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Risk and management of patients with mastocytosis and MCAS in the SARS-CoV-2 (COVID-19) pandemic: Expert opinions

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The coronavirus disease 2019 (COVID-19) (caused by severe acute respiratory syndrome coronavirus 2) pandemic has massively distorted our health care systems and caused catastrophic consequences in our affected communities. The number of victims continues to increase, and patients at risk can only be protected to a degree, because the virulent state may be asymptomatic. Risk factors concerning COVID-19–induced morbidity and mortality include advanced age, an impaired immune system, cardiovascular or pulmonary diseases, obesity, diabetes mellitus, and cancer treated with chemotherapy. Here, we discuss the risk and impact of COVID-19 in patients with mastocytosis and mast cell activation syndromes. Because no published data are yet available, expert opinions are, by necessity, based on case experience and reports from patients. Although the overall risk to acquire the severe acute respiratory syndrome coronavirus 2 may not be elevated in mast cell disease, certain conditions may increase the risk of infected patients to develop severe COVID-19. These factors include certain comorbidities, mast cell activation–related events affecting the cardiovascular or bronchopulmonary system, and

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chemotherapy or immunosuppressive drugs. Therefore, such treatments should be carefully evaluated on a case-by-case basis during a COVID-19 infection. In contrast, other therapies, such as anti–mediator-type drugs, venom immunotherapy, or vitamin D, should be continued. Overall, patients with mast cell disorders should follow the general and local guidelines in the COVID-19 pandemic and advice from their medical provider. (J Allergy Clin Immunol 2020;146:300-6.)

Key words: *Mast cells, mastocytosis, tryptase, KIT D816V, coronavirus, COVID-19, SARS-CoV-2, mast cell activation syndrome*

Abbreviations used
CM: Cutaneous mastocytosis
COVID-19: Coronavirus disease 2019
HSCT: Hematopoietic stem cell transplantation
ISM: Indolent systemic mastocytosis
MC: Mast cell
MCAS: Mast cell activation syndrome
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2
SM: Systemic mastocytosis

Mast cells (MCs) are proinflammatory effector cells of the immune system.[1-3] Upon activation by an allergen, microbes (including viruses), or toxins, MCs release a number of proinflammatory substances and lipid mediators, thereby contributing to tissue inflammation and allergic reactions.[1-3] Mastocytosis is a group of neoplasms characterized by an uncontrolled expansion and accumulation of neoplastic MCs in various organs, including the skin, the bone marrow, and the gastrointestinal tract.[1,3-7] Mastocytosis is divided into cutaneous mastocytosis (CM) and systemic mastocytosis (SM).[4-7] Most patients with CM are children,[8] whereas adult patients are usually diagnosed with SM.[4-7] Most patients with SM carry an activating *KIT* mutation, typically D816V.[4-7,9] In a smaller subset of patients, an advanced form of the disease is diagnosed.[4-7] These patients are usually older. In addition, patients with mastocytosis may suffer from the consequences of a massive release of MC-derived mediators.[4-9] In severe cases, an MC activation syndrome (MCAS) may be diagnosed.[10-12]

The outbreak of coronavirus disease 2019 (COVID-19) in Wuhan (China)[13-19] and its pandemic spread with substantial morbidity and mortality in numerous countries have raised fears and concerns in patients with MC disorders and their physicians. These concerns relate to the questions as to whether patients with mastocytosis and/or MCAS have an increased risk to acquire severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and/or an increased risk to develop a more severe course of COVID-19, whether MC mediator–related symptoms are aggravated by the viral infection, and how treatment of MC diseases might affect the course of COVID-19. In addition, patients are concerned about potential side effects that could be provoked by antiviral agents. Because solid data to answer these questions are as yet scant, and based on the complexity of CM/SM and MCAS, there is thus a need for expert advice and recommendations.

