



ORCHESTRA Delphi consensus: diagnostic and therapeutic management of SARS-CoV-2 infection in haematological patients

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ABSTRACT

Objectives: COVID-19 poses a significant risk to individuals with haematological malignancies (HM), as they are particularly vulnerable to severe disease progression and hospitalization due to their compromised immune systems. Many clinical decisions regarding the management of COVID-19 in these patients are yet to be fully addressed by existing guidelines, leading to variability in care.

Methods: A 28-item Delphi survey was developed to gather expert opinions on key areas of COVID-19 management in patients with HM, including risk stratification for severe COVID-19, diagnostic processes, and treatment decisions.

Results: Twenty-one experts with backgrounds in haematology and infectious diseases were enrolled. Of the 28 questions posed to the experts, consensus was reached on 15 statements.

Discussion: These Delphi consensus statements offer valuable suggestions with direct implications for clinical practice, addressing critical areas such as risk identification, appropriate diagnostic approaches, and tailored treatment strategies for patients with HM with COVID-19. The findings provide actionable

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Haematological malignancies
Risk of progression
Treatment

insights that may help fill gaps in current scientific literature, enhancing patient care and decision-making in this high-risk population. **Lorenzo Maria Canziani, *Clin Microbiol Infect* 2025;31:S26**
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Introduction

During 2022, the worldwide epidemiology, morbidity, and mortality of COVID-19 showed a favourable trend for public health compared with the previous years of the pandemic, with a reduction in the number of hospital admissions, intensive care unit (ICU) admissions, and mortality rates, as reported by WHO [1]. The main reasons for this change in epidemiology were the immunological coverage obtained with natural infection, the introduction of vaccines and monoclonal antibodies (MoAbs), used as early treatment but also in pre- and post-exposure prophylaxis, and the emergence of less virulent viral variants [2,3].

Despite the available preventive and therapeutic strategies, special attention is still needed for patients with immunocompromising conditions, and especially haematological malignancies (HM). Although COVID-19-related hospitalizations and deaths declined in this population in the last years [4–7], the risk of severe clinical manifestations is still higher than among the general population [8]. Vaccines show reduced immunogenicity because of acquired immunological deficiency [4,9,10], and MoAbs become obsolete with the emergence of new variants [11–15].

Prolonged viral shedding is another crucial aspect of SARS-CoV-2 infection in patients with HM, which may occur even in the absence of clinical symptoms [16,17], and can negatively impact the course of the underlying haematological disease [5,6,18].

In this complex and ever-changing scenario, and despite the available literature, a standardized approach for the prevention, diagnosis, and treatment of COVID-19 in patients with HM is lacking.

In the frame of the Horizon 2020 funded ORCHESTRA project ("Connecting European cohorts to increase common and effective response to SARS-CoV-2 Pandemic" <https://orchestra-cohort.eu/>) and specifically within the Work Package 4 (fragile population cohorts), a Delphi survey was conducted among selected experts in an endeavour to bridge these knowledge gaps. This structured and iterative approach, designed to achieve consensus among experts on complex issues, is precious when empirical evidence is limited [19]. The Delphi method has been successfully employed in various healthcare contexts, including managing haematological conditions and COVID-19 in the first phase of the pandemic [20].

Through the Delphi process, we leverage the collective expertise of haematologists and infectious disease (ID) specialists involved in managing patients with HM to address uncertainties surrounding COVID-19 management in this population. The aim of this study is to identify consensus on critical clinical issues, define shared statements, and ultimately provide physicians and policymakers worldwide with guidance to improve patient outcomes.

Methods

Study design and preparatory research

At the start of 2024, a 28-item online questionnaire was developed, reviewed, and piloted by a multidisciplinary group. This process was informed by a critical review of the existing literature, clinical experience, and anticipated gaps in guidelines and position papers. The introduction to the questionnaire included standard definitions from medical literature (see Supplementary Material).

The questionnaire was divided into three main domains: (a) the risk of progression to severe COVID-19; (b) screening and diagnostic processes; and (c) the management and treatment of patients with HM with asymptomatic or symptomatic SARS-CoV-2 infection. Relevant literature references were included to support the questionnaire items.

This study presents the statements reached through the survey and is structured according to the ACCORD (ACcurate CONsensus Reporting Document) reporting checklist for Delphi studies (Table S1) [21]. The study was not prospectively registered.

Selection of experts, recruitment process, and participation

Experts were initially invited to participate via the ORCHESTRA consortium. The invitation was later extended to the 'Infections in Haematology' Specialized Working Group of the European Hematology Association. Experts were required to have clinical expertise in haematology or ID within haematology. Experts were also invited to nominate other qualified professionals for participation. A target of 20 experts was set [19]. Patient advisory groups were not involved in the study.

The questionnaire was disseminated via a personalized and anonymized link through the REDCap platform [22], with technical assistance available to the experts if required. To ensure comprehensive input, experts were permitted to participate in the second or third round of the survey even if they had not responded to one of the previous rounds.

Delphi process and analysis

Three rounds of the Delphi process were conducted, during which the experts responded anonymously to the questions and had the opportunity to provide free-text comments. A six-point Likert scale was adopted to collect agreement (1—Strongly disagree, 2—Disagree, 3—Somewhat disagree, 4—Somewhat agree, 5—Agree, 6—Strongly agree).

At the end of each round, the responses were analysed. Total cumulative consensus was defined as the sum of percentages across two concordant and contiguous points of the Likert scale. Consensus was initially defined when total cumulative consensus reached at least 80% of the experts, but for an approximation based on the number of participants, consensus was redefined as agreement of at least 15 of the 19 expert respondents (79%) in the first and second rounds [23]. For assigning the strength of support, the six-point Likert scale was categorized into four tiers: strong disagreement (1—Strongly disagree, 2—Disagree); moderate disagreement (2—Disagree, 3—Somewhat disagree); moderate agreement (4—Somewhat agree, 5—Agree); strong agreement (5—Agree, 6—Strongly agree). Items were excluded from subsequent rounds once consensus was achieved. No other item was modified or removed during the process. In the second and third rounds, feedback was provided to the experts in both qualitative and quantitative forms. The frequency of scores and the associated comments was presented after each item.

Anonymity was maintained throughout the process, ensuring that neither the conductors of the survey nor the experts could identify individual responses. No data regarding the experts were

included in the questionnaire, and each round was analysed independently of the others. Study data were collected and managed using the REDCap electronic data capture tools [22].

Final statements were generated for each question that achieved consensus, accompanied by the strength of support (moderate or strong).

Ethical

This study was limited to expert feedback and did not involve research or data collection in human or animal subjects. As a result, Institutional Review Board approval was not required. All participants provided their consent and authorization to participate in the survey, understanding that their data would be used solely for scientific research.

Results

Twenty-one experts (8 female and 13 male) from seven European countries participated in the survey. Of these, 11 had a background in haematology and ten had a background in ID. The three rounds of the Delphi survey were conducted between August and September 2024. Nineteen experts participated in both the first and second rounds. During the first round, consensus was reached on five questions. In the second round, eight additional questions reached consensus. In the third round, 20 experts responded, and consensus was achieved on four more questions. All experts participated in at least one round of the survey. The list of consensus statements is provided in [Table 1](#), and the complete questionnaire is available in [Table S2](#).

