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Clinical characteristics and outcomes of COVID-19 in 1295 new cancer patients: Single-center, prospective cohort study from Iran

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Background: SARS-CoV-2 (Severe Acute Respiratory Syndrome–related CoronaVirus-2) pandemic is the most serious challenge facing public health worldwide. The pandemic imposes different challenges to patients with cancer. To clarify the clinical characteristics and outcomes of COVID-19 in a large cohort of new cancer cases referred to an oncology center in the north of Iran.

Methods: This prospective, observational cohort study was conducted in Babol Oncology center, Mazandaran, Iran, between Feb 1, 2020, and Sep 30, 2021 (before commencing a valid vaccination program in Iran). Patients with newly diagnosed cancer who consented to enter the study were included. Cancer patients diagnosed more than six months before recruitment or who had received anticancer treatments—such as radiotherapy, chemotherapy, endocrine therapy, immunotherapy, and targeted therapy—were excluded from the study. Patients were followed up for COVID-19 infection and its outcomes.

Results: During the study period, 1295 patients with new cancer a mean age of 58.7 years were enrolled. After median follow-up of 12 months (range, 6–24 months), 122 patients (9.4%) were diagnosed with COVID-19, among which 44 cases (3.4%) required hospitalization, and 10 cases (0.7%) were admitted to ICU and received mechanical ventilation. During the study, COVID-19 mortality was reported in 9 cases (0.6%) with a case fatality rate of 20.4%.

Conclusions: This study could pave the new way to understand the role of clinical characteristics and outcomes of COVID-19 infection in new cancer cases, which may lead to the development of preventative, diagnostic, and curative procedures in cancer patients. This cohort study showed that cancer type (most in hematologic malignancies) and treatment setting (palliative care) were significantly associated with COVID-19 infection. Moreover, cancer type (most in brain cancers), metastasis, and treatment setting (palliative care) were in direct relationship to death. Further investigations are needed to help us to get novel insights into the exact role of clinical characteristics in susceptibility to COVID infection in new cancer patients.

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Antitumor activity of zolbetuximab combined with chemotherapy and anti-mPD-1 antibody (anti-mPD-1) in a syngeneic mouse model and a virtual preclinical trial using a quantitative systems pharmacology (QSP) model

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Background: Zolbetuximab, a chimeric mouse/human IgG1 monoclonal antibody, binds to claudin 18.2 (CLDN18.2) and mediates cancer cell death via antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. A phase II study of zolbetuximab plus chemotherapy or without the anti-programmed cell death 1 (anti-PD-1) antibody nivolumab is ongoing. Here, the triple combination was evaluated in a syngeneic mouse model. In addition, a virtual preclinical trial was conducted using a QSP approach.

Methods: Immunocompetent mice were engrafted with gastric carcinoma cells lethally transfected with mouse CLDN18.2 (CLS-103/LVT-murinCLDN18.2) and randomized to treatment groups based on tumor volume at Day 2 (Table). Tumor growth inhibition (TGI, %) = 100 × (1 – mean of the total tumor volume of each group) × 100. A mouse QSP model was built on a published QSP model with in-house/published data, and the antitumor effect of the triple combination was simulated.

Results: Day 20 TGI was 88% with the zolbetuximab triple combination. TGIs of dual combinations of chemotherapy plus anti-mPD-1 antibody, zolbetuximab plus anti-mPD-1 antibody, or zolbetuximab plus chemotherapy were 65%, 78%, and 54%, respectively. The triple combination was associated with a higher percentage of regressed tumors (50%) than the dual combinations (31% in each combination group) or control (0%). Results of the virtual trial simulation by the established QSP model showed that interanimal variability of TGI was less with the triple combination than with any dual combination.

Table: 42P

| Groups (n = 16 each) | Control | Rituximab + vehicle + isotopic control Ab | Dual anti-mPD-1 Ab + chemotherapy | Dual anti-CLDN18.2 Ab + anti-mPD-1 Ab | Triplet anti-CLDN18.2 Ab + chemotherapy + anti-mPD-1 Ab |
|---------------------|---------|----------------------------------------|----------------------------------|----------------------------------|--------------------------------------------------|
|                     | 56.8%   | 65.9%                                  | 68.5%                            | 70.8%                            | 73.8%                                             |
|                     |         | Rituximab + 5-FU + oxaliplatin + anti- mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab |
|                     |         | 65.7%                                  | 69.9%                            | 71.2%                            | 73.7%                                             |
|                     |         | Rituximab + vehicle + isotopic control Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab |
|                     |         | 65.2%                                  | 68.8%                            | 70.1%                            | 72.6%                                             |
|                     |         | Rituximab + 5-FU + oxaliplatin + anti- mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab | 5-FU + oxaliplatin + anti-mPD-1 Ab |
|                     |         | 65.3%                                  | 68.9%                            | 70.2%                            | 72.7%                                             |

Conclusions: Zolbetuximab triple combination showed a more potent antitumor effect in the mouse model. The QSP model was able to reproduce the observed results not only as mean profiles but as profiles with different interanimal variability among treatments.