In this article, we provide a first expert opinion–based estimate of the risk and a guide and proposal for the management of MC diseases during the COVID-19 pandemic, based on case observations, reports of patients, and recommendations provided in other, similar, disease entities. In addition, we discuss risk factors concerning transmission and fatality of COVID-19 and propose therapeutic strategies in mastocytosis and MCAS that may help reduce the overall impact.

SYMPTOMATOLOGY OF COVID-19 AND RISK FACTORS PREDISPOSING FOR SEVERE DISEASE IN THE GENERAL POPULATION

The clinical course of a SARS-CoV-2 infection ranges from asymptomatic or mild upper respiratory tract illness to severe viral COVID-19 pneumonia, leading to respiratory failure and death due to acute respiratory distress syndrome and multiorgan failure.[13-19] More than 80% of all patients with SARS-CoV-2 infection have a mild form of the disease.[13-19] However, about 15% to 20% of the patients need hospitalization, and up to 5% develop a life-threatening pneumonia.[13-19] The most commonly reported symptoms are fever (>70%) and dry cough (>60%) (Table I).[13-19] Other typical symptoms are sore throat, anosmia and agneusia, and a skin rash (Table I).[13-19] Dyspnea, tachycardia, and fatigue are usually recorded when the disease progresses, and in the advanced phase of COVID-19, patients often need intensive care with or without oxygen supply. Less frequently reported symptoms are increased sputum production, headache, urticaria, myalgia, arthralgia, abdominal discomfort, vomiting, and diarrhea. Abdominal symptoms and headache are also seen frequently in patients with MC disorders (Table I). However, other symptoms and findings typically recorded in mastocytosis and/or MCAS, such as pruritus, flushing, or hypotension, are not considered typical presenting symptoms of a COVID-19 infection (Table I).

Severe illness and death due to SARS-CoV-2 are more commonly documented in elderly patients and those with preexisting comorbidities.[13-19] Most patients with a fatal outcome are older than 60 years, and the most vulnerable population are those older than 80 years. About half the critically ill patients have preexisting comorbidities, including diabetes mellitus, arterial hypertension, obesity, cardiovascular diseases, chronic respiratory tract diseases, cancer requiring chemotherapy, or immunologic disorders.[13-22] In cancer patients, involvement of the lung and treatment with cytotoxic chemotherapy (with subsequent cytopenia) may add to the preexisting risk.[23-25] In other patients, continuous treatment with glucocorticoids and other immunosuppressive drugs may play an aggravating role, although this issue remains in discussion.[26]

So far, little is known about the risk of COVID-19 progression and COVID-19–related deaths in patients with indolent (chronic) or advanced (aggressive/acute) hematologic neoplasms.[27] In acute leukemia or highly aggressive lymphomas, the dilemma is that the underlying hematologic disease is by far a more dangerous enemy but is even more critical when intensive treatment is started during a bacterial or viral pneumonia. Therefore, cytoreductive treatment is often delayed or bypassed with less toxic chemotherapy in these patients, if possible.

For chronic (indolent) hematologic neoplasms no reports are as yet available. A general problem is that these patients are usually older, often have cardiovascular or pulmonary comorbidities, and frequently receive cytoreductive, immunosuppressive, and/or targeted drugs for their disease. Also, these patients are

TABLE I. Clinical symptoms typically associated with local or systemic MCA and comparison to symptoms of COVID-19

Symptom	Typically found in patients with MCA*	Typically found in patients with COVID-19†
Urticaria	+	−
Flushing	+	−
Pruritus	+	−
Measles-like rash	−	±
Angioedema	+	−
Nasal congestion	±	±
Wheezing	+	±
Anosmia	−	++
Cough	−	++
Dyspnea	±	++
Hoarseness	±	±
Sore throat	±	+
Throat swelling	±	±
Agneusia	−	++
Fever	−	±
Headache	±	±
Hypotensive episode	±	−
Tachycardia	±	±
Abdominal cramping	±	−
Diarrhea	±	±

