Providence Holy Cross Outlines Steps for Ethical Distribution of a COVID Medication

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Providence Holy Cross Medical Center is a Level II trauma center located in the northern tip of Los Angeles. The hospital has a reputation for serving the community in the most difficult of situations, playing a major role in responding to disasters, from earthquakes and train crashes to school shootings and rampant fires.

Most recently, Holy Cross found itself in one of the COVID "hot spots," consistently recording the highest census of patients with a diagnosis of COVID-19 among the 51 hospitals in the Providence St. Joseph Health system.

At the beginning of the COVID-19 pandemic, we knew that demand for critical medical supplies would far outstrip what was available. Nationally, the initial focus was on the availability of ventilators. However, attention soon turned to the availability and allocation of a drug called remdesivir, which had shown potential in early drug trials to improve outcomes in patients with COVID-19. The Food and Drug Administration approved the use of remdesivir for patients under certain conditions and began distributing the limited supply.

On May 14, 2020, Providence Holy Cross Medical Center received its first allocation of remdesivir. The amount we were given was enough to treat, at most, four of the 61 COVID-positive patients that we were caring for at that time.

Following the recommendations of both the Providence Office of Theology and Ethics (the system's office for ethics) and the California Department of Public Health, the leadership team at Providence Holy Cross Medical Center formed a clinical discernment team to wrestle with questions about the just and ethical allocation of a scarce resource. Participants included physicians from palliative care and infectious disease, as well as hospitalists, intensivists and clinicians from infection control, pharmacy, nursing, administration and ethics.

The team began our discussion with (and would revisit several times) an awareness that unconscious or implicit bias had the potential to cloud our process. To safeguard against potential bias, we sought to establish a set of inclusion and exclusion criteria that were grounded in the existing medical evidence. Much of these criteria were drawn from the guidelines provided by the California Department of Public Health[1] and the initial findings of the remdesivir study.[2]

In order to be included in the pool of patients who might receive the medication, the patient must:

1. Be hospitalized with a positive test for COVID-19 virus.

2. Be over 18 years of age and not pregnant. (Remdesivir was available to these patients through a separate "compassionate use" process.)

3. Have a Creatinine Clearance of > 30mL/min. (Creatine clearance tests check renal function, or how well the kidneys work.)

4. Have ALT/AST levels < 5x the upper limit of normal. (The check of ALT/AST levels shows if a person has elevated alanine transaminase and/or aspartate transaminase. Elevated liver enzymes often indicate inflammation or damage to cells in the liver.)

Additionally, patients would be excluded from consideration if:

1. The patient is showing steady or significant improvement.
2. The patient is transitioning to a lower level of care.
3. The patient had a terminal diagnosis with less than six months to live.

To be clear, inclusion criteria did not automatically mean that the patient would receive the medication. While the discernment role was critical, the importance of an informed consent conversation between the attending physician and the patient or surrogate was equally important. Our Catholic health care system already had a strong commitment to honest and ongoing conversations with our patients regarding their goals of care, but this situation increased the necessity of such communications.

The clinical discernment team spent a significant amount of time discussing issues around quality of life and whether or not that should be a factor in discerning if the patient would be offered the medication. A review of the literature revealed a lack of consensus on this issue at the national level, with several articles raising concerns that quality of life measures might inadvertently discriminate against those with disabilities. Clearly, this is an area worth further discussion in search of a just and moral national consensus.

With our "screening process" established and the number of patients deemed most appropriate for the remdesivir treatment reduced from 61 to 34, our next task was to determine how we would select the patients who would be offered the treatment. The team agreed that a lottery system amongst those patients in a similar condition would be the best approach from both a clinical and ethical perspective.

To group our patients by similar condition, the clinical discernment team agreed upon three clinical variables that the preliminary research indicated were most critical in predicting outcome.

