Glo-BNHL Industry Information Pack

Guidance: submitting asset information to the Glo-BNHL Trial Steering Committee v4.0

Contact Details

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Background

The Glo-BNHL platform trial (NCT05991388) has been developed as a direct output of the 2nd ACCELERATE Paediatric Strategy Forum[1]. Following this forum, an International Working Group was formed to address the following specific goals:

Identify which of the many potential new drugs would have the optimal probability of improving rates of cure in paediatric patients with chemo-resistant B-cell malignancies.

Design and execute scientifically sound studies in a very small international population of children with relapsed mature B-cell malignancies.

Several challenges had to be overcome, including too many potential assets of interest to be evaluated in a rare paediatric population (estimated 50-70 patients with relapsed/refractory B- cell Non-Hodgkin Lymphoma (B-NHL) per year globally). International collaboration and a platform-trial infrastructure were recognised as requirements and have led to the development of the Glo-BNHL trial.

Overview

Glo-BNHL is an international, academic-led, early-phase clinical platform trial designed to efficiently assess multiple prioritised novel agents in paediatric patients with relapsed and refractory B-NHL. It is sponsored by the University of Birmingham and managed by the Birmingham Cancer Research UK Clinical Trials Unit (CRCTU).

CRCTU is one of the largest cancer trials units in the UK, with proven expertise in the management of international clinical trials of Investigational Medicinal Products.

Core-funded by Cancer Research UK, the CRCTU is a fully registered UK Clinical Research Collaboration (UKCRC) Clinical Trials Unit. The University of Birmingham has previously been independently reviewed and approved to act as the European Sponsor for the Innovative Therapies for Children with Cancer (ITCC) consortium multi-country, early-phase clinical trials in children with cancer.

This global trial will open at up to 45 sites across Europe, North America and Australasia. Using a well-established hub and spoke management model, the CRCTU will arrange Coordinating Centre Agreements with National Coordinating Centres (NCCs) in each country. The NCCs will be responsible for regulatory submission and management of the study within that country. As Sponsor and lead trial coordinating centre, the University of Birmingham and CRCTU will retain oversight of the conduct of the NCCs.

The trial will be run in compliance with national and international regulatory requirements as well as in accordance with the University of Birmingham's and CRCTU's quality management system and associated standard operating procedures. The conduct of the trial and the data generated will meet International Conference on Harmonisation Good Clinical Practice (ICH GCP) standards to facilitate regulatory submissions. The aim is to produce data to support marketing authorisation applications.

Glo-BNHL has obtained UK regulatory approval, and engagement with both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) has been favourable.

A letter of support from the EMA can be downloaded from the Glo-BNHL website.

Prioritisation of Potential Agents

Prioritisation of potential agents for inclusion in Glo-BNHL is a key element of the platform design, given the rarity of relapsed B-NHL in the paediatric population and the number of potential assets.

The primary class prioritisation was delivered through the multi-stakeholder ACCELERATE Paediatric Strategy Forum. The published consensus was that the following three classes of agents held the greatest potential for benefit in paediatric relapsed and refractory B-NHL, based on their mechanism-of-action [1].

T-cell engagers (Bi-specific antibodies)

Antibody-drug conjugates (excluding those carrying a vinca alkaloid-like drug)

Chimeric antigen receptor (CAR) T-cells

In addition, it was felt that new trials using cell signalling inhibitors should not commence until the final results of the SPARKLE trial [2] were known. An iterative 'living prioritisation' approach has been adopted to ensure this overarching mechanism-of-action prioritisation list remains reflective of the current landscape. Members of the Trial Steering Committee (TSC) have committed to conducting this re-prioritisation on a regular basis (every 18 months to 2 years), with earlier review if a significant change in the treatment landscape becomes apparent.

Specific agents within the three classes noted above will currently be prioritised for entry into Glo-BNHL, however consideration will be given to any proposed novel agent.

1. Pearson ADJ, Scobie N, Norga K, et al. ACCELERATE and European Medicine Agency Paediatric Strategy Forum for medicinal product development for mature B-cell malignancies in children. Eur J Cancer 2019; 110: 74-85

2. Burke GAA, Vinti L, Kabickova E, Beishuizen A, Tacyildiz N, Uyttebroeck A, Kang HJ, Luisi F, Minard-Colin V, Burkhardt B, Tamegnon M, Sun S, Curtis M, Deshpande S, Nottage K, Howes A, Srinivasan S, Bhojwani D, Norris R, Cairo M. Ibrutinib plus RICE or RVICI for relapsed/refractory mature B-cell non-Hodgkin lymphoma in children and young adults: SPARKLE trial. Blood Adv. 2023 Feb 28;7(4):602-610. doi: 10.1182/bloodadvances.2022008802.PMID: 36541957

Submitting Asset Information

Contact can be made with the Glo-BNHL trial management team by emailing the trial mailbox at Glo-BNHL@trials.bham.ac.uk.