MCA, Mast cell activation.
Score: ++, high specificity; +, moderate specificity; ±, low specificity; −, not considered to be indicative of MCA or COVID-19 when recoded as an individual symptom.
*In patients with MCA, the symptoms are typically episodic and recurrent and cannot be explained by other known disorders or conditions. In severe cases, an MCAS may be diagnosed.
†Most of the COVID-19–related symptoms are recorded only during the infection period, and are transient; however, chronic pulmonary damage with persistent dyspnea may be seen in rare, severe, COVID-19 cases.

sometimes hospitalized and/or handicapped. On the other hand, these patients are often isolated in social distancing and try to avoid infections as a general rule because of their health care provider's advice. In addition, some of the targeted drugs used to treat chronic myeloid neoplasms, such as the multikinase inhibitors, may exert an antiviral activity, although solid data in the corona context are not available.

Categories of mastocytosis and MCAS, clinical manifestations, and therapeutic options in various patient cohorts

Based on the World Health Organization classification, SM can be divided into indolent SM (ISM), smoldering SM, aggressive SM, SM with an associated hematologic neoplasm, and MC leukemia.[4-7,20,21] Although all age groups can be affected, advanced SM (aggressive SM, SM with an associated hematologic neoplasm, MC leukemia) occurs more frequently in older individuals (>60 years). Independent of age, the prognosis is grave in advanced SM.[4-7] Most of these patients require cytoreductive drugs and/or KIT-targeting tyrosine kinase inhibitors while others are treated with polychemotherapy and/or hematopoietic stem cell transplantation (HSCT).[20-22,28-32]

In most patients with mastocytosis, mediator-induced symptoms are recorded.[3-7,9-12] These symptoms may be mild, severe, or even life-threatening, especially when a concomitant IgE-dependent allergy is also present. In severe cases, MCAS may be diagnosed.[10-12] MCAS can also occur in the absence of mastocytosis.

By consensus, MCAS is classified into primary forms, where monoclonal MCs are found (with or without a known CM or SM), secondary forms where an IgE-dependent allergy is usually detected, and the idiopathic form of MCAS, where neither a clonal MC disease nor an underlying allergy or other underlying etiology is identified.[10-12] Patients with MCAS may present with episodic anaphylaxis. In these cases, MC involvement may be documented by an event-related, diagnostic increase in the serum tryptase level over the individual's baseline level.[10-12,33]

Patients with MCAS are usually treated with MC stabilizers, histamine receptor blockers, and/or glucocorticoids.[10-12] During an acute episode, epinephrine may be required. Patients with MCAS suffering from recurrent anaphylactic events due to IgE-dependent venom allergy are advised to undergo venom immunotherapy and/or are treated with anti-IgE antibodies (omalizumab) along with precautions to avoid the allergen.[34-36] The most dangerous form of MCAS is the mixed variant (primary plus secondary), where both clonal MC (±an MC neoplasm) and an IgE-dependent allergy are found.[36] These patients are at high risk to develop a fatal MCAS event.

THE IMMUNE SYSTEM IN MASTOCYTOSIS AND MCAS AND IMPLICATIONS FOR COVID-19

MCs are an integral component of the immune system and are thought to have an active role in various infectious diseases, including bacterial and viral infections as well as fungal and parasitic diseases.[2,37-42] In these conditions, MCs often become activated, and once activated, these cells can release a number of proinflammatory mediators. For example, viral infections, including SARS-CoV-2 infections, may manifest with acute urticaria. It is also worth noting that some of the MC-derived compounds are capable of degrading microbial toxins and/or are involved in the recruitment of other immune cells and phagocytes.[37-42] In viral diseases, MCs may also serve as a viral reservoir, as has been described for the HIV.[43] Overall, the possible role of MCs in coronavirus infections remains uncertain. Several observations suggest that MCs express coronavirus receptors such as CD26. MCs have also been discussed as possibly contributing to coronavirus-mediated inflammation in the lung.[44] Indeed, as mentioned before, MCs produce and release a number of proinflammatory mediators and cytokines in various organs.[1-3] It could also be that MCs play a protective role in an early phase of a coronavirus infection (because of the defensive functions MCs may provide), whereas in later stages when inflammation in the lung is a critical factor, MCs and their proinflammatory products (cytokines, histamine, others) may play a disease-aggravating role. However, definitive evidence is lacking and it remains unknown as to whether MCs play a defending or accelerating role in COVID-19. In mastocytosis, substantial lung infiltration by neoplastic MCs is rarely seen and no reports are available to suggest that patients with SM have a lower or higher risk to develop severe COVID-19.

