Syngeneic Models for Developing Cancer Therapeutics Targeting Immune System

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Abstract

Syngeneic tumor models have long been used in cancer research, from mechanistic study to developing cancer therapeutics, especially those that require intact immune system, such as the ADCC effect in many of the antibody therapeutics. Recently, cancer immunotherapy reignited to become one of the most promising therapies, largely because of the success of the clinical studies of CTLA-4, PD-1/PD-L1 antibodies. Researchers now believe there are many novel therapeutics, both small and large molecules, and many novel targets, to be discovered and developed in this field. To meet this demand, Crown has established a large collection of syngeneic models that covers most of the tumor types and mutational profiles. In addition, we've also profiled the models using anti-mouse PD1/PD-L1 antibodies. The syngeneic models display very different responses toward the immunotherapeutics, ranging from shrinking the tumor to stimulating the tumor growth. These results emphasize the need to carefully select models based on the development goals. A single agent development approach would require selecting the models with the best response, while a combination study design would require a model with suboptimal response. Our comprehensive list of syngeneic models and profiling data are essential in developing cancer immunotherapies that may one day benefit the patients.

Method

Animals: C57BL/6 and BALB/c mice purchased from Beijing HFK Bio-Technology Co. Ltd. (HFK, Beijing, China) and Shanghai Laboratory Animal Center (SLAC, Shanghai, China).

Tumor Inoculation: For subcutaneous syngeneic models, each mouse was inoculated at the right flank with tumor cells for tumor development.

Group and Treatment: The treatments for the therapeutic study were started when mean tumor size reached 100mm^3 in subcutaneous model.

Endpoints: Tumor volume was calculated as the formula: V (mm^3) = (a x b^2)/2, where a and b were the long and short diameters of the tumor, respectively.

Statistical Analysis: For comparison between two groups, an independent sample t-test were used. All data were analyzed using SPSS 18.0. $p < 0.05$ was considered to be statistically significant.

Results

Fig. 1 The Efficacy Evaluation of Immunotherapeutic Abs in the Treatment of Murine Syngeneic Model

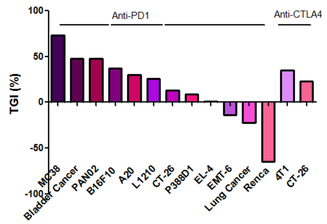

Figure 1 The Efficacy Evaluation of Immunotherapeutic Abs in the Treatment of Murine Syngeneic Model

Fig. 2 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous MC38 Murine Colon Carcinoma Model

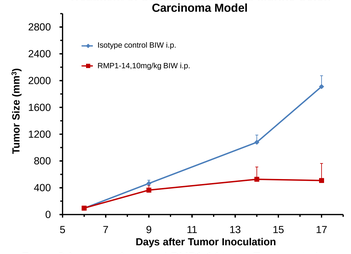

Figure 2 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous MC38 Murine Colon Carcinoma

Fig. 3 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous Murine Bladder Cancer Model

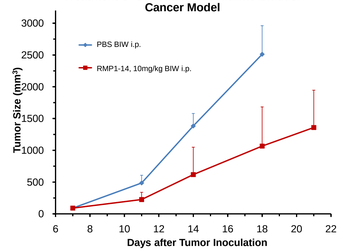

Figure 3 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous Murine Bladder Cancer Model

Fig. 4 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous PAN02 Murine Breast Cancer Model

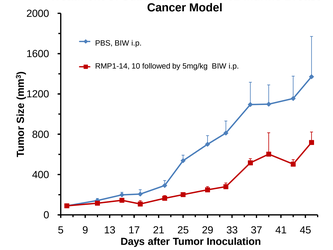

Figure 4 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous PAN02 Murine Breast Cancer Model

Fig.5 Antitumor Activity of RPM1-14 in the Treatment of Subcutaneous B16F10 Murine Melanoma Model

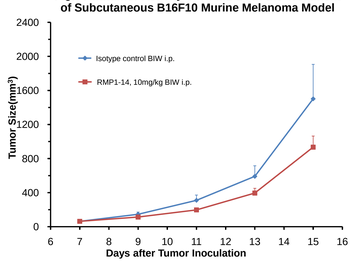

Figure 5 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous B16F10 Murine Melanoma Model

Fig.6 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous A20 Murine B lymphoma Model

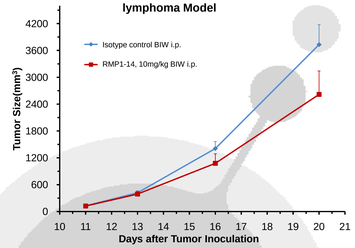

Figure 6 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous A20 Murine B lymphoma Model

Fig. 7 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous L1210 Murine Lymphoid Leukemia Model

