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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

innate pharma

Conflict of Interest Disclosure – Pierluigi Porcu

- Employment or leadership position: N/A
- Consultant or advisory role: Innate Pharma
- Stock ownership: N/A
- Honoraria: N/A
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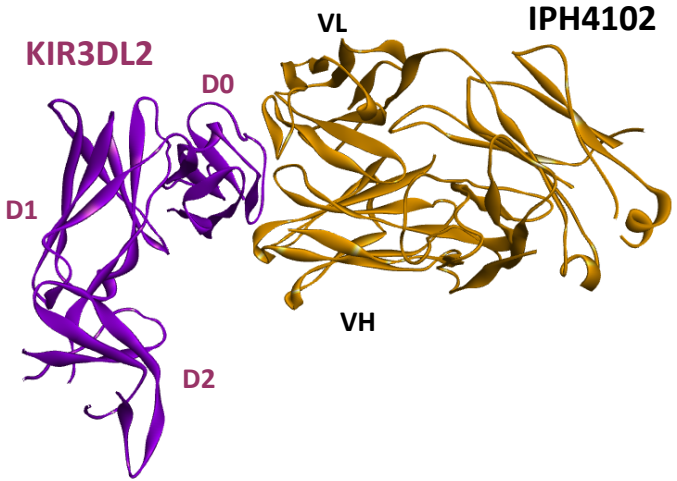
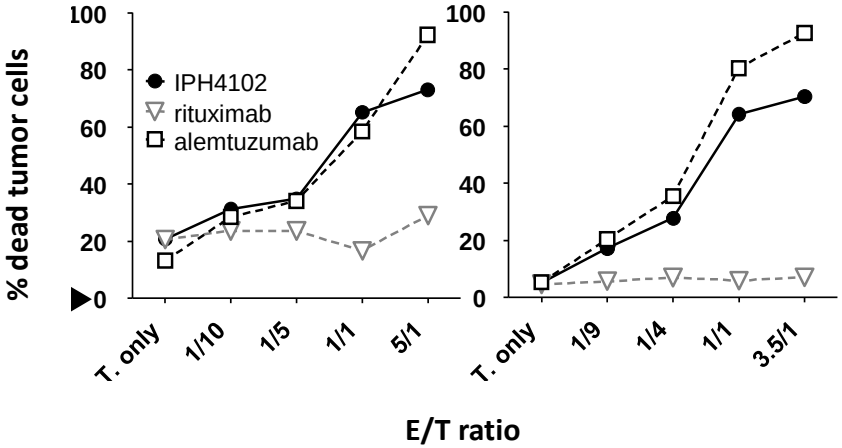
- Other remuneration: N/A

IPH4102
FIRST IN CLASS mAb DIRECTED AGAINST KIR3DL2



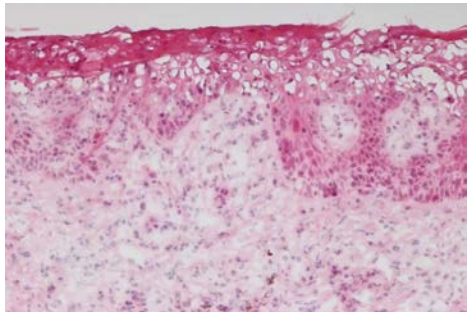
NK cells kill primary Sézary cells in *ex vivo* autologous model through IPH4102-mediated ADCC (2 representative SS patients)

