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# Biology of Blood and Marrow Transplantation



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**Position Statement** 

# American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group Position Statement on Pharmacy Practice Management and Clinical Management for COVID-19 in Hematopoietic Cell Transplantation and Cellular Therapy Patients in the United States



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## ABSTRACT

The coronavirus-19 (COVID-19) pandemic poses a significant risk to patients undergoing hematopoietic stem cell transplantation (HCT) or cellular therapy. The American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group Steering Committee aims to provide pharmacy practice management recommendations for how to transition clinical HCT or cellular therapy pharmacy services using telemedicine capabilities in the inpatient and outpatient settings to maintain an equivalent level of clinical practice while minimizing viral spread in a high-risk, immunocompromised population. In addition, the Steering Committee offers clinical management recommendations for COVID-19 in HCT and cellular therapy recipients based on the rapidly developing literature. As the therapeutic and supportive care interventions for COVID-19 expand, collaboration with clinical pharmacy providers is critical to ensure safe administration in HCT recipients. Attention to drug-drug interactions (DDIs) and toxicity, particularly QTc prolongation, warrants close cardiac monitoring and potential cessation of concomitant QTc-prolonging agents. Expanded indications for hydroxychloroquine and tocilizumab have already caused stress on the usual supply chain. Detailed prescribing algorithms, decision pathways, and specific patient population stock may be necessary. The COVID-19 pandemic has challenged all members of the healthcare team, and we must continue to remain vigilant in providing pharmacy clinical services to one of the most high-risk patient populations while also remaining committed to providing compassionate and safe care for patients undergoing HCT and cellular therapies.

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## INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) declared the new coronavirus, coronavirus-19 (COVID-19), a global pandemic [1]. This highly contagious illness poses a significant risk to immunocompromised patients, and patients undergoing hematopoietic stem cell transplantation (HCT) or cellular therapy are no exception. There are currently no reports on the outcomes of HCT/cellular therapy patients;

however, early accounts of the outcomes of patients with cancer infected with COVID-19 indicate a 3.5-fold greater risk of intensive care unit admission, need for mechanical ventilation, or death compared with patients without cancer [2]. As this virus continues to spread throughout the United States, many hospitals have worked rapidly to conserve resources and to protect patients in response to the COVID-19 pandemic. Avoiding exposure by adhering to good hygiene practices and social distancing are the sole available prevention strategies given the lack of approved treatment options or vaccine [3]. In many cases, patients with a hematologic malignancy undergoing HCT or cellular therapy cannot have their treatment delayed. There are limited recommendations for pharmacy practices working with HCT and cellular therapy patients. We remain a

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critical and required component of the health care team and must ensure we can continue to monitor patients, provide clinical recommendations, and provide critical education to patients in need [4]. The American Society for Transplantation and Cellular Therapy (ASTCT) Pharmacy Special Interest Group (SIG) Steering Committee provides this position statement for pharmacy practice management and clinical management recommendations for COVID-19 in HCT and cellular therapy recipients.

## PHARMACY PRACTICE MANAGEMENT CONSIDERATIONS

There have been published reports on managing cancer care during the COVID-19 pandemic, and resources are available from both the ASTCT and the European Society for Blood and Marrow Transplantation. However, to our knowledge, there are no reports specifically addressing pharmacist practice management in the inpatient and outpatient settings and leveraging telemedicine capabilities in these unprecedented circumstances [3,5,6]. In addition, many of our institutions include academic learning environments in which there are frequently students and pharmacy residents, and many changes have been implemented due to concerns for COVID-19. Consideration should always be given to institutional policies and procedures, and practices should be routinely reviewed and revised if needed.

## **Initial Preparations**

In these unprecedented times, priority should be given to protecting our vulnerable patient population while also ensuring a safe work environment and protecting the health of the frontline staff. Although we maintain that face-to-face communication is the most ideal model for patient care, we are fortunate to have technologies capable of supporting much of our work virtually if necessary. Many of these recommendations are also applicable to other vital members of the HCT team. When making initial preparations, consideration should be given to staffing models and exploring what work must be done in person versus work that can be done virtually. Attention should be given to staff members who are themselves immunosuppressed and or have family members that are at high risk for complications of COVID-19. These staff members should be the first considered when developing work-from-home practices.

