-19 vaccines	2021	**13 361**	**2 620 423**
Tetanus vaccine	1968	32	14 697
Measles vaccine	1992	35	3 696
Acetaminophen (Tylenol)	1968	3 865	> 146 000

World Health Organization | FDA | MERCK

Who Supports the Use of Remdesivir?

The research supporting Remdesivir is funded by drug companies such as Gilead and Pfizer and institutions such as the Bill and Melinda Gates Foundation, who incentivize hospitals and research journals to promote and use their products. Keep this in mind when looking at research or when visiting healthcare systems who use this drug for treatment.

THE PLAYERS

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Final Report

John H. Beigel, M.D., Kay M. Tomashek, M.D., M.P.H., Lori E. Dodd, Ph.D., Aneesh K. Mehta, M.D., Barry S. Zingman, M.D., Andre C. Kalil, M.D., M.P.H., Elizabeth Hohmann, M.D., Helen Y. Chu, M.D., M.P.H., Annie Luetkemeyer, M.D., Susan Kline, M.D., M.P.H., Diego Lopez de Castilla, M.D., M.P.H., Robert W. Finberg, M.D., et al., for the ACTT-1 Study Group Members*

Research Journals: See, for example, the disclosure section of this study

Acknowledgments

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Hospital Involvement: Receive money from the pharmaceutical industry

Hospitals' Incentive Payments for COVID-19

AAPS Association of American Physicians and Surgeons

The hospital payments include:

- A "free" required PCR test in the Emergency Room or upon admission for every patient, with government-paid fee to hospital.
- Added bonus payment for each positive COVID-19 diagnosis.
- Another bonus for a COVID-19 admission to the hospital.
- A 20 percent "boost" bonus payment from Medicare on the entire hospital bill for use of remdesivir instead of medicines such as ivermectin.
- Another and larger bonus payment to the hospital if a COVID-19 patient is mechanically ventilated.
- More money to the hospital if cause of death is listed as COVID-19, even if patient did not die directly of COVID-19.
- A COVID-19 diagnosis also provides extra payments to coroners.

Politics and Economic Greed Define Science

August 21, 2020

Print This Post

Editors of The Lancet and the New England Journal of Medicine: Pharmaceutical Companies are so Financially Powerful They Pressure us to Accept Papers

As uncovered by Science Defies Politics: 16 of the panel members selected by NIH to formulate the official COVID-19 Treatment Guidelines – including two of the three co-chairs – were paid by Gilead.

At least 7 (seven) members of the Panel on COVID-19 Treatment Guidelines, including 2 out of 3 Co-Chairs, have not disclosed their financial ties to Gilead Sciences (GILD), the patent owner and manufacturer of *remdesivir*.

February 1, 2022
1:46 PM EST
Last Updated 6 days ago

Healthcare & Pharmaceuticals

REUTERS

Gilead COVID drug takes top spot for U.S. hospital spending - report

By Deena Beasley

Gilead, which will report quarterly results on Tuesday, posted $4.2 billion in global Veklury sales in the first nine months of 2021.

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The Research

Below is a summary of research on Remdesivir (RDV). It was associated with:

- **A higher risk of mortality**
- **A higher chance that the patient would become more ill**
- **Longer hospital stays**
- **Risk of acute kidney injury or failure (AKI/AKF) rose by 4–20 times.**

HIGHER RISK OF SICKNESS AND DEATH

Research with significant results:

The risk of death was 460% higher

- A study by Kurniyanto et al., funded by Universitas Kristen Indonesia, involved retrospective data on 477 hospitalized patients in Indonesia. In the RDV group, RR 5.60, p 0.001, treatment 7 of 45 (15.6 %), and control 12 of 432 (2.8%). Seven out of 45 participants in the RDV group died, whereas only 12 out of 432 in the control group died.

Remdesivir causes increased mortality while hydroxychloroquine causes lower mortali c

- According to the study by Bowen et al., in 4,631 hospitalized patients in New York, **RDV use increased the risk of mortality by 57% at day 30.**
- The NIH's National Institute of Allergy and Infectious Diseases funded this research.