Table 1
Overview of statements

Statement	Level of support	TCC (%)	Round
1 The risk of progression to severe COVID-19 is elevated in patients with haematological malignancies, due to the interplay of disease-specific and treatment-related factors, in comparison with the general population. Individual risk stratification should consider the specific malignancy type and the related treatment regimen	Strong	84	2
2 The risk of progression to severe COVID-19 is elevated in haematopoietic cell transplantation (HCT) recipients and chimeric antigen receptor T-cell (CAR-T cell) therapy-treated patients in comparison with other patients with HM. Individual risk stratification should consider previous vaccination status, the interval between cellular therapy and SARS-CoV-2 infection diagnosis, and the underlying HM's progression status	Moderate	90	2
3 Patients with HM who do not develop protective vaccine-induced serological response with an updated vaccination schedule should be considered at higher risk of progression to severe COVID-19	Moderate	79	2
4 In hospitalized patients with HM with asymptomatic or clinically recovered COVID-19, routine repetition of nucleic acid amplification test (NAAT) on nasopharyngeal swab (e.g. every 48–72 hours) could be used to guide release from infection prevention and control indications	Moderate	79	2
5 All patients with HM receiving immunosuppressive treatment and diagnosed with SARS-CoV-2 infection should be considered for early COVID-19 treatment (nirmatrelvir/ritonavir, molnupinavir, remdesivir, effective anti-spike monoclonal antibodies), irrespective of the presence of symptoms	Strong	80	3
6 All HCT recipients and CAR-T cell-treated patients receiving immunosuppressive treatment should receive early treatment for SARS-CoV-2 infection (nirmatrelvir/ritonavir, molnupinavir, remdesivir, effective anti-spike monoclonal antibodies), regardless of the presence of symptoms	Strong	79	1
7 After having completed a course of early antiviral treatment (nirmatrelvir/ritonavir, molnupinavir, remdesivir, effective anti-spike monoclonal antibodies), for all patients with HM exhibiting COVID-19 symptoms with ongoing viral replication (e.g. those with low CT values or a positive rapid antigen test), a longer course or additional doses of antiviral treatment can be considered	Moderate	79	1
8 In case of mild or moderate COVID-19, temporary discontinuation of treatment with anti-CD20 antibodies should be considered after a clinical risk/benefit ratio assessment	Moderate	79	2
9 In case of mild or moderate COVID-19, dose reduction should be considered for glucocorticoids with haematological indication after assessing the clinical risk/benefit ratio	Moderate	85	3
10 In case of asymptomatic COVID-19, the HCT induction should be delayed, according to the clinical risk/benefit ratio assessment	Moderate	85	3
11 In case of asymptomatic or mild COVID-19, ongoing chemotherapy for acute leukaemia should be continued after assessing the clinical risk/benefit ratio	Moderate	89	2
12 In case of asymptomatic or mild COVID-19 in patients undergoing chemotherapy for myeloproliferative disorders, chemotherapy should be continued after assessment of the clinical risk/benefit ratio	Moderate	83	2
13 In case of asymptomatic or mild COVID-19 disease in patients with acute leukaemia, myelodysplastic syndrome, blast phase of myeloproliferative neoplasm or chronic myeloid leukaemia, the decision to cease or modify standard-of-care treatment should be individualized, considering the risk of progression of the HM	Moderate	85	3
14 In case of severe COVID-19 diagnosed during treatment for HM, the ongoing chemotherapy should be modified or stopped until COVID-19 resolution			
• In patient with acute leukaemia	Strong	84	1
• In patient with myeloproliferative disorder	Strong	94	2
• In patient with myelodysplastic syndrome, blast phase of myeloproliferative neoplasm or chronic myeloid leukaemia	Moderate	79	1
15 For haematological patients who have recovered from COVID-19, the initiation or re-initiation of haematological syndrome-directed therapy should be considered 1 wk after achieving viral clearance (i.e. SARS-CoV-2 not detectable by NAAT testing in two consecutive nasopharyngeal swabs)	Strong	84	1

CT, cycle threshold; HM, haematological malignancies; TCC, total cumulative consensus; Round, round of consensus reached.

Risk of progression to severe COVID-19

Statement 1. The risk of progression to severe COVID-19 is elevated in patients with HM, due to the interplay of disease-specific and treatment-related factors, in comparison with the general population. Individual risk stratification should consider the specific malignancy type and the related treatment regimen (moderately supported)

Patients with HM represent a highly selected population, although there is a wide spectrum of diseases under the same umbrella. Overall, they are at higher risk of contracting SARS-CoV-2 infection than the general population (hazard ratio [HR] 1.19; 95% CI: 1.13–1.25) and patients with solid cancer (HR 1.23; 95% CI: 1.16–1.30). They also show a significantly greater risk of 14-day hospitalization (HR 4.61; 95% CI: 4.13–5.15) and 28-day mortality (HR 7.67; 95% CI: 6.57–8.96) compared with patients with solid cancer, although both the risk of infection and progression to severe COVID-19 decreased with the number of COVID-19 vaccine doses received [8].

When stratified by type of HM, in the pre-vaccination era, the risk of progression to severe forms of COVID-19 and death was higher for patients affected by acute myeloid leukaemia (AML), myelodysplastic syndrome [24], and chronic lymphocytic leukaemia (CCL) [25]. Even after the introduction of COVID-19 vaccination, the risk of severe forms of COVID-19 has been shown to be higher for patients with HM with lymphoproliferative diseases (CCL, non-Hodgkin lymphoma), and especially if treated with Bruton tyrosine-kinase inhibitors [26]. Moreover, anti-CD20 treatments have been shown to be linked to unfavourable outcomes in this group [7,27].

On the other hand, the risk of death due to COVID-19 is influenced by factors common to different HMs, such as the severity and progression status of the HM, recent chemotherapy or recent termination of chemotherapy (within 12 months), or the suspension of HM treatment due to SARS-CoV-2 infection. Moreover, risk factors for COVID-19 mortality in the general population, such as the severity of COVID-19, older age, and the presence of comorbidities, have also been described in patients with HM [24,26,28–30].

Statement 2. The risk of progression to severe COVID-19 is elevated in haematopoietic cell transplantation recipients and chimeric antigen receptor T-cell therapy-treated patients in comparison with other patients with HM. Individual risk stratification should consider previous vaccination status, the interval between cellular therapy and SARS-CoV-2 infection diagnosis, and the underlying HM's progression status (moderately supported)

In the period before the availability of COVID-19 vaccines (hereafter referred to as the pre-vaccine period), 39% of haematopoietic cell transplantation (HCT) recipients experienced severe clinical manifestations of COVID-19, whereas 16% experienced critical manifestations. An overall COVID-19 attributable mortality of 16% was reported in HCT recipients, with an increased mortality of 52% seen among those with severe COVID-19 [31,32]. Higher hospital admission rates and intubation rates were reported in the pre-vaccine period compared with the post-vaccine period (44% vs. 14%, and 12% vs. 2%, respectively). Conversely, mild COVID-19 was experienced by 86% of HCT recipients in the post-vaccine period, compared with 48% during the pre-vaccine period. The mortality rate also decreased for this group in the post-vaccine period, with a 12-month overall survival rate of 89%, compared with 73% in the pre-vaccine period [7,33].

Chimeric antigen receptor T-cell (CAR-T) recipients have shown similar results, with 80% of subjects needing hospitalization after COVID-19 diagnosis and approximately 50% requiring oxygen

supplementation, in the pre-vaccine period. The COVID-19 attributable mortality was 41% at that time [34]. The proportion of patients hospitalized during a COVID-19 episode and the proportion of patients needing ICU admission decreased in the post-vaccine period compared with the pre-vaccine period (74.3% vs. 43.4%, and 33.8% vs. 5.7%, respectively). Also, the COVID-19 attributable mortality decreased from 22.9% to 43.6% in the pre-vaccine period to 7.5% in the post-vaccine period. Furthermore, only 6.4% of fully vaccinated patients died [5].

These changes over time, represented by time-dependent risk factors such as not being fully vaccinated before SARS-CoV-2 infection (HR 5.64) and diagnosis of SARS-CoV-2 infection in the pre-vaccine period (HR 3.37), may be explained by the protective effect of vaccination and the decreasing virulence of new circulating viral variants [5].

Few studies compare CAR-T and allogeneic HCT patients. It seems that CAR-T patients show a higher risk of severe COVID-19, compared with allogeneic HCT (OR 7.7) [7].

Interestingly, risk factors for mortality in these two groups of patients were not related to the specific underlying HM disease, but rather to its level of activity and to the time between cellular therapy infusion and SARS-CoV-2 infection (i.e. less than 3 months for CAR-T and less than 1 year for HCT). This denotes the role of the immune system in COVID-19-related outcomes [31,32]. A possible explanation may rely on the fact that patients undergoing cellular therapy have both an impaired humoral response to COVID-19 vaccination, and are also severely T-cell depleted due to the lymphodepletion chemotherapy. This is particularly the case for CAR-T patients in the early months after cellular infusion [5].

The evidence is discordant on the roles of acute and chronic graft vs. host disease (GVHD), type of HCT, and type of conditioning regimen as risk factors for severe COVID-19 and mortality. Even if evidence is lacking, additional risk factors identified by experts include the conditioning regimen type, in particular the use of bispecific antibodies or anti-CD20 therapy, and the presence of hypoglobulinaemia. However, more studies are needed to estimate these risks.

