Developing statewide remdesivir use criteria

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Purpose. This report describes our process of 4 health systems coming together to agree on standard use criteria for remdesivir as a coronavirus disease 2019 (COVID-19) treatment for patients in Utah. We hope our process provides a framework for remdesivir use in other states and insights on future use of other therapeutic agents that may also be in short supply, such as vaccines and monoclonal antibodies.

Summary. Emergency use authorization (EUA) criteria for COVID-19 treatments often allow for broad use of a treatment relative to limited supplies. Without national criteria, each health system must develop further rationing criteria. Health systems in Utah worked together as part of the state's crisis standards of care workgroup to develop a framework for how to limit the EUA criteria for remdesivir to match available supplies. The 4 largest health systems were represented by infectious diseases specialists, chief medical officers, and pharmacists. The group met several times online and communicated via email over a 9-day period to develop the criteria. The clinicians agreed to use this framework to develop criteria for future therapeutics such as monoclonal antibodies.

Conclusion. The unique collaboration of the 4 health systems in Utah led to statewide criteria for use of remdesivir for patients with COVID-19, ensuring similar access to this limited resource for all patients in Utah.

Keywords: COVID-19, remdesivir, shortage, supply and distribution

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On May 1, 2020, the US Food and Drug Administration (FDA) granted emergency use authorization (EUA) for remdesivir.[1] The criteria provided in the initial EUA were broad, allowing the use of remdesivir for adults and children hospitalized with suspected or confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and severe coronavirus disease 2019 (COVID-19). Initial details were unclear regarding how the drug would be distributed to hospitals. It was clear at the time there would likely not be enough supply of this medication to meet demands for months.

In early May, each health system in Utah independently began working on its own set of criteria for remdesivir allocation (briefly described below).

HCA Healthcare

HCA Healthcare has 8 hospitals in Utah. Only 1 facility was administering remdesivir before receipt of the state allocation as a participant in the "Expanded Access Treatment Protocol (EAP): Remdesivir (RDV; GS-5734) for the Treatment of SARS-CoV2 (CoV) Infection" study, sponsored by Gilead Sciences, Inc. (Foster City, CA).

On May 14, 2020, St. Mark's Hospital received the first shipment of state-issued remdesivir and served as the central repository for the other 7 HCA hospitals in Utah. In recognition of the limited supply of medication, HCA's Corporate Clinical Services Group provided guidance on the ethical framework for allocation of remdesivir, which was in alignment with the EUA. Since St. Mark's Hospital was still able to enroll patients in the

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EAP study, pharmacists were instructed to use the EAP study drug for all patients meeting inclusion/exclusion criteria and to only use the state-allocated drug for those outside the EAP criteria.

Intermountain Healthcare

Intermountain Healthcare is the largest healthcare provider in the Intermountain West, with 24 hospitals including a flagship hospital with 504 beds. Intermountain Healthcare's multidisciplinary COVID-19 Therapeutics Committee developed remdesivir allocation guiding principles and clinical criteria in early May. Intermountain committed to a process of equitable remdesivir allocation across all 23 hospitals, including critical access hospitals, using a central distribution model with drug allocated from the state of Utah stored at a central location. A system-wide remdesivir allocation subcommittee, comprised of infectious diseases pharmacists with infectious diseases and critical care physicians, was tasked with daily active surveillance to identify qualifying patients, contact providers, facilitate medication ordering, and monitor patients during therapy. Challenges overcome during implementation included communication with providers on how best to approach patient conversations, coordination of patient transfers, and clarification of clinical criteria rationale. Adjudication of patient eligibility was changed from daily to twice daily to increase medication access before ultimately pursuing a decentralized approach. Physician support was critical in assisting in the application of criteria to unique patient situations and fielding questions from providers about the process.

Steward Health Care

Steward Health Care operates 5 acute care hospitals in Utah as part of a large national health system. Before May 1, 2020, the Steward Utah hospitals did not have the ability to provide remdesivir as a therapeutic option to patients with COVID-19. When FDA issued the EUA for remdesivir, Steward, as well as the other health systems in Utah, were not scheduled to receive any allocations. At that time Steward leaders in Utah joined the national outreach to the Department of Health and Human Services (HHS) to express concern over the allocation process.

HHS quickly announced that a new allocation process would be used, in which Utah would be included among the states allocated an amount of donated remdesivir, and states would be responsible for distributing their allocated doses to individual hospitals within the state.

KEY POINTS

- State health authorities should partner with health systems when faced with allocating scarce resources.
- Stakeholder clinicians working collegially can quickly develop use criteria.
- Consensus-based criteria can help states equitably allocate scare resources.

University of Utah

University of Utah Health is the only academic medical center in the Mountain West with 5 hospitals, including the flagship University Hospital with 585 beds. University of Utah Health had experience with remdesivir as a participating site for two Gilead Sciences clinical trials evaluating 5- versus 10-day courses of remdesivir for moderate (GS-US-540-5774) and severe (GS-US-540-5773) COVID-19. On May 12, the system received notice that clinical trials of remdesivir would be ending on May 29 based on the announced EUA and lack of availability of remdesivir.

