Imprime PGG, a soluble yeast β-glucan PAMP, activates both innate and adaptive immune effector cells resulting in enhanced anti-tumor responses that synergize with anti-PD-1 antibody therapy

Poster # B009

Steven M. Leonardo, Ross B. Fulton, Kathryn A. Fraser, Takashi O. Kangas, Keith B. Gorden, Ben Harrison, Adria LB Jonas, Anissa SH Chan, Yumi Yokoyama, Nandita Bose, Jeremy R. Graff, and Mark Uhlik

Biothera Pharmaceuticals, Inc., Eagan, MN

Abstract

Immune checkpoint therapy has made a splash in the cancer world by providing long-term durable responses in patients across multiple cancer indications. However, not all patients respond to checkpoint intervention so this therapeutic relies on an underlying recognition and activation of T cells against the tumor. Furthermore, recent evidence suggests that acquired resistance to CPIs may occur through beta-2 microglobulin mutations and loss of MHC class I-restricted T cell recognition. In this study, we evaluate the potential to use a novel synergy between anti-PD-1 and a Toll-like receptor (TLR) agonist to enhance anti-tumor responses in established melanoma tumors. Here we employ a combination of experimental techniques, including both flow cytometry and multiplex immunohistochemistry (mIHC), to examine how Imprime modulates the anti-tumor response in the MC38 mouse adenocarcinoma model. C57BL/6 mice were injected s.c. with 5e5 MC38 tumor cells. When the tumors reached an average of ~50mm3, mice were randomized into 4 treatment groups (vehicle, Imprime alone, anti-PD1 alone, Imprime+anti-PD1) once tumors reached ~90mm3. After 2 weeks of treatment, mice were evaluated for inhibition of tumor growth, presence and activation of tumor-infiltrating immune cells by F4/80, Ly6C, Ly6G, MHCII) in the tumor of mice treated with the various treatment regimens. In these experiments Imprime was able to significantly reduce tumor burden, increase CD8+GranzymeB+ cells, and enhance the NK cytotoxic killing of the targets providing further evidence of a unique synergy between anti-PD-1 and Imprime treatment. These data demonstrate a unique synergy between anti-PD1 and Imprime treatment and provide potential therapeutic benefit to patients in our ongoing clinical trials.

Structure of Imprime PGG