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

1. Luke J, Powderly J, Merchan J, Barve M, Hotson A, Mobasher M, Kwei L, Luciano G, Buggy J, Piccione E, Miller R. Immunobiology, preliminary safety, and efficacy of CPI-006, an anti-CD73 antibody with immune modulating activity, in a phase 1 trial in advanced cancers. *J Clin Oncol* 2019; **37**:15 suppl, 2505.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0326>

326

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

¹Pedro Noronha*, ¹Georgia Paraschoudi, ¹Eric Sousa, ¹Jéssica Kamiki, ¹Patrícia António, ¹Carolina Condeço, ¹Inês Silva, ¹Andréia Maia, ¹Mireia Castillo-Martin, ¹António Beltran, ²Carlos Carvalho, ³Joana Lérias, ³Alimuddin Zumla, ¹Marius Maeuer. ¹Champalimaud Centre for the Unknown, Lisbon, Portugal; ²Champalimaud Clinical Centre, Lisbon, Portugal; ³University College London, London, UK

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 15 mers 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.

Acknowledgements We thank the Surgery, Pathology and Vivarium Units of Champalimaud Clinical Center (N. Figueiredo, A. Brandl, A. Beltran, M. Castillo, C. Silva).

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

1. Grifoni, A., Weiskopf, D., Ramirez, S. I., Mateus, J., Dan, J. M., Moderbacher, C. R., Rawlings, S. A., Sutherland, A., Premkumar, L., Jodi, R. S., Marrama, D., de Silva, A. M., Frazier, A., Carlin, A. F., Greenbaum, J. A., Peters, B., Krammer, F., Smith, D. M., Crotty, S., & Sette, A. (2020). Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. *Cell*, **181**(7), 1489–1501.e15. <https://doi.org/10.1016/j.cell.2020.05.015>
2. Mateus, J., Grifoni, A., Tarke, A., Sidney, J., Ramirez, S. I., Dan, J. M., Burger, Z. C., Rawlings, S. A., Smith, D. M., Phillips, E., Mallal, S., Lammers, M., Rubiro, P., Quiambao, L., Sutherland, A., Yu, E. D., da Silva Antunes, R., Greenbaum, J., Frazier, A., ... Weiskopf, D. (2020). Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. *Science*, eabd3871. <https://doi.org/10.1126/science.abd3871>
3. Le Bert, N., Tan, A. T., Kunasegaran, K., Tham, C. Y. L., Hafezi, M., Chia, A., Chng, M. H. Y., Lin, M., Tan, N., Linster, M., Chia, W. N., Chen, M. I.-C., Wang, L.-F., Ooi, E. E., Kalimuddin, S., Tambyah, P. A., Low, J. G.-H., Tan, Y.-J., & Beretoletti, A. (2020). SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. *Nature*, **584**(7821), 457–462. <https://doi.org/10.1038/s41586-020-2550-z>
4. Zhang, J., Wang, X., Xing, X. et al. Single-cell landscape of immunological responses in patients with COVID-19. *Nat Immunol* 2020;21:1107–1118. <https://doi.org/10.1038/s41590-020-0762-x>

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0326>

327

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

Jian Shi*, Baoen Shan, Junyan Wang, Jiayin Liu, Rongfeng Liu, Yujie Shan. Fourth Hospital of Hebei Medical University, shijiazhuang, China