IMMUNE RESPONSES TO COVID-19 VACCINATION IN CANCER PATIENTS

Roberta Campagna[1], Federica Dominelli[2], Maria Antonella Zingaropoli[2], Fabio Ciurluini[3], Giorgia Grilli[4], Alessandra Amoroso[4], Angelo De Domenico[4], Donatella Amatore[4], Maria Stella Lia[4], Claudio Maria Mastroianni[2], Maria Rosa Ciardi[2], Riccardo De Santis[2,4], Guido Antonelli[1], Ombretta Turriziani[1]

1 Dipartimento di Medicina Molecolare, Sapienza Università di Roma , 2 Dipartimento di Malattie Infettive e Sanità Pubblica, Sapienza Università di Roma, 3 Dipartimento di Scienze Radiologiche, Oncologiche e Patologiche, Sapienza Università di Roma, 4 Istituto di Scienze biomediche della Difesa, Roma, 5 Dipartimento di Oncologia Medica, Policlinico Umberto I, Sapienza Università di Roma

INTRODUCTION

Cancer patients (CPs) are more susceptible to infections and their potential complications, showing an increased risk of developing severe COVID-19 compared to the general population. In this study we evaluated humoral and cell-mediated responses one year after the administration of the third dose of anti-SARS-CoV-2 vaccine in CPs investigating immunotherapy effects on humoral and cell-mediated responses.

MATERIAL AND METHODS

Binding and Neutralizing Antibody (Ab) titers were quantified using chemiluminescence immunoassay and Plaque Reduction Neutralization Test (PRNT) respectively. Cell-mediated response was assessed by multiparametric flow cytometry. T-cells were labelled "responding" and "triple-positive" if producing at least one cytokine between IFNγ, IL2 and TNFα or all three cytokines, respectively. The population was stratified in "experienced" and "naïve" according to previous SARS-CoV-2 infection. CPs were also stratified according to treatment in "immunotherapy" and "non-immunotherapy".

RESULTS

Sixty-six CPs were enrolled, 47 received three vaccine doses (CPs-3), 19 received a fourth dose (CPs-4). Twenty-seven HDs vaccinated with three doses were included.

CPs-3 had lower Ab titer compared to CPs-4 (p=0.0209) and HDs (p=0.0079) (Fig. 1A). No significant differences were found when comparing neutralizing Ab titer against Wuhan strain and Omicron variant stratifying the population according to the number of doses (Fig. 1D, 1G). Naïve CPs-3 had lower binding and Neutralizing Ab titer when compared to both experienced CPs-3 (p=0.0004) and naïve HDs (p=0.0380; p=0.0045) and lower binding Ab titer compared to naïve CPs-4 (p=0.0060) (Fig.1B). No differences in both binding and Neutralizing Ab titers were found comparing immunotherapy and non-immunotherapy CPs (Fig. 1C, 1F). A positive correlation between the antibody level and both the PRNT50 titer against Wuhan (Figure 1H) and Omicron strains were found (Figure 1I).

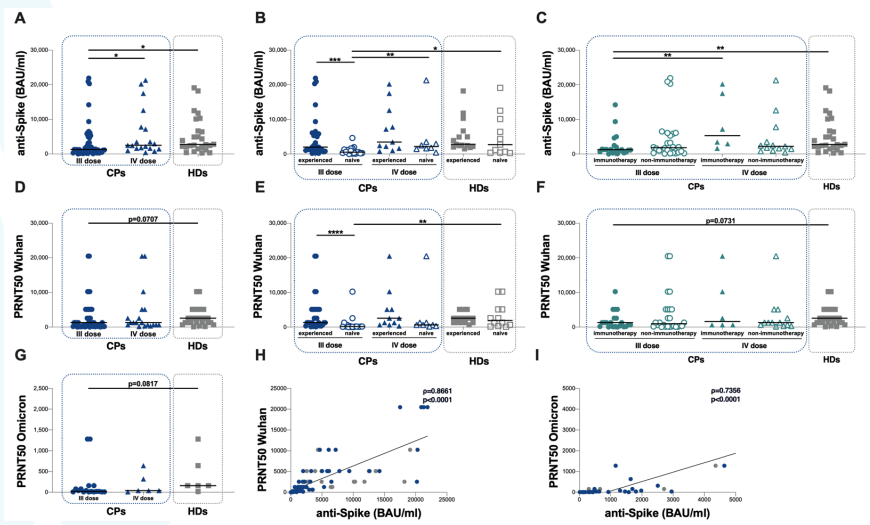

Figure 1. Evaluation of humoral response in the study population. Antibody anti-Spike titer in CPs stratified according to (A) the number of vaccine doses, (B) previous SARS-CoV-2 infection and (C) immunotherapy. PRNT50 titer against Wuhan strain in CPs stratified according to (D) the number dose of mRNA vaccine, (E) previous SARS-CoV-2 infection and (F) immunotherapy (G) PRNT50 titer against Omicron strain in CPs stratified according to the number of vaccine doses. (H) Positive correlation between anti-Spike antibody titer and PRNT50 against Wuhan. Linear correlation was evaluated by using the regression test (R^2=0.5848, p<0.0001). (I) Positive correlation between anti-Spike antibody titer and PRNT50 against Omicron strain (R^2=0.9075, p<0.0001). CPs: cancer patients; HDs: healthy donors; BAU: binding antibody units; PRNT50: Plaque Reduction Neutralization Test. ****: p<0.0001; ***: p<0.001; **: p<0.01; *: p<0.05.

