INTRODUCTION

• In recent years, understanding of tumor immunology has led to modulation of the tumor microenvironment (TME) and resulted in more potent antitumor activity. Effective immunotherapy requires an understanding of the role of TLR9 agonists in the TME.

• Several IDO-1 inhibitors in clinical development have led to significant advances in cancer immunotherapy. New approaches to modulate the TME are now being pursued, with IMO-2125, a Toll-like receptor (TLR) 9 agonist, to modulate the TME.

• A Phase 1/2 clinical trial of IMO-2125 in combination with ipilimumab in subjects with metastatic melanoma is ongoing (NCT02644967).

Rationale for the current studies

• The current studies are designed to evaluate the antitumor activity and the role of combination treatment with IDO-1 inhibitors in the TME.

• Combination treatment was shown to induce immune checkpoint suppression and cross-regulatory pathways including IDO-1 in tumors.

• In the current studies, combination of IMO-2125 is treated with IDO-1 inhibitor, resulted in multiple immune pathways that enhance antitumor activity.

• Analysis of tumor biopsies showed (Combination 1) expression and increased IDO-1 for the combination group compared to IMO-2125 alone.

• Combination treatment suppressed an IMO-2125–associated increase in IDO-1 checkpoint expression.

• The current clinical data confirmed that the combination of IMO-2125 is evaluable and that Combination 1 would lead to modulation of the TME and enhanced antitumor activity.

CONCLUSIONS

• IMO-2125 was shown to induce immune checkpoint suppression and cross-regulatory pathways including IDO-1 in tumors.

• Combination treatment with IDO-1 inhibitor resulted in multiple immune pathways that enhance antitumor activity.

• Analysis of tumor biopsies showed (Combination 1) expression and increased IDO-1 for the combination group compared to IMO-2125 alone.

• Combination treatment suppressed an IMO-2125–associated increase in IDO-1 checkpoint expression.

• The current clinical data confirmed that the combination of IMO-2125 is evaluable and that Combination 1 would lead to modulation of the TME and enhanced antitumor activity.

DISCUSSION

Creating the tumor microenvironment for effective immunotherapy: antitumor activity of intratumoral IMO-2125, a TLR9 agonist, is further enhanced by inhibition of indoleamine-pyrole 2,3-dioxygenase (IDO)

DISCUSSION

Creating the tumor microenvironment for effective immunotherapy: antitumor activity of intratumoral IMO-2125, a TLR9 agonist, is further enhanced by inhibition of indoleamine-pyrole 2,3-dioxygenase (IDO)

DISCUSSION

Creating the tumor microenvironment for effective immunotherapy: antitumor activity of intratumoral IMO-2125, a TLR9 agonist, is further enhanced by inhibition of indoleamine-pyrole 2,3-dioxygenase (IDO)

Creating the tumor microenvironment for effective immunotherapy: antitumor activity of intratumoral IMO-2125, a TLR9 agonist, is further enhanced by inhibition of indoleamine-pyrole 2,3-dioxygenase (IDO)