In the development of work-from-home strategies, employees should have a reliable internet connection and either a home computer or an employer-issued device to log into the institutional electronic medical record (EMR) to continue to provide clinical services. Employees should maintain a workspace that is free of other distractions. Instructions should be created for the staff working remotely on how to check voicemail when not in the office, how to access translator services if needed, and available technologies to be able to use personal cell phones to securely call patients. Most importantly, communication channels back to the clinical team should be created, and physicians and advanced practice providers should be aware of how to reach the pharmacists that are completing their work remotely. Regular contact with pharmacy leadership to ensure the staff working from home have the resources they need to complete their work and triage any barriers is highly recommended.

For staff members who must remain at work, policies and procedures should be in place for a strict "stay at home if sick" policy with clear guidelines for when staff can return to work and safely care for patients. In addition, guidance on the use of facemasks and personal protective equipment (PPE) should be outlined within institutional policies and procedures. Despite all initial preparations, flexible and frequent (typically daily) communication to staff is vital to ensure care continuity in this dynamic, rapidly evolving situation.

## **Recommendations for Inpatient Pharmacist Practice**

Clinical pharmacy services are an established practice within the HCT and cellular therapy team. The ASTCT Pharmacy SIG recommends continued pharmacist monitoring of these high-risk complex patients and access to the health care team for clinical decision making. The role of the HCT pharmacist is vital for the safety and optimal care of HCT recipients and must be maintained for FACT compliance [4].

Depending on the institution's model of inpatient rounds, our recommendation is to limit exposure to patients and other team members as much as possible. Recognizing the importance of onsite representation of inpatient clinical pharmacy services for urgent and emergent needs, a rotating model of working remotely for pharmacists is recommended to limit the number of pharmacists that may be exposed or exposing patients or colleagues. If attending in-person rounds is deemed necessary, we recommend the following steps: avoid entering patient rooms if possible, conserve PPE, remain 6 feet from other team members, and dress in scrubs that can be routinely laundered. Institution-provided scrubs and laundry service could be an ideal resource if available. Documentation, communication, and patient monitoring should be done in a workspace separate from other team members. Some practice models may have the ability to limit the pharmacist to exclusive virtual rounding. This allows the opportunity for individuals to work remotely during this critical time to preserve the healthcare system and workforce and supports the importance of protecting our communities from pandemic spread. Additional information on recommendations for using technology is provided later in this position statement.

Discharge counseling and education is one of the pillar clinical services that inpatient HCT pharmacists provide. Fortunately, there are available technologies that can be used, such as the EMR, to ensure that educational handouts are received (eg, Epic, MyChart) or to enroll patients into medication calendar applications, such as MedActionPlan Pro. If these technologies are not available, we encourage coordination with other team members who are already caring for the patient to ensure delivery of educational materials and customized calendars before planned education sessions, to minimize patient exposure. Patient counseling should occur over the phone when possible; however, virtual visits may be supported at some institutions. For patients with concerns about cognitive comprehension and limited telehealth capabilities, education can be completed in person with a caregiver; however, exposure should be limited and proper PPE as outlined by the institution should be worn.

Modern EMRs and supporting technology give pharmacists the ability to complete a profile review, pharmacokinetic monitoring (eg, immunosuppression), renal and hepatic adjustments, chemotherapy entry and verification, evaluation of DDIs and medication reconciliation remotely. In addition, we recommend that consideration be given to standardizing times of medication administration to limit the number of times nurses and respiratory therapists need to enter the patient's room. Consideration should also be given to plan for and mitigate potential drug shortages by identifying potential therapeutic alternatives and, if necessary, creating patient selection criteria to conserve supplies. Inpatient clinical pharmacy services for HCT and cellular therapy recipients should not be negatively impacted or sacrificed despite the need to limit face-toface patient and caregiver interactions.

#### **Recommendations for Outpatient Pharmacist Practices**

The outpatient clinic is critical to both acute management and long-term chronic management of HCT recipients. Care requires a multidisciplinary approach throughout the patient's entire transplantation journey. The HCT clinical pharmacist is a key member of the interdisciplinary team in the clinic. Education, drug therapy management, supportive care, and management of acute and chronic complications of HCT are among the services provided by clinical pharmacists in the clinic. Successful delivery of these services requires integration into clinic workflows. This integration is valuable for providers and patients alike. In the face of COVID-19, pharmacists are now challenged to identify creative and innovative ways to deliver these services to ambulatory HCT recipients while minimizing viral spread in a high-risk, immunocompromised population. This has required that pharmacists depend on established relationships with their teams to provide care while protecting the health of both of patients and their colleagues. This can be achieved by models that minimize the physical presence of the pharmacist, distribute work among resources, and leverage technology.