Moreover, most patients with mastocytosis and MCAS appear to have normal cellular and humoral immune systems, unless these patients are treated with continuous glucocorticoids, other immunosuppressive drugs, or chemotherapy. Although no results from controlled observational studies are yet available, at present

there are no reports suggesting that rates of viral, bacterial, or fungal infections in patients with CM, nonadvanced SM, and MCAS are either higher or decreased compared with otherwise healthy individuals. In patients with advanced SM, the situation may be different. In this group, patients may have an impaired immune system and the risk for infections is sometimes higher, especially when these patients have or develop severe neutropenia and/or are treated with cytoreductive chemotherapeutics or stem cell transplantation. Also, in patients treated with higher doses of glucocorticoids on a long-term basis, immunosuppression may occur and the risk to develop a bacterial, viral, or fungal infection is higher.

In contrast, anti–mediator-type drugs, including antihistamines, antileukotrienes, cromones, and omalizumab (anti-IgE), have been in use for many years, and there is no reasonable evidence to suggest that these drugs exert immunosuppressive effects, even when used over several years. Therefore, patients on anti–mediator-based treatment should continue therapy, with recognition that potential drug-drug interactions may occur between antihistamines such as rupatadine and certain antiviral drugs, including lopinavir or ritonavir used as exploratory agents in the coronavirus context. It is also worth noting that antacids may decrease absorption of hydroxyl-chloroquine. Finally, it should be noted that there is no evidence to suggest that antiviral drugs, such as remdesivir, ritonavir, or others, induce or aggravate MC activation in patients with allergies, patients with mastocytosis, or patients with MCAS.

RISK OF ACQUISITION AND TRANSMISSION OF SARS-CoV-2 IN MASTOCYTOSIS AND MCAS

At the time of writing this report, no epidemiologic studies in patients with both mastocytosis and COVID-19 are available. Based on experience with CM/SM and MCAS in general, other hematologic neoplasms, and the biology of SARS-CoV-2, there is yet no reason to conclude that patients with mastocytosis or MCAS have a higher risk to acquire a SARS-CoV-2 infection. Rather, because many of these patients live in more or less coherent isolation and avoid public meetings and crowded places, their risk may thus be lower compared with the general population.

Once a SARS-CoV-2 infection has been diagnosed (and 2-4 days before it has been diagnosed) in a patient with CM/SM or MCAS, the risk of transmission to other individuals may well be the same as in the general population. The risk, however, may be increased within specific disease categories and be influenced by associated situations. For example, an older patient with comorbidities who needs continuous care and medical support because of SM or MCAS, or suffers from an aggressive form of mastocytosis, may transmit more readily, especially in hospitals, compared with a young asymptomatic (or slightly symptomatic) patient with indolent SM living in relative isolation who may not transmit the virus at all.

