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# IPH4102, a first-in-class anti-KIR3DL2 monoclonal antibody, in patients with relapsed or refractory cutaneous T-cell lymphoma: an international, first-in-human, open-label, phase 1 trial

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## Summary

### Background

IPH4102 is a first-in-class monoclonal antibody targeting KIR3DL2, a cell surface protein that is expressed in cutaneous T-cell lymphoma, and predominantly in its leukaemic form, Sézary syndrome. We aimed to assess the safety and activity of IPH4102 in cutaneous T-cell lymphoma.

### Methods

We did an international, first-in-human, open-label, phase 1 clinical trial with dose-escalation and cohort-expansion parts in five academic hospitals in the USA, France, the UK, and the Netherlands. Eligible patients had histologically confirmed relapsed or refractory primary cutaneous T-cell lymphoma, an Eastern Cooperative Oncology group performance score of 2 or less, were aged 18 years or older, and had received at least two previous systemic therapies. Ten dose levels of IPH4102, administered as an intravenous infusion, ranging from 0.0001 mg/kg to 10 mg/kg, were assessed using an accelerated 3 + 3 design. The primary endpoint was the occurrence of dose-limiting toxicities during the first 2 weeks of



ent, defined as toxicity grade 3 or worse lasting for 8 or more days, except for lympho  
response by cutaneous T-cell lymphoma subtype was a secondary endpoint. Safety a



analyses were done in the per-protocol population. The study is ongoing and recruitment is complete. This trial is registered with [ClinicalTrials.gov](https://clinicaltrials.gov), number [NCT02593045](https://clinicaltrials.gov/ct2/show/study/NCT02593045).

## Findings

Between Nov 4, 2015, and Nov 20, 2017, 44 patients were enrolled. 35 (80%) patients had Sézary syndrome, eight (18%) had mycosis fungoides, and one (2%) had primary cutaneous T-cell lymphoma, not otherwise specified. In the dose-escalation part, no dose limiting toxicity was reported and the trial's safety committee recommended a flat dose of 750 mg for the cohort-expansion, corresponding to the maximum administered dose. The most common adverse events were peripheral oedema (12 [27%] of 44 patients) and fatigue (nine [20%]), all of which were grade 1–2. Lymphopenia was the most common grade 3 or worse adverse event (three [7%]). One patient developed possibly treatment-related fulminant hepatitis 6 weeks after IPH4102 discontinuation and subsequently died. However, the patient had evidence of human herpes virus-6B infection. Median follow-up was 14·1 months (IQR 11·3–20·5). A confirmed global overall response was achieved in 16 (36·4% [95% CI 23·8–51·1]) of 44 patients, and of those, 15 responses were observed in 35 patients with Sézary syndrome (43% [28·0–59·1]).

## Interpretation

IPH4102 is safe and shows encouraging clinical activity in patients with relapsed or refractory cutaneous T-cell lymphoma, particularly those with Sézary syndrome. If confirmed in future trials, IPH4102 could become a novel treatment option for these patients. A multi-cohort, phase 2 trial (TELLOMAK) is underway to confirm the activity in patients with Sézary syndrome and explore the role of IPH4102 in other subtypes of T-cell lymphomas that express KIR3DL2.

## Funding

Innate Pharma

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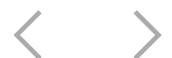
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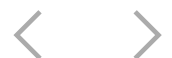
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