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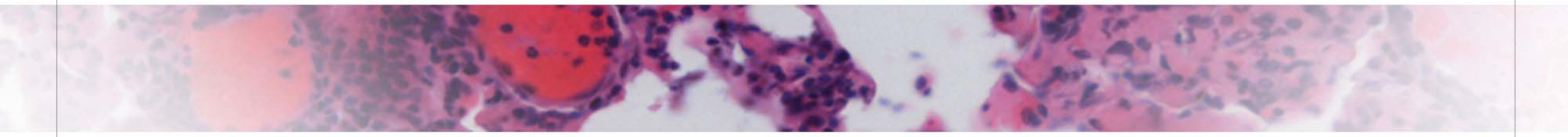

GIO-BNHL

A Global Study of Novel Agents in Paediatric and Adolescent Relapsed and Refractory B-cell Non-Hodgkin Lymphoma (B-NHL)

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Prioritisation

- Novel agents showing greatest promise prioritised for inclusion

- Classes currently prioritised for inclusion
  - **Treatment Arm I: bispecific antibodies (BsAbs)**
  - **Treatment Arm II: antibody-drug conjugates (ADCs) combined with standard chemotherapy** (modified R-ICE: dexamethasone, rituximab, ifosfamide, carboplatin, etoposide)
  - **Treatment Arm III: chimeric antigen receptor (CAR) T-cell products**

- Robust systematic assessment for individual novel agents

Population

Key inclusion criteria*	Key exclusion criteria*
Aged ≤25 years	Uncontrolled infection
Radiologically or histologically proven relapsed (≥first) or refractory B-NHL with evaluable disease	On-going moderate or severe toxicities
Adequate organ function	Primary immunodeficiency
Negative pregnancy test	Recent stem cell transplant
Agreement to use effective contraception	Recent investigational treatment
Written informed consent	Recent craniospinal irradiation

**Full detailed platform and treatment arm-specific inclusion and exclusion criteria are specified within protocol*

Treatment

- **Treatment Arm I: Odronextamab** (Regeneron)
  - Human CD20xCD3 bispecific antibody
  - Monotherapy as intravenous infusion weekly for 12 weeks
  - Then decreasing frequency until progression or up to two years if response

- **Treatment Arm II: Loncastuximab tesirine** (ADC Therapeutics)
  - Humanised CD19-targeting monoclonal antibody with PBD dimer cytotoxin
  - Intravenous infusion with each cycle of modified R-ICE chemotherapy
  - Up to three cycles

- **Treatment Arm III: Product negotiations on-going**

Outcome measures

Primary outcomes	Secondary outcomes
Treatment Arm I Objective response after 12 weeks of treatment	• Event-free survival • Progression-free survival • Overall survival time • Best overall response • Duration of response • Adverse events • Pharmacokinetic profile • Pharmacodynamic markers
Treatment Arm II Complete response within a maximum of three cycles of treatment	
Treatment Arm III Objective response following CAR T-cell infusion	

Statistical Design

- **Bayesian design enables meaningful evaluation with small numbers**
- **Transition analysis**
  - Initial cohorts of 15 patients
- **Confirmatory analysis**
  - Expansion stage for agents showing sufficient promise
  - Up to 30 patients
- Anticipated global recruitment
  - 30 patients per year

	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

Conclusion

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