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Association of immunotherapy and immunosuppression with severe COVID-19 disease in patients with cancer

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includes external validation using other large datasets of patients with COVID-19 and cancer.

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502P Association of immunotherapy and immunosuppression with severe COVID-19 disease in patients with cancer

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Background: Cytokine storm due to COVID-19 can cause high morbidity and mortality. Patients with cancer treated with immunotherapy (IO) and those with immunosuppression may have higher rates of cytokine storm due to immune dysregulation. We sought to evaluate the association of IO and immunosuppression with COVID-19 outcomes and cytokine storm occurrence among patients with cancer and COVID-19, based on data from the COVID-19 and Cancer Consortium (CCC19).

Methods: A registry-based retrospective cohort study was conducted on patients reported to the CCC19 registry from March 2020 to September 2021. The primary outcome was defined as an ordinal scale of COVID-19 severity. The secondary outcome was the occurrence of a cytokine storm using CCC19 variables, defined as biological and clinical evidence of severe inflammation, with end-organ dysfunction (Fajgenbaum D.C. et al., N Engl J Med., 2020). The association of IO or immunosuppression with the outcomes of interest were evaluated using a multivariable logistic regression balanced for covariate distributions through inverse probability of treatment weighting (IPTW).

Results: A total of 10,214 patients were included, among which 482 (4.7%) received IO, 3,715 (36.4%) received non-IO systemic therapies, and 6,017 (58.9%) were untreated in the 3 months prior to COVID-19 diagnosis. No difference in COVID-19 severity or the development of a cytokine storm was found in the IO group compared to the untreated group (aOR: 0.77; 95%CI:0.45-1.32, and aOR: 1.06; 95%CI:0.42-2.67, respectively). On multivariable analysis, baseline immunosuppression was associated with worse outcomes both in relation to COVID-19 severity (aOR: 1.89; 95%CI:1.51-2.35) and the presence of a cytokine storm (aOR: 1.75; 95%CI:1.30-2.35).

Conclusions: Administration of IO was not associated with severe outcomes in patients with cancer and COVID-19, whereas pre-existing baseline immunosuppression appears to be independently associated with worse clinical outcomes including cytokine storm.

Legal entity responsible for the study: COVID-19 and Cancer Consortium (CCC19).

Funding: National Institutes of Health (NIH) National Cancer Institute (NCI).

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503P The IMPRESS-Norway trial: Improving public cancer care by implementing precision cancer medicine in Norway

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Background: There is a high demand for precision cancer treatment. Methods for advanced molecular diagnostics are available, and a considerable number of drugs are already approved on specific indications. However, these drugs are only to be used within subgroups of patients with the specific diagnostics determined by clinical studies. Some drugs targeting a specific pathway or gene aberration, might just as well be efficient in patients with other tumour types, not yet tested.

Methods: In this national, investigator-initiated, prospective, open-label, non-randomized combined basket- and umbrella-trial, patients are enrolled into multiple parallel treatment cohorts. Patients with progressive disease with no further standard therapy, are eligible. Each cohort is defined by the patient's tumour type, molecular profile of the tumour, and study drug. Treatment outcome in each cohort is monitored by using a Simon two-stage-like 'admissible' monitoring plan to identify evidence of clinical activity. All drugs available in IMPRESS-Norway are regulatory approved. Molecular diagnostics with the TSO-500 gene panel are funded by the public health care system. In addition, patients included in IMPRESS-Norway are screened by analyses of ctDNA. Currently, 17 drugs are provided by five different pharmaceutical companies / research grants. The primary objective in the study is clinical benefit of treatment at 16 weeks of treatment, defined as complete response, partial response, or stable disease.

Results: The trial opened for accrual April 1st 2021. As of April 25, 2022, 359 patients had been included in the molecular screening, and 295 had completed evaluation in the national molecular tumour board. 67 patients were allocated to therapy in an IMPRESS-Norway treatment-cohort. Early aggregated data at 16-weeks show clinical benefit in 43% (12/26 of the first patients reaching 16 weeks of treatment). Updated results will be presented.

Conclusions: Patients with advanced cancer progressing on standard treatment are eligible for IMPRESS-Norway. Genetic alterations indicating benefit of the drugs currently available in the study, are detected in 23% of the patients.

Clinical trial identification: EudraCT: 2020-004414-35; NCT04817956.

Legal entity responsible for the study: Oslo University Hospital.

Funding: Funding from the regional health authorities, The Norwegian Cancer Society, Radiumhospitalets legater, Drug and funds from Roche, Novartis, Incyte, Eli Lilly and AstraZeneca.

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504P SARS-CoV-2 Omicron (B.1.1.529) variant infection leads to high morbidity and mortality in unvaccinated patients with cancer

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Background: Evidence is lacking as to the impact of SARS-CoV-2 Omicron (B.1.1.529) variant in oncological patients.

Methods: Capitalizing on OnCovid study data (NCT04393974), we analysed COVID-19 morbidity and case fatality rate at 28 days (CFR_{28}) of unvaccinated patients across 3 phases defined following the evolution of the pandemic in Europe, according to date of COVID-19 diagnosis: "Pre-vaccination" phase (27/02/2020-30/11/2020), "Alpha-Delta variant" phase (01/12/2020-14/12/2021), "Omicron variant" phase (15/12/2021-31/01/2022).

Results: By the data lock of 04/02/2022, 3820 patients from 37 institutions across 6 countries were entered. Out of 3473 eligible patients, 2033 (58.6%), 1075 (30.9%) and 365 (10.5%) were diagnosed during the Pre-vaccination, Alpha-Delta and Omicron phases. In total 659 (61.3%) and 42 (11.5%) were unvaccinated in the Alpha-Delta and Omicron. Unvaccinated patients across the Omicron, Alpha-Delta and Pre-vaccination phases experienced similar CFR_{28} (27.5%, 28%, 29%). Following propensity score matching, 42 unvaccinated Omicron patients were matched with 122 and 121 patients from the Pre-vaccination and Alpha-Delta phases respectively, based on country of origin, sex, age, comorbidity burden, primary tumour, cancer stage and status, and the receipt of systemic anticancer therapy at COVID-19. Unvaccinated Omicron patients experienced improved COVID-19 outcomes in comparison to patients diagnosed during the Pre-vaccination phase. Morbidity and mortality were comparable to those of unvaccinated patients diagnosed during the Alpha-Delta phase.

Table: 504P

	Omicron vs Pre-vaccination OR (95%CI)	Omicron vs Alpha-Delta OR (95%CI)
CFR_{28}	0.43 (0.19-0.94)	0.56 (0.25-1.24
Hospitalization	0.30 (0.12-0.72)	1.07 (0.46-2.51)
Oxygen therapy	0.39 (0.18-0.84)	0.77 (0.35-1.66)
COVID-19 complications	0.47 (0.22-1.01)	0.84 (0.39-1.79)

Conclusions: Despite time-dependent improvements in outcomes reported in the Omicron phase, patients with cancer remain highly vulnerable to SARS-CoV-2 in absence of vaccinal protection. This study provides unequivocal evidence in support of universal vaccination of patients with cancer as a protective measure against morbidity and mortality from COVID-19.