Strategies for minimizing physical presence in the clinic depend on existing infrastructure and pharmacist resources. Pharmacists who are the sole HCT pharmacist in their clinic can consider rescheduling patients in a way that allows for onsite care on specific days of the week and remote care on other days of the week, relieving the need for their physical presence at the clinic every day. Alternatively, some institutions may have a team of clinic-based HCT pharmacists. These pharmacists can implement rotations that allow them to maintain onsite direct patient care services while simultaneously limiting the personnel in the clinic. This may involve pharmacists rotating onsite coverage by certain days of the week or adopting a week-long rotation for improved continuity. Finally, pharmacists in the ambulatory HCT setting may also have administrative days built into their staffing model. These days are usually when pharmacists are not engaging in direct patient care visits but are conducting indirect patient care activities including progress note documentation, phone call follow-up and medication and care coordination. These indirect patient care days are ideal opportunities for pharmacists to work remotely to limit exposure and contact.

When considering onsite and remote models, pharmacists should consider which services are best provided onsite and which can be maintained remotely and distribute those services among resources accordingly. Clinic pharmacists can perform order verification responsibilities, chemotherapy order preparation, or treatment plan implementation remotely. Clinical services such as laboratory follow-up, therapeutic drug monitoring, transplant education, oral chemotherapy counseling and follow-up, and medication reconciliation can also be performed via phone by an offsite resource. Pharmacists who maintain an onsite presence can provide immediate support to their clinic teams for issues that may arise in the delivery of care that require a timelier response, such as rapid responses and codes. If able, providing this at-the-elbow support onsite can help maintain clinic workflow efficiency and throughput. Pharmacists onsite may continue to see patients in clinic as needed, but should identify ways to minimize contact with patients, such as routing information and/or materials through a primary provider who will be interfacing with patients.

#### **Recommendations for Optimizing Technology Resources**

The modern technologies provided within our institutions can support remote clinical pharmacy services for both the inpatient and outpatient settings and are critical to the successful delivery of care when there is an effort to limit patient contact (Table 1). Many centers may already have a developed and implemented model for telemedicine in place, and other

## Table 1

Inpatient and Outpatient Considerations for Pharmacy Practice Management

Inpatient Considerations	Outpatient Considerations				
Limiting exposure to staff and patients					
Limiting physical presence <ul> <li>Attending clinical rounds or huddles virtually</li> <li>Rotating pharmacy staff on- and off-site</li> <li>Pharmacists to avoid accessing patient rooms (not seeing patients directly)</li> <li>If rounding in person, maintaining 6 feet from other team members</li> </ul>	Limiting physical presence <ul> <li>Concentrating visits on particular days to allow for non-patient visit days</li> <li>Rotating pharmacy staff on- and off-site</li> <li>Pharmacists to avoid accessing patient rooms (not seeing patients directly)</li> </ul>				
Distribution of services					
Onsite • Urgent/emergent needs (rapid responses/codes) • Collaboration with other team members • Discharge education Offsite • Medication education and reconciliation • Patient own medication identification • Therapeutic drug monitoring • Order verification, including chemotherapy • Medication adjustments based on renal and liver function • Drug-drug interaction management	Onsite Urgent/emergent needs (rapid responses/codes) Help maintain clinic workflow efficiency/throughput Collaboration with other team members Offsite Medication education and reconciliation Oral chemotherapy education and follow-up Conditioning and transplant education Laboratory follow up Therapeutic drug monitoring Order verification Chemotherapy order preparation				
Technology					
Messaging <ul> <li>Chat mechanisms (EMR real-time, Cureatr, Voatle, Skype for Business)</li> <li>EMR messaging functions</li> <li>Email</li> <li>Handouts or medication calendars sent to patient via EMR or through program</li> </ul>	is such as MedActionPlanPro				

Audiovisual

• Audio call resources (Doximity, Jabber phone, blocked calls from personal line)

• Virtual visit capabilities (eg, webcam)

Zoom/Webex/Skype for Business (for communicating with team members) (if approved for use by IT department)

institutions are actively working toward this capability. Pandemics such as this create the opportunity for teams to scale and leverage those services to a greater population of patients. Home access through virtual private network clients and Citrix platforms allow for easy access to the necessary data to complete clinical responsibilities and are readily available to the clinical team. We recommend partnering with the information technology (IT) department within the organization for guidance on available options and implementation of telemedicine capabilities, which can vary from institution to institution. These modes of communication, although extremely convenient, should be first be approved by the institution to ensure that patient confidentiality is maintained and accounts are secure.