Statement 3. Patients with HM who do not develop protective vaccine-induced serological response with an updated vaccination schedule should be considered at higher risk of progression to severe COVID-19 (moderately supported)

Higher anti-spike IgG titres correlate with high neutralizing antibody titres [9], with a lower risk of severe COVID-19 progression and COVID-19-related mortality [4]. Overall, the serological response of patients with HM to SARS-CoV-2 vaccines is sufficient after a full vaccination course and is even improved after booster doses [35]. However, after a full vaccination course, the specific serological response in this population is worse if compared with that of patients with solid cancer and the general population (64% vs. 96% vs. 98%, respectively) [10]. Different levels of serological response can be identified by stratifying patients on the type of haematological disease, with lower response levels seen in those with CCL (50%) or aggressive/indolent non-Hodgkin lymphoma (58% and 61%, respectively), when compared with those with Hodgkin lymphoma (91%), myeloproliferative neoplasms (83%) or multiple myeloma (76%). Antibody titres are also influenced by the status of the HM and its specific treatment, as shown by the low pooled response for patients on active chemotherapy (35%), anti-CD20 therapy during the previous year (15%), Bruton kinase inhibition (23%), venetoclax (26%), ruxolitinib (42%), and CAR-T (42%) [10,36]. On the contrary, the pooled response for allogeneic and autologous HCT is better (82% and 83%, respectively) [10,37].

However, some studies found that even if the serological response is low in patients with HM, COVID-19-related mortality improves after vaccination [24]: this lack of direct correlation between serological response and survival might be explained by the role of anti-SARS-CoV-2 cellular immunity [24,38,39]. Data explicitly examining the impact of T-cell responses in these patients are limited, which hinders a comprehensive assessment of their protective capacity against severe COVID-19. This knowledge gap emphasizes the importance of further research to understand how both humoral and cellular immune responses contribute to COVID-19 risk in patients with HM, which is essential for refining vaccination and treatment strategies in this high-risk group.

This statement does not consider known risk factors for COVID-19 progression, such as older age, male sex, smoking, obesity, multimorbidity, pre-existing lung disease, chronic kidney disease, diabetes, hypertension, and coronary heart disease.

Diagnosis

Statement 4. In hospitalized patients with HM with asymptomatic or clinically recovered COVID-19, routine repetition of nucleic acid amplification test on nasopharyngeal swab (e.g. every 48–72 hours) could be used to guide release from infection prevention and control indications (moderately supported)

SARS-CoV-2 nucleic acid amplification test (NAAT) tests are the reference standard for diagnosing SARS-CoV-2 infection in patients with HM inside and outside hospitals [40,41]; their performance should be evaluated for newly emerging variants.

SARS-CoV-2 genome quantification of cycle-thresholds values > 30–35 in an upper respiratory tract sample is associated with reduced risk of transmission and this value has been used as a clinical cut-off to diagnose a persistent infection, although its routine use for clinical decision-making is still not recommended [42,43].

Patients affected by HM could be persistently positive for SARS-CoV-2 even after specific treatment and complete recovery from symptomatic COVID-19. Prolonged virus shedding can last months, mainly affecting patients with B-cell lymphoma who have previously received immunotherapies such as anti-CD20 antibodies, and other B-cell-depleted patients [44].

Prolonged SARS-CoV-2 shedding has several therapeutic, preventive and epidemiological implications: (a) it may lead to inflammatory or fibrotic-like pulmonary changes, which are only partially reversible after the inhibition of viral replication; (b) it may defer chemotherapy or other procedures, including peripheral blood stem cell mobilization, bone marrow harvest, T-cell collection, and conditioning/lymphodepletion, which could facilitate progression of the underlying HM; (c) it may favour the selection of new viral variants; (d) it may place limitations on hospital/home management of the patient, in terms of infection prevention and control measures [11,45–47].

Therefore, hospitalized patients with HM with persistent COVID-19 symptoms should be monitored for persistent viral shedding with a PCR test every 48–72 hours. Testing could be performed less frequently in COVID-19 asymptomatic and clinically stable patients with HM, mainly to release infection prevention and control indications.

Treatment and management

Statement 5. All patients with HM receiving immunosuppressive treatment and diagnosed with SARS-CoV-2 infection should be considered for early COVID-19 treatment (nirmatrelvir/ritonavir, molnupinavir, remdesivir, effective anti-spike

MoAbs), irrespective of the presence of symptoms (strongly supported)

Early treatment with nirmatrelvir/ritonavir, molnupinavir, remdesivir, and MoAbs has been proven to be effective in reducing the risk of hospitalization in high-risk patients, including immunosuppressed patients [48–50]. However, the trials from which these results emerged suffered many limitations. First, the enrolled population mainly represented people with hypertension, obesity, or older age, whereas people with cancer represented less than 5% of the enrolled population. Moreover, the trials were conducted in unvaccinated individuals. There are considerable clinical limitations of the aforementioned drugs, including: the unavailability of molnupinavir in Europe; the current unavailability of any MoAbs against SARS-CoV-2 variant of concerns; the limited logistics of remdesivir as an intravenous drug; the potential interference of nirmatrelvir/ritonavir with the metabolism of other drugs as it is a strong CYP3A inhibitor [51]. Nevertheless, data regarding the use of early therapy in patients with HM have been derived from observational studies that showed reduced mortality for this population [2,52,53].

COVID-19-related risk of hospitalization and mortality remains higher in patients with HM than the general population (see Statements 1–3), with a higher expected benefit from treatment than the standard population. The results of the previously mentioned trials could therefore be generalized to patients with HM. Considering the intrinsic limitations of early therapy, the experts of this consensus survey agreed to define the risk of patients with HM receiving immunosuppressive therapy as worthy of early treatment for SARS-CoV-2 infection, when possible.

Statement 6. All HCT recipients and CAR-T cell-treated patients receiving immunosuppressive treatment should receive early treatment for SARS-CoV-2 infection (nirmatrelvir/ritonavir, molnupinavir, remdesivir, effective anti-spike MoAbs), regardless of the presence of symptoms (strongly supported)

The evidence regarding the efficacy of early treatment against SARS-CoV-2 infection in HCT recipients and CAR-T cell-treated is quite scarce.

In a retrospective study including 59 patients with HM/HCT with mild–moderate COVID-19 receiving SARS-CoV-2-specific MoAb between November 2020 and September 2021, 46 patients (78%) received MoAb as outpatients. Only two patients subsequently visited the Emergency Department for COVID-19 symptoms between 10 and 35 days after MoAb administration, with no hospitalization needed. Of the subjects in the outpatient group, 52% were in remission, 5 (11%) had GVHD, and 10 (22%) were receiving immunosuppressive medications. Among the 13 patients that received MoAb as inpatients, only three were admitted for COVID-19 symptom monitoring, the remaining 5 (38%) for neutropenic fever, 4 (31%) were already hospitalized for transplantation and cellular therapy, and one for acute kidney injury. Two hospitalized patients required mechanical ventilation, and three (23%) died within 60 days of MoAb administration. The three patients who died were on active chemotherapy and were not vaccinated [54].

A prospective observational study conducted in Spain during the Omicron wave collected data on 60 adults with high-risk HM treated with remdesivir after a median time of 2 days from diagnosis, of whom, 95% were vaccinated. All patients were hospitalized: 8 (13%) had asymptomatic COVID-19, 17 (28%) had pneumonia, and all the other presented cough, fever, and pharyngitis. Only 6.7% of patients required ICU admission. Within the first 60 days of SARS-CoV-2 infection, three (5%) patients died of non-COVID-19-related causes [55].

Guidelines recommend early treatment in patients with mild–moderate COVID-19 [40,41]. Without clear evidence, the same treatment strategy is proposed for asymptomatic infection in the most severely immunocompromised patients to reduce the risk

of progression and length of viral shedding [41]. Although SARS-CoV-2 vaccination profoundly reduced the risk of progression to severe COVID-19 and death in both HCT recipients and CAR-T-treated patients, these patients remain at risk of worse SARS-CoV-2 infection outcomes [5,7]. The short interval between cellular therapy infusion and the diagnosis of SARS-CoV-2 infection (less than 3 months for CAR-T and less than 1 year for HCT) is one of the most important risk factors for mortality in these populations [31,32].

In line with this evidence, the experts broadly agreed, after the first round of consultation, on the universal administration of COVID-19 early treatment (nirmatrelvir/ritonavir, molnupinavir, remdesivir, effective MoAbs) for all HCT recipients and CAR-T cell-treated patients undergoing immunosuppressive therapy, in particular in cases of recent cellular infusion or active GVHD [56,57].

Statement 7. After having completed a course of early antiviral treatment (nirmatrelvir/ritonavir, molnupinavir, remdesivir, effective anti-spike MoAbs), for all patients with HM exhibiting COVID-19 symptoms with ongoing viral replication (e.g. those with low CT values or a positive rapid antigen test), a longer course or additional doses of antiviral treatment can be considered (moderately supported)

After the first round of the survey, the experts agreed on the extension of SARS-CoV-2 antiviral therapy for patients with HM with ongoing viral replication following an initial antiviral course. Available reports of extended antiviral therapy suggest additional doses and sequential or combination treatment with multiple antivirals [16,58–61]. It was suggested that treatment decisions should be made on a case-by-case basis, with patients receiving anti-CD20 therapy identified as a primary group that could necessitate prolonged antiviral therapy. As no study has established this population's optimal drug or treatment duration, the experts strongly encourage exploring this knowledge gap with ad hoc designed studies.

