INTRODUCTION

- New immunotherapy regimens involving multiple agents represent a highly promising area of cancer research; a challenge is to identify optimal combinations.
- Investigations of checkpoint inhibitors such as ipilimumab, nivolumab, and pembrolizumab have shown a correlation between clinical activity and checkpoint gene expression.
- Preclinical data have demonstrated that intratumoral administration of IMO-2125, a novel TLR9 agonist shown to induce interferon-α, modulates the tumor microenvironment and induces antitumor immune responses.
- The current study was undertaken to evaluate the tumor microenvironment following intratumoral IMO-2125 therapy. This evaluation includes analysis of checkpoint expression in treated tumors as well as in distant tumors.

METHODS AND RESULTS

Intratumoral IMO-2125 induced potent antitumor activity and tumor checkpoint expression compared to subcutaneous administration in an A20 lymphoma model

STUDY DESIGN

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CHANGES IN TUMOR VOLUME AND TIL INFILTRATION

- CD3+ TILs
- PBMCs
- IMO-2125 3 x 10^6 cells
- IMO-2125 6 cells

CHANGES IN CHECKPOINT GENE EXPRESSION

- IDO1
- TIM3
- PDL1
- CTLA4

CT26 colon carcinoma model

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A20 lymphoma model

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CONCLUSIONS

- Intratumoral IMO-2125 stimulated potent antitumor activity in preclinical models of lymphoma, colon carcinoma and melanoma.
- Treatment led to increases in CD3+ TILs.
- Intratumoral IMO-2125 induced a systemic antitumor effect.
- Treatment led to decreases in tumor volume in treated and distant tumors.
- Intratumoral IMO-2125 modulated immune checkpoint gene expression, including IDO1, PD1L, TIM3, LAG3 and CTLA4, in both treated and distant tumor nodules.
- Together, these data showed that intratumoral IMO-2125 sensitized the tumor microenvironment for potential combinatorial effects with various checkpoint inhibitors.
- Planning for a clinical trial of intratumoral IMO-2125 in combination with ipilimumab, an anti-CTLA4 monoclonal antibody, in patients with metastatic melanoma is currently underway with study initiation expected in 4Q 2015.