When assigning a score for each of these variables, the patients were evaluated by at least two physicians using objective criteria. The three variables considered were length of stay, a measurement of the level of oxygen in the patient's blood, and the degree of inflammation as measured by a marker referred to as C Reactive Protein.

Variable	1 Point	2 Points	3 Points
Length of stay (days)	> 10	6–10	1–5
Hypoxia (% FiO2)	< 40	40–60	> 60
C Reactive Protein	At least 15	—	—

With the identifying factors blinded to the members of the clinical discernment team, we now had four patients with a score of six. Using the consent process described below, each of those four patients (or their surrogate decision-maker) was approached and offered the remdesivir treatment. Three of these four patients accepted the recommended plan of care, and were started on the remdesivir regimen, leaving us with enough remaining vials for a single patient.

Next, we considered the group of 10 patients who had a score of five. As noted above, we elected to use a lottery process that randomized this group of patients to establish the order in which they would be considered (we used random.org). We then re-assembled the clinical discernment team and elected to review each of the cases with a twofold purpose in mind. First, a final review of the patient's entire clinical condition seemed warranted before administering such a scarce resource. Just as importantly, we wanted to begin refining our criteria for appropriateness so that it could be applied consistently to reduce bias and variation. As we reviewed each patient, we were acutely aware that each decision we made set the standard for future evaluations.

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Two patients had a history of failed attempts to extubate, combined with extremely poor kidney function. Two patients were not necessarily terminal (as defined by death being expected within six months) but had already decided to focus their efforts on comfort measures without additional escalation of care. This caused us to further refine our exclusion criteria. A fifth patient had improved significantly in the past 24 hours and was now on a path to discharge within 48 to 72 hours. The sixth patient appeared likely to benefit from remdesivir. That patient was offered and received the final regimen of the medication.

In the midst of so many medical experts and an overwhelming amount of articles in the medical journals, it seemed particularly important to engage with the patient or surrogate in a carefully crafted consent process. While some physicians and even systems have thought that administering remdesivir should fall under the general consent as a part of the conditions of admission, our clinical discernment team felt strongly that an informed consent conversation was ethically critical.

Part of our process was influenced by requirements laid down by the FDA as conditions for receiving the drug. The FDA provided an information sheet that we were required to share with the patient/surrogate. It served to remind all of us that there was no vaccine for this virus and no cure. There was enough clinical evidence to suggest that remdesivir might help, but there was not sufficient evidence to provide any guarantees. We were able to offer it only through a process whereby the FDA authorizes the use of a medication prior to the completion of clinical trials. This process is known as an Emergency Use Authorization (EUA).

Those requirements alone were consistent with a typical informed consent conversation.

INFORMED CONSENT TEMPLATE FOR ADMINISTRATION OF REMDESIVIR

I am recommending the administration of remdesivir for this patient. I have verified that the patient is:

- ☐ 1. Covid-19 positive
- ☐ 2. 18 years of age or older[1]
- ☐ 3. Not pregnant[2]
- ☐ 4. SpO2 < 94% on room air or requiring supplemental oxygen or mechanical ventilation (SpO2 is a measurement of the level of oxygen saturation in the blood.)
- ☐ 5. Has a Creatinine clearance greater than or equal to 30 ml/min
- ☐ 6. LFT (liver function test) including an ALT/AST levels less than 5x the upper limit of normal.
- ☐ 7. Not preparing to be discharged
- ☐ 8. Not on hospice or comfort care

☐ The patient and/or their surrogate decision maker has been informed of the known and potential benefits of remdesivir as well as the purpose of and details related to the administration of this treatment. I have also explained that remdesivir is an unapproved drug that is authorized for use under the Food and Drug Administration's Emergency Use Authorization. I have informed the patient/surrogate of the risks and benefits of and the alternatives to receiving this medication, including the option to refuse the medication and the risks of doing so.

☐ No adequate and well-controlled studies of remdesivir use in pregnant women have been conducted. Remdesivir should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus. If the patient is pregnant, I have informed the patient that we have no information regarding the presence of remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production. I have strongly encouraged the patient to suspend breast-feeding while taking this medication.

