IKS03: CD19-directed ADC for B cell cancers

TARGET: CD19

ANTIBODY: Anti-CD19 monoclonal IgG1

LINKER: Site-specific conjugation of β-glucuronide, with a 2nd β-glucuronide moiety attached to the 2nd dimer of the PBD prodrug for increased hydrophilicity and added protection against unwanted binding to plasma proteins

DRUG/PAYLOAD: DNA cross-linker; a PBD prodrug (LCB20-0187)

DRUG DESCRIPTION: IKS03 is a class-leading ADC that incorporates an anti-CD19 antibody conjugated to highly potent DNA cross-linking payload (talirine-like PBD) via site-specific conjugation, with tumour-selective payload activation and release: a 'PBD prodrug'.

PRECLINICAL STUDIES: Preclinical studies have demonstrated best-in-class efficacy (MED in mouse xenografts) and safety (HNSTD NHPs), resulting in a TI which is >5-fold that of Zynlonta (loncastuximab tesirine).

In xenograft models for B-cell cancers, including B-cell lymphoma, DLBCL and MCL, IKS03 induced complete regression with doses of 0.3mg/kg. For comparison, Zynlonta induced complete regression at 1mg/kg.

IKS03 also induced complete regression in high-grade triple hit, refractory & MYC-amplified lymphoma PDX models at doses of ≥0.3mg/kg.

In GLP toxicology studies, HNSTD was >1.5mg/kg, more with a corresponding TI of >5. By comparison, the HNSTD for Zynlonta is ≥0.6mg/kg, below the efficacious dose and with an associated TI of <1.

DEVELOPMENT STATUS: **First in human Phase 1**

CLINICAL INDICATION: Advanced B-cell Non-Hodgkin Lymphomas:

- B-cell Non-Hodgkin Lymphoma
- Diffuse Large B Cell Lymphoma (DLBCL)
- Follicular Lymphoma
- Mantle Cell Lymphoma (MCL)
- B-cell Lymphoma

CLINICAL TRIALS

IKS03 in patients with advanced B Cell Non-Hodgkin Lymphomas NCT05365659

https://classic.clinicaltrials.gov/ct2/show/NCT05365659

The study consists of 2 parts: dose-escalation (Part 1) and dose-expansion (Part 2).

Part 1 of the study is to evaluate the safety and tolerability of increasing dose levels of IKS03 to establish a recommended dose for expansion (RDE).

Part 2 of the study is to further evaluate the safety, pharmacokinetics/pharmacodynamics, and efficacy of IKS03 at the RDE.

Estimated enrolment: 140 patients

Enrolment sites: US, Canada, Australia

PARTNERING STATUS

Available for license: WW or Regional territories

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