Due to concerns regarding the limited supply of remdesivir in the setting of increasing cases of COVID-19, the medical director of our antimicrobial stewardship program, in cooperation with the principal investigator for our remdesivir trials, drafted criteria for use on May 13 that encompassed the broad EUA criteria, but further limited use based on the severely limited number of doses available. The next day, based on an initial allocation of 40 vials, the University of Utah Health Clinical Services Core Committee (representing hospitalists and critical care, infectious diseases, medical ethics, and pharmacy professionals) met to revise and approve criteria for how this limited supply of remdesivir could best be used. The initial use criteria followed all guidance in the EUA but, due to limited supplies, were further limited to patients who were in the early course of illness and those not eligible for consent or uninterested in ongoing remdesivir clinical trials. The intent was to provide therapy to patients who were most likely to benefit. Additionally, the criteria advised using a 5-day course whenever possible to allow more patients to be treated. These decisions were made with only limited information available from a National Institutes of Health press release[2] of the Adaptive COVID-19 Treatment Trial (ACTT-1) preliminary results, as no literature had been published yet. These criteria were approved by the pharmacy and therapeutics committee, and a process was put in place for daily review of all inpatients with COVID-19 by the antimicrobial stewardship team. Ability to prescribe remdesivir was limited to the antimicrobial stewardship team, and upon daily review, providers caring for eligible patients were contacted to offer the drug and obtain verbal consent. The antimicrobial stewardship team then left a progress note for all patients prescribed remdesivir outlining daily laboratory monitoring and parameters for discontinuation and adverse event reporting. As previously noted, other health systems in the area were working on their own sets of rationing criteria, and University of Utah Health suggested that statewide criteria would

be beneficial to ensure similar access to this limited resource for all patients in Utah.

Developing statewide use criteria

Utah has been proactive in crisis management. Work on crisis standards of care (CSC) guidelines began during the 2009 H1N1 pandemic with a first set of CSC being approved by the state in 2010. On March 27, 2020, Utah's governor officially convened a workgroup to address CSC during the COVID-19 pandemic. The group was charged with developing a fair method for prioritizing scarce resources during the COVID-19 pandemic. Initial work focused on resources that were expected to be limited, such as intensive care unit beds and ventilators. One additional principle that the group agreed to was the concept of "load leveling," that to the degree possible hospitals should not be forced to limit care or resources until all of the resources in the state had been depleted.[3] Enacting this principle would require potential sharing of resources or patients.

The Utah CSC committee recognized the need for developing statewide remdesivir use criteria, noting the varied guidance available at each health system, and on May 21, 2020, this group formed an Allocation of Scarce Medications Subcommittee with representation from the Department of Health, Utah Hospital Association, medical directors and infectious diseases specialists from all major health systems, pharmacy representatives, rural hospital representatives, and a medical ethicist. The group met for 2 hours on May 21, 2020, with email follow-up, and held a second meeting on May 26, 2020, to agree on a single set of criteria that would be used at all health systems in Utah. During this time, preliminary results of the ACTT-1 trial[4] were published, in addition to data on patients with severe disease described by Goldman and colleagues,[5] which helped inform the criteria approved on May 28, 2020.

Critical points of discussion for the Utah CSC committee centered around ensuring that remdesivir would be used for patients who were the most likely to benefit from this limited resource without engaging in discrimination. Another consideration was use in patients with lesser supplemental oxygen needs or in patients who were already mechanically ventilated. The group also discussed whether treatment should begin as early as possible, or if that might disadvantage patients who may not have early access to care. Each health system also developed a standardized method to identify patients who might qualify for remdesivir treatment and allocate individual courses on a daily basis. While each health system had originally developed its own set of criteria, everyone agreed to use the single set of criteria beginning May 26, 2020.

Hospitals in Utah were allocated the donated remdesivir based on COVID-19 census. Those health systems with greater numbers received larger allocations. Allocations were simply a number of vials per hospital and not a per-patient allocation. For example, if 6 vials were not required for a patient, those vials could be used for other patients. Hospitals evaluated patients for eligibility to receive remdesivir based on the criteria on a daily basis. If the number of eligible patients exceeded the number of vials, the patients were entered into a lottery. The Utah CSC committee checked in via email to report on whether the criteria were still working and if any changes were needed. Health systems were not required to report back overall usage or compliance with the use criteria due to concerns regarding reporting burden and lack of enforceable repercussions. For example, if a hospital chose not to follow the criteria, no repercussions could be enforced. The group selected the honor system and collegiality in recommending adjustments to the criteria. No hospitals reported having insufficient inventory requiring the use of a lottery. In 2 instances, University of Utah Health transferred remdesivir to rural sites that had not received a statewide allocation and were unaffiliated with Intermountain, HCA, or Steward.

After commercially available remdesivir became available on June 28 and hospitals were satisfied that supplies had truly improved, the criteria were further revised July 22 to allow for broader use (ie, in newly intubated patients treated within 12 hours) while including contingencies if supplies became very scarce. Clinical criteria were also slightly adjusted to allow for earlier use of remdesivir by allocating courses at any point in time during the day rather than a single time point. On August 20, supplies were sufficient to further expand criteria to allow use in a larger group of patients (those hospitalized and receiving at least 2 L/min of supplemental oxygen). On August 28, with supplies plentiful and with the broadened EUA criteria, the need for rationing a scarce resource was negated. The latest edition of the criteria is available online.[6]

Summary

In this article, we share our process of 4 different health systems coming together to agree on standard use criteria for remdesivir for all patients in Utah. We hope our process will provide a framework for remdesivir use in other states and insights on future use of other therapeutic agents that may also be in short supply, such as vaccines and monoclonal antibodies. We would like to thank the Utah Hospital Association for its leadership in bringing together all of the hospital systems in the state and facilitating the collaboration that led to quick, thoughtful, and effective actions. We are also grateful for the collaborative spirit in which all health systems in the state and the Utah Department of Health have worked to develop this framework.

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Disclosures

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