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LETTER TO THE EDITOR

Immune Checkpoint Inhibitor Therapy in HIV-Positive Patients with Advanced-Stage Cancer: a Golden Card to Be Played?

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Immune checkpoint inhibitor (ICI) therapy has recently been reported to be safe and effective among HIV-positive patients with advanced stage cancer [1, 2]. Moreover, no associations with adverse changes in HIV load or CD4 cell count have been observed [1]. HIV infection has been historically considered an exclusion criterion for immunotherapy because of its involvement in regulation of the immune system [1]. Patients affected by HIV infection appear to be at increased risk for cancer which represents the leading cause of death among non-AIDS–defining conditions [1, 2]. The anti-tumor action of ICI therapy has been documented in a number of advanced-stage cancer types including non-small cell lung cancer (NSCLC), melanoma and Kaposi sarcoma [1]. Among the different types of immunotherapy, anti-programmed death receptor-1(PD-1) antibodies such as nivolumab and anti-cytotoxic T –lymphocyte antigen 4 (anti-CTLA-4) antibodies including ipilimumab appear to be particularly successful [3]. It has been stated that activation of PD-1 and CTLA-4 on T cells results in T cell exhaustion and ultimately promotes tumor progression [3]. Telomere length of NSCLC tissues has been advised to be an independent prognostic factor in patients with surgically resected early stage NSCLC [4]. Patients suffering from NSCLC with the shortest telomere length have been revealed to experience a significantly worse overall survival and disease-free survival in comparison to patients with longer telomeres [4]. Short telomeres have emerged to predict poor survival in patients with different cancers [5]. Telomere shortening has been found to cause genomic instability that determines oncogenesis through the activation of telomerase and the generation of other mutations necessary for tumor progression [4]. Decreased telomere length has also been shown to predict poor survival in melanoma subgroups [5]. It has been written that there is a link between patients with short telomere and a poor-melanoma-specific survival in comparison with patients with long telomeres [5]. Immunosenescence has been connected with presence of Kaposi's sarcoma [6]. The progressive loss of immunological memory during aging has been associated with a reduced proliferative capacity and shortened telomeres of T cells [6]. HIV infection has been associated with a large and quantifiable shortening of telomeres [7]. Decreased peripheral leukocyte telomere length has long been associated with HIV infection [7]. Early combination antiretroviral therapy initiation has been linked to subsequent suppression of HIV viral replication leading to the normalization of the rate of telomere attrition and telomere length shortening [7]. It has been stated that HIV-1-specific CD8 + T cells from HIV-1 controllers exhibit long telomeres and high levels of constitutive telomerase activity, while HIV-1-specific CD8 + T cells from HIV-1 progressors demonstrate telomere shortening with limited telomerase activity [8]. Telomere shortening has been proposed to have a causal role in the functional deficiency of HIV-1-specific CD8 + T cells in chronic progressive infection [8]. Telomere lengths and telomerase activities have been recognized to be actively increased by blocking the programmed death receptor-1(PD-1)/programmed death ligand 1 (PD-L1) pathways in HIV-1-specific CD8 + T cells from progressors implying an active reversibility of the process of telomere shortening [8]. Disruption of CTLA-4 expression on peripheral blood CD8 + T cell has been shown to enhance anti-tumor efficacy [9]. Blockage of CTLA-4 has been demonstrated to allow expansion of enzyme telomerase-specific T cell clones [10]. All these contentions led me to hypothesize that HIV patients with advanced cancer-stage might benefit most from ICI. I suppose that HIV patients affected by advanced stage cancer may result benefits from taking ICI as a result of increased telomere length, given that telomere shortening and telomerase activity appear to represent a major underlying causal

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pathological dynamic in both several cancers and HIV infection. Further research is warranted to define the interaction between ICI therapy and telomere length in HIV-positive patients with advanced-stage cancer.

Compliance with Ethical Standards

Conflict of Interest The author declares no conflict of interest.

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