Greater mortality in all age groups

- The study by Mitsushima et al., which was an independent investigation and retrospective analysis of 18,566 hospitalized patients in Japan, revealed **greater mortality in all age groups of 44% (P=0.01) with RDV treatment.**

A 58.9% higher risk of disease progression

- A prospective investigation by Punzalan et al., of 400 hospitalized patients in the Philippines showed disease progression, RR 1.59, p = 0.001, with Remdesivir treatment accounting for 93 of 224 (41.5%) and control for 46 of 176 cases (26.1 %) and **greater mortality rate of 42%** (treatment: 47 of 224; 21.0%; control: 26 of 176; 14.8%); without statistical significance (p=0.12).

The Research

HIGHER RISK OF SICKNESS AND DEATH

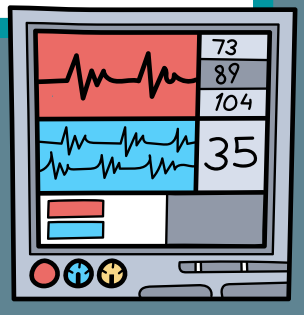
Ironically, even some pharmaceutical company-sponsored research produced negative results with RDV use:

The risk of progression was 509% higher

- A study by Schmidt et al., which was a retrospective analysis of 1,106 prostate cancer patients, revealed that the **risk of progression was 509% higher with RDV treatment**, OR 6.09, p 0.001, treatment 43, control 434, adjusted per study.
- Some authors received fees from Bristol Myers, Bayer, Janssen, Pfizer, Astellas, and Merck.)

Death risk was 6% higher

- The study by Ohl et al., (funded by Gilead and the VA) **found a link between routine Remdesivir use and higher 30-day mortality and hospital stay**: **Death risk was 6% higher**, HR 1.06, p = 0.66, adjusted per study at day 30 of treatment.
- **Hospitalization time was 100% longer.**



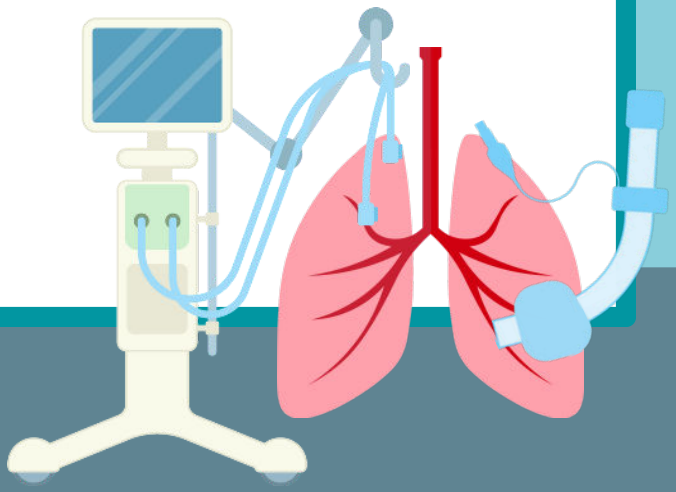
The Research

HIGHER RISK OF SICKNESS AND DEATH

Death risk was 100% higher; Mechanical ventilation risk was 250% greater

Death risk was higher and ventilation risk was greater

- Another research project by Ullah et al., funded by Roche, Gilead, and Abbvie. The results did not support the use of RDV even though the results were not statistically significant. **Death risk was 100% higher (double)**, treatment 8 of 30 (26.7%) and control 4 of 30, RR 2.00, p = 0.33. (13.3%). **Mechanical ventilation risk was 250% greater**, RR 3.50, p = 0.15, treatment rate was 23.3%, control rate was 23% for each of the 30 subjects (6.7%).
- In the study by Oku et al., several of the authors received funding from Eli Lilly and Chugai Pharma, yet the findings were against the usage of RDV. **The risk of death was 40% greater**, RR 1.40, p = 0.59, treatment 3 of 46 (6.5%), control 8 of 174 (4.5%), unadjusted, odds ratio converted to relative risk.

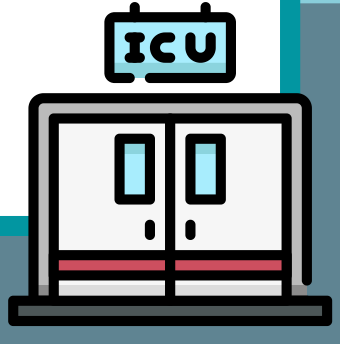


The Research

Here is a summary of studies that have produced interesting results but are not statistically significant. These studies illustrate important findings of how Remdesivir can cause reactions within the body.