ADDITIONAL POTENTIAL RISK FACTORS FOR PROGRESSION TO SEVERE COVID-19 IN MASTOCYTOSIS AND MCAS

The risk of progression of COVID-19 to fatal pneumonia, with acute respiratory distress syndrome and cytokine storm, in patients with CM, SM, and MCAS remains unknown at the time of writing this article. In those with CM and ISM who are often children (CM) or younger adults (ISM), the risk may not be higher as in other patients with chronic hematologic neoplasms or healthy individuals. However, in patients with advanced SM (aggressive SM, SM with an associated hematologic neoplasm, or MC leukemia), the risk may be increased for several reasons. First, these are usually patients at an advanced age. Moreover, the number of MCs is higher in patients with SM compared with healthy individuals, so that more mediators and cytokines are released once these cells are activated, which could in turn promote the SARS-CoV-2–induced cytokine storm. Another evident reason is an impaired immune system that may be further suppressed by antineoplastic drugs (such as cladribine) or glucocorticoids. Patients with advanced SM are also at a higher risk concerning bacterial or fungal infections, especially when treated with intensive polychemotherapy and/or HSCT. However, there is no definitive evidence as of yet to suggest that patients with mastocytosis or MCAS are at a higher risk for developing severe COVID-19 because of treatment with targeted drugs, glucocorticosteroids, or cytotoxic drugs.

There are also additional risk factors and comorbidities (unrelated to CM/SM or MCAS) that may further increase the risk for developing severe COVID-19, such as arterial hypertension, pulmonary disease, or diabetes mellitus (Table II).[13-19]

Other possible risk factors include associated respiratory allergies, or hypersensitivity or intolerance against certain drug classes used during COVID-19. In particular, severe and uncontrolled allergic pulmonary inflammation may well represent a significant risk for more severe disease.

Recent data suggest that extra copy numbers in the alpha tryptase gene, also known as hereditary alpha tryptasemia (found in about 4%-6% of the general population), may predispose to severe allergic symptoms and severe mediator-related symptoms in MC diseases and atopic disorders.[45-47] Whether hereditary alpha tryptasemia also predisposes to a more severe form of COVID-19 in otherwise healthy people, individuals with allergies, or patients with CM, SM, or MCAS remains at present unknown.

Additional, less obvious factors may also have a role, including the nutritional status and vitamin deficiencies.[48-52] For example, obesity is frequently seen in patients with COVID-19 admitted to intensive care units. It has also been reported that vitamin D deficiency may predispose individuals to more frequent and more severe infections with a number of respiratory viruses, including coronaviruses, and the antiviral activity of vitamin D has been reported repeatedly.[48-52] However, to date, proof documenting a role for vitamin D in SARS-CoV-2 infections is lacking. Male sex, smoking habits, allergies affecting the respiratory tract, and additional lung diseases have also been implicated as risk factors for severe COVID-19 inflammation. Unfortunately, these factors may often act together (older smokers often are males, who often develop lung diseases). Whether these risk factors are also applicable to patients with CM/SM and MCAS remains unknown. However, it is worth noting that patients with CM, SM, and MCAS tend to be nonsmokers, of younger age, and when osteoporosis and/or vitamin D deficiency is diagnosed, they are treated with vitamin D. Furthermore, during systemic events, patients with CM/SM or MCAS more commonly experience hypotension rather than arterial hypertension.

TABLE II. Potential risk factors predisposing for severe COVID-19

Established/reported*:
Male sex
Advanced age (>60 y)
Arterial hypertension
Diabetes mellitus
Severe bronchial or pulmonary disease
Clinically overt cardiac diseases
Active advanced cancer (solid tumor)
Active advanced hematologic neoplasm
Hereditary or acquired immunodeficiency
Cytotoxic chemotherapy inducing cytopenia
Continuous immunosuppressive therapy
Severe uncontrolled allergic asthma
Not established but discussed†:
Nicotine consumption
No previous exposure to other coronaviruses
Initial viral load
Moderate or severe adipositas
Treatment with NSAID
Treatment with ACE inhibitors or ARB
Vitamin D deficiency
Vitamin C deficiency
Copper and/or zinc deficiency
Allergy—atopic disorders
Chronic pulmonary disease due to air pollution and smog
Bacterial superinfection in the lung
Chronic bronchitis
Pulmonary hypertension
Blood group A, B, or AB

ACE, Angiotensin-converting enzyme; *ARB*, angiotensin II type 1 receptor blocker; *NSAID*, nonsteroidal anti-inflammatory drug.
*Reported in peer-reviewed journal with solid data (any evidence level).
†Some of these factors may be underestimated and may also play a role in other models of viral infections.