For communication with the clinical team, pharmacists can use chat and messaging functions that may be embedded in, or exist outside of, the medical record to communicate directly with colleagues (eg, Epic Inbasket, Epic chat, Jabber chat, Cureatr, Voalte, Skype for Business).

With institutions limiting or in many cases prohibiting visitors, providing education to patients and caregivers has become difficult, and alternative measures need to be used, such as email, telephone, Facetime, or Zoom technology. Communication with patients can be achieved through electronic messaging or calling. Requested patient resources, such as medication calendars and/or customized education sheets, can often be sent via electronic portals including email or messaging through the EMR (eg, Epic MyChart). More involved education discussions and/or updates to care plans can be completed via phone visits using telephonic audio services (eg, Doximity, Jabber phone). If the technology is available, virtual visits with webcams can be implemented, allowing for audiovisual capabilities. Pharmacists should collaborate with their IT departments to identify options. The ability to bill for these remotely provided services varies widely depending on individual state laws.

#### **Recommendations for Students/Interns/ Resident Learners**

In response to the COVID-19 outbreak, many schools of pharmacy have chosen to cancel in-person classes and favor an online approach. As such, many student clinical rotations have been cancelled or changed to virtual learning. This presents a unique challenge, because case-based learning is so beneficial. The ASTCT Pharmacy SIG recommends that students remaining on clinical rotations work remotely to review patients and provide potential clinical interventions after discussion with their primary preceptor. Patient discussions, recommendations, topic discussions, and other required assignments can be completed with the primary preceptor via such platforms as Zoom or Skype for Business. Students also may be assigned to more academic- or research-type rotations to minimize their exposure to patients.

The COVID-19 pandemic presents a unique challenge for current residents. However, we believe that it is in the best interest of residents to be treated the same as clinical staff. Resident exposure should be limited, and they should complete clinical duties remotely when able. Patient monitoring and topic discussion with preceptors can be completed remotely as well. Pharmacy residents may also be requested to assist with other departmental needs, such as planning, communication, drug information requests, and staffing. It is ultimately the responsibility of the residency program director to ensure that pharmacy residents continue to meet the goals and objectives outlined to meet the requirements for graduation.

## CLINICAL MANAGEMENT CONSIDERATIONS

Novel data supporting potential COVID-19 treatment options are emerging at a record pace, fueling heavy debate regarding study design and optimal strategies [3,6,7]. The use of any of the proposed agents in the HCT patient population requires careful consideration regarding clinical condition, comorbidities, and current drug therapy. Currently, more than 300 clinical trials for various COVID-19 interventions are posted on ClinicalTrials.gov [8]. Here we review the most common COVID-19 therapeutic options, relevant DDIs, and safety and administrative concerns with medications commonly used in the HCT setting (Table 2). For a complete list of DDIs with potential COVID-19 treatments, visit http://www.covid19-druginteractions.org/.

#### Chloroquine/Hydroxychloroquine

Chloroquine (CQ) and hydroxychloroquine (HCQ) have garnered significant interest as potential options for treating COVID-19. In vitro data demonstrates possible viral inhibition by increasing the pH of intracellular lysosomes and endosomes, leading to decreased viral membrane fusion [9]. Other mechanisms of viral inhibition involve altering the glycosylation of ACE2, as well as blocking transport and subsequent release of the viral genome [9–11]. Pharmacodynamically, both CQ and HCQ are readily bioavailable (~89% and 74%, respectively) with rapid peak concentrations and display multicompartment pharmacokinetics with significant tissue distribution and long terminal half-lives (30 to 40 days) [11–14]. They are converted to active metabolites by cytochrome P450 enzymes CYP3A4, CYP2D8, and, to a lesser extent, CYP2D6. Both drugs have also been shown to moderately inhibit CYP2D6 [15]. Based on metabolic pathways, administration with a CYP3A4 or CYP2D8 inhibitor may result in decreased active CQ/HCQ concentrations, and coadministration with a CYP2D6 substrate may increase the concentration of the coadministered drug. There have been 2 case reports of significantly elevated cyclosporine concentrations when given in combination with CQ but no documented DDIs with tacrolimus, suggesting the interaction was not CYP-mediated [16,17]. The frequency, significance, and mechanism for the reported interaction with cyclosporine are unknown, and routine pharmacokinetic monitoring is recommended. Regarding administration of either agent, avoiding antacid administration within 4 hours is recommended to help ensure absorption. In

