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

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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

Methods

ABBV-085 Administration:
• Two doses, 6 mg/kg and 12mg/kg, once a week for 4 weeks via intraperitoneal injection were tested in 2 patient derived xenografts (PDX) models; remaining models were tested at 6mg/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
• Two control cohorts that received vehicle and isotype MMAE-linked antibody were included for each PDX model
• Tumor volume was monitored in all cohorts with event defined as 4x initial tumor growth
• 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

RNA and Protein Expression of LRRC15 in OS

Discussion and Conclusions

• ABBV-085 demonstrated significant anti-tumor activity in OS with significant 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