Abstract #TPS7095

A Phase 1/2, Open-Label, Multicenter Trial Investigating the Safety, Tolerability, and Preliminary Antineoplastic Activity of IPH6501, a First-in-Class NK Cell Engager, in Patients with Relapsed and/or Refractory CD20-expressing Non-Hodgkin Lymphoma (NCT06088654)

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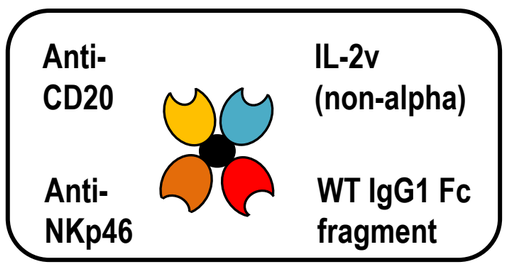
SCAN ME

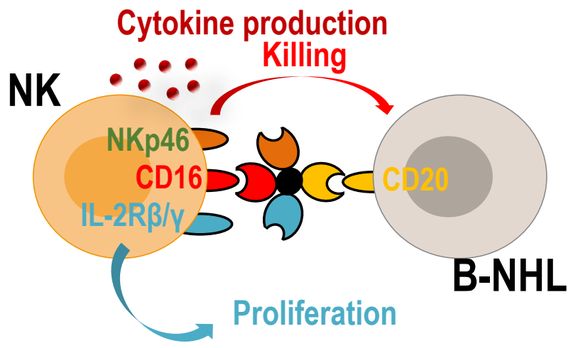
The therapeutic landscape for relapsed and/or refractory (R/R) B-cell non-Hodgkin lymphoma (B-NHL) is evolving to include targeted T-cell based immunotherapies. However, there remains an unmet medical need for patients who are refractory to, relapsing from, or are ineligible for these therapies.

Leveraging natural killer (NK) cells emerges as a promising strategy in hematological malignancies, as demonstrated in a Phase 1 study with IPH6101/SAR'579 in R/R AML (*Stein, ASCO 2023; Bajel, ASH 2023*).

IPH6501 is a first-in class tetraspecific NK cell engager, based on ANKET®-platform, that simultaneously targets the CD16a and NKp46 receptors on NK cells and CD20 on B-NHL cells, and includes an IL-2 variant designed to avoid binding to CD25 (IL-2Rα), limiting Treg activation and potential IL-2 related side effects.

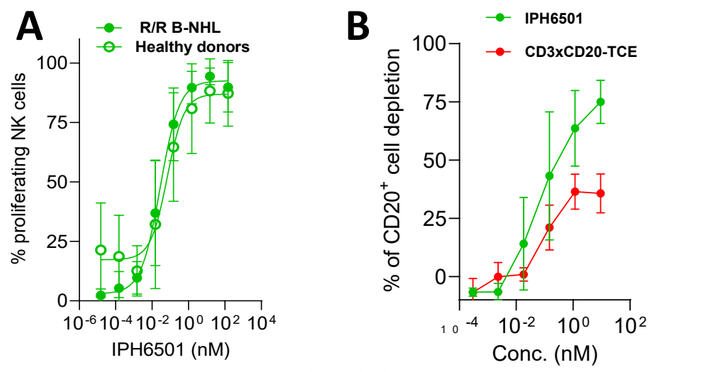


In preclinical *in vitro* and *in vivo* models, IPH6501 boosts NK cell proliferation and activation, and CD20+ target cell elimination (Abstract #7030). In PBMC obtained from R/R B-NHL patients, IPH6501 demonstrated greater killing efficacy compared to a CD3xCD20 T-cell engager.



NK cell proliferation

Higher B cell depleting activity than CD3xCD20 TCE



(A) Increasing concentrations of IPH6501 induced similar immune cell proliferation in PBMC from HD and R/R B-NHL patients.
(B) **% of** B cell depletion upon increasing doses of IPH6501 or a CD20-TCE in PBMC from R/R patients with a leukemic form of B-NHL (n=3).

