A Cancer Research UK phase I/IIa trial of BT1718 (a first in class Bicycle Toxin Conjugate) given intravenously in patients with advanced solid tumours.

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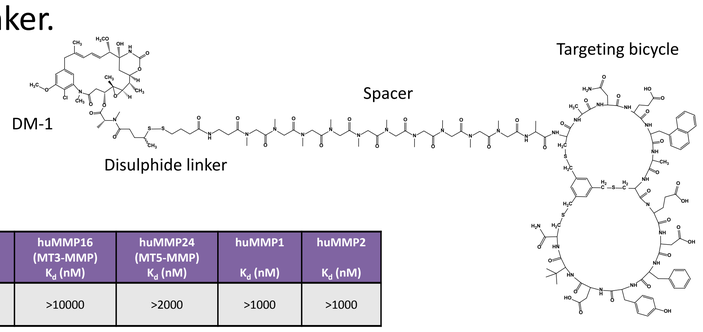
Background - Target

MT1-MMP (MMP-14) - surface metalloproteinase involved in tissue remodelling through proteolysis of extracellular matrix components

- Highly expressed in tumours with unmet medical need, including triple negative breast cancer (TNBC) and non small cell lung cancer (NSCLC)
- Strong link with cell invasion, metastasis
- Expression correlated to poor outcomes
- High adjacent tumour stroma expression
- Low expression in adult normal tissue

Background - Drug

BT1718 - novel first in class bicyclic targeting peptide that binds MT1-MMP and is linked to the maytansinoid tubulin inhibitor DM1 by a cleavable disulfide linker.

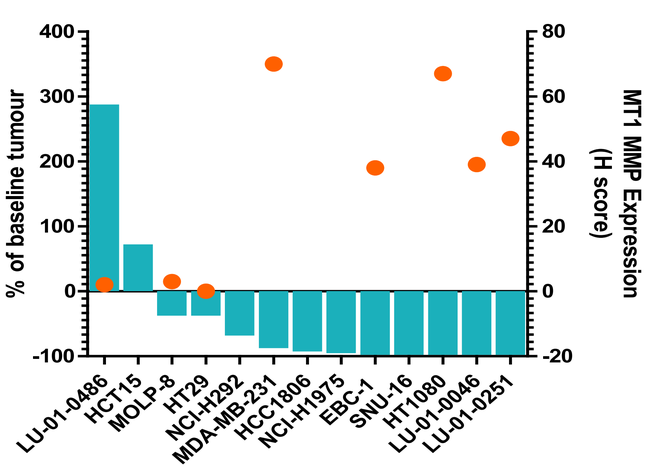


huMMP14 (MT1-MMP) K_d (nM)	moMMP14 (MT1-MMP) K_d (nM)	huMMP15 (MT2-MMP) K_d (nM)	huMMP16 (MT3-MMP) K_d (nM)	huMMP24 (MT5-MMP) K_d (nM)	huMMP1 K_d (nM)	huMMP2 K_d (nM)
2.6	1.8	>10000	>10000	>2000	>1000	>1000

Bicycle Toxin Conjugates have a low molecular weight in comparison to other conjugated toxin approaches, enabling rapid penetration and a short systemic half-life, potentially reducing toxicity.