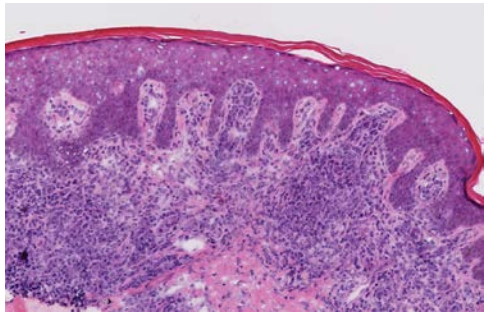


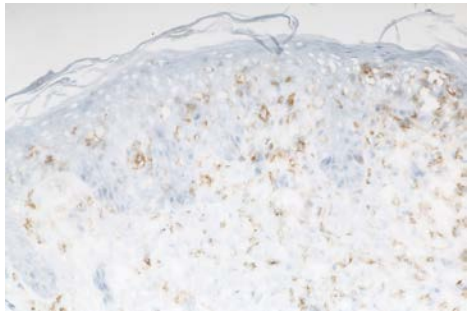
Marie-Cardine A et al, Cancer Res 2014

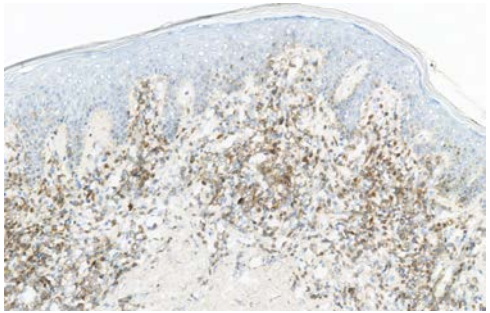
KIR3DL2 IS EXPRESSED IN CUTANEOUS T CELL LYMPHOMA

	% of samples with at least 5% of cells expressing KIR3DL2
Mycosis fungoides	~50%
Sézary Syndrome	~85%









KIR3DL2 expression in **Mycosis Fungoides**

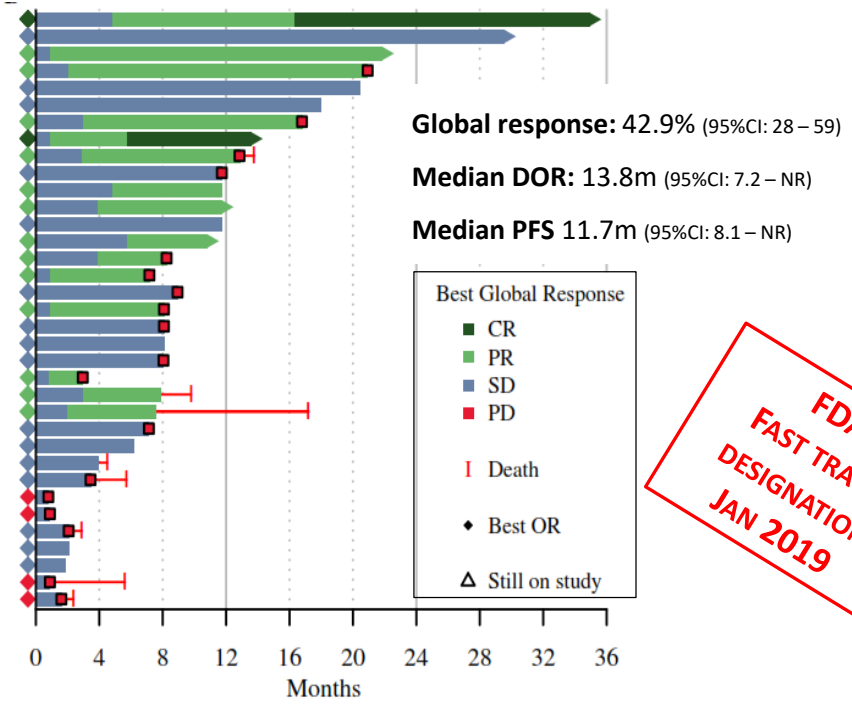
KIR3DL2 expression in **Sézary syndrome**