HIGHER RISK OF SICKNESS AND DEATH

- An independent investigation by Kim et al., that looked back at 167 nosocomial COVID-19 patients in South Korea. The study showed 14 deaths were in the RDV group. **The risk of death is 1,612.4% higher**, RR 17.12, p = 0.22, treatment 14 of 145 (9.7%), control 0 of 22 (0.0%).
- The study by Mulhem et al., was an independent investigation. **The risk of death was 76.5% higher in RDV group**, RR 1.76, p = 0.47, treatment 5 of 34 (14.7%), and control 3 of 36 (8.3%), and the risk of mechanical ventilation was 111.8% higher in the RDV group, RR 2.12, p = 0.42, treatment 4 of 34 (11.8%), and control 2 of 36, respectively (5.6%).
- Study by Mahajan et al., which was not sponsored by a pharmaceutical company, **showed a 58.9% greater disease progression.**



The Research

Here is a summary of studies that have produced interesting results but are not statistically significant. These studies illustrate important findings of how Remdesivir can cause reactions within the body.

HIGHER RISK OF SICKNESS AND DEATH

- The Barrt-Due et al., study was funded by the National Clinical Therapy Research in the Specialist Health Services in Norway. According to the study, **the risk of mortality was 35.7% greater** with RDV treatment (RR 1.36, p = 0.70, treatment 3 of 42, 7.1%; control 3 of 57, 5.3%), day 60). **The risk of death was 24% higher in the RDV group**, OR 1.24, p = 0.87, treatment 32, control 7,126, adjusted per study, multivariable, day 30, and RR approximated with OR.
- The Research Committee from the Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran, showed **the risk of death was 24% higher in the RDV group**, OR 1.24, p = 0.87, treatment 32, control 7,126, adjusted per study,
- Malundo et al., conducted a separate investigation and found that the risk of death was **16.5% higher in the RDV group**, with RR 1.17, p = 0.45, treatment 24 of 115 (20.9%) and control 197 of 1,100 (17.9%).
- According to a study by Burhan et al., without external funding, **the risk of death is 14.8% greater with RDV treatment**, RR 1.15, p = 0.23, treatment 33 of 43 (76.7%), and control 345 of 516 (66.9%).

The Research

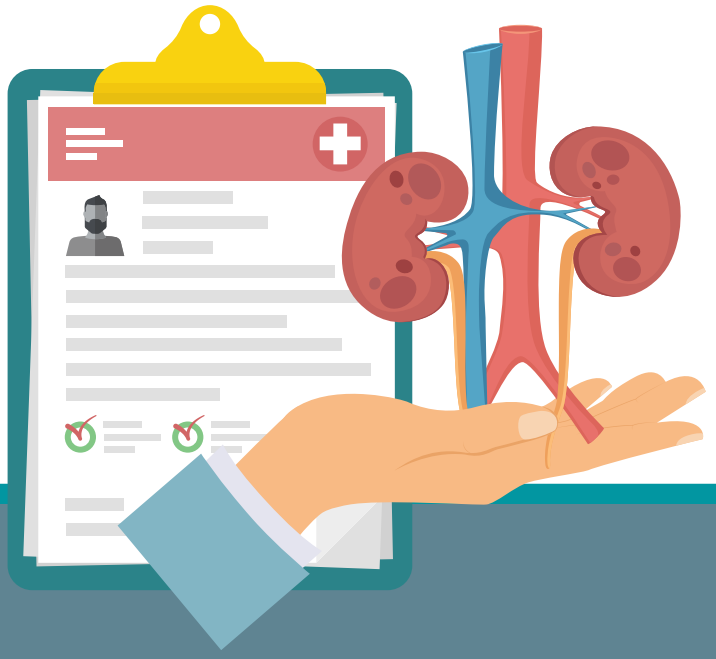
HIGHER RISK OF SICKNESS AND DEATH

- Retrospective research by Aweimer et al., revealed 149 patients in Germany receiving invasive mechanical ventilation (without outside funding) had a probability of death was **13% higher in the RDV group**, RR 1.13, p = 0.33, treatment 40 of 51 (78.4%), control 68 of 98 (69.4%), and day 100.
- An independent retrospective study by Nadeem et al., observed in 132 hospitalized COVID-19 patients in the USA **had a greater mortality of 11%** (p=1) with Remdesivir.
- An independent study by Elhadi et al., found that the probability of death was **10.9% greater in the RDV group**, RR 1.11, p = 0.65, treatment 14 of 21 (66.7%), control 267 of 444 (60.1%), at day 60.
- A small independent RCT by Wang et al., looked at 237 hospitalized patients in China with severe COVID-19. The risk of disease progression was **47.6% greater in the RDV group**, RR 1.48, p=0.76.

