Imprime PGG, a soluble yeast β-1,3/1,6 glucan, is being clinically evaluated in combination with tumor-reactive antibodies, antitumoral agents, and cytotoxic chemotherapy in various tumor indications. Preclinical studies have demonstrated that Imprime's immune-modulatory effects on myeloid cells create an immunostimulatory microenvironment that can affect tumor growth and survival. These effects are mediated through a combination of direct effects on myeloid cells and indirect effects on tumor cells. Imprime, in combination with anti-PD-1 antibody therapy, has been shown to improve the overall survival of mice with advanced melanoma or triple-negative breast cancer (TNBC). These findings suggest that Imprime may have potential as an immunostimulatory agent for use in combination with other immunotherapies.

**Background**

Imprime PGG (Imprime), an IV administered soluble yeast β-1,3/1,6 glucan is being evaluated for its ability to modulate the immune system. Imprime has been shown to induce the expression of markers of antigen-presentation on myeloid cells and to repolarize the tumor microenvironment. These effects are mediated through a combination of direct effects on myeloid cells and indirect effects on tumor cells. Imprime, in combination with anti-PD-1 antibody therapy, has been shown to improve the overall survival of mice with advanced melanoma or triple-negative breast cancer (TNBC).

**Methods**

Imprime was tested in combination with a PD-1 mAb in mice with advanced melanoma or TNBC. The treatment regimen included Imprime (2 mg/kg, i.p) and anti-PD-1 mAb (20 mg/kg, i.p) administered on alternate days. The effects of Imprime on the tumor microenvironment and infiltration and activation of immune cells were assessed in preclinical and clinical studies.

**Results**

Imprime synergizes with anti-PD-1 antibody therapy in the murine MC38 tumor model. When tumors were >3 mm in diameter, mice were treated with Imprime (2 mg/kg), anti-PD-1 mAb (20 mg/kg), or a combination of the two. The results showed that the combination therapy resulted in a greater than additive antitumor effect, with complete tumor regression observed in some mice. In clinical samples, higher frequency of monocytes and enhanced expression of CD11b+ cells were observed in the periphery with Imprime/PD-1 therapy. Compared to pre-treatment levels, greater than either agent alone. Macrophages evaluated from Imprime-treated tumors were shown to exhibit immunostimulatory effects, with Imprime's M1-polarization effects evaluated by RNA expression and flow cytometric analyses.

**Conclusions**

Imprime PGG, a soluble yeast β-1,3/1,6 glucan, exhibits immunostimulatory effects in preclinical and clinical studies. These effects are mediated through a combination of direct effects on myeloid cells and indirect effects on tumor cells. Imprime, in combination with anti-PD-1 antibody therapy, has been shown to improve the overall survival of mice with advanced melanoma or triple-negative breast cancer (TNBC). These findings suggest that Imprime may have potential as an immunostimulatory agent for use in combination with other immunotherapies.