Abstract 10037

Testing of B7-H3 Targeting Antibody-Drug Conjugate (ADC) MGC018 in Models of Pediatric Solid Tumors by the Pediatric Preclinical Testing Consortium (PPTC)


1. Introduction

- B7-H3 (encoded by the CD276 gene) is a checkpoint molecule that is highly expressed in pediatric solid tumors, with limited expression in normal tissues (Du, et al. 2016).
- Overexpression of B7-H3 is correlated with tumor progression, metastasis, and poor clinical outcome across a variety of malignancies (Ye, et al. 2016).

2. Study Methods

- MGC018 is a duocarmycin-based ADC (drug-to-antibody ratio = 2.7) targeting B7-H3, showing robust in vivo activity against a range of adult cancer models, and a favorable pharmacokinetic and safety profile in cynomolgus monkeys (Stobinoff, et al. 2020).
- MGC018 is being evaluated in a phase 1/2 trial (NCT03729596) in pediatric cancer preclinical models showed.

3. CD276 mRNA and Protein Expression

- CD276 expression by IHC was highest for OS. NB expressed more CD276 mRNA expression was higher in pediatric solid tumor specimens in vivo.

4. Results

- Objective response categories are as described by Houghton, et al. 2007.

5. Discussion and Conclusions

- RNAseq data showed elevated CD276 expression levels in pediatric solid tumors, which is consistent with protein expression data from clinical specimens (Majzner, et al. 2019 and Kendersky, et al. 2021). Protein levels of CD276 are highest in OS and lowest in EwS, with RMS and NB having intermediate levels.

6. References

- More Information
- Corresponding Author: Dr. Raushan Kurmasheva
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- Poster available at: http://www.ncipptc.org/publications