ELSEVIER

Blood 142 (2023) 3097–3099

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

A Global Study of Novel Agents in Paediatric and Adolescent Relapsed and Refractory B-Cell Non-Hodgkin Lymphoma (Glo-BNHL)

Emma Seaford[1], Shanna Maycock, MSc[2], Sarah Alexander, MD[3], Auke Beishuizen, MD PhD[4], Birte Wistinghausen, MD[5], Veronique Minard-Colin, MD PhD[6], Charlotte Rigaud, MD[6], Charles A Phillips, MD[7], James B. Ford, DO[8], Pamela R. Kearns, PhDFRCPC[2], Anna Lawson, BSc[2], Ellie Williams[9], Zahra Ahmed[2], Mahnoor Muzaffar[2], Rhianna Parsons[2], Lia Gore, MD[10,11], Nicole Scobie[12], Victoria Buenger[13], Carl Allen[14], Karin Mellgren[15], Catherine M. Bollard, MD[5], Anne Auperin[6], Lucinda Billingham[2], Gladstone Austin Amos Burke, MB, PhD[16]

[1] University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom
[2] Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom
[3] The Hospital For Sick Children, Toronto, CAN
[4] Princess Máxima Center For Pediatric Oncology, Utrecht, NLD
[5] Children's National Hospital, Washington, DC
[6] Gustave Roussy, Villejuif, France
[7] Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, PA
[8] University of Nebraska Medical Center, Omaha, NE
[9] Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom
[10] Children's Hospital Colorado, Aurora, CO
[11] Center for Cancer and Blood Disorders, University of Colorado Cancer Center, Aurora, CO
[12] Zoé4life, Sullens, Switzerland
[13] Coalition Against Cancer, Philadelphia, PA
[14] Texas Children's Cancer Center, Houston, TX
[15] Queen Silvia Children's Hospital, Gothenburg, SWE
[16] Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Overview
Glo-BNHL is an adaptive prospective international academic-led multicentre platform clinical trial designed to evaluate the efficacy and safety of the most promising novel agents as monotherapy or in combination with existing therapies for the treatment of children, adolescents, and young adults with relapsed or refractory (r/r) B-cell Non-Hodgkin Lymphoma (B-NHL). A direct output of the second ACCELERATE multi-stakeholder Paediatric Strategy Forum (Pearson, 2019), Glo-BNHL was designed in collaboration with patient advocates, is supported by the Regulatory Authorities, and the intent is for trial data to support filing for marketing authorisation.
Rationale
Outcomes for r/r paediatric B-NHL are extremely poor with long term cure rates lower than 30%. Glo-BNHL fulfils the critical need for a single collaborative global approach to find new treatments for these rare patients for whom current therapy is inadequate. It allows for a rational approach to investigating the array of potentially promising agents currently in development for adults.
The classes of agents currently prioritised for inclusion in Glo-BNHL are:

- Treatment Arm I: bispecific antibodies (BsAbs)
- Treatment Arm II: antibody-drug conjugates (ADCs) combined with standard chemotherapy
- Treatment Arm III: chimeric antigen receptor (CAR) T-cell products

A robust systematic assessment of each asset is undertaken before a decision to include in the platform is made (published separately).
Population

Glo-BNHL will enrol participants in ≥45 sites in 18 countries spanning Europe, Asia, North America and Australasia. Eligible patients are aged ≤25 years with radiologically or histologically proven relapsed (≥ first) or refractory B-NHL with evaluable disease, adequate organ function, negative pregnancy test, agreement to use effective contraception and written informed consent. Key exclusion criteria include recent stem cell transplant, craniospinal radiation or investigational treatment, on-going moderate or severe acute toxicities, uncontrolled infection or primary immunodeficiency. Patients may be enrolled into any of the available treatment arms for which they are eligible.

Statistical Design

In this rare population we anticipate global enrolment of 30 patients per year. The Bayesian design enables initial cohorts of 15 patients to be meaningfully evaluated. A transition analysis will estimate with ≥80% certainty whether the true efficacy of the treatment exceeds the pre-defined target response rate. Agents demonstrating sufficient promise will be further evaluated in an expansion stage, following discussion with regulators to clarify data requirements to enable subsequent approval of the agent. Confirmatory analyses of all evaluable patients will estimate with ≥95% certainty whether the true efficacy exceeds the target response rate ("GO"). During both initial and expansion stages patients will be closely monitored, with regular interim futility analyses employed, allowing a treatment arm to stop early if there is very little probability of efficacy ("NoGO").

Outcome measures

Primary outcomes measures are occurrence of an objective response after 12 weeks of treatment (Treatment Arm I), occurrence of complete response within a maximum of three cycles of treatment (Treatment Arm II) and occurrence of an objective response following CAR T-cell infusion (Treatment Arm III). Secondary outcome measures include event-free survival, progression-free survival, overall survival time, best overall response, duration of response, adverse events, pharmacokinetic profile and pharmacodynamics markers.

Treatment

Treatment Arm I: Odronextamab (Regeneron) - a human CD20xCD3 bispecific antibody - monotherapy will be given as an intravenous infusion weekly for 12 weeks, then at a decreasing frequency until progression or up to two years for responding patients.

