**INTRODUCTION**

BT1718 is a novel first in class bicyclic targeting peptide that selectively binds MT1-MMP (MMP-14) and is linked to the maytansinoid tubulin inhibitor DM1 by a cleavable disulfide linker. Bicycle Toxic Conjugates have a low molecular weight compared to other conjugated toxin approaches, enabling rapid tumour penetration and a short systemic half-life (<1h). These properties limit the body’s exposure to payload to minimize damage to normal tissue.

**STUDY DESIGN**

Open-label, first in human phase I/IIa study of twice weekly (BIW) and once weekly (QW) dosing schedules in patients with advanced solid tumours. 

**STUDY STATUS: Characteristic**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SW Patients</th>
<th>QW Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Median (range)</td>
<td>Median (range)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>13/15</td>
<td>8/7</td>
</tr>
<tr>
<td>Median age</td>
<td>58 (27 – 72)</td>
<td>59 (22 – 77)</td>
</tr>
</tbody>
</table>

**RESULTS: Pharmacokinetics**

Summary of adverse events: table shows drug exposure vs time after first doses in cycles 1 & 2

<table>
<thead>
<tr>
<th>Drug Exposure vs Time</th>
<th>BIW</th>
<th>QW</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIW AUC</td>
<td>7.2 mg/m²</td>
<td>10 mg/m²</td>
</tr>
<tr>
<td>BIW t½ life</td>
<td>2.4 h</td>
<td>1.2 h</td>
</tr>
</tbody>
</table>

**CONCLUSIONS / SUMMARY**

• AUC of BT1718 (following a 1h IV infusion) increases with dose, and is consistent between Cycles 1 and 2. Preliminary analysis of total DM1 levels in tumour indicates localisation of DM1 at tumour; further plasma and tumour DM1 analysis is ongoing to assess extent of DM1 retention in tumour.

• RP2D for twice weekly dosing determined as 7.2 mg/m². A greater total BT1718 dose per cycle was achieved using once weekly dosing (dose escalation ongoing at 32 mg/m²); therefore, RP2D used in the expansion phase was selected for on-treatment schedule.

• Although no RECIST objective responses were seen in an unselected population, an encouraging number of patients had stable disease and there has been evidence of tumour shrinkage. Once weekly RP2D will be assessed for efficacy in patients selected for tumoural MT1-MMP expression.

**AUTHOR AFFILIATIONS / ACKNOWLEDGEMENTS**

The authors declare no conflict of interest to declare. The study is sponsored by Bicycle Research UK.

York Bioscientific Solutions Limited determined BT1718 concentrations in plasma. Pharmacokinetic pilot conducted data analysis.

Thank you to all the patients who have kindly participated in this trial.

**REFERENCES**

1. University of Manchester & Christie NHS Foundation Trust, Manchester, UK; Institute of Cancer Research & Rosal Margen NHS Foundation Trust, Sutton, UK; University of Glasgow & Western of Scotland Cancer Centre, Glasgow, UK; Cancer Research UK Centre for Drug Development, London, UK; Bicycle Therapeutics, Cambridge, UK; formerly at Bicycle Therapeutics; currently Ranger Therapeutics; University of Edinburgh, Edinburgh UK. Corresponding author Stefan Symeonides@ed.ac.uk

Pharmacokinetic (PK) assessment of BT1718: A phase 1/2a study of BT1718, a first in class binary toxin conjugate (BTC), in patients with advanced solid tumours

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**RESULTS: Safety and Efficacy**

No objective responses (RECIST 1.1) observed to date in this unselected population. 13/24 patients had stable disease at the 8 week timepoint; one patient had ~14% reduction in target lesions at end of cycle 2 with 6.4% decrease in one lesion. Mean number of cycles received was 3 months (±8). 

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