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Abstract 325 Figure 1 Antibody responses to SARS-CoV-2 spike protein in patients treated with CPI-006

represents a novel therapy for COVID-19 aimed at stimulating more robust and prolonged anti-SARS-CoV-2 immunity potentially after infection or with vaccination.

Trial Registration NCT04464395

Ethics Approval

The study was approved by Temple University Hospital’s Ethics Board, Western IRB, approval number 1-1317457-1.

REFERENCE


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SARS-COV-2 SPECIFIC T-CELLS IN TIL FROM PATIENTS WITH EPITHELIAL CANCER

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Background

SARS-CoV-2 primarily infects the upper and lower airway system, yet also endothelial cells and multiple tissues/organ systems. Anti-SARS-CoV-2 directed cellular immune responses may be deleterious or may confer immune protection – more research is needed in order to link epitope-specific T-cell responses with clinically relevant endpoints.1 Analysis of epitope reactivity in blood from healthy individuals showed pre-existing (CD4+) reactivity most likely due to previous exposure to the common old coronavirus species HCoV-OC43, HCoV-229E, - NL63 or HKU1, or – not mutually exclusive - cross-reactive T-cell responses that would recognize SARS-CoV-2, yet also other non-SARS-CoV-2 targets.2,3 Detailed single cell analysis in PBMCs from patients with COVID-19 showed strong T-cell activation and expansion of TCR gamma – delta T-cells in patients with fast recovery or mild clinical symptoms.4 Previous studies examining antigen-specific T-cell responses in tumor-infiltrating T-cells (TIL) showed that EBV or CMV-specific cellular immune responses in TIL from patients with melanoma or pancreatic cancer. Such virus -specific T-cells may represent bystander’ T-cell activation, yet they may also impact on the quality and quantity of anti-tumor directed immune responses. We tested therefore TIL expanded from 5 patients with gastrointestinal cancer, who underwent elective tumor surgery during the COVID-19 pandemic for recognition of a comprehensive panel of SARS-CoV-2 T-cell epitopes and compared the reactivity, defined by IFN-gamma production to TIL reactivity in TIL harvested from patients in 2018, prior to the pandemic.

Methods

A set of 187 individual T-cell epitopes were tested for TIL recognition using 100IU IL-2 and 100 IU IL-15. Different peptide epitopes were selected: i) all epitopes were not shared with the 4 common old coronavirus species, ii) some peptides were unique for SARS-CoV-2, and iii) others were shared with SARS-CoV-1. Antigen targets were either 15mers or 9mers for MHC class II or class I epitopes, respectively, derived from the nucleocapsid, membrane, spike protein, ORF8 or the ORF3a. The amount of IFN-gamma production was reported as pg/10e4 cells/epitope/5 days. Controls included CMV and EBV peptides.

Results

We detected strong IFN-gamma production directed against antigenic ‘hotspots’ including the ORF3a, epitopes from the SARS-CoV-2 nucleocapsid and spike protein with a range of 12 up to 30 targets being recognized/TIL.

Conclusions

SARS-CoV-2 epitope recognition, defined by IFN production, can be readily detected in TIL from patients who underwent surgery during the pandemic, which is not the case for TIL harvested prior to the circulating SARS-CoV-2. This suggests a broader exposure of individuals to SARS-CoV-2 and shows that SARS-CoV-2 responses may shape the quality and quantity of anti-cancer directed cellular immune responses in patients with solid epithelial malignancies.

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Ethics Approval

This study was approved by the Champalimaud Foundation Ethics Committee.

Consent

All donors provided written consent and the study was approved by the local ethics committee. The study is in compliance with the Declaration of Helsinki.

REFERENCES


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STUDY OF ANTI-PD-1 ANTIBODY MULTIMODAL COMBINATION AS FIRST-LINE TREATMENT ON TIME WINDOW OF ADVANCED SOLID TUMOR

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Background Immune checkpoint inhibitors (ICIs) targeting the programmed cell death-1 (PD-1) has dramatically shifted the therapeutic paradigm of advanced tumor. However, a large proportion of patients do not achieve durable responses with anti-PD-1 monotherapy. Strategically combining immunotherapies with other systemic therapies to harness potential synergies is critical for maximizing their clinical activity and realizing the greatest benefits for patients with cancer. Chemotherapy drugs induce a form of tumor cell death that is immunologically active, thereby inducing an adaptive immune response specific for the tumor. Apatinib (VEGFR2 inhibitor) in combination with an anti-PD-1 has demonstrated synergistic antitumor effects. In our previous research, steady-state of apatinib (250 mg qd) plasma drug concentration was achieved by day 3. Camrelizumab and sintilimab are humanized anti-PD-1 antibody. We aim to assess time window, efficacy and safety of patients who receive anti-PD-1 antibody multimodal combination as first-line treatment of advanced solid tumor.