Table 2

Drug Interactions with Experimental COVID-19 Therapies and Common Immunosuppressants [32]

0 1	1					
Drug	CQ/HCQ	RDV	RBV	LPV/r	TCZ	RUX
Tacrolimus	$\uparrow$	$\leftrightarrow$	$\leftrightarrow$	↑	↓ (weak)	$\leftrightarrow$
Cyclosporine	$\uparrow$	$\leftrightarrow$	$\leftrightarrow$	↑	↓ (weak)	$\leftrightarrow$
Sirolimus	1	$\leftrightarrow$	$\leftrightarrow$	↑ (strong)	↓ (weak)	$\leftrightarrow$
Mycophenolate	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$
ATG	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$

RDV indicates remdesivir; RBV, ribavirin; LPV/r, lopinavir/ritonavir; TCZ, tocilizumab; RUX, ruxolitinib; ATG, antithymocyte globulin. Arrow depicts the effect on immunosuppressant concentration.

patients with compromised oral intake (eg, mucositis), HCQ cannot be crushed at the bedside and must be compounded to a solution once the external layer is removed [18].

Potentially more significant in the HCT and cellular therapy populations are the overlapping toxicities with concomitant medications. CQ and HCQ are associated with QTc prolongation, especially problematic in HCT patients receiving multiple other QTc- prolonging agents, such as azole antifungals, fluoroquinolones, macrolides (azithromycin), 5-HT3 antagonists, and others [19,20]. Electrocardiography should be performed before starting antiviral therapy with CQ/HCQ. Early reports of dual therapy with HCQ and azithromycin have raised a considerable concern for QTc prolongation and warrant a discussion of risk versus benefit [7]. Vigilant electrolyte repletion is also recommended, given that HCT recipients commonly have significant electrolyte disturbances, further increasing the risk of cardiac arrhythmias. A rare but notable adverse effect seen with both agents is altered insulin metabolism, leading to hypoglycemic events. Patients receiving concurrent therapy for diabetes should be monitored closely [21].

Other toxicities noted on drug labeling include elevated liver function tests, ophthalmic changes, and glucose-6-phosphate dehydrogenase (G6PD) deficiency-related anemia. Ophthalmic toxicities are typically associated with consistent drug concentration of 6.5 mg/kg/day for >5 years [21,22], and G6PD-associated toxicity was not observed in a retrospective review of patients receiving HCQ for autoimmune disease [23]. Given the short course and risk/benefit ratio of initiating COVID-19 directed therapy, these potential toxicities are less concerning; however, G6PD assessment would be ideal.

#### Remdesivir

Remdesivir (GS-5734) is an investigational compound with broad-spectrum antiviral activity developed during the Ebola outbreak in 2014 [24,25]. A nucleotide prodrug, remdesivir is metabolized to its active nucleoside triphosphate form. It then binds RNA-dependent RNA polymerase, acting as a delayed RNA chain terminator [26,27]. Remdesivir has demonstrated in vitro and in vivo activity in animals first against SARS-CoV-1 and MERS-CoV, and now with potent in vitro activity against SARS-CoV-2 [10,28]. The dosage currently under study is 200 mg i.v. on day 1, followed by 100 mg i.v. once daily for 10 days [7]. In the United States, remdesivir is available on clinical trial or via compassionate use; however on March 23, 2020, Gilead Inc had to temporarily halt its use on an individual compassionate basis owing to the overwhelming number of requests [29]. It is still available for pregnant women and children age <18 years with severe COVID-19 infection outside of a clinical trial at this point. Although remdesivir is described as a substrate for CYP2C8, CYP2D6, and CYP3A4 in vitro, it is thought that inhibitors or inducers of CYP3A4 are unlikely to cause significant drug interactions, because remdesivir's metabolism is likely mediated by hydrolase activity [7,29,30].

## Ribavirin

Ribavirin, a nucleoside inhibitor that terminates RNA synthesis [31], was discovered in the 1970s and has been used to treat hepatitis C infection, respiratory syncytial virus infection, and viral hemorrhagic fever. In combination with other drugs, such as corticosteroids or interferon, ribavirin at very high doses (1.2 to 2.4 g every 8 hours) has been used to treat for SARS-CoV-1 and MERS-CoV; this dosage was associated with excessive toxicity, however [32–34]. Ribavirin is currently being studied in combination with interferon and lopinavir/ ritonavir against COVID-19. Ribavirin has minimal drug interactions of note; however, it may be associated with an increasedrisk for myelosuppression when given in combination with azathioprine, linezolid, and amphotericin B [30].

