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LETTER TO THE EDITOR

Response to Dr Derhovanessian "Impact of cytomegalovirus infection on immune signatures in cancer patients"

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Dear Editors

We thank Dr. Derhovanessian for the comments on our article "Immune impairment in patients with terminal cancers: influence of cancer treatments and cytomegalovirus infection" pointing out an important yet less studied role of CMV in modulating immune status in patients with cancer. Theoretically, we also believe that CMV serostatus could be an useful marker in predicting a patient's immune outcome following treatment and disease progression. In the early phase of enrollment, we had 65 participants being tested for their CMV serostatus (14 normal; 13 stage I treatment-naïve; 20 stage III/IV treatment-naïve; 18 stage IV heavily treated). Only 2 patients in stage I were CMV IgG-negative and the other 63 were positive. It was therefore practically impossible to enroll a sufficient number of sero-negative patients to demonstrate the power of CMV serostatus.

Our data suggested that a number of factors including stage of disease, treatment and CMV reactivation could contribute to the deviation of immune status in stage IV heavily treated patients from stage III/IV treatment-naïve patients. While we strongly believe that repetitive treatment-associated CMV reactivation is the main factor exhausting their immune integrity in cancer patients, we were unable to demonstrate this based on current data. Indeed, the amount of CMV-specific T cells was not different between stage I treatment-naïve patients (not included in the current article) and stage III/IV treatment-naïve patients, supporting the notion that CMV-associated immune signatures may well be a consequence of treatments. On the other hand, if when we compared those stage I treatment-naïve patients with a normal group and those stage III/IV treatment-naïve patients, some stage-associated differences in immune status were found; for instance CD27, CD127 in naïve populations and IL-6. Therefore, the impact of CMV infection on immune status may not be the sole factor compromising immune functions in patients with cancer. Still, among these factors, we may be in a better position to control CMV than cancer. One way to identify the impact of CMV infection on immune status is to study patients with pre-emptive therapy during chemotherapy. Our unpublished data show that some of the immune parameters can be reversed in vitro in PBMC from stage IV patients by treatment with ganciclovir. The impact of CMV infection in patients with cancer during treatment somehow looks like accelerating the process of immune senescence. Whether pre-emptive treatment will be helpful in preserving patients' immunity is not known at this time, but our data encourage the development of strategies to control CMV reactivation.

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