Statement 8. In case of mild or moderate COVID-19, temporary discontinuation of treatment with anti-CD20 antibodies should be considered after a clinical risk/benefit ratio assessment (moderately supported)

Data collected before the availability of vaccines have shown that recent administration of anti-CD20 therapy is a risk factor for prolonged length of hospital stay and death in patients with lymphoma hospitalized for COVID-19 [62]. Many case reports have also described delayed clinical, microbiological, and/or radiological recovery after SARS-CoV-2 infection in patients on anti-CD20 therapy [47,63,64]. After introducing SARS-CoV-2 vaccines, doubts have been raised about their efficacy in patients with altered B-cell immunity. Specifically, in patients treated with anti-CD20 therapy, data have been published demonstrating seroconversion failure after COVID-19 vaccination [65,66].

Anti-CD20 therapy is associated with high COVID-19 mortality and persistent COVID-19 [67]. A study on patients with HM vaccinated against SARS-CoV-2 and treated with anti-CD20 therapy within 12 months of a breakthrough infection described that 47% of the patients required hospitalization, 67% required oxygen support, and 10% needed ventilation. COVID-19-related death was 17%, and among fatal COVID-19 cases, the median time from the most recent administration of anti-CD20 therapy to the onset of symptoms was 82 days. Among survivors, 31% presented respiratory symptoms 60 days after the COVID-19 diagnosis, and in 57% of cases, there were also radiological signs. After 60 days, 70% of patients had still positive nasopharyngeal swab in a SARS-CoV-2 PCR test, with 50% at 90 days [67].

Partially discordant results emerged from a cohort of adult patients with lymphoproliferative diseases, with only 21% vaccinated

with at least two doses. Severe COVID-19 reached 50% of cases, with high COVID-19-related mortality (69%), but anti-CD20 therapy was not significantly associated with severe COVID-19 nor did it influence the survival rate [26].

Considering the risk of prolonged SARS-CoV-2 infection and death in patients treated with anti-CD20 antibodies, as well as the risk of progression of the underlying disease in case of discontinuation, the decision to discontinue this treatment should be considered on a case-by-case basis.

Statement 9. In case of mild or moderate COVID-19, dose reduction should be considered for glucocorticoids with haematological indication after assessing the clinical risk/benefit ratio (moderately supported)

In the general population, the use of dexamethasone has shown reduced mortality in severe COVID-19 but for mild and moderate COVID-19, it has shown increased mortality, albeit not statistically significant [68]. Similar reports are available for patients with HM [69]. Patients with HM may receive glucocorticoids for different indications (i.e. GVHD). Decisions regarding systemic glucocorticoids must be individualized, depending on the dose and indication for the glucocorticoid. In the case of mild–moderate COVID-19, glucocorticoids may be temporarily discontinued. The recommendations for managing COVID-19 in patients with HM from the 2022 European Conference on Infections in Leukaemia nine underline that dexamethasone should not be used in the early treatment of mild–moderate COVID-19 [41].

Statement 10. In case of asymptomatic COVID-19, the HCT induction should be delayed, according to the clinical risk/benefit ratio assessment (moderately supported)

To reduce the risk of severe COVID-19 in SARS-CoV-2 positive but asymptomatic HCT/CAR-T candidates, the most recent guidelines for COVID-19 management in HCT and CAR-T recipients recommend deferring for at least 14 days the following procedures: peripheral blood stem cell mobilization, bone marrow harvest, T-cell collection, and conditioning [40]. If early infusion is desired, however, retesting at 5 to 7 days and then proceeding, if the SARS-CoV-2 test is negative, is an option, as long as the patient remains asymptomatic.

Given the known prolonged viral shedding in this population, a suggested alternative approach consists of deferring until 20 days from the first SARS-CoV-2 positive test and then deciding on a case-by-case basis; weighing the risks and benefits of delaying therapy and consequently risking underlying disease relapse and/or progression [41].

The experts converged through multiple rounds of Delphi to the same approach reported in [41]. The individual risk–benefit ratio should consider the severity of the underlying HM and its risk of progression, the specific conditioning regimen and the patient's overall history. Additionally, COVID-19 early treatment (nirmatrelvir/ritonavir, molnupinavir, remdesivir, MoAbs) can be considered to reduce the time of SARS-CoV-2 shedding.

Statement 11. In case of asymptomatic or mild COVID-19, ongoing chemotherapy for acute leukaemia should be continued after assessing the clinical risk/benefit ratio (moderately supported)

COVID-19-related mortality ranges from 20% to 52% in patients with acute leukaemia (AL), with higher rates in adult AML (40%) compared with adult acute lymphoblastic leukaemia (26%) [70].

In a cohort study that categorized treatment for AML with concurring COVID-19 as: finished before COVID-19, not delayed, delayed, or discontinued, treatment discontinuation was associated with higher mortality (HR 4.4, 95% CI: 2.3–8.4; $p < 0.001$), as opposed to treatment delay, which was found to be protective (HR 0.37, 95% CI: 0.15–0.89; $p 0.027$) [29]. In particular, the overall

mortality rate changed based on the chemotherapy indication, being higher for patients in induction (67.1%) or re-induction (77.7%) than for patients receiving consolidation (20%, $n = 10$) during the last month before COVID-19 ($p < 0.001$) [29].

These findings support the opinion of Delphi's expert group, which disagreed with delaying or discontinuing ongoing chemotherapy in patients with AL with asymptomatic SARS-CoV-2 infection or even mild COVID-19.

Because the mortality rate of patients with ongoing or recent (<1 month before COVID-19 diagnosis) AML treatment was significantly higher than that of patients receiving therapy until 3 months or less before the diagnosis COVID-19 ($p < 0.001$) [29], the decision to continue chemotherapy must take into account also the severity of the AL, the vaccination status of the patient and the timeliness in starting early COVID-19 therapy. Early therapy for COVID-19 should be instituted to mitigate the risk of severe COVID-19 progression.

Statement 12. In case of asymptomatic or mild COVID-19 in patients undergoing chemotherapy for myeloproliferative disorders, chemotherapy should be continued after assessment of the clinical risk/benefit ratio (moderately supported)

Myeloproliferative disorders primarily affect older individuals, with factors such as frailty, comorbidities, and age playing a critical role in predicting COVID-19-related mortality in this population [71]. One report identifies a neutrophil-to-lymphocyte ratio of four or higher as a significant predictor of hospitalization (OR: 7.04, $p < 0.001$) [72]. Additionally, active immunosuppressive treatment has been associated with an increased risk of hospitalization (OR: 2.19; $p < 0.001$) and mortality (HR: 2.14; $p < 0.001$) [71]. However, some studies suggest that JAK inhibitors, particularly baricitinib, may reduce the risk of death among patients with COVID-19 [73].

JAK inhibitors have been reported to reduce systemic inflammation caused by SARS-CoV-2 and mortality in hospitalized adults with COVID-19 [74]. Ruxolitinib discontinuation has been linked to worse outcomes in patients infected with SARS-CoV-2 [72]. Nonetheless, the broad immunosuppressive potential of JAK inhibitors, especially ruxolitinib, raises concerns, as prolonged exposure has been shown to limit both T-cell and humoral responses to mRNA vaccines [75].

In line with published guidelines [41], for patients with myeloproliferative disorders who develop asymptomatic or mild COVID-19, the experts suggested that the decision to continue chemotherapy should be based on a thorough assessment of the clinical risk/benefit ratio. Early therapy for COVID-19 should be instituted to mitigate the risk of COVID-19.

Statement 13. In case of asymptomatic or mild COVID-19 disease in patients with AL, myelodysplastic syndrome, blast phase of myeloproliferative neoplasm or chronic myeloid leukaemia, the decision to cease or modify standard-of-care treatment should be individualized, considering the risk of progression of the HM (moderately supported)

Individualized care is a crucial strategy in managing patients with asymptomatic or mild COVID-19 who have aggressive HM, such as AL, myelodysplastic syndrome and the blast phase of myeloproliferative neoplasms or chronic myeloid leukaemia. Clinicians must carefully balance two critical factors when deciding whether to adjust or continue treatment: the risk of malignancy progression vs. the potential harm of delaying or modifying active HM therapy [29]. These decisions should be made on a case-by-case basis, balancing the patient's disease status and the risk of COVID-19 progression [20,26,41]. Notably, before the introduction of vaccines, chemotherapy in the month before COVID-19 was observed as an essential risk factor for mortality. However, patients who experienced treatment delays also faced increased mortality [29]. Since the introduction of vaccination [24], mortality has

considerably decreased, altering the risk–benefit balance in this complex decision-making process. Early treatment (with nirmatrelvir/ritonavir, molnupinavir, remdesivir or effective MoAbs) should be administered to reduce the risk of COVID-19 progression and its complications.

