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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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.

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. Among cancer patients, those with hematological cancers are at particularly high risk of severe disease or death. 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. 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

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Pearsom method$^*$ reveals the linear relationship between the two variables. The severity of COVID-19 evaluated by World Health Organization (WHO) score, as emphasized by the Pearson method$^*$, shows the clinical and biological parameters associated with viremia in patients with hematological malignancies. Viremia was detected by SARS-CoV-2 RT-PCR on blood (as indicated in the methods appendix) at day 1 of hospitalization. Overall, 21 patients were investigated for viremia, 10 were positive and 11 were negative. For each factor, the median value calculated over the entire population ($N = 51$ patients) was used to determine the cut-off for each variable in subgroup. The relative risk and its 95% confidence interval (CI) as well as the $P$ value for the interaction, calculated by Fisher’s exact test, are shown for each parameter in the table. Gray bars in the figure indicate 95% CI.

**Figure 1.** Main laboratory parameters in patients hospitalized for coronavirus disease (COVID-19) and having hematological cancers.

(A) Correlation matrix between the quantitative variables observed in patients included in the study. The correlation matrix computed 14 numeric variables using the statistical Pearson method ($^*$P value for interaction <0.05). A positive correlation between two variables was illustrated by a blue color, whereas a negative correlation was in red. A thin ellipse meant that the relationship between the two variables was linear. The severity of COVID-19 evaluated by World Health Organization (WHO) score, as emphasized by the Pearson method$^*$, shows the clinical and biological parameters associated with viremia in patients with hematological malignancies. Viremia was detected by SARS-CoV-2 RT-PCR on blood (as indicated in the methods appendix) at day 1 of hospitalization. Overall, 21 patients were investigated for viremia, 10 were positive and 11 were negative. For each factor, the median value calculated over the entire population ($N = 51$ patients) was used to determine the cut-off for each variable in subgroup. The relative risk and its 95% confidence interval (CI) as well as the $P$ value for the interaction, calculated by Fisher’s exact test, are shown for each parameter in the table. Gray bars in the figure indicate 95% CI.

**Figure 2.** SARS-CoV-2 cycle threshold (Ct) by nasopharyngeal RT PCR.

(B) The comparison method was extra sum-of-squares F test and the $P$ value was 0.05. The curves representing SARS-CoV-2 RT-PCR for each data set were different with $P$ value for interaction, calculated by Fisher’s exact test, are shown for each parameter in the table. Gray bars in the figure indicate 95% CI. ANC, absolute neutrophil count; BMI, body mass index; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase; NA, not available; naso., nasopharyngeal; RT-PCR, reverse-transcriptase PCR; SARS-CoV-2, severe acute respiratory syndrome coronavirus; WHO, World Health Organization.
γ-globulins by the correlation Pearson statistics method \( r = -0.43; P = 0.0018 \) (Figure 1A). The intensity of viral replication, studied by kinetics of cycles threshold (Ct) of SARS-CoV-2 RT-PCR by nasopharyngeal swabs, was higher in patients with hypogammaglobulinemia \( \leq 6 \text{g/l} \) (\( P = 0.0033 \)) (Figure 1B). The duration of carrier status of the SARS-CoV-2 virus by SARS-CoV-2 RT-PCR in nasopharyngeal swabs tended to be prolonged in severe COVID-19 patients \([\text{range 16-101} \text{ days versus 27 (range 2-143) days in mild to moderate COVID-19 patients (} P = 0.1750)]\) (Supplementary Table S3, available at https://doi.org/10.1016/j.annonc.2021.07.002). This led to the hypothesis that in patients with hematological cancers, spread of the SARS-CoV-2 virus related to humoral immunosuppression, rather than cytokine storm, could drive the COVID-19 severity. To address this hypothesis we retrospectively assessed SARS-CoV-2 viremia in 21 patients by RT-PCR in whole blood.

Ten out of 21 patients tested had detectable viremia (48%) at day 1 of hospitalization. Viremia was associated with a relative risk of progression to severe COVID-19 and COVID-19 death of 5.33 [95% confidence interval (CI) 1.47-19.30; \( P = 0.0019 \)] and 2.83 (95% CI 1.49-5.39; \( P = 0.0351 \)), respectively (Figure 1C).

We compared the SARS-CoV-2 viremia in patients hospitalized for COVID-19 on the day of admission to hospital in patients with hematological cancers versus a control population with solid tumors. Viremia was more often positive in patients with hematologic cancer as compared to patients with solid tumors (47.6% versus 18.2%; \( P = 0.0099 \)) (Supplementary Figure S1, available at https://doi.org/10.1016/j.annonc.2021.07.002).

The main limitation in the interpretation of our results is the focus on a reduced population size with hematologic malignancies. Our results suggest hypogammaglobulinemia and SARS-CoV-2 viremia were two relevant determinants of COVID-19 severity in patients with hematological cancers. Viremia was recently reported as correlating with disease severity. Our findings suggest that in patients with hematological cancers, the coronavirus infection itself, rather than a cytokine storm, leads to severe and lethal COVID-19. We suggest that humoral immunocompromised patients may be considered as a specific population to manage for COVID-19. Thus, corticosteroids or anticytokine drugs such as anti-interleukin 6 receptor therapies may worsen immunosuppression and should probably be used with caution in such patients. Therapeutics supporting immunity against SARS-CoV-2, such as hyperimmune convalescent plasma, deserve to be specifically investigated for immunocompromised patients.

