Intratumoral IMO-2125 treatment in combination with anti-CTLA-4 mAb induces durable anti-tumor responses associated with tumor-specific memory in preclinical studies

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INTRODUCTION

Mechanism of action of I.T. IMO-2125

- IMO-2125 is a synthetic agonist of Toll-like receptor (TLR) 9
  - TLR9 is a key receptor of the innate immune system and is expressed on human dendritic cells and B-cells
  - Activation of TLR9 leads to induction of interferon alpha and other Th1-type cytokines, thereby activating an innate cascade, and bridging adaptive immunity

- Data from preclinical studies has shown that
  - I.T. IMO-2125 demonstrates dose-dependent anti-tumor activity in the treated tumor, as well as distant tumors
  - I.T. IMO-2125 in combination with agents targeting CTLA-4, PD-1, and PD-1/PDL-1 inhibitors has shown potent anti-tumor activity
  - The anti-tumor activity of I.T. IMO-2125 is associated with increased Tumor Infiltrating Lymphocytes (TILs), most of which are CD8+ T-cells

- Our current clinical trials have shown encouraging results that IMO-2125 in combination with other molecules promotes anti-PD-1 (Pembrolizumab) therapy resistance in melanoma patients

DISCUSSION

Durability of the anti-tumor activity during the follow-up period

Combination therapy with I.T. IMO-2125 and anti-CTLA-4 mAb increased plasma soluble IL-1R antagonist and plasma anti-tumor IgG2a

Tumor-free mice developed tumor-specific memory responses following I.T. IMO-2125 and anti-CTLA-4 mAb treatment

Durable anti-tumor activity is associated with tumor-specific immune responses

CONCLUSIONS

- Combination treatment with I.T. IMO-2125 and anti-CTLA-4 mAb was well tolerated in preclinical models
- Combination treatment showed potent systemic anti-tumor activity compared to either agent alone
- Combination therapy with I.T. IMO-2125 given for 1 to 2 weeks with anti-CTLA-4 mAb lead to potent anti-tumor activity, and showed durable responses
- In the combination treatment group, all mice remained tumor free at both injected and distant tumor sites for 360 days
- Durable anti-tumor activity was associated with tumor-specific immune responses

References

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