Background - Predictive Biomarker

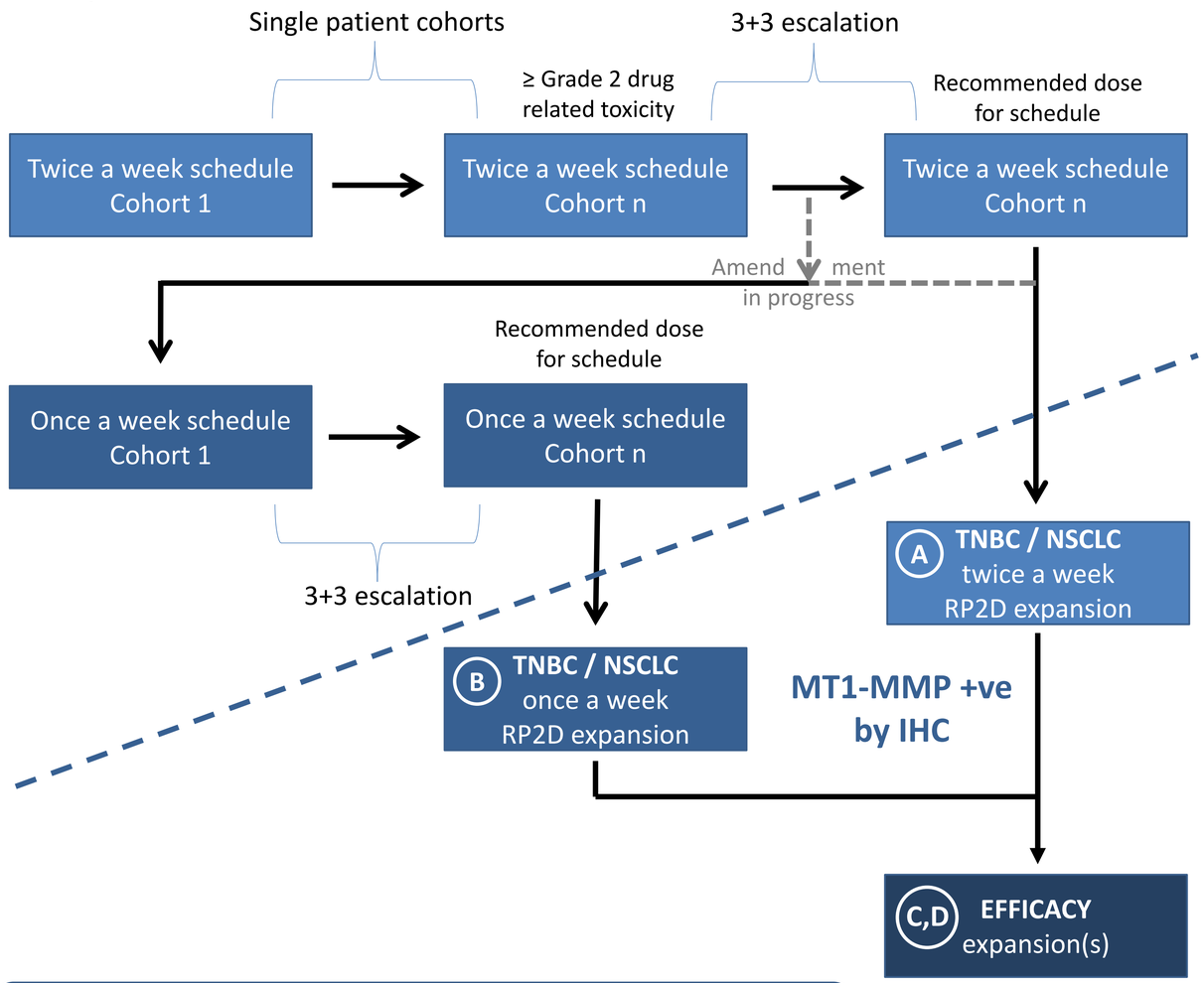
Regression in MT1-MMP expressing xenografts



Trial Design

Open label first in human phase I/IIa study - primary objective to propose a recommended phase 2 dose (RP2D) and schedule of BT1718. Secondary objectives include pharmacokinetic (PK) parameters, and preliminary clinical responses in biomarker pre-defined cohorts of patients. Tertiary objectives include correlative blood and tissue biomarker studies.

- Accelerated dose escalation design with single patient cohorts until grade 2 drug related toxicity, then a 3+3 design to maximum tolerated dose and RP2D
- Starting with twice a week schedule IV; will also explore once a week schedule
- Parallel expansions in MT1-MMP +ve patients, exploring clinical & biological activity, to refine schedule, biomarkers & population for final efficacy expansions



Current Status

Cohorts 1, 2 & 3 have been completed without DLT and single patient escalation continues. Our thanks to all the patients that have kindly participated in the trial.