J. M. Michot1*, T. Hueso1, N. Ibrahimii, F. Pomerret3, C. Willekens1, E. Colomba1, S. Francis1, A. Baye1, P. H. Courrède3, M. Merad1, S. Foulon3, L. Albige3, B. Gachot6, F. Barlesi7,8, J. C. Soria7, V. Ribrag1 & F. Griscelli4

1Departments of Hematology; 2Biostatistics; 3Cancer Medicine; 4Biopathology, Gustave Roussy, Paris-Saclay University, Paris; 5Biostatistics, Gustave Roussy, Paris-Saclay University, Paris; 6Department of Interdisciplinary Cancer Course, Gustave Roussy, Paris-Saclay University, Paris; 7Oncological Department, Gustave Roussy, Paris-Saclay University, Paris; 8Oncological Department, Aix Marseille University, CNRS, INSERM, CRCM, Marseille, France (*E-mail: jean-marie.michot@gustaveroussy.fr).

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Updated treatment recommendations for newly diagnosed epithelial ovarian carcinoma from the ESMO Clinical Practice Guidelines

The following ESMO Clinical Practice Guideline has been recently updated with new treatment recommendations:

**Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.**

**UPDATE**

View the ESMO eUpdate here: [https://www.esmo.org/guidelines/gynaecological-cancers/newly-diagnosed-and-relapsed-epithelial-ovarian-carcinoma/eupdate-newly-diagnosed-epithelial-ovarian-carcinoma-treatment-recommendations](https://www.esmo.org/guidelines/gynaecological-cancers/newly-diagnosed-and-relapsed-epithelial-ovarian-carcinoma/eupdate-newly-diagnosed-epithelial-ovarian-carcinoma-treatment-recommendations)

**FRONT-LINE CHEMOTHERAPY FOR EPITHELIAL OVARIAN CANCER (FIGO STAGE II-IV)**

The text has been updated for targeted therapy and ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) scores summarised in a new table (Table 3).

**Targeted therapy**

Three phase III trials (SOLO-1, PAOLA-1/ENGOT-ov25 and PRIMA/ENGOT-OV26) in newly diagnosed high-grade epithelial ovarian cancers (including fallopian tube and peritoneal) have investigated maintenance therapy with the poly-adenosine diphosphate (ADP)-ribose polymerase (PARP) inhibitors olaparib or niraparib after surgery and chemotherapy (ChT). In another trial (VELIA/GOG-3005), veliparib was given with ChT followed by maintenance. All four trials have demonstrated significant improvements in progression-free survival (PFS).

SOLO1 assessed first-line maintenance monotherapy with olaparib given for 2 years in women with FIGO (Fédération Internationale de Gynécologie et d’Obstétrique) stage III-IV ovarian cancer and a BRCA mutation with a partial or complete response to platinum-based ChT. Primary results from SOLO1 showed that maintenance with olaparib significantly reduced the risk of disease progression by 70% [hazard ratio (HR) 0.30, 95% confidence interval (CI) 0.23-0.41, P < 0.001] compared with placebo. Extended follow-up has demonstrated sustained long-term benefit, with 5-year follow-up showing a median PFS of 56 months with olaparib versus 14 months with placebo (HR 0.33, 95% CI 0.25-0.43). At 5 years, 48% of patients treated with olaparib remained progression-free compared with 21% in the placebo group. Olaparib has been approved by both the European Medicines Agency (EMA) and Food and Drug Administration (FDA) as maintenance therapy in BRCA-mutated patients in first remission after platinum-based therapy.

The PRIMA/ENGOT-OV26 trial evaluated niraparib as maintenance therapy for up to 3 years in patients with stage III-IV disease at high risk of treatment failure, with or without BRCA mutation. Patients with stage III ovarian cancer and no residual disease after primary debulking surgery were excluded and 67% of patients had received neoadjuvant ChT. Patients were stratified according to homologous recombination repair deficiency (HRD) status of the tumour using the Myriad myChoice assay (defined as an HRD score of ≥42). The primary analysis was performed on the HRD population, followed hierarchically by the all-comer population. The study showed a significant improvement in PFS in the HRD population (HR 0.43, 95% CI 0.31-0.59, P < 0.001) and in the overall population (HR 0.62, 95% CI 0.50-0.76, P < 0.001). An exploratory subgroup analysis showed that the greatest benefit occurred in women with a BRCA mutation and showed a significant, but lesser, benefit in women who were BRCA wild type with HRD. There was also an increase of 2.7 months in the median PFS in the HRD-negative, sometimes termed homologous recombination repair proficient, population (HR 0.68, 95% CI 0.49-0.94, P = 0.020). Niraparib has been approved by both the EMA and FDA as maintenance therapy for unselected patients in first remission after platinum-based therapy.

In the PAOLA-1/ENGOT-ov25 trial, patients with stage III-IV ovarian cancer, with or without residual tumour after surgery, were treated with ChT and bevacizumab and, after ChT, randomised to maintenance therapy with olaparib tablets or placebo for 2 years, as well as completing 15 months of bevacizumab therapy in both arms of the trial. The study included all patients who had no residual disease after surgery and no evidence of disease or achieved a complete or partial response after ChT and bevacizumab. Randomisation to olaparib or placebo was stratified based on tumour BRCA mutation status and response to first-line treatment. The primary analysis in the all-comer, intention-to-treat (ITT) population showed a significant benefit in PFS in patients receiving olaparib and bevacizumab with a median PFS of 22.1 months compared with 16.6 months with placebo and bevacizumab (HR 0.59, 95% CI 0.49-0.72, P < 0.001). Exploratory subgroup analyses showed the greatest benefit among women with a BRCA mutation (HR 0.31, 95% CI 0.20-0.47) followed by HRD-positive women (defined using the