Study objectives

- Characterizing
- Identifying
- Class anti-KIR3DL2 mAb. It selectively depletes KIR3DL2+ cells. IPH4102 has shown potent efficacy in preclinical models, in particular in vivo assays using primary CTCL cells. IPH4102-101 (NCT02593045) is a first-in-Human dose-finding phase I study evaluating repeated administrations of IPH4102 in relapsed/refractory CTCL. The primary objective is to assess safety and tolerability of ascending doses of IPH4102 by characterizing dose-limiting toxicity (DLT) and adverse events (AE). The study comprises a dose-escalation followed by cohort expansion. The dose-escalation portion has a 3+3 design with accelerated titration and aims to determine the maximal tolerated dose (MTD) or recommended Phase 2 dose (RP2D). Secondary objectives include pharmacokinetics (PK), immunogenicity and signals of anti-neoplastic clinical activity. 

Enrollment started in November 2015. Dose levels 1-7 were completed without DLT, with 16 patients evaluable for safety and clinical activity assessments. These comprise 13 SS, 2 MF and 1 CD4+ TCL CTCL patients. Preliminary safety and clinical activity results from patients treated up to dose-level 7 (cut-off date 10SEP16) are presented below.

Key eligibility criteria

- Patients with relapsed/refractory primary CTCL who have received at least 2 previous systemic antineoplastic therapies
- For MF/SS patients: clinical stage ≥ II
- Centrally assessed KIR3DL2 expression (>5%) on malignant cells in blood or in at least 1 skin lesion

Patient disposition & baseline characteristics

Nineteen patients were screened. Sixteen were treated in dose-cohorts #1 to #7 and were evaluable for safety and clinical activity assessments. They comprise 13 SS, 2 MF and 1 CD4+ TCL CTCL patients.

Preliminary global ORR is 38% in the evaluable population and 38% in Sézary Syndrome patients. Results of exploratory endpoints such as pharmacodynamics in skin and blood are in line with clinical activity. Additionally, preliminary global ORR in Sézary Syndrome patients is 38% and 38% in SS patients. There is a trend for dose-response relationship:
- At lower doses, responses seem to appear earlier in blood than in skin.
- At intermediate dose-levels, in SS patients, response in skin can occur before response in blood.
- CR tend to appear in skin or blood with higher doses and/or increased duration of exposure.
- All responses are still ongoing and a few responses need to be confirmed.

Conclusions on preliminary safety and clinical activity

- Sixteen patients were evaluatable for safety and efficacy. Including 13 SS, 2 MF and 1 CD4+ TCL NOS.
- IPH4102 is well tolerated in an elderly and heavily pretreated patient population.
- Seven dose-levels were completed (0.0001 to 1.5 mg/kg) and no DLT was reported.
- The majority of AE is typical for CTCL or reflects low grade infusional related reactions.
- Preliminary global ORR is 38% in the evaluable population and 38% in Sézary Syndrome patients.
- CR tend to appear in skin (n=2) and in blood (n=3) with higher doses and/or increased duration of exposure.
- Results of exploratory endpoints such as pharmacodynamics in skin and blood are in line with clinical activity results (see poster 0-11).
- With a relatively short observation time (med. 126+ days), all responders are still ongoing.
- Three additional dose-levels (3, 6 and 10 mg/kg) remain to be evaluated.