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**LBA78** A microsimulation model to assess the impact of SARS-CoV-2 on cancer outcomes, healthcare organization and economic burden

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**Background:** SARS-CoV-2 pandemic has deeply modified healthcare seeking and services in Europe since February 2020 with delays in treatment delivery and changes in the standards of care. The organization of cancer centers (CC) has been transformed to minimize virus exposure in cancer patients (pts). Real-time assessment of the impact on cancer outcomes can optimize decision-making for future epidemic episodes.

**Methods:** A discrete-event simulation (DES) model was developed to model individual pt pathways during the pandemic in a context of constrained medical resources. Cancer pt care is modeled based on pandemic-adapted guidelines for medical practice. Pt flow is derived from medico-administrative databases using time series methods to estimate the proportion of punctual / late visits and associated delay and to extrapolate future flows. Finally, the impact of modified care on survival is estimated using literature data.

**Results:** From March to December 2020, based on data from Gustave Roussy CC in France (n= 4877 included pts), estimated overall treatment delay is <= 7 days in 86,6% of pts and 5,2% of pts have a delay higher than 2 months. More than 94% of this duration is delay in pt request for care, causing 99 pts to suffer a major prognosis change upon arrival. Delayed pt flows result in a highly time-variable use of medical resources, with important queues forecast for surgery care and chemotherapy. The handling of such queues will require intensified healthcare professionals effort. Projections show that, in the best-case scenario, ie without a 2nd pandemic wave, treatment delays and modifications will result in around 49 additional 5-year cancer-specific deaths (+ 2,25% of 5-year deaths), mainly in liver, sarcomas and head and neck cancer pts.

**Conclusions:** In a resource-constrained context, optimization of the benefit-risk ratio between COVID-19 and cancer care is key. Simulations of individual projections from actual hospital data, show a 2.25% increase of the 5-year risk of death and that pandemic-related cancer burden is mainly due to patient-induced lateness in seeking care. Defining optimal strategies in terms of screening, monitoring and prioritization for care could minimize the impact of future pandemic episodes.

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**LBA79** Dutch oncology COVID-19 Consortium (DOCC): Outcome of COVID-19 in patients with cancer in a nationwide cohort study

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**Background:** The coronavirus disease 2019 (COVID-19) pandemic is having significant impact on oncological care (Joode et al, Eur J Cancer 2020;136:132-139) and patients with cancer might have an increased risk for severe outcome of COVID-19. In order to identify risk factors associated with a worse outcome of COVID-19, a nationwide registry was developed for patients with cancer and COVID-19.

**Methods:** This ongoing multicentre nationwide observational cohort study was designed as a quality of care registry and is executed by the Dutch Oncology COVID-19 Consortium (DOCC), a collaboration of oncology physicians in the Netherlands. A questionnaire was developed to collect pseudonymised patient data on patients' characteristics, cancer diagnosis, cancer treatment, and outcome of COVID-19. All patients with COVID-19 and a cancer diagnosis or cancer treatment in the past 5 years were eligible for inclusion.

**Results:** To date, > 600 cancer patients diagnosed with COVID-19 have been registered by 45 Dutch hospitals. Data of 442 registered patients with at least 4 weeks follow-up were cleaned and 351 patients could be included for the first analyses. The main cancer diagnoses were non-small cell lung cancer (13.4%), breast cancer (13.4%), and chronic lymphocytic leukaemia (8.8%). Overall, 114 (32.3%) out of 351 patients with cancer died from COVID-19. In multivariate analyses, age  $\geq$  65 years ( $p < 0.001$ ), male gender ( $p = 0.035$ ), prior or other malignancy ( $p = 0.045$ ), and active diagnosis of haematological malignancy ( $p = 0.046$ ) or lung cancer ( $p = 0.003$ ) were independent risk factors for a fatal outcome of COVID-19. In a subgroup analysis of patients with active malignancy, the risk for a fatal outcome was mainly determined by tumour type (haematological malignancy or lung cancer) and age ( $\geq$  65 years).

**Conclusions:** The findings in this registry indicate that patients with a haematological malignancy or lung cancer have an increased risk of a worse outcome of COVID-19. During the ongoing COVID-19 pandemic, these vulnerable patients should avoid exposure to SARS-CoV-2, whereas treatment adjustments and prioritizing vaccination, when available, should also be considered.

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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 Committee of University Hospitals - KU Leuven. File number S63881.

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