Supplementary Material 4

Screening and Registration

D.4 Screening and Registration

D.4.1 Informed consent

- Prior to formal screening process patients were required to provide written informed consent. Before performing any non-standard of care assessments written informed consent was obtained.
- Eligible patients were invited to participate by their consultant and the trial was explained to them. A trial PIS was provided and the patients had a minimum of 24 hours to consider the information before giving written informed consent. The right to refuse to participate without giving reasons was respected.
- If the patient expressed an interest in participating in the trial, they were asked to sign and date the latest version of the ICF. The Principal Investigator (PI) or Co-Investigator with documented, delegated responsibility witnessed, signed and dated the ICF.
- Patients that provided written informed consent for screening were allocated a screening number.
- Patients were then invited to participate in the formal screening process.
- An Eligibility Checklist was completed by the Investigator to document fulfillment of the inclusion criteria for all patients considered for the trial and subsequently included or excluded patients. Details of all patients approached about the trial were recorded on the Patient Screening/Enrolment Log. Each site was provided with a Patient Screening Enrolment log, which was pre-populated with site-specific screening numbers.
- The original signed ICF was retained in the Investigator Site File (ISF), with a copy in the hospital notes and a copy provided to the patient. The patient specifically consented for their General Practitioner (GP) to be informed of their participation in the trial.
- The screening process consisted of two visits (Visit 1 and 2).

D.4.2 Pre-registration

After the results of the screening process (Visits 1 and 2) were available, the following information was verified by the local site PI and/or Co-Investigators before registering the patient onto the trial:

- Patients ICF,
- Confirmation of all the inclusion criteria,
- Review of all the exclusion criteria,

- Patient's screening number,
- Completion of Registration Form.

D.4.3 Registration

Eligible patients were registered via the Trial Office. All patients were registered for trial entry with the CRCTU at the University of Birmingham and were allocated a unique Trial Number. Completed Eligibility Checklists and Registration Forms were sent to the Trial Office. A copy of the patient's ICF was also sent to the Trial Office, if the patient had given explicit consent for this.

Patient Registration During Dose Confirmation Phase:

- During the dose confirmation phase of the trial all participating centres were required to contact the Trial Office directly before approaching any potential patient to confirm a treatment slot.
- PIs were also required to keep the Trial Office informed of any circumstances (patient refusal, screen failure, previously recruited patients fail to reach Visit 7 [Day 50] etc.) that may mean that previously allocated slots become available.

Patient Registration During Dose Expansion Phase (Via Electronic Remote Data Capture System):

- All eligible patients that have provided informed consent were registered via the online electronic remote data capture system (eRDC).
- Informed consent was obtained prior to registration. An Eligibility Checklist was also completed and faxed to the Trials Office before the online Registration Form was completed.
- In the expansion phase of the trial, registration of patients could be achieved by logging onto: https: //www.cancertrials.bham.ac.uk.

D.4.4 Trial Intervention

BTT1023 was formulated at 20 mg/ml in a buffer containing 20 mM sodium citrate, 100 mM sodium chloride, 1.5% D-mannitol, 20 μM diethylenetriaminepentaacetic acid and 0.02% polysorbate 80 in water for injection; the pH is 7.0 ± 0.5.

BTT1023 was contained in single-use 10 mL clear type I glass vials with a white-coloured cap. Each vial was filled to the nominal volume of 5.0 mL of the sterile concentrate solution, thus each vial contained a nominal total of 100.0 mg of BTT1023. BTT1023 required dilution prior to administration by infusion. The amount of diluent to be added to the BTT1023 concentrate was calculated to consistently provide a total diluted drug product infusion volume of 50 mL. The amount of diluent required was based on the calculated dosage for each patient according to instructions provided to the administering clinicians.

The diluent product was designated as BTT1023 IV Infusion Diluent, 10 mL. It contained 0.9% sodium chloride and 0.02% polysorbate 80 in water for injection; the osmolality is 310 ± 30 mOsmol/kg, within the range for typical physiological value. It was contained in single-use 20 mL clear type I glass vials with a blue-coloured cap. Each vial was filled to the nominal volume of 10.0 mL of the sterile diluent solution. BTT1023 and its diluent were stored at 2-8°C.

BUTEO was a single-arm trial, all patients registered on the trial received the same treatment. Patients received

multiple doses of BTT1023 (maximum of 7 doses) at 8, 12 or 16 mg/kg body weight. All patients received one-dose level and no dose reductions were permitted.

Table S1: BTT1023 Drug Infusion Table

Visit Number	Infusion number	Dose	Infusion time*
3	1	8, 12, or 16 mg/kg	120 minutes
4-9	2-7	8, 12, or 16 mg/kg	60 minutes

Note:
*Infusion rate for subsequent visits were increased if the individual patient did not experience a break in infusion due to AEs in the previous visit.