RECOMMENDATIONS FOR MANAGEMENT OF PATIENTS WITH MASTOCYTOSIS AND MCAS DURING THE COVID-19 PANDEMIC

The basic recommendation for patients with mastocytosis and MCAS is to adhere to local and regional guidelines and recommendations in each country during the COVID-19 pandemic and to avoid as much as possible any situation that might be associated with an elevated risk of acquiring and/or distributing the infection. In addition, patients and doctors should avoid any situation that is associated with an increased risk of a severe course of COVID-19 (Table III). This includes, among other preventive measures, avoidance of immunosuppressive agents, heavily cytoreductive treatments, or lymphocyte-depleting drugs (eg, rituximab, alemtuzumab, or cladribine) if such treatment can be postponed or can be avoided (Table III). For example, for a young patient with *KIT* D816V+ advanced SM in need of cytoreduction, who is planned for chemotherapy and consecutive HSCT, it may be wise to postpone the chemotherapy + HSCT approach and to treat the disease with a KIT D816V blocker, such as midostaurin, ripretinib, or avapritinib and/or with hydroxyurea, depending on the COVID-19 infection rate in the area, aggressiveness of the diseases, and the possibility to isolate the patient (Table III). Of note, these drugs, including hydroxyurea, are not regarded as immunosuppressive agents unless high doses are applied over a longer time period. It is also worth noting that some of these agents, such as ripretinib or avapritinib, are currently only available within clinical trials and that these trials usually require frequent laboratory monitoring and hospital visits. To accommodate the isolation requirements, investigators and sponsors are now making adjustments to patients' protocols to allow less frequent visits, reflected in a reduction in evaluations and response assessments. Video visits and investigational drug shipments directly to patients are now also being permitted by oversight regulators, which may help avoid further viral spread and may help promote continuous treatment of all patients in clinical trials. In some patients with mastocytosis or MCAS suffering from acute anaphylaxis, and in some cases with advanced disease, systemic glucocorticoids may be prescribed. In those who are on high-dose glucocorticoids, it may be wise to switch to omalizumab (anti-IgE) therapy and to taper the corticosteroid dose at least until a potent drug or vaccination against COVID-19 is available.

Once the diagnosis of SARS-CoV-2 infection is established, the patients should be treated for COVID-19 on the basis of local guidelines and with recognition that the patients may react to antiviral drugs or anti-inflammatory drugs because these patients have a low but measurable risk to react against some drugs with hypotension and anaphylaxis. We also recommend that patients with mastocytosis or MCAS should be tested for COVID-19 quite early, and that those showing signs of progression or requiring antiviral therapies be hospitalized when a SARS-CoV-2 infection has been diagnosed to monitor the patients clinically for anaphylactic episodes and to better observe (or exclude) viral disease progression. In patients with asymptomatic SARS-CoV-2 infection, the best management is to keep the patients at home and to stay in contact with them to confirm the asymptomatic state and to relieve the patient's fears. All patients with mastocytosis should continue their anti–mediator-type drugs, bisphopshonates, and KIT-targeting kinase blocker (Table III). Other drugs should be administered with caution and on the basis of COVID-19 severity, aggressiveness of mastocytosis, and the overall situation in each case (Table III). If possible, glucocorticoids and cytoreductive drugs should be dose-reduced or postponed. However, there are no published data on the impact of such treatment during an active COVID-19 infection.

It should also be noted that there is no evidence for an increased prevalence of severe hypersensitivity reactions to antiviral drugs, such as remdesivir, other anti-infective agents, or nonsteroidal anti-inflammatory drugs used in the COVID-19 context in patients with mastocytosis or MCAS, although data from controlled clinical studies again are lacking. Thus, it cannot be ruled out with certainty that some of the antiviral drugs or other drugs used in patients with COVID-19 may provoke adverse reactions or aggravate disease in patients with mastocytosis or MCAS.

