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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 Gl response by cutaneous T-cell lymphoma subtype was a secondary endpoint. Safety a ivi

analyses were done in the per-protocol population. The study is ongoing and recruitment is complete. This trial is registered with ClinicalTrials.gov, number 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.

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