**INTRODUCTION**

MT1-MMP is a membrane-type matrix metalloproteinase (MMP) involved in extracellular matrix degradation.

- Established role in cell invasion and metastasis
- Various tumor types have reportedly high MT1-MMP expression including breast, ovarian, lung, and bladder cancer
- MT1-MMP expression is associated with poor outcomes in various tumor types
- MT1-MMP is expressed at low levels in normal tissue
- MMPs are difficult pharmacological targets due to their high sequence similarity and compensatory roles

**METHODS**

- A clinical grade MT1-MMP IHC assay was developed on the Ventana platform using a Millipore MT1-MMP primary antibody (MAB3328) at 1:6000 and detected using Optiview chemistry
- TMAs (n=8) were selected covering multiple cancer indications (Figure 1A) with reportedly high MT1-MMP expression. After staining, MT1-MMP expression levels were estimated by consensus of two pathologists using an H-score (staining intensity*percent positivity). H-scores (0-300) were derived separately for tumor membrane (TM), cytoplasm (TC), and stroma (TS) for each TMA slide.

**RESULTS**

**DISTRIBUTION ANALYSIS**

Figure 1: Tumor membrane, tumor cytoplasm and stromal staining of MT1-MMP was quantified for ~600 tumor cores

**SQUAMOUS HISTOLOGY ANALYSIS**

Figure 2: Squamous tumors are enriched for higher MT1-MMP tumor membrane expression relative to non-squamous tumors

**CONCLUSION/SUMMARY**

- An indication and patient selection strategy was developed for BT1718 using a novel IHC scoring method to determine MT1-MMP expression levels on tumor sub cellular compartments.
- Expansion cohorts with prospective selection were selected for the BT1718 Phase 1/2 trial to increase the enrollment of patients with tumors that have high MT1-MMP expression.
- Expansion to expansion cohorts will commence following establishment of the one-weekly BT1718 RP2D; dose escalation is ongoing.

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**REFERENCES**