A confidentiality agreement can be executed, if required, prior to submission. Information regarding a potential asset for consideration for inclusion in the trial should be submitted electronically to the trial mailbox and must include a completed Asset Submission Form and the following information, where available:

1. **Primary target, mechanism-of-action and scientific rationale for the target**
2. **Pre-clinical data**
   - Details of cell lines and models used
   - Concentration range tested and relation to human dosing
   - Observed responses and validation
3. **Clinical data**
   - Safety data in adults including severity and frequency of Adverse Events, ability to support/modify toxicity and details of population in whom tested
   - Efficacy data in adults including details of tumour types, population, dosing regimens, study design and end-points
   - Any early safety/efficacy data in paediatrics if available (any disease)
4. **Feasibility in paediatrics**
   - Plans for development of paediatric formulation (if applicable)
   - Pharmacokinetic studies or modelling supporting starting dose decision in children (if available)

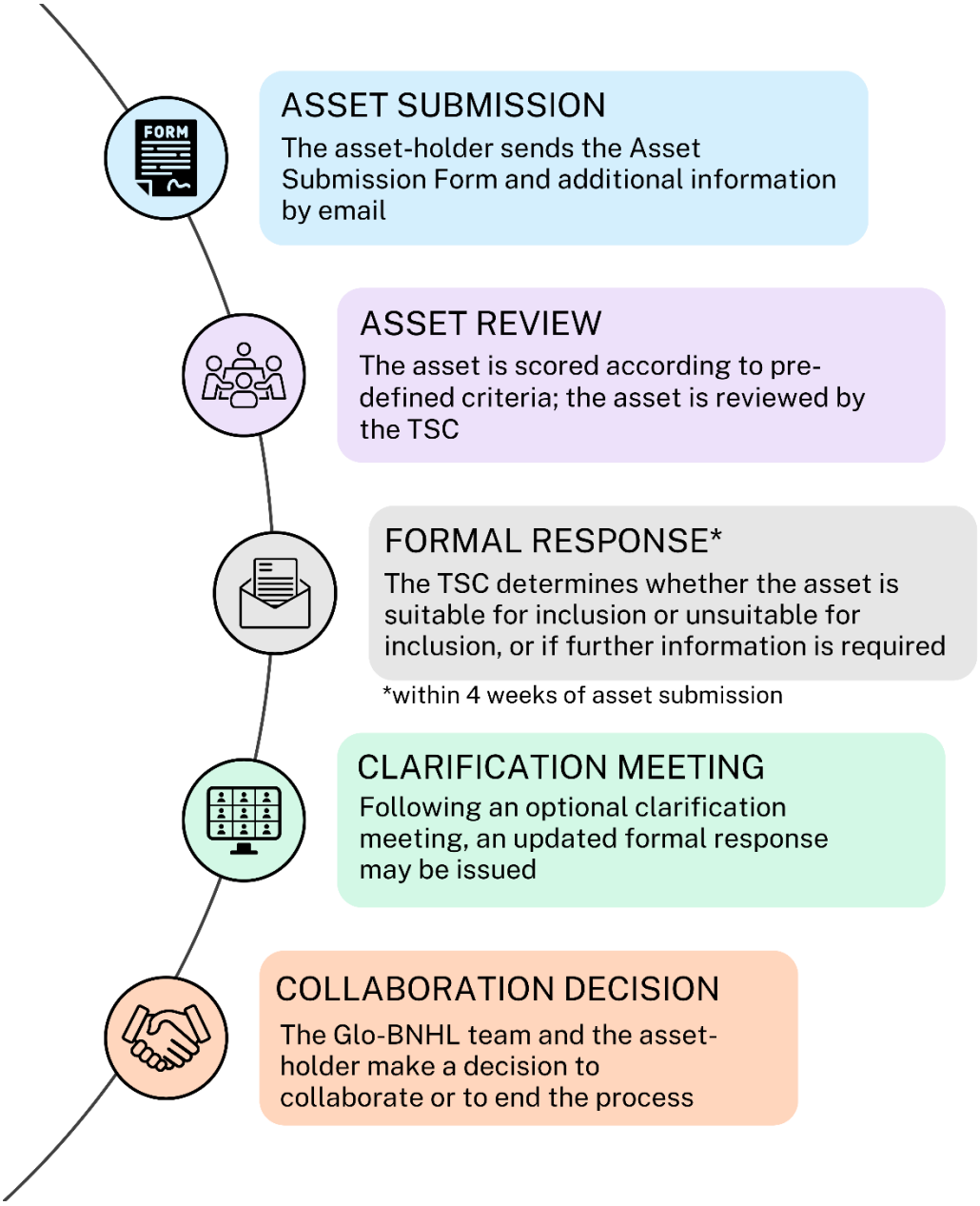
Asset submission deadlines can be found on the Glo-BNHL website. A formal response will be returned in writing within 4 weeks of receipt, along with a detailed summary of the rationale to facilitate the asset-holder's subsequent interaction with the relevant regulatory bodies.

Asset Review

The TSC includes the following voting members: Independent Chair, Chief Investigator, Sponsor representative, globally representative academic clinicians, statisticians and patient and public representatives. Additionally, trial management group representatives sit on the TSC as non-voting members. The TSC are bound by the TSC Charter and a Confidentiality Agreement with the University of Birmingham.

A robust scientific, systematic approach comprising pre-defined scoring criteria is used to assess the suitability of assets for inclusion in the trial. An indication of the likelihood of inclusion cannot be provided prior to submission to the TSC. The submission process detailed here is essential to allow the TSC to review and respond appropriately.

It is important that formal responses to asset submissions are shared with regulatory authorities – the asset-holder's consent for this is sought on the Asset Submission Form.



A decision will be reached by way of offline review and a TSC teleconference. Every reasonable effort will be made for all TSC members to be present, however the minimum attendees required for the TSC to be quorate is at least seven members, including a statistician, one trial management group member and three clinicians (including the Chair, unless otherwise agreed).

Where required for clarification prior to a final decision, a teleconference will be arranged with the asset-holder. This will be arranged by the Sponsor.

Where possible, it is preferable to engage with the platform early in the drug development pathway so that the Glo-BNHL Trial Management Group can advise on aspects of the asset-holder's Paediatric Investigations Plan (PIP) and/or Paediatric Study Plan (PSP). There may be a fee for this service.

For further information please contact the team at Glo-BNHL@trials.bham.ac.uk. A document entitled "Glo-BNHL Industry Information Pack: post-asset inclusion" is available upon request.