Statement 14. In case of severe COVID-19 diagnosed during treatment for HM, the ongoing chemotherapy should be modified or stopped until COVID-19 resolution (moderately supported for myelodysplastic syndrome, blast phase of myeloproliferative disorders or chronic myeloid leukaemia; strongly supported for ALs, myeloproliferative disorders)

In line with other published expert opinions and guidelines [20,41], the experts of this study widely agreed on the necessity to modify or discontinue the standard-of-care treatment for various HM in case of severe COVID-19. Severe COVID-19 continues to be a major cause of short-term mortality in this population, with reported COVID-19-related mortality of about 5% [5], which remains a priority concern for healthcare providers. For patients with HM, where balancing treatment of the underlying malignancy with the risks posed by a severe viral infection is critical, experts emphasized the importance of adapting therapeutic strategies to focus on stabilizing and managing COVID-19 [20,41]. This consensus reflects the ongoing need to prioritize the immediate risk of life-threatening complications associated with severe COVID-19 while ensuring that adjustments to HM therapies are made with careful consideration of each patient's clinical status and the progression of the haematological condition [8,63].

Statement 15. For haematological patients who have recovered from COVID-19, the initiation or re-initiation of haematological syndrome-directed therapy should be considered 1 week after achieving viral clearance (i.e. SARS-CoV-2 not detectable by NAAT testing in two consecutive nasopharyngeal swabs). (strongly supported)

The experts agreed in the first round of the survey that the initiation or re-initiation of directed therapy for the baseline haematological malignancy should be considered only 1 week after achieving SARS-CoV-2 viral clearance. The two main components in this decision were the risk of recurrence of COVID-19 and the need for haematological therapy. Before the introduction of vaccines, the risk of recurrence of COVID-19 was prioritized because of the impaired immune response of individuals with HM and the reported high case–fatality ratio [5,8]. The introduction of preventive treatment (vaccination, MoAbs, protease inhibitors) and increasing experience in the management of COVID-19 shifted the focus for this decision from reducing the risk of COVID-19 to reducing the risk of HM [5]. Persistent COVID-19 can be identified in cases of failed viral clearance [76]. Moreover, some of this study's experts proposed starting active therapy just after the clinical resolution of symptoms in cases of mild/moderate disease and previous vaccination, which differs from other previously published expert opinions [20,41]. One notable exception to this strategy was regarding anti-CD20 therapy, which would need a 1-month waiting period after achieving viral clearance. Overall, the experts agreed that after achieving viral clearance (i.e. SARS-CoV-2 not detectable by NAAT testing in two consecutive nasopharyngeal swabs), haematological syndrome-directed therapy should be started after 1 week.

Questions that did not reach consensus

Out of 28 questions included in this survey, 11 did not reach consensus (Table S2). All three questions related to the risk of progression reached consensus. Six questions on screening and diagnosis, as well as five questions on treatment and management, failed to reach an agreement. In many cases, a bimodal distribution of responses prevented consensus from being established.

Regarding the diagnostic process and screening, experts did not reach a consensus on several key aspects. These included the need for routine screening of asymptomatic patients before initiating HM-directed treatment, the preferred diagnostic test (antigenic vs. nucleic acid amplification testing) for patients with HM with mild-to-moderate clinical symptoms lasting less than 5 days, and whether viral genomic sequencing should be performed for all patients with HM to identify the viral variant.

There was also no consensus on the use of viral genome quantification, both for distinguishing between re-infection and prolonged viral shedding and for guiding treatment decisions in patients with persistently positive NAAT results. Similarly, the benefit of serological testing 4 months after vaccination to assess immune response remained unclear.

In patients with HM with COVID-19 symptoms and ongoing viral replication, no consensus was reached on the use of combination therapy (i.e. remdesivir and effective MoAb) or the role of convalescent plasma. The use of effective MoAb for pre-exposure or post-exposure prophylaxis in patients with HM remains a subject of debate. Additionally, in cases of asymptomatic COVID-19, no consensus was reached for the start of induction for autologous HSCT.

Discussion

In this Delphi survey involving experts in haematology and ID, 15 consensus statements were developed, each with direct implications for the clinical management of patients with HM with COVID-19. These statements represent a collaborative synthesis of expert opinions, supported by the available literature, and offer practical guidance on key areas of patient care. In summary, the experts agreed on the higher risk of COVID-19 in patients with HM, the use of early therapy, the timing of HM-directed treatment in asymptomatic COVID-19, and the temporal suspension of HM-directed treatment in cases of severe COVID-19.

This study has several notable strengths, one being the heterogeneity of the participating experts in terms of clinical background and geographical representation. The multidisciplinary approach used ensured that the perspectives on managing patients with HM with COVID-19 were multi-faceted, comprehensive, and clinically relevant. The geographical diversity of the experts helped to reduce potential national biases, and contributed to more balanced and generalizable statements that are applicable across various healthcare systems and settings. Additionally, the study achieved a balanced representation of male and female experts, enhancing the inclusivity of viewpoints.

The robust Delphi methodology ensured a structured and iterative process, allowing for a refinement of consensus based on expert feedback. Crucially, the anonymity of participants was preserved throughout all rounds, minimizing the risk of peer influence and fostering independent contributions. These factors collectively strengthen the reliability and clinical relevance of the consensus statements generated by this study.

Despite the valuable insights gained from this study, limitations should be acknowledged. First, the survey did not include specific questions tailored to the context of low- and middle-income countries. This may limit the applicability of the statements in resource-limited settings. Second, patient advisory groups were not involved in the study. Although this limits the inclusion of patient-centred perspectives, focusing on expert consensus ensures that the recommendations remain firmly rooted in clinical expertise. In cases of uncertainty, assessing the clinical risk–benefit ratio was frequently cited as a guiding principle, and patient preferences should be consistently incorporated where applicable. Third, emerging treatment options for HM such as bispecific antibodies were not discussed within the questionnaire.

Finally, it is important to note that Delphi studies inherently produce expert opinion, and therefore represent a low level in the hierarchy of evidence [19]. That said, in areas where high-quality evidence is lacking, such as the rapidly evolving management of patients with HM with COVID-19, expert consensus can contribute to guiding practice until more robust evidence becomes available.

The Delphi method has been proven to be an efficient tool for rapidly generating expert consensus, particularly in producing timely recommendations for managing vulnerable populations, such as patients with HM, during crises like the ever-changing COVID-19 pandemic [20,41]. Its speed and flexibility make it especially valuable for pandemic preparedness, where urgent decision-making is required, and high-quality evidence may be limited. The ability to quickly synthesize expert opinion helps to provide crucial guidance for clinical practice in dynamic and rapidly evolving situations.

Author contributions

The authors confirm their contribution to the paper as follows: LMC, AMA, AS, JRB, and ET were responsible for study conception and design. LMC, AMA, AS, and ET were responsible for review of evidence. LMC was responsible for accessing and verifying data. LMC and AMA were responsible for analysis and interpretation of results. LMC, AMA, and JS-G were responsible for draft manuscript preparation. All authors reviewed the results and approved the final version of the manuscript.

Transparency declaration

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Data availability

Data will be available from the corresponding author on reasonable request.

