Imprime PGG, a soluble yeast β-glucan PAMP, in combination with Pembrolizumab induces infiltration and activation of both innate and adaptive immune cells within tumors in melanoma and triple-negative breast cancer (TNBC) patients

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Imprime is a novel, IV administered 1,3β-D-glucan PAMP (pathogen-associated molecular pattern) that activates immune cells through its interaction with Toll-like receptor (TLR) 2 and TLR 13 in dendritic cells (DCs) and macrophages within the tumor microenvironment and as such the induction of professional antigen-presenting cells. These events culminate in the expansion and activation of T cells and their subsequent infiltration into the tumor microenvironment; this has previously demonstrated that Imprime enhances the anti-tumor efficacy of immune checkpoint inhibitors (CPIs) in multiple clinical models. Here we report the first-in-human clinical trial to test the mechanistic basis for our preclinical findings. The addition of Imprime to pembrolizumab (Pembro) significantly increased infiltration and infiltration of stress and adaptive immune cells in tumors of melanoma and TNBC patients. In a phase 1/2 trial (NCT03196664) combining Imprime with pembrolizumab (Pembro) in metastatic melanoma patients (n=18) has been found in metastatic melanoma patients who have failed previous chemotherapy, but with checkpoint inhibitor resistance. From these data, we demonstrated that Imprime augmented the anti-tumor effect of pembrolizumab through: 1) increased T cell infiltration of the tumor microenvironment and infiltration of stress and adaptive immuners in tumors of melanoma and TNBC patients.

Conclusions

- Collectively, these data recapitulate our preclinical findings and provide the first evidence that Imprime/Pembrolizumab mechanistically triggers the infiltration and activation of immune cells in tumors of patients with advanced melanoma and triple-negative breast cancer.
- The increased infiltration of both innate and adaptive immune cells within tumors of patients treated with Imprime/Pembrolizumab is associated with enhanced anti-tumor efficacy.
- These findings support the clinical development of Imprime/Pembrolizumab in patients with advanced melanoma and triple-negative breast cancer.

Abstract

Image show staining of Imprime Tumor (DAPT) access from the Tumor Microenvironment IHC Panel. The set of images in each of these panels was generated from patient MEL1 pre-treatment on MEL1 on treatment (Rx) (MEL1 on Rx). Approximately 0% of CD163+ cells are positive for Imprime staining in this on Rx samples.

Lymphoid Staining Panel – Images and Data

Conclusions

- Imprime/PGG is a PAMP that acts to degrade a coordinated anti-tumor immune attack.
- Multiphase imaging of pre- and post-treatment biopsies from patients receiving Imprime/Pembrolizumab therapy have demonstrated an increase in the infiltration of CD80+ myeloid cells (M1 phenotype) within tumor regions with significant infiltration of the three highlighted cell types.
- Presence of Imprime-bound cells within the tumor microenvironment.
- Increased infiltration of myeloid cells and their polarization towards the M1 phenotype. 
- Increased expression of FOXP3 and tumor-infiltrating CD80+ cells.
- Identification of Imprime-bound cells and CD80+ myeloid cells within the tumor microenvironment.
- Colocalization of Imprime-bound cells, activated myeloid cells and advanced T cells within the tumor microenvironment.

1) Tissue harvest
2) Staining
3) Multispectral Imaging and Analysis Workflow
4) Tumor Microenvironment Staining Panel – Imprime Staining
5) Convert imaging data into the software Histoflow
6) Unmixed Image Segmentation Phenotyping
7) IHC Quantitative Data Summary

Images from stained biopsy MEL1 On Rx that show various regions of accumulation for various infiltrating cell types. Images show high levels of Imprime (blue) from the Tumor Microenvironment IHC Panel. Middle image shows an expression map of CD163+ myeloid cells. Far right image (MEL1 On Rx) highlights regions of CD163+ myeloid cells that represent tumor regions with significant infiltration of the three highlighted cell types.