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



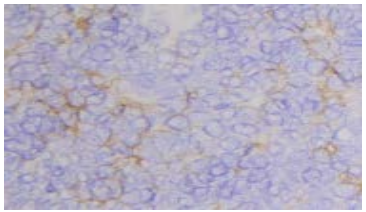
FDA FAST TRACK DESIGNATION JAN 2019

Bagot M et al, Lancet Oncol 2019, in press

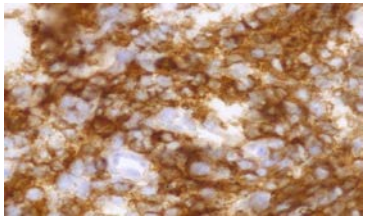
IPH4102 IN PERIPHERAL T-CELL LYMPHOMA
RATIONALE

Expression of KIR3DL2 in PTCL subtypes

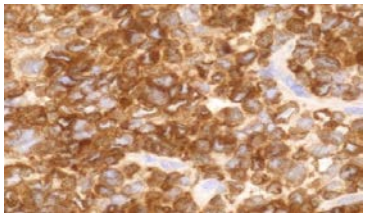
AITL
(9/25, 36%)



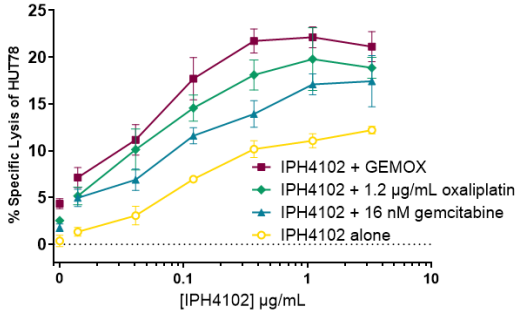
PTCL-NOS
(7/20, 35%)



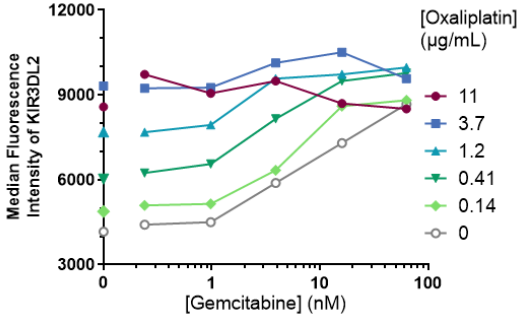
ALCL
(8/14, 57%)



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

TELLOMAK : T-CELL LYMPHOMA ANTI-KIR3DL2 THERAPY
A Multi-cohort International Phase 2 Trial

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N~60	**Sézary Syndrome** ≥ 2 prior systemic therapies that must include mogamulizumab	IPH4102 single agent
Cohort # 1		
N~90	**Mycosis Fungoides** ≥ 2 prior systemic therapies including biological agents	
Cohort # 2	KIR3DL2 expressing	
Cohort # 3	KIR3DL2 non-expressing	
N~100	**Peripheral T Cell Lymphoma** ≥ 1 prior systemic therapy including anthracycline-based chemo	IPH4102 + GEMOX
Cohort # 4	KIR3DL2 expressing	
Cohort # 5	KIR3DL2 non-expressing	

KEY ELIGIBILITY CRITERIA

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Sézary Syndrome	Mycosis Fungoides	Peripheral T Cell Lymphoma
• Relapsed/refractory SS	• Relapsed refractory MF	• Relapsed PTCL (ALCL, AITL, PTCL-NOS subtypes)
• ≥ 2 prior systemic therapies, must include mogamulizumab;	• ≥ 2 prior systemic therapies;	• ≥ 1 prior systemic therapies;
• At least 1 skin biopsy at screening	• At least 1 skin biopsy at screening	• 1 lymph node biopsy at screening
• B2 at screening (central flow cytometry assessment);	• KIR3DL2 expressing (cohort 2), or non-expressing (Cohort 3) using central IHC assessment	• KIR3DL2 expressing (cohort 4), or non-expressing (Cohort 5) using central IHC assessment;
• No evidence of LCT (central assessment)	• No evidence of LCT (central assessment)	• Presence of at least one target lesion on PET/CT

SCHEDULE OF ADMINISTRATION & DISEASE EVALUATION

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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/m^2 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

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- **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

KEY FACTS

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- 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**