Abstract 5206

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 and may be more common in patients with cancer treated with immunotherapy (IO) due to immune system activation.
- 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 between baseline immunosuppression and/or IO-based therapies with COVID-19 severity and cytokine storm in patients with cancer, based on data from the COVID-19 and Cancer Consortium (CCC19).

METHODS

- We conducted a registry-based retrospective study on patients reported to the CCC19 registry from March 2020 to May 2022.
- Baseline immunosuppression status was defined as recent history of stem cell transplant, or receipt of standard immunosuppressive medications, corticosteroids, bruton kinase inhibitors, or anti-CD20, prior to COVID-19.
- IO was defined as receipt of PD-(L)1 and/or CTLA-4 inhibitors, BiTE or CAR T-cell therapies within 3 months of COVID-19 diagnosis. Non-IO therapy was defined as receipt of cytotoxic chemotherapy, targeted therapies or endocrine therapies within 3 months of COVID-19 diagnosis.
- The primary outcome was a five-level ordinal scale of COVID-19 severity. The secondary outcome was the occurrence of cytokine storm, defined as biological and clinical evidence of severe inflammation, with end-organ dysfunction.
- We conducted a multivariable logistic regression balanced for covariate distributions through inverse probability of treatment weighting (IPTW), and adjusted for demographic and clinical variables. As baseline immunosuppression might modify the effect anti-cancer systemic therapies, we included the interaction terms of cancer treatment and immunosuppression in the regression models. When the interaction terms were significant, additional subgroup analyses were computed to clarify the effect of the exposures in each stratum.

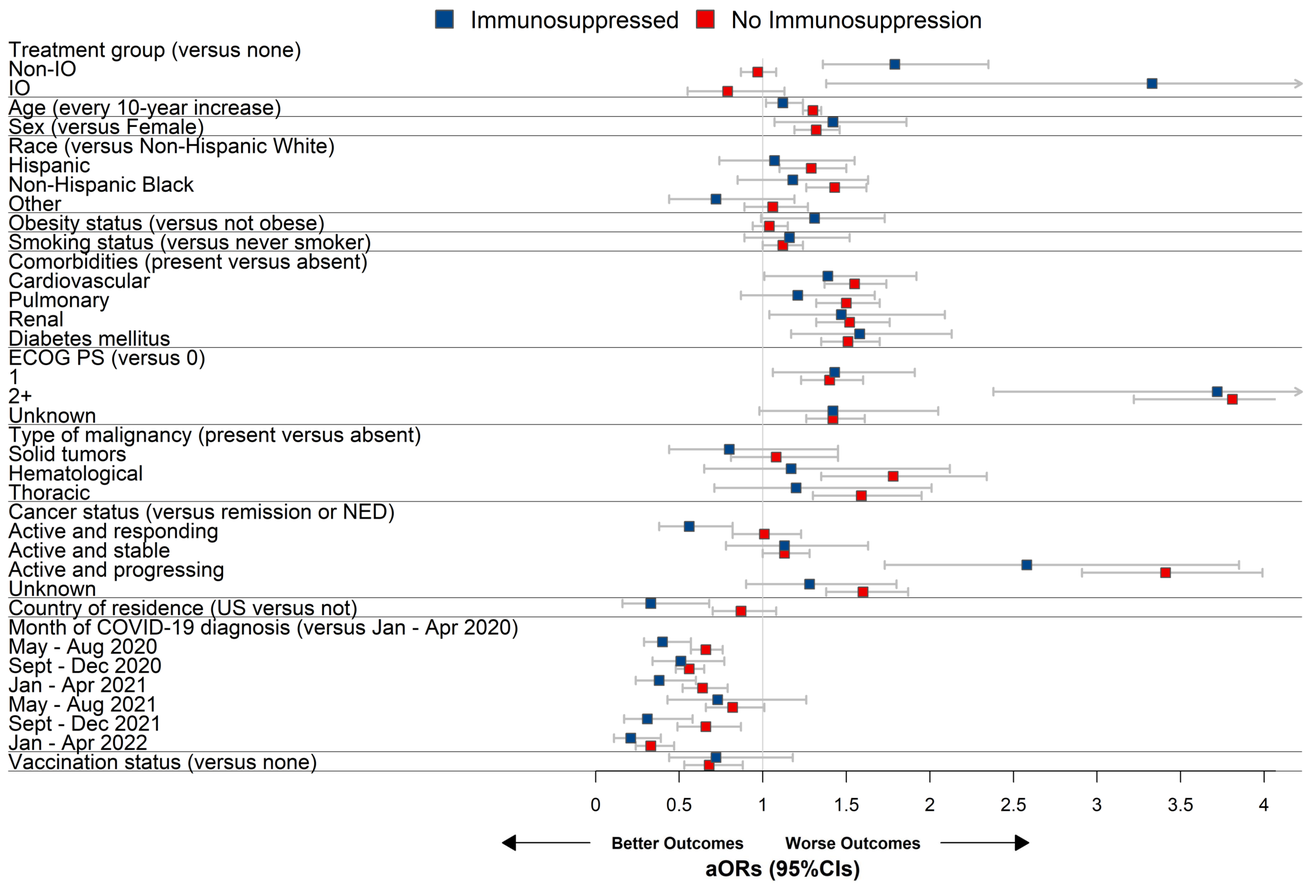

Figure 1: Forest plots of adjusted odds ratios (aORs) for COVID-19 severity, stratified by immunosuppression status.

Patients with cancer with baseline immunosuppression and COVID-19 may experience worse outcomes when treated with IO or non-IO systemic anti-cancer therapy.

CONCLUSION

In patients with cancer and COVID-19, administration of systemic anti-cancer therapies, especially IO, in the context of baseline immunosuppression was associated with severe clinical outcomes and the development of cytokine storm.

RESULTS

- A total of **12,046 patients** were included. Median age was 65 years (interquartile range: 54-74 years).
- Overall, **5.0% (n=599)** of patients were in the **IO group**, while **35.9% (n=4,327)** received **non-IO therapies** and **59.1% (n=7,120)** were not administered any anti-neoplastic regimen (**untreated group**).
- In the IO group, 23% (n=138) of patients died, compared to 20% (n=856) in the non-IO group, and 16% (n=1,124) in the untreated group. **The raw incidence of cytokine storm was comparable across all groups** at 12% with n=68, 533 and 860 for the IO, non-IO, and untreated groups, respectively.
- In the regression analysis, the interaction term of IO (vs. untreated) group and immunosuppression presented a strong, but non-significant trend towards worse clinical outcomes (aOR: 3.12; 95%CI: 0.93-10.47), and was significantly associated with the development of a cytokine storm (aOR: 6.36; 95%CI: 1.56-25.95). The interaction term of non-IO (vs. untreated) group and baseline immunosuppression was significantly associated with more severe COVID-19 (aOR: 1.44; 95%CI: 1.08-1.90) and a higher risk of cytokine storm (aOR: 1.69; 95%CI: 1.02-2.80).
- Based on these results, multivariate analyses stratified by immunosuppression status, **both the IO (vs. untreated) and non-IO (vs. untreated) groups were associated with worse COVID-19 outcomes in the context of pre-existing immunosuppression** (aOR: 3.33; 95%CI: 1.38-8.01 and aOR: 1.79; 95%CI: 1.36-2.35, respectively) (**Figure 1**). Additionally, **similar findings were observed in relation to the development of cytokine storm**.

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