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Appendix A. Supplementary data

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References

- Cheng L, Dhiyebi HA, Varia M, Atanas K, Srikanthan N, Hayat S, et al. Omicron COVID-19 case estimates based on previous SARS-CoV-2 wastewater load, regional municipality of Peel, Ontario, Canada. *Emerg Infect Dis* 2023;29:1580–8. <https://doi.org/10.3201/eid2908.221580>.
- Marchesi F, Salmanton-García J, Buquicchio C, Itri F, Besson C, Dávila-Valls J, et al. Passive pre-exposure immunization by tixagevimab/cilgavimab in patients with hematological malignancy and COVID-19: Matched-paired analysis in the EPICOVIDEHA registry. *J Hematol Oncol* 2023;16:32. <https://doi.org/10.1186/s13045-023-01423-7>.
- Salmanton-García J, Marchesi F, Farina F, Weinbergerová B, Itri F, Dávila-Valls J, et al. Decoding the historical tale: COVID-19 impact on haematological malignancy patients—EPICOVIDEHA insights from 2020 to 2022. *eClinicalMedicine* 2024;71:102553. <https://doi.org/10.1016/j.eclinm.2024.102553>.
- Best AF, Bowman M, Li J, Mishkin GE, Denicoff A, Shekfeh M, et al. COVID-19 severity by vaccination status in the NCI COVID-19 and cancer patients study (NCCAPS). *J Natl Cancer Inst* 2023;115:597–600. <https://doi.org/10.1093/jnci/djad015>.
- Spanjaart AM, Ljungman P, Tridello G, Schwartz J, Martínez-Cibrián N, Barba P, et al. Improved outcome of COVID-19 over time in patients treated with CAR T-cell therapy: Update of the European COVID-19 multicenter study on behalf of the European Society for Blood and Marrow Transplantation (EBMT) Infectious Diseases Working Party (IDWP) and the European Hematology Association (EHA) Lymphoma Group. *Leukemia* 2024;38:1985–91. <https://doi.org/10.1038/s41375-024-02336-1>.
- Nimgaonkar I, Yoke LH, Roychoudhury P, Flaherty PW, Oshima MU, Weixler A, et al. Outcomes in hematopoietic cell transplant and chimeric antigen receptor T-Cell therapy recipients with pre-cellular therapy SARS-CoV-2 infection. *Clin Infect Dis* 2024;79:86–95. <https://doi.org/10.1093/cid/ciae116>.
- Infante M-S, Nemirovsky D, Devlin S, DeWolf S, Tamari R, Dahi PB, et al. Outcomes and management of the SARS-CoV2 omicron variant in recipients of hematopoietic cell transplantation and chimeric antigen receptor T cell therapy. *Transplant Cell Ther* 2024;30. <https://doi.org/10.1016/j.jtct.2023.09.027>. 116.e1–12.
- Hosseini-Moghaddam SM, Shepherd FA, Swayze S, Kwong JC, Chan KKW. SARS-CoV-2 infection, hospitalization, and mortality in adults with and without cancer. *JAMA Netw Open* 2023;6:e2331617. <https://doi.org/10.1001/jamanetworkopen.2023.31617>.
- Hill JA, Martens MJ, Young J-AH, Bhavsar K, Kou J, Chen M, et al. SARS-CoV-2 vaccination in the first year after hematopoietic cell transplant or chimeric antigen receptor T-cell therapy: A prospective, multicenter, observational study. *Clin Infect Dis* 2024;79:542–54. <https://doi.org/10.1093/cid/ciae291>.
- Gagelmann N, Passamonti F, Wolschke C, Massoud R, Niederwieser C, Adjalé R, et al. Antibody response after vaccination against SARS-CoV-2 in adults with hematological malignancies: A systematic review and meta-analysis. *Haematologica* 2022;107:1840–9. <https://doi.org/10.3324/haematol.2021.280163>.
- Gupta A, Konnova A, Smet M, Berckell M, Savoldi A, Morra M, et al. Host immunological responses facilitate development of SARS-CoV-2 mutations in patients receiving monoclonal antibody treatments. *J Clin Invest* 2023;133:e166032. <https://doi.org/10.1172/JCI166032>.
- Huygens S, GeurtsvanKessel C, Gharbharan A, Bogers S, Worp N, Boter M, et al. Clinical and virological outcome of monoclonal antibody therapies across SARS-CoV-2 variants in 245 immunocompromised patients: A multicenter prospective cohort study. *Clin Infect Dis* 2024;78:1514–21. <https://doi.org/10.1093/cid/ciae026>.
- Imai M, Ito M, Kiso M, Yamayoshi S, Uraki R, Fukushi S, et al. Efficacy of antiviral agents against omicron subvariants BQ.1.1 and XBB. *N Engl J Med* 2023;388:89–91. <https://doi.org/10.1056/NEJMc2214302>.
- Wang Q, Iketani S, Li Z, Liu L, Guo Y, Huang Y, et al. Alarming antibody evasion properties of rising SARS-CoV-2 BQ and XBB subvariants. *Cell* 2023;186. <https://doi.org/10.1016/j.cell.2022.12.018>. 279–86.e8.
- Lee J, Naoe Y, Bang U, Nakagama Y, Saito A, Kido Y, et al. Neutralization sensitivity of SARS-CoV-2 omicron variants FL.1 and GE.1 by therapeutic antibodies and XBB sera. *Virology* 2024;595:110067. <https://doi.org/10.1016/j.virol.2024.110067>.
- Maruyama S, Wada D, Kanayama S, Shimazu H, Miyano Y, Inoue A, et al. The evaluation of risk factors for prolonged viral shedding during anti-SARS-CoV-2 monoclonal antibodies and long-term administration of antivirals in COVID-19 patients with B-cell lymphoma treated by anti-CD20 antibody. *BMC Infect Dis* 2024;24:715. <https://doi.org/10.1186/s12879-024-09631-3>.
- Ichikawa T, Tamura T, Takahata M, Ishio T, Ibata M, Kasahara I, et al. Prolonged shedding of viable SARS-CoV-2 in immunocompromised patients with haematological malignancies: A prospective study. *Br J Haematol* 2024;204:815–20. <https://doi.org/10.1111/bjh.19143>.
- Janssen M, Leo A, Wolf C, Stenzinger M, Bartschlagler M, Brandt J, et al. Treatment of chronic COVID-19 with convalescent/postvaccination plasma in patients with hematologic malignancies. *Int J Cancer* 2024;155:618–26. <https://doi.org/10.1002/ijc.34988>.
- Beiderbeck D, Frevel N, Von Der Gracht HA, Schmidt SL, Schweitzer VM. Preparing, conducting, and analyzing Delphi surveys: Cross-disciplinary practices, new directions, and advancements. *MethodsX* 2021;8:101401. <https://doi.org/10.1016/j.mex.2021.101401>.
- Buske C, Dreyling M, Alvarez-Larrán A, Apperley J, Arcaini L, Besson C, et al. Managing hematological cancer patients during the COVID-19 pandemic: An ESMO-EHA interdisciplinary expert consensus. *ESMO Open* 2022;7:100403. <https://doi.org/10.1016/j.esmoop.2022.100403>.
- Gattrell WT, Logullo P, Van Zuuren EJ, Price A, Hughes EL, Blazey P, et al. ACCORD (Accurate COnsensus reporting document): A reporting guideline for consensus methods in biomedicine developed via a modified Delphi. *PLOS Med* 2024;21:e1004326. <https://doi.org/10.1371/journal.pmed.1004326>.
- Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 2019;95:103208. <https://doi.org/10.1016/j.jbi.2019.103208>.
- Diamond IR, Grant RC, Feldman BM, Pencharz PB, Ling SC, Moore AM, et al. Defining consensus: A systematic review recommends methodologic criteria for reporting of Delphi studies. *J Clin Epidemiol* 2014;67:401–9. <https://doi.org/10.1016/j.jclinepi.2013.12.002>.
- Pagano L, Salmanton-García J, Marchesi F, Blennow O, Gomes Da Silva M, Glenthøj A, et al. Breakthrough COVID-19 in vaccinated patients with hematologic malignancies: Results from the EPICOVIDEHA survey. *Blood* 2022;140:2773–87. <https://doi.org/10.1182/blood.2022017257>.
- Blixt L, Bogdanovic G, Buggert M, Gao Y, Hober S, Healy K, et al. COVID-19 in patients with chronic lymphocytic leukemia: Clinical outcome and B- and T-cell immunity during 13 months in consecutive patients. *Leukemia* 2022;36:476–81. <https://doi.org/10.1038/s41375-021-01424-w>.
- Infante MS, Salmanton-García J, Fernández-Cruz A, Marchesi F, Jaksic O, Weinbergerová B, et al. B-cell malignancies treated with targeted drugs and SARS-CoV-2 infection: A European hematology association survey (EPICOVIDEHA). *Front Oncol* 2022;12:992137. <https://doi.org/10.3389/fonc.2022.992137>.

