Evaluation of ABBV-085, an antibody-drug conjugate targeting LRRC15, in Osteosarcoma by the Pediatric Preclinical Testing Consortium

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Methods

ABBV-085 Administration:

- Two doses, 6 mg/kg and 12 mg/kg, once a week for 4 weeks via intraperitoneal injection were tested in 2 patient derived xenografts (PDX) models; remaining models were tested at 6 mg/kg dose with a single model (OS-33) also tested at 3 mg/kg.

Study Design and Analysis:

- Four high LRRC15 expressing (OS1, OS33, OS42-SJ and OS60) and two low LRRC15 expressing PDX (OS9, OS34-SJ) were heterotopically injected into the flanks of CB17SC scid- mice

- Tumor growth, Event Free Survival (EFS) compared between treatment and control groups

- P-values were two-sided and considered statistically significant if p <0.05

Introduction

• Survival rates for patients with metastatic and recurrent osteosarcoma (OS) have remained stagnant at <30% for several decades

• Data from genome sequencing has failed to reveal recurrent genetic aberrations that are therapeutically targetable in a large proportion of patients

• Identification of cell-surface proteins that are strongly expressed in a majority of tumors and can be targeted directly or indirectly provides a novel therapeutic avenue

• Antibody-drug conjugates (ADC) are novel therapeutic agents with a monoclonal antibody against a cell surface protein linked to a cytotoxic payload via a linker that releases the payload inside the cell

• ABBV-085 is an ADC against LRRC15, a highly expressed cell surface protein in OS, linked to a tubulin inhibitor MMAE.

• The PPTC sought to evaluate the potential anti-cancer efficacy of ABBV-085 against in vivo OS models

ABBV-085 demonstrated significant anti-tumor activity in OS with a marked prolongation of EFS in 3/5 PDX

OS33 demonstrated a maintained complete response

Response was related to tumor LRRC15 expression

ABBV-085 should be further studied in a clinical trial of patients with OS

References
