MGC018, a Duocarmycin-based Antibody-drug Conjugate Targeting B7-H3, Exhibits Immunomodulatory Activity and Enhanced Antitumor Activity in Combination with Checkpoint Inhibitors

Juniper A. Scribner, Michael Oliwio, Pam Li, Thomas San, Jeff Hooley, Ying Li, Anushka De Costa, Peter Lung, Nicholas Yee-Toy, Francine Chen, Zhuangyu Pan, Bhavesh Baral, Christina Wolff, Valentina Ciccocciro, James Tamura, Scott Keenig, Chet Bohar, Ian Wighton, Paul A. Moore, Elio Bonvini, Deryk Lee

Abstract

MGC018 is a Clinical-stage Anti-B7-H3 ADC Therapeutic

Background

MGC018 Antitumor Activity Toward Patient-derived Xenograft (PDX) Models

Synergistic Mouse Model System

Dosing

Results

Antitumor Activity of MGC018 is Enhanced on Human B7-H3 Expression

Antitumor Activity of MGC018 in Combination with Anti-PD-1 in C26 Model: Induction of Immunological Memory

MGC018 Increases Infiltration of Lymphocytes into MC38/B7-H3 Tumor Xenografts

Conclusions

Acknowledgements

References

MGC018 and B7-H3 are highly expressed in a variety of solid cancers and as a result, MGC018 is a promising treatment for cancer, interest has grown in understanding the potential of cytotoxic agents to promote immune surveillance or stimulate a promising treatment for cancer. The potential of MGC018 to promote immune surveillance or stimulate an immune response in vivo was evaluated in syngeneic mouse models. Depletion of CD8+ T cells led to reduced antitumor responses, indicating that CD8+ T cells contribute to MGC018-mediated antitumor responses.

MGC018 and anti-PD-1 combined treatment in vivo led to improved antitumor activity compared to MGC018 or anti-PD-1 alone, indicating that MGC018 can cooperate with anti-PD-1 to enhance antitumor activity. Our findings support a clinical strategy that combines MGC018 with checkpoint inhibitors to enhance antitumor responses.

MGC018 is a novel, human B7-H3-targeting ADC that demonstrates antitumor activity toward heterogeneous B7-H3-expressing solid cancers. MGC018 treatment increased infiltration of CD4+ T cells and Granzyme B+ cells, indicating an immunomodulatory activity of MGC018. Tumor cells are originally derived from the same genetic background as the tumor initiating cell and tumor associated vasculature.

MGC018 was combined with anti-PD-1. Treatment with MGC018 alone, or in combination with anti-PD-1 led to complete antitumor responses, and the prospect to combine with checkpoint inhibitors to enhance antitumor responses.

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