Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Pending additional data, we would highly recommend vaccination for family and friendship circles, to provide an indirect protection against COVID-19 to this population.

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Plitidepsin for the management of a cancer patient infected with SARS-CoV-2 while receiving chemotherapy

Plitidepsin is a cyclic peptide that inhibits the host protein elongation factor alpha 1 (EF1A), thus blocking viral replication. A hospitalized patient with stage IIIB gastric signet ring cell carcinoma and multiple comorbidities developed COVID-19 shortly after receiving his first chemotherapy course. He was treated with plitidepsin on a compassionate use basis. The patient showed a substantial acute reduction in viral load 4 days after initiating plitidepsin treatment and was negative for SARS-CoV-2 by day 14. Therapy was well tolerated, and no COVID-19-related complications were observed. The patient was discharged 18 days after plitidepsin treatment, having received a full second course of chemotherapy, with only a 1-week delay from the planned schedule.

Patients with cancer who are also infected with SARS-CoV-2 have a poor prognosis and increased risk of all-cause mortality.1-3 Furthermore, cancer treatments are almost always withheld from patients with COVID-19, leading to an increased risk of tumor-related morbidities, and potential onset of progressive disease in the absence of therapy.

Recently, a study with plitidepsin in adults with SARS-CoV-2 infection and who requiring hospital admission assessed that the discharge rates by days 8 and 15 after the start of plitidepsin were 56.8% and 81.8%, respectively.4 Likewise, a mean −4.2 log10 reduction in viral load from baseline was attained by day 15.

The antiviral mechanism of action of plitidepsin is mediated through inhibition of the host protein EF1A.5 Notably, the nucleocapsid protein of SARS-CoV-2 has been shown to interact directly with EF1A and is essential for viral replication as demonstrated by a significant reduction in viral replication capability following EF1A knockdown.

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Grounded on our own experience in the aforementioned clinical trial, we requested authorization for the use of plitidepsin for this patient on a compassionate use approved by the Spanish Agency for Medicinal Products (AEMPS) (AUT334100148189/21). PharmaMar provided the study drug as well as operational and regulatory support. The patient signed informed consent for treatment and before manuscript preparation.

This hospitalized patient with stage IIIB gastric signet ring cell carcinoma and multiple comorbidities developed COVID-19 shortly after receiving his first chemotherapy course. He was treated with plitidepsin on a compassionate use basis. The patient showed a substantial acute reduction in viral load 4 and 7 days after initiating plitidepsin treatment and was negative for SARS-CoV-2 by day 9 after therapy (Figure 1). The patient was discharged 18 days after plitidepsin treatment, having received a full second course of chemotherapy with only a 1-week delay from the planned schedule (full description in Supplementary Material, available at https://doi.org/10.1016/j.annonc.2021.07.003).

**DISCUSSION**

In this report, we present our experience using a potential antiviral, plitidepsin, as rescue therapy for SARS-CoV-2 infection in an adult patient with stage IIIB gastric cancer. To our knowledge, this is the first evidence of an acute, pharmacologically-induced, negative SARS-CoV-2 conversion in a patient with cancer, possibly preventing the potential onset of life-threatening Covid-19 pneumonia. Both of these outcomes allowed the patient to quickly resume his planned anticancer therapy. All three cycles of FOLFOX-4 were well tolerated by the patient, with no signs of bone marrow or organ toxicities. Importantly, the dosing and schedule of plitidepsin used here (2.5 mg once daily for 3 days) did not induce any safety signals that would interfere with anticancer therapy. The estimated terminal half-life of plitidepsin is a
maximum of 144 h (6 days); given that a FOLFOX-4 cycle was administered beyond this period of time suggests that any drug interactions would be improbable.

This compassionate use case study has obvious limitations in that it only describes one patient who also had a rapidly progressive underlying disease. Nevertheless, given the patient’s poor prognosis at the time of infection, the rapid, positive outcomes observed here are unlikely to be the result of spontaneous disease resolution in a patient with advanced gastric cancer.

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Severe COVID-19 in patients with hematological cancers presenting with viremia

The coronavirus disease (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), poses a danger to the health of populations around the world. Cancer is one of the comorbidities identified as being at risk of developing severe COVID-19.1 Among cancer patients, those with hematological cancers are at particularly high risk of severe disease or death.2,4 The reasons for developing severe COVID-19 in patients with hematological cancers, however, remain poorly understood. Here, we investigate clinical factors associated with higher risk for severe COVID-19 in patients with hematological cancers.

Characteristics of all patients with hematological cancers hospitalized for COVID-19 at Gustave Roussy in France from 20 March 2020 to 17 November 2020 were analyzed. Overall, 51 adult patients with lymphoma (n = 26; 51%), acute leukemia (n = 15; 29%), myeloma (n = 9; 18%) or other type of hematological cancer (n = 1; 2%) were included. The clinical and biological characteristics at day 1 of hospital admission are shown in Supplementary Table S1, available at https://doi.org/10.1016/j.annonc.2021.07.002.

During hospitalization, 24 (47%) of the 51 patients had progressed to severe COVID-19 as assessed by the 10-points World Health Organization (WHO) scale.5 At day 1 of hospitalization, patients who progressed to severe COVID-19 were characterized by significantly lower γ-globulin levels in their serum (P = 0.0312) and tended to have more advanced age (64.7 versus 57.6 years; P = 0.0503). Lymphopenia was not significantly associated with increased risk of developing severe COVID-19 (P = 0.1006) (Supplementary Table S1, available at https://doi.org/10.1016/j.annonc.2021.07.002).

By linear logistic regression, hypogammaglobulinemia remained the most significant factor associated with progression to severe COVID-19 (Supplementary Table S2, available at https://doi.org/10.1016/j.annonc.2021.07.002). The severity of COVID-19 correlated negatively with serum