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### LBA80 Outcome and prognostic factors of SARS CoV-2 infection in cancer patients: A cross-sectional study (SAKK 80/20 CaSA)

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**Background:** There is ongoing controversy regarding the outcome of COVID-19 in cancer patients. This is one of few registries on the impact of COVID-19 in cancer patients in a country severely affected by the pandemic.

**Methods:** This cohort study is collecting data on symptomatic Sars-CoV-2 infected patients with a cancer diagnosis from 23 Swiss sites, starting March 1, 2020. The main objective of the study is to assess the outcome of COVID-19 infection in patients with solid and hematological malignancies, while the main secondary objective is to define prognostic factors of COVID-19 outcome.

**Results:** With a cutoff date of July 16, 2020, 357 patients with a diagnosis of cancer and symptomatic COVID-19 were included into this first analysis. The most frequent malignancies were breast in 63 cases (18%), lung in 40 cases (11%), prostate cancer in 24 cases (7%) and myeloma in 16 cases (5%), with 104 (38%) patients having non-curative disease. Anticancer treatment within 3 months prior to the diagnosis of COVID-19 included chemotherapy in 65 patients (18%), targeted therapy in 54 patients (15%), steroids in 39 (11%), checkpoint inhibitors in 22 (6%) or no anticancer treatment in 155 patients (43%). 230 patients (65%) were hospitalized for COVID-19 or were already in hospital; 167 of the hospitalized patients (73%) required oxygen treatment, 43 patients (19%) intensive care, 31 (14%) invasive ventilation. 63 patients died from COVID-19 infection, resulting in a mortality rate of 18%. Significant risk factors for death included age  $\geq 65$  versus  $< 65$  (HR 5.84,  $p < 0.001$ ) and non-curative versus curative disease (HR 2.34,  $p = 0.01$ ). Neither male versus female gender (HR 1.59,  $p = 0.12$ ), type of cancer, geographic region, chemotherapy (HR 1.31,  $p = 0.44$ ), cardiovascular disease (HR 2.25,  $p = 0.09$ ) nor pulmonary comorbidity (HR 0.93,  $p = 0.86$ ) were significant risk factors for death.

**Conclusions:** We found a COVID-19 mortality rate in real-world cancer patients in a country with a decentralized, high-quality health care system that is substantially higher than in all COVID-19 infected patients in Switzerland (18% versus 5%). The rate of hospitalization and intensive care from COVID-19 in cancer patients is substantial.

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### LBA81 Keeping exhausted T-cells in check in COVID-19

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**Background:** Clinical data suggest an aggravated COVID-19 disease course in cancer patients treated with immune checkpoint inhibitors (ICI). European guidelines advise to defer ICI therapy until complete resolution of COVID-19. However, mechanistic insight into how ICI impacts COVID-19 immunopathology is absent.

**Methods:** We performed single-cell RNA- and T-Cell Receptor-sequencing (TCR-seq) on bronchoalveolar lavage fluid of COVID-19 pneumonia (n=19) and non-COVID pneumonia (n=10), and co-analyzed CD8+ T-cells with publicly available tumor-infiltrating T-cell data of treatment-naïve and ICI-treated patients (Sade-Feldman, Cell, 2018; Lambrechts, Nat Med, 2018). Cell lineages were determined by trajectory inference (Slingshot, Monocle v2) and stratified per condition. Pathogen- or tumor-directed T-cells were defined based on clonal selection (Zhang, Nature, 2018). To identify ICI responsive cells, we calculated a score derived from a validated gene set denoting ICI reactivity (Okamura, J. Autoimmun, 2019).

**Results:** We identified 3 CD8+ T-cell lineages, with 'Naïve' T-cells transitioning into 'Effector Memory' cells and then branching into either 'Recently Activated Effector Memory (T<sub>EMRA</sub>)', 'Exhausted (T<sub>EX</sub>)' or 'Resident Memory (T<sub>RM</sub>)' T-cells. In COVID-19, clonal expansion indicating a SARS-CoV-2 antigen-specific T-cell response, was mainly observed in the highly cytotoxic T<sub>EMRA</sub> lineage. In contrast, tumor-specific T-cells were found in the T<sub>EX</sub> lineage. Of importance, the ICI responsiveness score was significantly higher in the non-pathogen-directed T<sub>RM</sub>' and T<sub>EX</sub>' cells in COVID-19. In cancer, T<sub>EX</sub>' cells were shown to be ICI responsive as expected.

Table: LBA81 Demographics and characteristics of study cohort

	COVID-19 pneumonia (n=19)	Non-COVID pneumonia (n=10)
Age (y)	60 [55.5-69]	69.5 [62.75-75.25]
Men	14 (74)	5 (50)
Women	5 (26)	5 (50)
Time from illness onset to sampling (d)	19 [16-25]	15 [9-19]
SARS-CoV-2 PCR positive	6 (32) <sup>a</sup>	0 (0)
Other viral PCR positive	4 (21) <sup>b</sup>	1 (10) <sup>c</sup>
Bacterial culture positive	3 (16)	2 (20)
PJP PCR positive	0 (0)	4 (40)
Respiratory support	19 (100)	7 (70)
Oxygen via nasal cannula	0 (0)	4 (40)
Non-invasive ventilation	0 (0)	1 (10)
Invasive ventilation	15 (79)	2 (20)
Extracorporeal membrane oxygenation	4 (21)	0 (0)
Antiviral therapy (<7d)	13 (68) <sup>d</sup>	0 (0)
Antibiotics (<7d)	19 (100)	8 (80)
Immunomodulatory therapy (<7d)	5 (26) <sup>e</sup>	0 (0)

**Conclusions:** We are the first to provide a mechanistic rationale for an aggravated COVID-19 disease course in ICI-treated patients. Whereas ICI reactivates tumor-directed 'exhausted' T-cells in cancer, it preferentially potentiates non-pathogen-directed T-cells in COVID-19, thereby contributing to lung damage without boosting the antiviral immune response.

**Clinical trial identification:** In-depth Immunological Investigation of COVID-19 (CONtAGIous). - Clinical Trial identifier: NCT04327570. - Ethical approval obtained by the Ethics Committee of University Hospitals - KU Leuven. File number S63881.

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