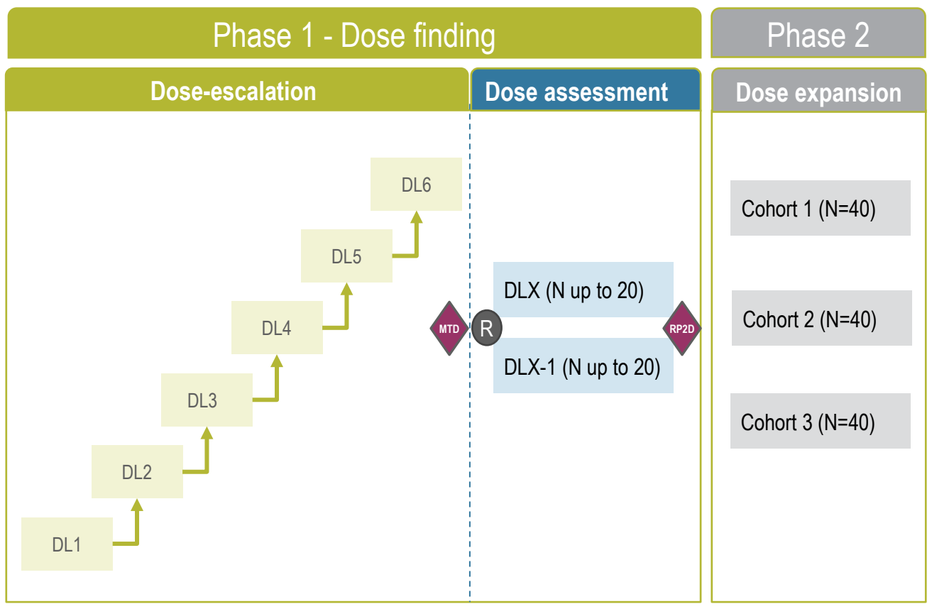
- **Leveraging NK cells emerges as a promising strategy in hematological malignancies and offers a novel approach that could complement or provide an alternative to T-cell therapies.**
- **IPH6501 is a first-in-class tetraspecific antibody-based NK cell engager including an IL-2 variant, that boosts NK cell proliferation and activation, and CD20+ target cell elimination, as presented in preclinical results of IPH6501 (abstract #7030).**

SCAN ME

- **This first-in-human Phase 1/2 study is ongoing to evaluate safety, tolerability and to determine RP2D of IPH6501 in patients with R/R B-NHL.**

Study Design

- The Phase 1 part will consist of:
  - dose escalation part which will follow a 3+3 design to determine the maximum tolerated dose (MTD) or the highest dose to be tested as defined in protocol if the MTD has not been reached.
  - dose assessment part randomizing at least 2 dose levels to determine the recommend Phase 2 dose (RP2D). RP2D will be selected by pooling all available PK, PD, efficacy, safety and tolerability data in Phase 1.
- The Phase 2 part will enroll one or more cohorts of selected B-NHL subtypes to be determined at the end of Phase 1.
- In total, up to 184 subjects will be enrolled.



Objectives and Endpoints

Primary objective

To evaluate the safety profile (including dose limiting toxicities (DLT), MTD or highest tested dose), tolerability according to NCI-CTCAE v5.0 and to determine the RP2D of IPH6501.

Primary endpoints

1. Incidence of DLTs
2. Safety and tolerability: AEs, clinical laboratory and ECG abnormalities.

Secondary objectives

1. To investigate any preliminary antitumor activity of IPH6501.
2. To characterize the pharmacokinetic profile of IPH6501
3. To evaluate the immunogenicity of IPH6501.

Secondary endpoints

1. Overall Response Rate (CR or PR). CR Rate, PFS
2. IPH6501 concentrations, C_{max}, AUC.
3. Incidence of antidrug antibodies against IPH6501.

Key Inclusion Criteria

- Advanced CD20+ B-NHL (WHO 2016), including DLBCL NOS; HGBL NOS; PMBLC, FL; MCL, MZL.
- R/R B-NHL without established alternative therapy.
- Must have received at least 2 prior systemic therapies including at a minimum anti-CD20 antibody therapy.
- ECOG performance status of ≤ 2.
- Adequate organ and hematological function.
- Must have measurable disease.
- Able to provide a fresh biopsy from a safely accessible site (or recent biopsy).

Key Exclusion Criteria

- Patients with another invasive malignancy in the last 2 years.
- Prior chemotherapy, immunotherapy or other anti-cancer therapy within 4 weeks prior to study drug administration.
- Autologous SCT or treatment with CAR-T cell therapy within 100 days prior to first dose of study drug.
- History of central nervous system lymphoma.
- Known history of infection with HIV or hepatitis B or C.
- Major surgery within 4 weeks.
- Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of study results.

The study is open for enrollment in the United States, Australia and France.

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