The Research

HIGHER RISK OF SICKNESS AND DEATH

- Retrospective database analysis by Tsuzuki et al., funded by the Health and Labor Sciences Research Grant, of 12,487 hospitalized patients in Japan revealed a **4% greater risk of death in RDV group**, HR 1.04, p = 0.21, treatment 69 of 824 (8.4%), control 285 of 11,663 (2.4%), adjusted per study, day 30.
- In an independent investigation, Hagman et al., discovered that the risk of progression was **40% greater with RDV.**



The Research

Studies below show the risk of acute kidney injury/failure (AKI/AKF) with Remdesivir was increased by a factor of 4–20.

HIGHER RISK OF KIDNEY INJURY AND FAILURE

- **Risk of ARF increased by up to 20-fold**
- The study by Gérard et al., confirmed the link between AKI and the use of popular COVID-19 inhibitors, particularly Remdesivir and Tocilizumab, in diabetic patients.
- When the terms "acute renal failure" and "Remdesivir" were combined, 138 observed cases, as opposed to the 9 expected, produced a statistically significant disproportionate signal.
- The risk of AKF **increased by 30-fold when Remdesivir was used** (confidence interval 0.95 [24.6–42.2], P < 0.0001).
- Remdesivir was observed by Zhou et al., to be strongly linked with AKI in COVID-19 patients with diabetes, and **RDV use increased the incidence of AKI by about six times** (ROR: 5.65, 95%, CI: 4.06-7.87).
- A significant association between AKI occurrences and Remdesivir therapy was found in COVID-19 patients in a different study by Wu et al., by mining FAERS real-world big data and was **significantly associated with AKI** by the authors: ROR = 2.81, 95% CI (2.48, 3.18).
- **The risk of getting AKI with Remdesivir was almost four times higher** after the propensity score matching ROR = 3.85, 95 percent CI (3.11, 4.78), was considered.
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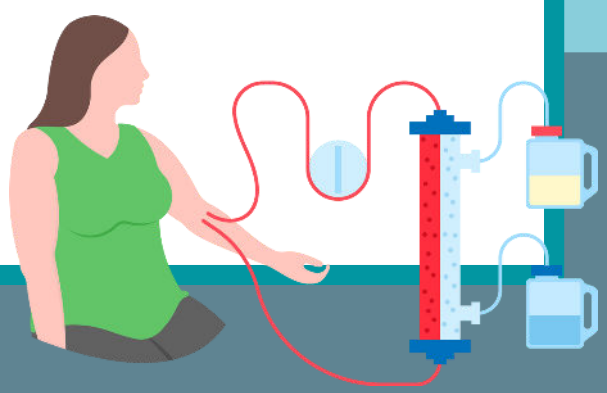

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In The Hospital

If you find yourself in the hospital in a situation where the care protocol involves receiving Remdesivir, know how to navigate this situation.

KNOW YOUR RIGHTS AND OPTIONS

- You have the right to informed consent.
- You have the right to ask for a copy of your medical records.
- If you find yourself in a difficult situation, call upon a nurse advocate for help.
  - https://www.graithcare.com/
  - www.remnantnursing.org
  - intergritylnconsultants@gmail.com
- Here are some resources we created in case you have to go to the hospital.
  - https://covid19criticalcare.com/hospital-guide/
  - https://covid19criticalcare.com/tools-and-guides/anesthesia-in-the-covid-era/
  - https://covid19criticalcare.com/tools-and-guides/what-is-informed-consent/
  - https://covid19criticalcare.com/tools-and-guides/remdesivir-vs-ivermectin/
  - https://covid19criticalcare.com/protocol/math-covid-hospital-treatment/
- Before you get sick, have a treatment plan in place.
  - Find a provider

The References Summarized

REFERENCES

- Visit https://c19early.org/smeta.html to access all the papers mentioned above in section I.
- Remdesivir and Acute Renal Failure: A Potential Safety Signal from Disproportionality Analysis of the WHO Safety Database Gérard et al., Clinical Pharmacology & Therapeutics, doi:10.1002/cpt.2145
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