Case Report

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Is safety a concern when using blinatumomab therapy for COVID-19 infection?

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ABSTRACT

SARS-CoV-2 infection and serious sickness may be more likely to strike patients with acute lymphoblastic leukemia. For patients with refractory or relapsed B-cell precursor acute lymphoblastic leukemia, blinatumomab is the cornerstone of current treatment. We report on a patient who developed a positive SARS-CoV-2 test while receiving blinatumomab therapy for relapsed acute lymphoblastic leukemia. Regarding the choice of whether to keep these patients on blinatumomab treatment or to stop it altogether, there are no official guidelines. Given that SARS-CoV-2 is predicted to persist, more research on this topic is necessary.Adult patients with relapsed or refractory B-cell precursor ALL benefit from blinatumomab, a new bispecific monoclonal antibody that targets both CD3 and CD19 and increases overall survival with reduced toxicity. Hypogammaglobulinemia, a blunted B-cell response, and impaired B-cell-dependent T-cell activation are anticipated side effects of its use.A substantial risk for multiple infections, such as bloodstream and urinary tract infections, invasive fungal infections, cytomegalovirus-related diseases, pneumonia (viral, non-viral, Pneumocystis jirovecii), enteroviral encephalitis, and cytomegalovirus-related illnesses, was noted in the most recent consensus of the European Society of Clinical Microbiology and Infectious Diseases on the safety of targeted and biological therapies (2018).gradual multifocal brain damage. As of right now, blinatumomab and SARS-CoV-2 are not specifically advised against. Therefore, weighing the advantages and disadvantages of stopping therapy is important. In patients who test positive for SARS-CoV-2 while receiving treatment, should we stop blinatumomab therapy? Since there isn't a guideline for this situation, we talk about a patient with relapsed ALL who finished blinatu- momab therapy without experiencing any worsening of their clinical condition.

Case : In December 2020, a 47-year-old female patient with a medical history of arterial hypertension, hypothyroidism, and a minor SARS-CoV-2 infection was diagnosed with common precursor B ALL, with a high risk due to age; an identical donor with the same HLA was available. Her achieved a full response with negative minimum residual illness after receiving induction therapy in accordance with the PETHEMA ALL HR 2011 chemotherapeutic protocol. Flow cytometry in a control bone marrow aspiration revealed 9.3% of lymphoblasts, consistent with refractory disease, before to transplantation and right after consolidation therapy was finished. In May 2021, she was admitted to begin blinatumomab rescue therapy. Among the medications she was using at the time were losartan 50 mg BID, levo-thyroxine 100 µg QD, esomeprazole 40 mg QD, allopurinol 300 mg QD, and acyclovir 400 mg BID. SARS-CoV-2 vaccination was still not available. The entrance lab workup and physical examination were unremarkable. A negative result was obtained from a real-time polymerase chain reaction (RT-PCR) for SARS-CoV-2 in accordance with institutional practice. She did not exhibit symptoms of cytokine release syndrome, and glucocorticoids were not prescribed. Blinatumomab was started with an appropriate tolerance. Following a fortnight of in-hospital surveillance, the patient manifested with rhinorrhea and odynophagia without hypoxemia. An RT-PCR test for SARS-CoV-2 revealed a positive result, and the laboratory workup was within normal ranges. SARS-CoV-2-related mild reinfection was identified through a multidisciplinary assessment conducted by specialists in hematology and infectious diseases. The multidisciplinary board determined that she would benefit from continued blinatumomab treatment under close observation because of the patient's high risk of malignant development, her clinical stability, and the absence of data supporting a higher risk for severe illness. Following a 28-day induction therapy, the patient's upper respiratory symptoms disappeared and there was no further decline in their condition. Her hematological results were resistive to blinatumomab, thus the IDA-FLAG rescue chemotherapy treatment was initiated.

Discussion : In accordance with global protocols, our patient underwent screening for SARS-CoV-2 infection prior to blinatumomab induction, which commenced upon a negative test outcome. She showed signs of minor illness and turned positive during therapy. A hyperinflammatory condition referred to as "cytokine storm" has been identified as a contributing factor to severe disease in COVID-19. The usage of blinatumomab has been linked to a related condition called "cytokine release syndrome" (CRS). A CRS episode was

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reported by 16% of participants in the blinatumomab arm of the pivotal research.4. Thus, a potential risk factor for an increased chance of CRS in those who have previously been exposed to SARS-CoV-2 has been proposed.Twelve In order to lower the risk of CRS, high-dose dexamethasone is therefore regarded as first-line therapy in cases of CRS and as a preventative measure before starting blinatumomab medication. The use of dexamethasone for COVID-19 is supported by evidence in this line.13 However, as our patient was not given glucocorticoids, their protective benefits during an active infection were not linked to clinical stability. Moreover, we could not completely rule out the possibility that the absence of a CRS incident was due to a lack of reaction to blinatumomab.

We have seen from our experience that patients who do not have CRS typically do not go into remission. Real-world studies ought to investigate this clinical experience-derived understanding. Is blinatumomab a safe medication to take while sick with SARS-CoV-2? Growing data points to a greater chance of serious disease linked to COVID-19 in patients receiving rituximab treatment.Eleven Data, however, are sparse about the detrimental effects of other B-cell-depleting treatments, such as blinatumomab. As a result of its mode of action, circulating CD-19+ B-cells and bone marrow depletion over time should result in a decrease in immunoglobulin concentration.14. Present data, however, indicates that only 6% of individuals exhibit overt hypogammaglobulinemia.4. To speculate that our patient's lack of a severe sickness was related to a potentially safer blinatumomab risk profile would be audacious.Since neutralizing antibodies are linked to a decreased probability of illness symptoms, we hypothesise that prior exposure to SARS-CoV-2 provided natural immunity.15. Due to our patient's resistance to blinatumomab therapy, there would have been insufficient depletion of immune-globulin-producing cells; this phenomena has been previously observed in non-respondents.14. Furthermore, the memory T-cell response against SARS-CoV-2 may have also survived.

Conclusion : Blinatumomab is the cornerstone of current treatment for patients with refractory or relapsed B-cell precursor ALL. If treatment is delayed, these people have a significant chance of the condition worsening and having unfavorable outcomes. Patients who test positive for SARS-CoV-2 during therapy should therefore be evaluated individually when deciding whether to continue, stop, or postpone blinatumomab treatment; collaborative and informed decision-making is encouraged. Since SARS-CoV-2 is anticipated to persist, more research examining this matter is necessary.

KeyWords : Blinatumomab, precursor cell lymphoblastic leukemia-lymphoma, COVID-19, SARS-CoV-2

INTRODUCTION

Individuals diagnosed with hematological malignancies are at a higher risk of contracting SARS-CoV-2 infection1 and developing a severe disease linked to COVID-19.2. Due to immunosuppression secondary to the disease (low immunoglobulin levels, myelosuppression) and its treatment (steroid exposure, impaired B-cell response, pulmonary, cardiac, or renal toxicities), patients with acute lymphoblastic leukemia (ALL) may be especially vulnerable.Reduced intensity regimens and switching to outpatient settings for therapeutic infusion are two of the many options that have been proposed to lower the rate of infection and serious sickness. The decision-making process to delay, withhold, limit, or continue therapy is therefore governed by the particular circumstances of each patient.

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