**Poster #22**

**LB-199**

**Imprime PGG modulates immunosuppressive myeloid components of the tumor microenvironment and drives enhanced anti-tumor efficacy in combination with checkpoint inhibitor therapies**

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**Abstract**

Checkpoint inhibitor therapies [CI] have shown great promise, however, is a limited percentage of patients. One of the key mechanisms behind the limited efficacy of CI therapy is immune resistance mediated by immunosuppressive myeloid cells at the tumor microenvironment (TME), namely M2 macrophages and myeloid-derived suppressor cells (MDSC). Multiple therapeutic interventions are being developed to target these cell types with the intention of reactivating the TME and enhancing the effector functions of the infiltrating cytotoxic T cells.

Molecules containing goguhon-gated molecular patterns (GMPs) are one of the unique combined partners that can sensitize tumors to respond to CI. Imprime PGG (Imprime), an intravenously administered soluble goat IL-12-like glucan IMMP, is being clinically developed in combination with tumor-targeting antibodies, antiangiogenesis, and CPI. Imprime has shown promising results in the randomized phase 2 studies in non-small cell lung cancer. Mechanistic studies have shown Imprime to reprogram M2 macrophages and MDSC in vivo humans as well as in preclinical models. The objective of this study was to evaluate Imprime’s ability to counteract immunosuppressive and thereby influence the effector functions of T cells in a syngeneic tumor model. To this end, we analyzed the anti-tumor efficacy of Imprime in combination with PD-1 (PDL-1/PD-L1) blocking or anti-IL-12B in the MC38 colon cancer model and found both combinations to be synergistic against the tumor. Flow cytometric evaluation of single cell suspensions of spleen and tumor tissue after one week of Imprime dosing revealed that the tumor-associated macrophages showed a shift to an M1-like phenotype with increased expression of PD-L1, CD40, CD80, L1-A, iNOS, and TNF. Mouse colon tumors with macrophage CD11c were increased intravenously with Imprime. Moreover, when M1 macrophages were injected on day 10, mice treated with and Imprime exhibited increased CD11c and IL-12P70 expression in the tumor cells as a result of tight activation observed in the spleen. Mouse macrophage gradient showed increased intravenous expression of M1 markers. Furthermore, increased number of CD68 cells in the spleen were of effective phagocytic phenotype with enhanced expression of PD-L1, granzyme A and B. At the tumor site, the CD68 cells from Imprime treated mice demonstrated increased proliferation and cytotoxic producing capabilities (CD10, CD48, and TNFγ) in response to COLO205. Collectively, these data show the ability of Imprime’s ability to revert the TME such that the malignant are less suppressive and the cytotoxic T cells are more functionally active can have a tremendous impact on overcoming resistance to CPI therapy.

**Background**

Imprime PGG Impacts Multiple Points of the Cancer Immunity Cycle

**Objective**

To evaluate the ability of Imprime to counteract immunosuppression and thereby influence the effector functions of T cells in a syngeneic tumor model.

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**Results**

**Imprime enhances efficacy of CPI in syngeneic mouse models**

**Imprime administration alters the suppressive M2-like TAM phenotype and function – MC38 Model**

**Imprime administration elicits maturation of both M-MDSC and PMN-MDSC**

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**Imprime treated macrophages, in vivo, are more M1-like and can elicit a CD8 T cell expansion**

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**Conclusions**

We demonstrated that Imprime, a systemically administered PAMP can:

- Synergizes with checkpoint inhibitors to reduce tumor burdens
- Mediates regulation of the TME
- Matures M-MDSC and PMN-MDSC
- Elicits effector T cells that are more functionally responsive

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For additional questions, please contact: release@biothera.com

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