Methods This multicentre, open-label, exploratory cohort study. Eligible patients were aged 18–70 years, and had historically or cytologically confirmed advanced solid tumors, an Eastern Cooperative Oncology Group performance status of 0 or 1, and received no previous anti-tumor treatment for advanced disease. 180 patients were assigned to three group: Camrelizumab/sintilimab (200 mg, iv, d4, q3w, 24 months) plus standard chemotherapy (d1-3), Camrelizumab/sintilimab (200 mg, iv, d4, q3w, 24 months) plus apatinib (250 mg, po, d1, qd), Camrelizumab/sintilimab (200 mg, iv, d7, q3w, 24 months) plus standard chemotherapy (d1-3) and apatinib (250 mg, po, d1, qd). Tumor tissue and matched blood of all patients will be collected for NGS-based 727 genes panel assay, and the blood samples will be collected until disease progression. Meanwhile, plasma drug concentrations were detected by daily measurement of trough and peak concentrations(d0, 1, 2, 3, 21, 42, 63). The primary endpoint of this study is progression free survival (PFS), and the secondary endpoints include objective response rate (ORR), disease control rate (DCR), overall survival (OS) and safety. In addition, exploratory analysis was performed to comprehensively assess the relationship between gene status and efficacy, plasma drug concentrations and biological effects. This study is registered with ClinicalTrials.gov, number NCT04282278.

Results N/A

Conclusions N/A

Trial Registration ClinicalTrials.gov, number NCT04282278.

Ethics Approval The study was approved by the Fourth Hospital of Hebei Medical University Institution’s Ethics Board, approval number 2020012.

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Background Platinum-based regimens, such as FOLFOX (fluouracil [5-FU], leucovorin, oxaliplatin), are recommended standard of care first-line options in metastatic colorectal cancer (CRC). Maintenance therapy with a less intensive treatment regimen in metastatic CRC patients who do not progress during intensive first-line platinum–based induction therapy can enhance clinical benefit and reduce toxicity associated with long-term exposure to oxaliplatin. The phase 3 CAIRO3 study demonstrated PFS benefit and a trend toward OS benefit in patients who discontinued oxaliplatin and switched to a maintenance regimen of fluoropyrimidine and bevacizumab. Olaparib is an oral PARP inhibitor that has shown efficacy in platinum-sensitive cancers. LYNK-003 is a randomized, open-label, phase 3 trial evaluating the efficacy and safety of olaparib, alone or in combination with bevacizumab, compared with bevacizumab plus 5-FU in patients with unresectable or metastatic CRC that has not progressed following first-line induction with FOLFOX plus bevacizumab.

Methods Adult (≥18 years) patients with histologically confirmed unresectable or metastatic CRC that has not progressed following a first-line induction course of ≥6 cycles of FOLFOX plus bevacizumab and who can no longer tolerate oxaliplatin are eligible. Patients are required to have ECOG performance status 0–1, adequate organ function, and provide tumor tissue for biomarker analysis. Patients will be randomly assigned 1:1:1 to olaparib 300 mg twice-daily (BID) plus bevacizumab 5 mg/kg every 2 weeks (Q2W), olaparib 300 mg BID, or 5-FU 2400 mg/m2 over 46–48 hours Q2W plus bevacizumab 5 mg/kg Q2W. Treatment will be stratified according to response to prior FOLFOX plus bevacizumab induction (stable disease [SD] vs partial response [PR]/complete response [CR]), mutation status (BRAFmut and/or RASmut vs BRAFwt plus RASwt), and number of cycles of prior FOLFOX plus bevacizumab induction (6–8 vs >8 cycles). Responses will be assessed by computed tomography/contrast-enhanced magnetic resonance imaging per RECIST 1.1 by blinded independent central review (BICR) every 8 weeks during the first year and every 12 weeks thereafter. Study treatments will continue until documented progressive disease, unacceptable toxicity, intercurrent illness that prevents further administration of study intervention, investigator’s decision to discontinue the patient, consent withdrawal, pregnancy, or administrative reasons requiring cessation of study intervention. The primary endpoint is PFS per RECIST 1.1 by BICR and the key secondary endpoint is OS. Additional secondary endpoints are objective response rate and duration of response; safety and tolerability will also be reported. Approximately 525 patients will be enrolled.

Results N/A

Conclusions N/A

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Trial Registration ClinicalTrials.gov, ID number NCT04456699

Ethics Approval The study protocol and all amendments were approved by the relevant Institutional Review Board or ethics committee at each study site. All patients provided written informed consent to participate in the clinical trial.

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