INTRODUCTION

Toll-like receptors (TLRs), which activate the innate immune system and play an important role in adaptive immune responses, and immunostimulatory agents that regulate T cell activity, such as cyclophosphamide-associated antigens (CAA), have been used as tumor vaccines in multiple clinical studies leading to clinical responses in a broad range of solid tumors. In addition, TLR9 agonists have been shown to enhance antitumor immunity. However, TLR9 agonists are not generally well tolerated in multiple clinical studies involving more than 300 healthy volunteers and patients with viral, cachexic, or late stage disease.

IMO-2055 is a potent and selective TLR9 agonist designed to stimulate an immune response. In previous preclinical studies, IMO-2055 demonstrated synergistic or additive effects when combined with tyrosine kinase inhibitors and monoclonal antibodies. However, the antitumor effect of IMO-2055 was generally well tolerated. In the present studies, we studied IMO-2055 alone and in combination with ipilimumab, an approved mAb against CTLA-4, to evaluate antitumor immune activity and effects on treated and distant tumors.

METHODS AND RESULTS

Evaluation of intratumoral injections of IMO-2055 monotherapy in the murine bladder carcinoma CT26 model

Evaluation of intratumoral injections of IMO-2055 and CTLA-4 mAb on directly treated tumors and systems in vivo. Tumor regression was monitored by measuring tumor volume and calculating tumor size on days 0, 4, 8, 12, and 16. Tumors were excised on day 16 after tumor implantation for histological analysis. Tumors were treated once at day 6. Tumors were excised on day 16 after tumor implantation for histological analysis. Tumors were treated once at day 6.

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