## Lopinovair/Ritonavir

The combination of lopinavir and ritonavir, in conjunction with other antiviral agents, is an antiviral regimen currently approved to treat HIV-1. Lopinavir and ritonavir are protease inhibitors coformulated based on their pharmacokinetic profiles, with ritonavir increasing the plasma half-life of lopinavir via inhibition of CYP3A metabolism [35]. Lopinavir/ritonavir is considered a strong CYP3A4 inhibitor and increases serum levels of CYP3A4 substrates, necessitating dosage adjustment or drug avoidance, depending on the specific drug substrate.

Lopinavir/ritonavir was first identified as having antiviral activity against SARS-CoV as both initial and rescue therapy when added to a regimen of ribavirin and steroids. This combination showed reductions in overall death rate, intubation rate, adverse events (ie, development of acute respiratory distress syndrome), nosocomial infections, and need for rescue pulsed steroids for severe respiratory deterioration [36,37]. Unfortunately, this benefit has not been carried over thus far in patients receiving this therapy for COVID-19 [38]. In a trial of 199 hospitalized patients with severe COVID-19 infection receiving lopinavir/ritonavir (400 mg/100 mg twice daily for 14 days), there was no improvement above standard care, and gastrointestinal adverse events were more common in the lopinavir/ritonavir group. There are currently 15 open studies evaluating the use of lopinavir/ritonavir for treating COVID-19, with future results hopefully helping define a place in therapy for this novel treatment regimen [39].

### **Convalescent Plasma**

Administration of convalescent plasma containing SARS-CoV-2-specific antibody (IgG) from previously infected patients was reported recently [40]. This brief case report included 5 patients with acute respiratory distress syndrome who displayed clinical improvement (improved fever, Sequential Organ Failure Assessment score, and arterial oxygen partial pressure/fraction of inspired oxygen, decreased viral loads) within 12 days of infusion. Further investigations of this strategy are underway, and the results are highly anticipated. Interactions with concomitant drug therapy seem unlikely. Special consideration is needed for ABO-mismatched patients, with use of AB plasma likely the optimal approach.

#### Tocilizumab

Tocilizumab has been ueed as adjunct therapy in COVID-19-positive patients displaying signs of cytokine-release syndrome (CRS) [41]. As a monoclonal antibody directed toward the IL-6 receptor, it does not undergo any CYP metabolism and is eliminated after binding to the target [30]. Elevated levels of IL-6 during extreme inflammation can suppress CYP enzyme function; thus, the impact of a drop in IL-6 level after tocilizumab administration is unknown [42]. Tocilizumab is an important agent in the treatment of CRS occurring after chimeric antigen receptor (CAR) T cell therapy; anticipation of future CAR T cell patients and sequestration of stock may be warranted. Creation of separate order sets or treatment defining indications for CAR T cell CRS versus COVID-19 CRS could help pharmacies maintain separate stocks. HCT pharmacists may also be consulted for their expertise with CRS management in treating COVID-19-infected patients.

# Ruxolitinib

The oral JAK1/2 inhibitor ruxolitinib is commonly used in the HCT population to treat steroid-refractory acute graft-versus-host disease. Its potent immunosuppressive properties also being investigated in treating patients with COVID-19 with CRS in upcoming Phase III trials [43]. Ruxolitinib is extensively metabolized by CYP3A4, necessitating dose adjustment with strong inhibitors/inducers [44]. Dose adjustment for renal dysfunction is also warranted. Myelosuppression and infection are the most common toxicities when ruxolitinib is used in the setting of graft-versus-host treatment; however, these effects might not be as profound when it is used for short courses to treat COVID-19 infection.

## CONCLUSION

The COVID-19 pandemic is challenging all members of the healthcare team, necessitating major restructuring of staffing models while providing optimal clinical management of infected HCT recipients in the face of rapidly evolving knowledge of potential treatments. Numerous clinical trials involving various treatment options are underway and others, are being designed. In this environment, we must continue to remain vigilant in providing pharmacy clinical services for patients receiving HCT and cellular therapies and remain committed to providing compassionate and safe care for this high-risk patient population.

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