- [27] Jones J, Faruqi A, Sullivan J, Calabrese C, Calabrese L. COVID-19 outcomes in patients undergoing B cell depletion therapy and those with humoral immunodeficiency states: A scoping review. *Pathog Immun* 2021;6:76–103. <https://doi.org/10.20411/pai.v6i1.435>.
- [28] Castelo-Branco L, Tsourti Z, Gennatas S, Rogado J, Sekacheva M, Viñal D, et al. COVID-19 in patients with cancer: First report of the ESMO international, registry-based, cohort study (ESMO-CoCARE). *ESMO Open* 2022;7:100499. <https://doi.org/10.1016/j.esmooop.2022.100499>.
- [29] Marchesi F, Salmanton-García J, Emarah Z, Piukovics K, Nucci M, López-García A, et al. COVID-19 in adult acute myeloid leukemia patients: A long-term follow-up study from the European hematology association survey (EPICOVIDEHA). *Haematol* 2022;108:22–33. <https://doi.org/10.3324/haematol.2022.280847>.
- [30] Ehsan H, Britt A, Voorhees PM, Paul B, Bhutani M, Varga C, et al. Retrospective review of outcomes of multiple myeloma (MM) patients with COVID-19 infection (two-center study). *Clin Lymphoma Myeloma Leuk* 2023;23:273–8. <https://doi.org/10.1016/j.clml.2023.01.006>.
- [31] Busca A, Salmanton-García J, Marchesi F, Farina F, Seval GC, Van Doesum J, et al. Outcome of COVID-19 in allogeneic stem cell transplant recipients: Results from the EPICOVIDEHA registry. *Front Immunol* 2023;14:1125030. <https://doi.org/10.3389/fimmu.2023.1125030>.
- [32] Schaffrath J, Brummer C, Wolff D, Holtick U, Kröger N, Bornhäuser M, et al. High mortality of COVID-19 early after allogeneic stem cell transplantation: A retrospective multicenter analysis on behalf of the German cooperative transplant study group. *Transplant Cell Ther* 2022;28(337). <https://doi.org/10.1016/j.jctct.2022.03.010>. e1–10.
- [33] Ljungman P, Tridello G, Piñana JL, Ciceri F, Sengeloev H, Kulagin A, et al. Improved outcomes over time and higher mortality in CMV seropositive allogeneic stem cell transplantation patients with COVID-19; An infectious disease working party study from the European Society for Blood and Marrow Transplantation registry. *Front Immunol* 2023;14:1125824. <https://doi.org/10.3389/fimmu.2023.1125824>.
- [34] Spanjaart AM, Ljungman P, De La Camara R, Tridello G, Ortiz-Maldonado V, Urbano-Ispizua A, et al. Poor outcome of patients with COVID-19 after CAR T-cell therapy for B-cell malignancies: Results of a multicenter study on behalf of the European Society for Blood and Marrow Transplantation (EBMT) Infectious diseases working party and the European Hematology Association (EHA) lymphoma group. *Leukemia* 2021;35:3585–8. <https://doi.org/10.1038/s41375-021-01466-0>.
- [35] Giuliano A, Kuter B, Pilon-Thomas S, Whiting J, Mo Q, Leav B, et al. Safety and immunogenicity of a third dose of mRNA-1273 vaccine among cancer patients. *Cancer Commun (Lond)* 2023;43:749–64. <https://doi.org/10.1002/cac2.12453>.
- [36] Aleissa MM, Little JS, Davey S, Saucier A, Zhou G, Gonzalez-Bocco IH, et al. Severe acute respiratory syndrome coronavirus 2 vaccine immunogenicity among chimeric antigen receptor T cell therapy recipients. *Transplant Cell Ther* 2023;29(398). <https://doi.org/10.1016/j.jctct.2023.03.005>. e1–5.
- [37] Barkhordar M, Chahardouli B, Bigliari A, Ahmadvand M, Bahri T, Alaeddini F, et al. Three doses of a recombinant conjugated SARS-CoV-2 vaccine early after allogeneic hematopoietic stem cell transplantation: Predicting indicators of a high serologic response—A prospective, single-arm study. *Front Immunol* 2023;14:1169666. <https://doi.org/10.3389/fimmu.2023.1169666>.
- [38] Martín-Vicente M, Almansa R, Martínez I, Tedim AP, Bustamante E, Tamayo L, et al. Low anti-SARS-CoV-2 S antibody levels predict increased mortality and dissemination of viral components in the blood of critical COVID-19 patients. *J Intern Med* 2022;291:232–40. <https://doi.org/10.1111/joim.13386>.
- [39] Einarisdóttir S, Martner A, Waldenström J, Nicklasson M, Ringlander J, Arabpour M, et al. Deficiency of SARS-CoV-2 T-cell responses after vaccination in long-term allo-HSCT survivors translates into abated humoral immunity. *Blood Adv* 2022;6:2723–30. <https://doi.org/10.1182/bloodadvances.2021006937>.
- [40] Dioveri V, Boghdadly ZE, Shahid Z, Waghmare A, Abidi MZ, Pergam S, et al. Revised guidelines for coronavirus disease 19 management in hematopoietic cell transplantation and cellular therapy recipients (August 2022). *Transplant Cell Ther* 2022;28:810–21. <https://doi.org/10.1016/j.jctct.2022.09.002>.
- [41] Cesaro S, Mikulska M, Hirsch HH, Styczynski J, Meylan S, Cordonnier C, et al. Update of recommendations for the management of COVID-19 in patients with haematological malignancies, haematopoietic cell transplantation and CAR T therapy, from the 2022 European conference on infections in Leukaemia (ECIL 9). *Leukemia* 2023;37:1933–8. <https://doi.org/10.1038/s41375-023-01938-5>.
- [42] Santarelli IM, Manzella DJ, Gallo Vaulet L, Rodríguez Fermepín M, Fernández SI. Descriptive analysis of cycle threshold in patients with hematologic malignancies infected with SARS-CoV-2. *Rev Fac Cien Med Univ Nac Cordoba* 2023;80:47–51. <https://doi.org/10.31053/1853.0605.v80.n1.38171>.
- [43] Jefferson T, Spencer EA, Conly JM, Rosca EC, Maltoni S, Brassey J, et al. Viral cultures, cycle threshold values and viral load estimation for assessing SARS-CoV-2 infectiousness in haematopoietic stem cell and solid organ transplant patients: A systematic review. *J Hosp Infect* 2023;132:62–72. <https://doi.org/10.1016/j.jhin.2022.11.018>.
- [44] Götz V, Mathé P, Agarwal P, Hornuss D, Pfau S, Panning M, et al. Clinical phenotype and outcome of persistent SARS-CoV-2 replication in immunocompromised hosts: A retrospective observational study in the Omicron era. *Infection* 2024;52:923–33. <https://doi.org/10.1007/s15010-023-02138-0>.
- [45] Manuelpillai B, Zendt M, Chang-Rabley E, Ricotta EE, Stuck in pandemic uncertainty: A review of the persistent effects of COVID-19 infection in immune-deficient people. *Clin Microbiol Infect* 2024;30:1007–11. <https://doi.org/10.1016/j.cmi.2024.03.027>.
- [46] Scendoni R, Cingolani M. What do we know about pathological mechanism and pattern of lung injury related to SARS-CoV-2 Omicron variant? *Diagn Pathol* 2023;18:18. <https://doi.org/10.1186/s13000-023-01306-y>.
- [47] Choi B, Choudhary MC, Regan J, Sparks JA, Padera RF, Qiu X, et al. Persistence and evolution of SARS-CoV-2 in an immunocompromised host. *N Engl J Med* 2020;383:2291–3. <https://doi.org/10.1056/NEJM2031364>.
- [48] Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with Covid-19. *N Engl J Med* 2022;386:1397–408. <https://doi.org/10.1056/NEJMoa2118542>.
- [49] Jayk Bernal A, Gomes Da Silva MM, Musungu DB, Kovalchuk E, Gonzalez A, Delos Reyes V, et al. Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. *N Engl J Med* 2022;386:509–20. <https://doi.org/10.1056/NEJMoa2116044>.
- [50] Gottlieb RL, Vaca CE, Paredes R, Mera J, Webb BJ, Perez G, et al. Early remdesivir to prevent progression to severe Covid-19 in outpatients. *N Engl J Med* 2022;386:305–15. <https://doi.org/10.1056/NEJMoa2116846>.
- [51] Tiseo G, Barbieri C, Galfo V, Occhineri S, Matucci T, Almerigogna F, et al. Efficacy and safety of nirmatrelvir/ritonavir, molnupiravir, and remdesivir in a real-world cohort of outpatients with COVID-19 at high risk of progression: The PISA outpatient clinic experience. *Infect Dis Ther* 2023;12:257–71. <https://doi.org/10.1007/s40121-022-00729-2>.
- [52] Salmanton-García J, Marchesi F, Gomes da Silva M, Farina F, Dávila-Valls J, Bigin YM, et al. Nirmatrelvir/ritonavir in COVID-19 patients with haematological malignancies: A report from the EPICOVIDEHA registry. *ECLINIMed* 2023;58:101939. <https://doi.org/10.1016/j.eclinm.2023.101939>.
- [53] Salmanton-García J, Marchesi F, Koehler P, Weinbergerová B, Colović N, Falces-Romero I, et al. Molnupiravir compared to nirmatrelvir/ritonavir for COVID-19 in high-risk patients with haematological malignancy in Europe. A matched-paired analysis from the EPICOVIDEHA registry. *Int J Antimicrob Agents* 2023;62:106952. <https://doi.org/10.1016/j.ijantimicag.2023.106952>.
- [54] Jabr R, Khatri A, Anderson AD, Garcia LC, Viotti JB, Natori Y, et al. Early administration of SARS-CoV-2 monoclonal antibody reduces the risk of mortality in hematologic malignancy and hematopoietic cell transplant patients with COVID-19. *Transpl Infect Dis* 2023;25:e14006. <https://doi.org/10.1111/tid.14006>.
- [55] Aiello T-F, Puerta-Alcalde P, Chumbita M, Lopera C, Monzó P, Cortes A, et al. Current outcomes of SARS-CoV-2 Omicron variant infection in high-risk haematological patients treated early with antivirals. *J Antimicrob Chemother* 2023;78:1454–9. <https://doi.org/10.1093/jac/dkac105>.
- [56] Mushtaq MU, Shahzad M, Chaudhary SG, Luder M, Ahmed N, Abdelhakim H, et al. Impact of SARS-CoV-2 in hematopoietic stem cell transplantation and chimeric antigen receptor T cell therapy recipients. *Transplant Cell Ther* 2021;27(796):e1–7. <https://doi.org/10.1016/j.jctct.2021.07.005>.
- [57] Mirgh S, Gokarn A, Punatar S, Chichra A, Singh A, Rajendra A, et al. Clinical course of severe COVID19 treated with tocilizumab and antivirals post-allogeneic stem cell transplant with extensive chronic GVHD. *Transpl Infect Dis* 2021;23:e13576. <https://doi.org/10.1111/tid.13576>.
- [58] Liu C, Yoke LH, Bhattacharyya P, Cassaday RD, Cheng G-S, Escobar ZK, et al. Successful treatment of persistent symptomatic coronavirus disease 19 infection with extended-duration Nirmatrelvir-Ritonavir among outpatients with hematologic cancer. *Open Forum Infect Dis* 2023;10:ofad306. <https://doi.org/10.1093/ofid/ofad306>.
- [59] Rosen EA, Krantz EM, McCulloch DJ, Wilson MH, Tverdek F, Kassamali Escobar Z, et al. COVID-19 Outcomes among hematopoietic cell transplant and chimeric antigen receptor T-cell recipients in the era of SARS-CoV-2 omicron variants and COVID-19 therapeutics. *Transplant Cell Ther* 2024;30. <https://doi.org/10.1016/j.jctct.2024.08.010>. 1108.e1–11.
- [60] Longo BM, Venuti F, Gaviraghi A, Lupia T, Ranzani FA, Pepe A, et al. Sequential or combination treatments as rescue therapies in immunocompromised patients with persistent SARS-CoV-2 infection in the omicron era: A case series. *Antibiotics (Basel)* 2023;12:1460. <https://doi.org/10.3390/antibiotics12091460>.
- [61] Pasquini Z, Toschi A, Casadei B, Pellegrini C, D'Abromo A, Vita S, et al. Dual combined antiviral treatment with remdesivir and nirmatrelvir/ritonavir in patients with impaired humoral immunity and persistent SARS-CoV-2 infection. *Hematol Oncol* 2023;41:904–11. <https://doi.org/10.1002/hon.3206>.
- [62] Duléry R, Lamure S, Delord M, Di Blasi R, Chauchet A, Hueso T, et al. Prolonged in-hospital stay and higher mortality after Covid-19 among patients with non-Hodgkin lymphoma treated with B-cell depleting immunotherapy. *Am J Hematol* 2021;96:934–44. <https://doi.org/10.1002/ajh.26209>.
- [63] Piñana JL, Vazquez L, Heras I, Aiello TF, López-Corral L, Arroyo I, et al. Omicron SARS-CoV-2 infection management and outcomes in patients with hematologic disease and recipients of cell therapy. *Front Oncol* 2024;14:1389345. <https://doi.org/10.3389/fonc.2024.1389345>.
- [64] Kos I, Balensiefer B, Roth S, Ahlgrimm M, Sester M, Schmidt T, et al. Prolonged course of COVID-19-associated pneumonia in a B-cell depleted patient after rituximab. *Front Oncol* 2020;10:1578. <https://doi.org/10.3389/fonc.2020.01578>.
- [65] Ghione P, Gu JJ, Attwood K, Torka P, Goel S, Sundaram S, et al. Impaired humoral responses to COVID-19 vaccination in patients with lymphoma receiving B-cell-directed therapies. *Blood* 2021;138:811–4. <https://doi.org/10.1182/blood.2021012443>.
- [66] Passamonti F, Romano A, Salvini M, Merli F, Porta MGD, Bruna R, et al. COVID-19 elicits an impaired antibody response against SARS-CoV-2 in patients with