Finally, although there are a few sporadic reports of adverse reactions to vaccines (particularly live vaccines in patients with diffuse CM), most patients with mastocytosis tolerate vaccination well and the benefits of such vaccination may outweigh the risk (of complications) by far. Therefore, we also recommend that all patients with CM, SM, or MCAS undergo vaccination for SARS-CoV-2, once this vaccination treatment is available.

SUMMARY AND FUTURE PERSPECTIVES

Although solid data on which to base recommendations are not yet available, we herein attempt to contextualize the risk and first

TABLE III. Recommendations for management of distinct forms of mastocytosis during COVID-19

Category of mastocytosis	Recommendations for management during the COVID-19 pandemic
Nonadvanced mastocytosis	
CM	Continue to carry adrenaline autoinjector and emergency medications Continue H1 and H2 antihistamines Stop or reduce systemic glucocorticoids if possible If necessary, adjust systemic glucocorticoids to the phase of COVID-19* Continue vitamin D Postpone nonurgent medical visits for routine check-up
ISM	Continue to carry adrenaline autoinjector and emergency medications Continue H1 and H2 antihistamines Continue cromolyn sodium Stop or reduce systemic glucocorticoids if possible If necessary, adjust systemic glucocorticoids to the phase of COVID-19* Continue hymenoptera venom immunotherapy Continue omalizumab Continue vitamin D Continue bisphosphonates and/or denosumab Postpone nonurgent medical visits for routine check-up
Advanced mastocytosis	
Aggressive SM (ASM)	Continue midostaurin or other KIT-targeting tyrosine kinase inhibitors Stop or reduce systemic glucocorticoids if possible If necessary, adjust systemic glucocorticoids to the phase of COVID-19* Stop cladribine or other cytotoxic chemotherapy if possible Reduce or stop IFN-α if possible; stop IFN-α during active COVID-19 Reduce hydroxyurea doses, if possible, during active COVID-19 Continue H1 and H2 antihistamines Continue to carry adrenaline autoinjector and emergency medications Continue vitamin D Continue bisphosphonates and/or denosumab
SM with associated hematologic neoplasm	Continue midostaurin or other KIT-targeting tyrosine kinase inhibitors Stop or reduce systemic glucocorticoids if possible If necessary, adjust systemic glucocorticoids to the phase of COVID-19* Postpone cytotoxic chemotherapy, if possible, during active COVID-19 or switch to KIT-targeting drugs such as midostaurin Reduce or stop IFN-α, if possible, during active COVID-19 Reduce hydroxyurea doses, if possible, during active COVID-19 Continue H1 and H2 antihistamines Continue to carry adrenaline autoinjector and emergency medications Continue vitamin D Continue bisphosphonates and/or denosumab
Mast cell leukemia (MCL)	Continue midostaurin or other KIT-targeting tyrosine kinase inhibitors Stop or reduce systemic glucocorticoids if possible If necessary, adjust systemic glucocorticoids to the phase of COVID-19* Postpone cytotoxic chemotherapy if possible; stop cytotoxic chemotherapy during active COVID-19 Stop or postpone cladribine if possible Reduce or stop IFN-α, if possible, during active COVID-19 Reduce hydroxyurea doses, if possible, during active COVID-19 Continue H1 and H2 antihistamines Continue to carry adrenaline autoinjector and emergency medications Continue vitamin D Continue bisphosphonates and/or denosumab

*Depending on the phase of COVID-19, systemic glucocorticoids are either avoided (earlier phases) or even recommended (to block life-threatening lung inflammation).

recommendations concerning management of patients with mast cell disorders in the COVID-19 pandemic. We believe that the suggestions we offer today may be helpful in reducing fears and answering questions from our patients and their caregivers. As the natural history of the COVID-19 crisis unfolds, and more data become available regarding the consequences of infection in patients with MC disorders, more specific recommendations with higher levels of evidence will be generated.

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