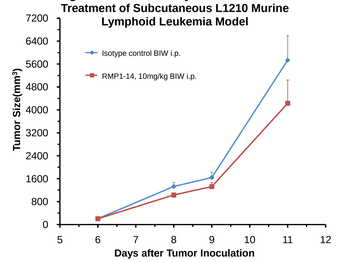

Figure 7 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous L1210 Murine Lymphoid Leukemia Model

Fig.14 Antitumor Activity of Anti-CTLA4 Ab in the Treatment of Subcutaneous 4T1 Murine Breast Cancer Model

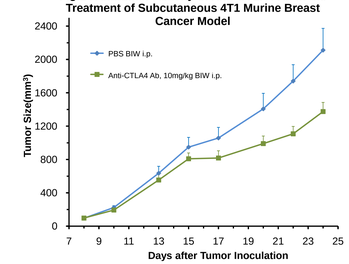

Figure 14 Antitumor Activity of Anti-CTLA4 Ab in the Treatment of Subcutaneous 4T1 Murine Breast Cancer Model

Fig. 8 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous CT-26 Murine Colorectal Cancer Model

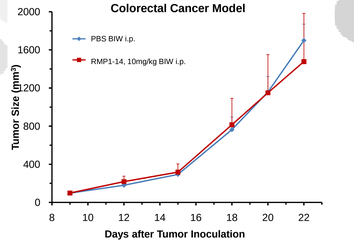

Figure 8 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous CT-26 Murine Colorectal Cancer Model

Fig. 9 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous P388D1 murine lymphoma Model

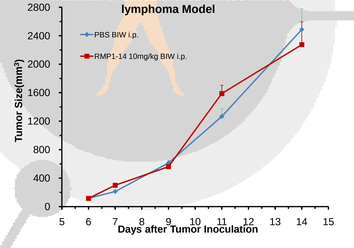

Figure 9 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous P388D1 murine lymphoma Model

Fig. 10 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous EL-4 Murine Lymphoma Model

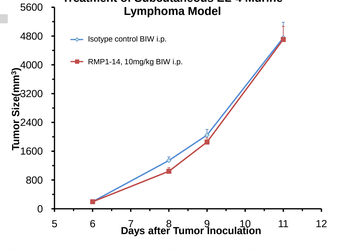

Figure 10 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous EL-4 Murine Lymphoma Model

Fig.15 Antitumor Activity of Anti-CTLA4 in the Treatment of Subcutaneous CT-26 Murine Colorectal Cancer Model

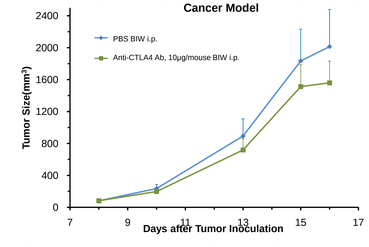

Figure 15 Antitumor Activity of Anti-CTLA4 in the Treatment of Subcutaneous CT-26 Murine Colorectal Cancer Model

Fig. 11 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous EMT-6 Murine Breast Cancer Model

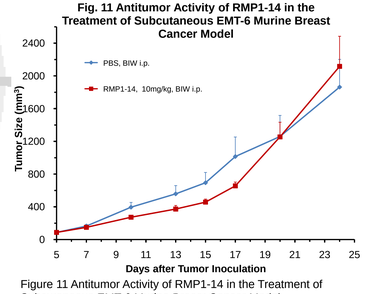

Figure 11 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous EMT-6 Murine Breast Cancer Model

Fig. 12 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous Murine Lung Cancer Model

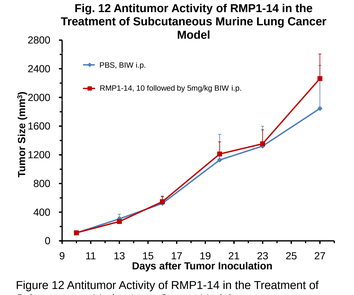

Figure 12 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous Murine Lung Cancer Model

Fig.13 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous Renca Murine Kidney Cancer Model

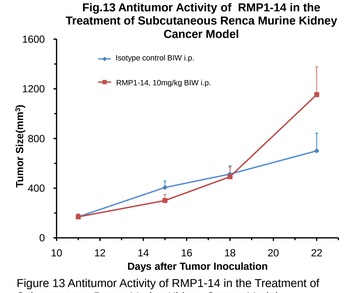

Figure 13 Antitumor Activity of RMP1-14 in the Treatment of Subcutaneous Renca Murine Kidney Cancer Model

Conclusions

The syngeneic models display very different responses toward immunotherapeutics.

Careful selection of models based on development goals are necessary, be it single agent or combination therapy.

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