Treatment Arm II: Loncastuximab tesirine (ADC Therapeutics) - a humanised CD19-targeting monoclonal antibody with PBD dimer cytotoxin - will be given as an intravenous infusion with each cycle of modified R-ICE chemotherapy (rituximab, ifosfamide, carboplatin, etoposide and dexamethasone) for up to three cycles.

Treatment Arm III: product negotiations are on-going

Conclusion

Glo-BNHL addresses an urgent unmet clinical need through an innovative trial design serving as a paradigm for evaluation of novel agents in very rare diseases.

Disclosures Minard-Colin: *Aztra:* Consultancy; *BMS:* Consultancy; *Adaptimmune Therapeutics plc:* Consultancy; *Roche:* Consultancy. **Phillips:** *Merck Group:* Consultancy. **Gore:** *Amgen:* Consultancy; *Novartis:* Consultancy; *Roche:* Consultancy. **Allen:** *Sobi:* Consultancy. **Bollard:** *Cabaletta Bio, Catamaran Bio:* Current equity holder in private company, Current equity holder in publicly-traded company, Current holder of *stock options* in a privately-held company, Membership on an entity's Board of Directors or advisory committees, Patents & Royalties: Patent applications in CAR-NKs; *Roche:* Consultancy. **Auperin:** *MSD France:* Consultancy. **Burke:** *Novartis:* Consultancy.

Table 1. Glo-BNHL trial operating characteristics

	Treatment Arm Ia	Treatment Arm Ib	Treatment Arm II	Treatment Arm III
Population	1st relapse	≥2nd relapse	≥1st relapse	≥1st relapse
Novel Agent	BsAb	BsAb	ADC + chemotherapy	CAR-T cell product
Primary outcome	OR after 12 weeks	OR after 12 weeks	CR within 3 cycles	OR post-CAR T-cell
Target response rate	OR > 40%	OR > 10%	CR > 20%	OR > 10%
Transition analysis "GO" decision rule	Probability ≥ 0.8 (True OR rate > 40%)	Probability ≥ 0.8 (True OR rate > 10%)	Probability ≥ 0.8 (True CR rate > 20%)	Probability ≥ 0.8 (True OR rate > 10%)
Minimum responses "GO" transition analysis	8/15	3/15	5/15	3/15
Power for initial stage (n=15)	>0.8 for true OR rate ≥61%	>0.8 for true OR rate ≥27%	>0.8 for true CR rate ≥41%	>0.8 for true OR rate ≥27%
One-sided type I error rate for initial stage	<0.05 for true OR rate ≤30%	<0.05 for true OR rate ≤5%	<0.05 for true CR rate ≤14%	<0.05 for true OR rate ≤5%
Confirmatory analysis "GO" decision rule	Probability ≥ 0.95 (True OR rate > 40%)	Probability ≥ 0.95 (True OR rate > 10%)	Probability ≥ 0.95 (True CR rate > 20%)	Probability ≥ 0.95 (True OR rate > 10%)
Minimum responses "GO" confirmatory analysis	17/30	6/30	10/30	6/30
Power for overall design (n=30)	>0.8 for true OR rate ≥65%	>0.8 for true OR rate ≥29%	>0.8 for true CR rate ≥43%	>0.8 for true OR rate ≥29%
One-sided type I error rate for overall design	<0.05 for true OR rate ≤41%	<0.05 for true OR rate ≤9%	<0.05 for true CR rate ≤20%	<0.05 for true OR rate ≤9%

BsAb = bispecific antibody; ADC = antibody-drug conjugate; CAR T-cells = chimeric antigen receptor T- cell; OR = objective response; CR = complete response

Figure 1. Glo-BNHL trial schema

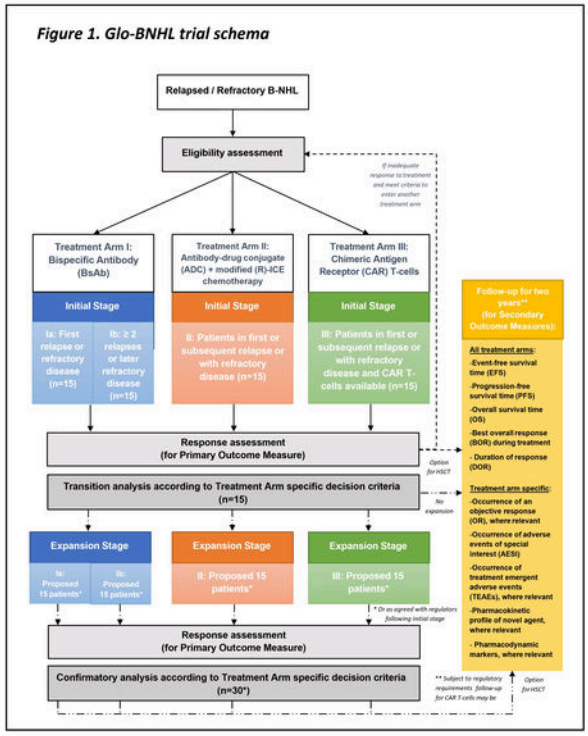

Figure 1

https://doi.org/10.1182/blood-2023-178658