Cancer Research

Immunology

Abstract 5626: Investigation of T cell activation by anti-human PD-1 antibodies Nivolumab, Pembrolizumab and BGB-A317 using tumor-infiltrating lymphocytes (TILs) from colorectal cancer and colorectal liver metastasis patients

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DOI: 10.1158/1538-7445.AM2017-5626 Published July 2017

Proceedings: AACR Annual Meeting 2017; April 1-5, 2017; Washington, DC

Abstract

Blockade of the PD-1 pathway with anti-PD-1 antibody, such as nivolumab (nivo) and pembrolizumab (pembro), has led to remarkable clinical responses in patients with many different cancer types. In this study, we investigated the activation of tumor-infiltrating lymphocytes (TILs) from patients with colorectal cancer (CRC) and colorectal liver metastasis (CLM) by nivo, pembro and BGB-A317, a novel humanized IgG4 anti-PD-1 antibody under clinical development. BGB-A317 has a unique binding signature to PD-1 with high affinity. Additionally, it is engineered to remove Fc gamma receptor (FcγR) binding, including FcγRI, FcγRIIA, FcγRIIB and FcγRIIIA. In our studies, all three anti-PD-1 antibodies showed significant increases in IFN-γ and TILs proliferation in a 3D tumor spheroid model. In both CRC and CLM patients, BGB-A317 treatment at concentration levels of 0.1, 1 and 10 μg/mL led to higher IFN-γ production than that in nivo and pembro treated groups. The enhanced TILs function was associated with a high density of $CD8^+$ T cells, but inversely correlated with the percentage of $CD11b^+$ myeloid cells in CRC tumors. Of

Citation Format: Lusong Luo, Xiaoran Wu, Tong Zhang, Chunyan Fu, Yanjuan Zhang, Amy Guo, Dongping Zhou, Lianhai Zhang, Kun Wang, Baocai Xing, Jiafu Ji, Lai Wang, Kang Li. Investigation of T cell activation by anti-human PD-1 antibodies Nivolumab, Pembrolizumab and BGB-A317 using tumor-infiltrating lymphocytes (TILs) from colorectal cancer and colorectal liver metastasis patients [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2017; 2017 Apr 1-5; Washington, DC. Philadelphia (PA): AACR; Cancer Res 2017;77(13 Suppl):Abstract nr 5626. doi:10.1158/1538-7445.AM2017-5626

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