TELLOMAK: **T-CELL LYMPHOMA ANTI-KIR3DL2 THERAPY**

An open label, multi-cohort, multi-center, international phase II study evaluating the efficacy and safety of IPH4102 alone or in combination with chemotherapy in patients with advanced T-cell lymphoma

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15-ICML Focus on ongoing trials Session
Conflict of Interest Disclosure – Pierluigi Porcu

- Employment or leadership position: N/A
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- Stock ownership: N/A
- Honoraria: N/A
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- Other remuneration: N/A
NK cells kill primary Sézary cells in *ex vivo* autologous model through IPH4102-mediated ADCC (2 representative SS patients)

Marie-Cardine A et al, Cancer Res 2014
**KIR3DL2 IS EXPRESSED IN CUTANEOUS T CELL LYMPHOMA**

<table>
<thead>
<tr>
<th>Condition</th>
<th>% of samples with at least 5% of cells expressing KIR3DL2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycosis Fungoides</td>
<td>~50%</td>
</tr>
<tr>
<td>Sézary Syndrome</td>
<td>~85%</td>
</tr>
</tbody>
</table>

KIR3DL2 expression in **Mycosis Fungoides**

KIR3DL2 expression in **Sézary syndrome**

Porcu P, 15-ICML 2019

Battistella M et al, Blood 2017
RESULTS OF FIRST-IN-HUMAN PHASE 1 STUDY
GOOD SAFETY PROFILE AND HIGH ACTIVITY OF IPH4102 IN SÉZARY SYNDROME

- Phase 1: N=44 Advanced CTCL, 80% (n=35) were Sézary Syndrome
- ≥ 2 prior systemic therapies, 39% ≥ 5th line of therapy
- Median age: 69 years
- No DLT, MTD not reached
- Recommended phase 2 dose: 750mg IV infusion
- Most common AE: lymphopenia, fatigue (mostly grade 1-2)
- Only 3/44 (9%) stopped IPH4102 for AE

Global response: 42.9% (95%CI: 28 – 59)
Median DOR: 13.8m (95%CI: 7.2 – NR)
Median PFS 11.7m (95%CI: 8.1 – NR)

Bagot M et al, Lancet Oncol 2019, in press
Expression of KIR3DL2 in PTCL subtypes

**AITL**
(9/25, 36%)

**PTCL-NOS**
(7/20, 35%)

**ALCL**
(8/14, 57%)

In vitro combination of IPH4102 with gemcitabine / oxaliplatin (GEMOX)

Enhanced ADCC of IPH4102 by GEMOX

Increased surface KIR3DL2 expression by GEMOX

AITL: Angio-Immunoblastic T cell Lymphoma, PTCL-NOS: Peripheral T Cell Lymphoma, non-otherwise specified, ALCL: Anaplastic T Cell Lymphoma.

Cheminant M et al, 15-ICML 2019

Porcu P, 15-ICML 2019
TELLOMAK: T-CELL LYMPHOMA ANTI-KIR3DL2 THERAPY
A Multi-cohort International Phase 2 Trial

N~60
Cohort # 1
Sézary Syndrome
≥ 2 prior systemic therapies that must include mogamulizumab

N~90
Cohort # 2
Mycosis Fungoides
≥ 2 prior systemic therapies including biological agents
Cohort # 3
KIR3DL2 expressing
KIR3DL2 non-expressing

N~100
Cohort # 4
Peripheral T Cell Lymphoma
≥ 1 prior systemic therapy including anthracycline-based chemo
Cohort # 5
KIR3DL2 expressing
KIR3DL2 non-expressing

IPH4102 single agent
IPH4102 + GEMOX

Clinicaltrials.gov: NCT03902184
Porcu P, 15-ICML 2019
KIR3DL2 expressing ≥ 1%
<table>
<thead>
<tr>
<th>Sézary Syndrome</th>
<th>Mycosis Fungoides</th>
<th>Peripheral T Cell Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Relapsed/refractory SS</td>
<td>• Relapsed refractory MF</td>
<td>• Relapsed PTCL (ALCL, AITL, PTCL-NOS subtypes)</td>
</tr>
<tr>
<td>• ≥ 2 prior systemic therapies, must include mogamulizumab;</td>
<td>• ≥ 2 prior systemic therapies;</td>
<td>• ≥ 1 prior systemic therapies;</td>
</tr>
<tr>
<td>• At least 1 skin biopsy at screening</td>
<td>• At least 1 skin biopsy at screening</td>
<td>• 1 lymph node biopsy at screening</td>
</tr>
<tr>
<td>• B2 at screening (central flow cytometry assessment);</td>
<td>• KIR3DL2 expressing (cohort 2), or non-expressing (Cohort 3) using central IHC assessment</td>
<td>• KIR3DL2 expressing (cohort 4), or non-expressing (Cohort 5) using central IHC assessment;</td>
</tr>
<tr>
<td>• No evidence of LCT (central assessment)</td>
<td>• No evidence of LCT (central assessment)</td>
<td>• Presence of at least one target lesion on PET/CT</td>
</tr>
</tbody>
</table>
SCHEDULE OF ADMINISTRATION & DISEASE EVALUATION

Cohorts 1-3 (SS & MF)

**Single agent IPH4102 750mg (30 minute IV infusion)**
- weekly x 4, every 2 weeks x 10, every 4 weeks until progression or unacceptable toxicity.
- Disease evaluation after 1 month and then every 2 months x 1 year followed by every 3 months thereafter.

Cohorts 4-5 (PTCL)

**IPH4102 750mg + GEMOX chemotherapy**
- **IPH4102**: weekly x 4, every 2 weeks x 10, every 4 weeks until progression or unacceptable toxicity.
- **Gemcitabine**: 800 – 1000mg/m² every 2 weeks x 8 administrations (max).
- **Oxaliplatin**: 75 – 100mg/m² every 2 weeks x 8 administrations (max).
- Disease evaluation by PET/CT every 2 months x 1 year followed by every 3 months thereafter.
STUDY ENDPOINTS

• Primary endpoint
  > Overall response rate
    • Cohort 1-3 (International consensus criteria, Olsen 2011)
    • Cohort 4-5 (Lugano criteria, Cheson 2014)

• Key secondary endpoints
  > Toxicity;
  > Duration of response, PFS, OS at 1 and 2 years;
  > Quality of life (QoL);
  > PK and immunogenicity
• Open in US, France, Italy, UK, Germany and Spain with target activation of around 40 centers.

• Target recruitment ~ 250 patients, with Simon 2-stage biomarker-stratified design in cohorts 2-5 to allow early stopping for futility.

• Governed by IDMC to ensure patient safety and study progress.

• First patient screened on 22 Mai 2019

• If interested to participate, contact christine.paiva@innate-pharma.fr