- haematological malignancies. *Br J Haematol* 2021;195:371–7. <https://doi.org/10.1111/bjh.17704>.
- [67] Feuth E, Nieminen V, Palomäki A, Ranti J, Sucksdorff M, Finnilä T, et al. Prolonged viral pneumonia and high mortality in COVID-19 patients on anti-CD20 monoclonal antibody therapy. *Eur J Clin Microbiol Infect Dis* 2024;43:723–34. <https://doi.org/10.1007/s10096-024-04776-0>.
- [68] The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 2021;384:693–704. <https://doi.org/10.1056/NEJMoa2021436>.
- [69] Aiello TF, Salmanton-García J, Marchesi F, Weinbergerova B, Glenthøj A, Van Praet J, et al. Dexamethasone treatment for COVID-19 is related to increased mortality in hematologic malignancy patients: Results from the EPICOVIDEHA registry. *Haematologica* 2024;109:2693–700. <https://doi.org/10.3324/haematol.2023.284678>.
- [70] Modemann F, Ghandili S, Schmiedel S, Weisel K, Bokemeyer C, Fiedler W. COVID-19 and adult acute leukemia: Our knowledge in progress. *Cancers (Basel)* 2022;14:3711. <https://doi.org/10.3390/cancers14153711>.
- [71] Marchetti M, Salmanton-García J, El-Ashwah S, Verga L, Itri F, Ráčil Z, et al. Outcomes of SARS-CoV-2 infection in Ph-neg chronic myeloproliferative neoplasms: Results from the EPICOVIDEHA registry. *Ther Adv Hematol* 2023;14:204062072311547. <https://doi.org/10.1177/20406207231154706>.
- [72] Barbui T, Carobbio A, Ghirardi A, Iurlo A, Sobas MA, Elli EM, et al. Determinants of early triage for hospitalization in myeloproliferative neoplasm (MPN) patients with COVID-19. *Am J Hematol* 2022;97:E470–3. <https://doi.org/10.1002/ajh.26732>.
- [73] Kow CS, Ramachandram DS, Hasan SS. Effect of JAK inhibitors on the risk of death in patients with moderate to severe COVID-19: A systematic review and meta-analysis of randomized controlled trials. *Can J Hosp Pharm* 2024;77:e3493. <https://doi.org/10.4212/cjhp.3493>.
- [74] Marconi VC, Ramanan AV, de Bono S, Kartman CE, Krishnan V, Liao R, et al. Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): A randomised, double-blind, parallel-group, placebo-controlled phase 3 trial. *Lancet Respir Med* 2021;9:1407–18. [https://doi.org/10.1016/S2213-2600\(21\)00331-3](https://doi.org/10.1016/S2213-2600(21)00331-3).
- [75] Palumbo GA, Cambria D, La Spina E, Duminuco A, Laneri A, Longo A, et al. Ruxolitinib treatment in myelofibrosis and polycythemia vera causes suboptimal humoral immune response following standard and booster vaccination with BNT162b2 mRNA COVID-19 vaccine. *Front Oncol* 2023;13:1117815. <https://doi.org/10.3389/fonc.2023.1117815>.
- [76] Machkovech HM, Hahn AM, Garonzik Wang J, Grubaugh ND, Halfmann PJ, Johnson MC, et al. Persistent SARS-CoV-2 infection: Significance and implications. *Lancet Infect Dis* 2024;24:e453–62. [https://doi.org/10.1016/S1473-3099\(23\)00815-0](https://doi.org/10.1016/S1473-3099(23)00815-0).