☐ A copy of the *Fact Sheet for Patients: Emergency Use Authorization (EUA) of Remdesivir for Coronavirus disease 2019 (COVID-19)* has been reviewed with and provided directly to the patient or will be made available to the surrogate decision maker as soon as practicable.

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1, 2 Patients who were under the age of 18 or pregnant would be able to receive remdesivir directly from Gilead, the manufacturer of this drug, so they are excluded from receiving the medication provided to us under the Emergency Use Authorization (EUA).

Beyond that, common sense and a respect for patient autonomy suggested that most people would want to have the opportunity to discuss options before having a drug that was untested and unapproved for general usage administered to them.

Recognizing that these were atypical informed consent conversations, we developed a standardized note that our physicians could access through our electronic medical record. This provided them with language that we believed would be helpful and reminded the physicians of the numerous requirements that were a part of the entire process. (For this article, the form has been amended slightly, with some additional details for readers.)

The very nature of responding to a pandemic makes a full review of any issue challenging. Our discussions raised several other issues that we recognize are worthy of additional reflection. We name three of them here in the interests of advancing the conversation and inviting such reflection.

- Dr. Ezekiel Emmanuel, in his article entitled "Fair Allocation of Scarce Medical Resources in the Time of Covid-19," recommends that critical health care and infrastructure workers receive preference for scarce medical resources. While Providence St. Joseph Health ultimately discerned that our system would not include a preference for key workers as a factor in the discernment process, accepting this decision was difficult for some members of the clinical discernment team. While every member was supportive of a commitment to care based on the patient's clinical condition without regard to race, age, ethnicity or any other protected status, some were supportive of Dr. Emmanuel's recommendation. We benefited from a well-articulated, ethically grounded statement from our system, but the lack of consensus on this issue at the national level was reflected by the passionate debate we experienced locally.
- Should the patient's pre-existing quality of life be a factor in determining who will receive scarce resources? If a patient could be returned to a quality of life that they had previously found to be acceptable, should that decision be subject to review in light of the scarce resources? Specifically, what are the benefits and risks of using such scales as the Eastern Cooperative Oncology Group (ECOG) or Sequential Organ Failure Assessment (SOFA)?
- Given that intubated patients are recommended to receive twice the amount of remdesivir, should they be excluded from consideration in order to treat a larger number of patients? Or should they receive a higher priority because they are sicker? Is the priority to treat the most number of patients or to treat the sickest? What ethical rationale would ground either decision?

The COVID-19 pandemic highlighted the need for a discernment process that removed bias when selecting patients to receive a scarce resource such as remdesivir where demand outstrips supply. Such discernment is not unique to COVID-19; it will certainly become an issue in other scenarios when demand is greater than supply. Having objective criteria and an objective scoring system in place that has been agreed to by a representative group of clinicians will take some of the subjectivity out of the patient selection process.

The importance of having sound ethical counsel at the table to guide the conversation and ensure that the ministry as a whole remains true to its values cannot be underestimated. The hope is that our experience will provide some details and direction on how best to approach such difficult times. As we continue to learn from one another and from each situation we encounter, we must all continue to refine our practices, ensuring the best care for our patients and minimizing the moral distress of both the patient and all those at the bedside.

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NOTES

1. John H. Beigel et al., "Remdesivir for the Treatment of Covid-19 - Preliminary Report," *The New England Journal of Medicine*, May 22, 2020, https://www.nejm.org/doi/full/10.1056/NEJMoa2007764.
2. California Department of Public Health, Remdesivir Public Distribution Fact Sheet, May 29, 2020, https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/Remdesivir-Distribution-Fact-Sheet-.aspx.

ADDITIONAL INFORMATION:

Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of Remdesivir for Coronavirus Disease 2019 (COVID-19), Federal Drug Administration, https://www.fda.gov/media/137565/download.

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