XMT-1660 is a Dolasynthen Antibody Drug Conjugate (ADC) targeting B7-H4 and carrying a Dolasynthen payload with a directed bystander effect. B7-H4 is an immunoregulatory protein that is expressed in breast, ovarian and endometrial cancers. 4 The expression of B7-H4 has been described in both tumor cells and in tumor-associated macrophages, and B7-H4 shows frequent co-expression with PD-L1, suggesting distinct immunoregulatory functions. 5 XMT-1660 is built on the Dolasynthen platform which incorporates several advantages, including site-specific bioconjugation and precise control over drug-to-antibody ratio (DAR). 6 Previously, we demonstrated the cytotoxic efficacy of XMT-1660 in cell line xenografts and patient derived xenograft models of breast cancer known to have B7-H4 over expression. 7 The purpose of the study was to evaluate the anti-tumor activity of XMT-1660 across an untreated panel of breast cancer patient derived xenograft (PDX) models, evaluate the level of B7-H4/XMT-1660 activity compared to B7-H4-positive models, and assess the correlation between B7-H4 expression and anti-tumor activity following a single dose of XMT-1660.

**Introduction**

**Results**

**Figure 2** In the model set, 12/28 (43%) of primary breast carcinoma models achieved a median best response of 30% (shown as 0.3 on the Y-axis) or better prior to final dose escape of 400 mg/kg XMT-1660. Tumor volume reductions were seen in 12/30 (40%) models. Of the 32 PDX in which a median best response of 30% was achieved, 10 were derived from known treated tumors. The anti-tumor effect of XMT-1660 of 30% or more was more frequent in TNBC models (5/10, 50%; compared to 12/28, 43%; does not color by receptor status). Two additional B7-H4 positive models, originally proposed for this study, were excluded from summary analysis due to unexpectedly rapid growth/mouse tumor phenotype or very slow growth in vehicle animals.

**Summary**

**Figure 4** TPS ranged from 0-100 and was calculated based on immunoreactivity: cytoplasmic reactivity; if none, it was not included in the score. Higher B7-H4 (IHC) TPS values were associated with response in this sample set (A) A similar trend was observed when XMT-1660 was administered using an I4-Score method. Employing a cut-off of 40 TPS (IHC) (High x75, TPS >7) identified 12/15 (77%) of responding models, below a cut-off of TPS 28 (TPS <25) 3/16 (19%) models were non-responders, when response was considered to be MBR ≥ 3 following a single dose of XMT-1660. Representative images of breast cancer xenografts are shown with associated scores (MBR); tumor color corresponds to receptor status (green: ER-, blue: ER+).