Overall, lower percentages of CD4+ and CD8+, responding and triple-positive T-cells, were found in CPs compared to HDs (Fig. 2A) and a predominance of monofunctional T-cells producing TNFα was observed (p<0.0001) (Fig. 2B). Experienced CPs had higher percentages of responding and triple-positive T-cells when compared to naïve CPs, but lower when compared to HDs (Fig. 3).

Higher percentages of responding and triple-positive T-cells were observed in CPs under immunotherapy compared to non-immunotherapy (Fig. 4).

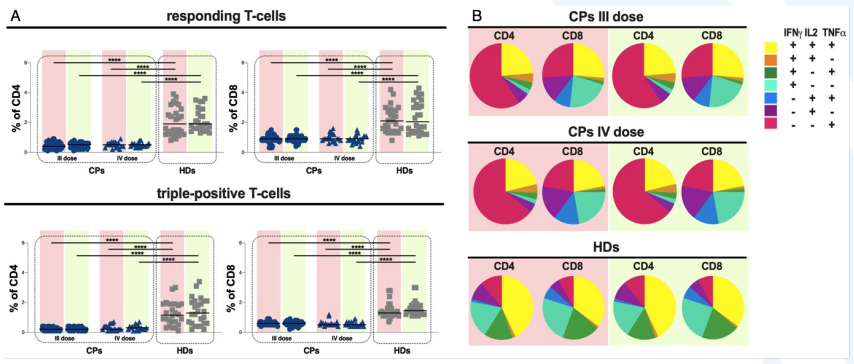

Figure 2. Evaluation of S-specific T-cell response in study population. (A) Percentage of responding and triple-positive T-cells in CPs and HDs. Data are shown as median (lines). (B) Pie charts representing multifunctional cytokine analysis of specific T-cells in CPs and HDs. In pink and green are reported data regarding stimulation using wild-type and omicron peptides, respectively. CPs: cancer patients; HDs: healthy donors. ****: p<0.0001; ***: p<0.001; **: p<0.01; *: p<0.05.

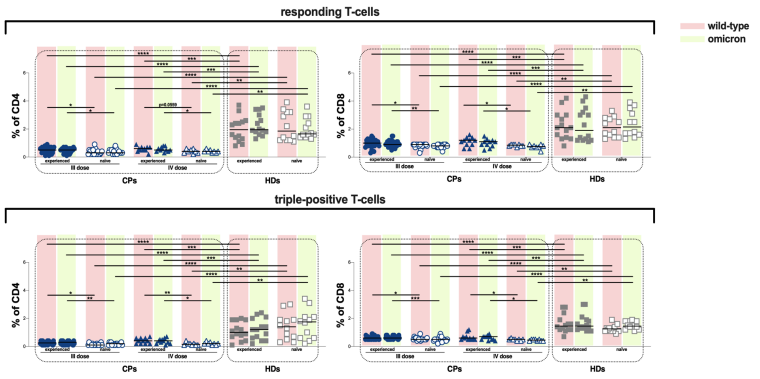

Figure 3. Evaluation of S-specific T-cell response in CPs and HDs stratified according to previous SARS-CoV-2 infection. In pink and green are reported data regarding stimulation using wild-type and omicron peptides, respectively. Data are shown as median (lines). CPs: cancer patients; HDs: healthy donors. ****: p<0.0001; ***: p<0.001; **: p<0.01; *: p<0.05.

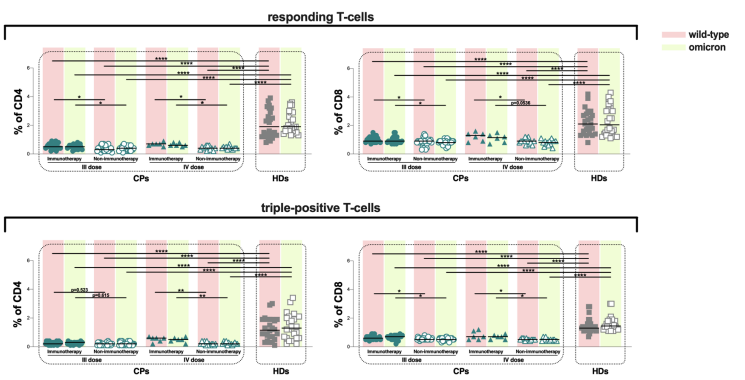

Figure 4. Evaluation of S-specific T-cell response in CPs and HDs stratified according to immunotherapy. In pink and green are reported data regarding stimulation using wild-type and omicron peptides, respectively. Data are shown as median (lines). CPs: cancer patients; HDs: healthy donors. ****: p<0.0001; ***: p<0.001; **: p<0.01; *: p<0.05.

CONCLUSIONS

Our results emphasize the importance of additional vaccine doses in cancer patients to strengthen the immune response. The stronger T-cell response observed in patients undergoing immunotherapy is in agreement with the purpose of the treatment to reinvigorate the immune system. These observations emphasize the need to adjust the vaccination schedule in this population and suggests that the possible effect of different therapies should be considered when vaccinating cancer patients.