

IPH4102 TELLOMAK KOL CALL

INTERNATIONAL CONFERENCE ON MALIGNANT LYMPHOMAS (ICML)

THURSDAY, JUNE 20, 2019

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IPH4102 TELLOMAK KOL CALL

INTRODUCTION

PIERRE DODION

CHIEF MEDICAL OFFICER
INNATE PHARMA

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AGENDA

Pierre Dodion, CMO, Innate Pharma

- IPH4102 Overview
- Introduction Pierluigi Porcu

Pierluigi Porcu, TELLOMAK principal investigator

- CTCL: treatment landscape and IPH4102 clinical results
- PTCL: treatment landscape and rationale for IPH4102
- TELLOMAK study design

Pierre Dodion, CMO, Innate Pharma

- TELLOMAK strategy, time-lines and commercial potential

CTCL: cutaneous T- cell lymphoma PTCL: peripheral T-cell lymphoma

IPH4102 OVERVIEW

- IPH4102 is being developed for the treatment of certain subtypes of T cell lymphomas (TCLs) including:
  - > Cutaneous TCL (CTCL): Sézary Syndrome (SS), Mycosis Fungoides (MF)
  - > Peripheral TCL (PTCL)

- IPH4102 has a differentiated profile (ASH 2018)
  - > To date, high and durable responses, favorable safety profile, and substantial improvement in quality of life
  - > FDA fast track designation for adult patients with relapsed/refractory Sézary who have received > 2 two prior systemic therapies

- IPH4102 currently in multi-cohort Phase II study - TELLOMAK
  - > Sézary Cohort with potential to support registration
  - > MF and PTCL cohorts

INNATE ICML-15 SYMPOSIUM

PRESENTATION:

TELLOMAK: T-cell lymphoma anti-KIR3DL2 therapy: An open label, multicohort, 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

Pr. Pierluigi Porcu, MD,
TELLOMAK Principal Investigator

POSTERS:

- *KIR3DL2 is expressed in peripheral T cell lymphomas and may be a therapeutic target*

  M. Cheminant, Paris (France)
  poster Nr. 157, poster discussion

- *KIR3DL2 contributes to delineate the Acute-type and is a therapeutic target in Adult T-cell leukemia/lymphoma*

  M. Cheminant, Paris (France)
  poster Nr. 218, poster discussion

PIERLUIGI PORCU, MD
TELLOMAK PRINCIPAL INVESTIGATOR



- Director, Division of Medical Oncology and Hematopoietic Stem Cell Transplantation at Jefferson University Hospital, Philadelphia, PA
- Lymphoma-focused hematologic oncologist
- Long track record of advocacy and education for patients with cutaneous lymphoma
- Listed in U.S. News & World Report Top Cancer Doctors in America, and Newsweek's Top Hematology Doctors.
- Past Positions:
  - Professor of Medicine with tenure and was a member of the Viral Oncology Program of The Ohio State University Comprehensive Cancer Center
  - Program leader T cell lymphoma at Ohio State University
  - Director of the Cutaneous Lymphoma Program, an integrated translational research program that included a multimodality cutaneous lymphoma clinic



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TELLOMAK STUDY

PIERLUIGI PORCU

JEFFERSON UNIVERSITY HOSPITAL,
PHILADELPHIA, PA

TELLOMAK

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

Pierluigi Porcu [1], Youn H. Kim [2], Pier Luigi Zinzani [3], Helene Sicard [4], Hatem A. Azim Jr [4], Martine Bagot [5], on behalf of study investigators.

1 *S. Kimmel Cancer Center, Jefferson, Philadelphia, PA,* ***2*** *Stanford Cancer Institute - Palo Alto, CA, USA,* ***3*** *University of Bologna, Italy,* ***4*** *Innate Pharma, Marseille, France,* ***5*** *Hôpital Saint Louis, Paris, France.*



15-ICML Focus on ongoing trials Session

innate pharma



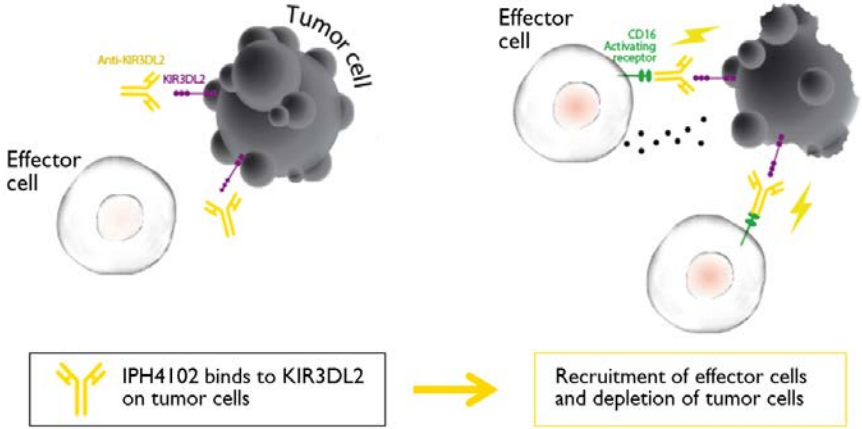
IPH4102 TELLOMAK KOL CALL

IPH4102 MECHANISM OF ACTION

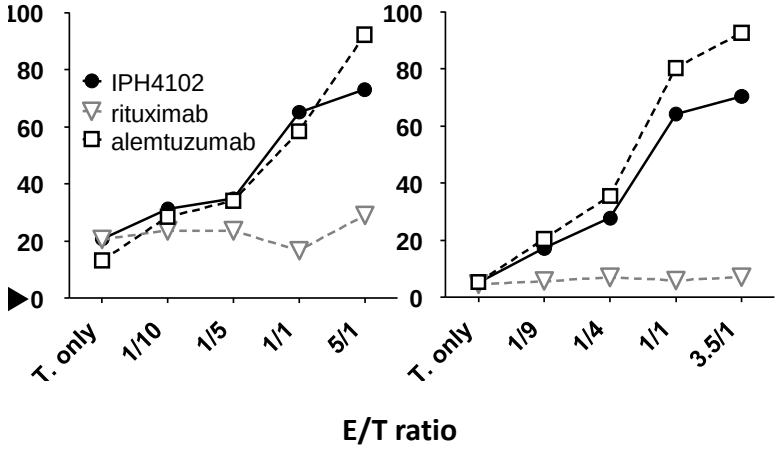
STRATEGIC IMPLICATIONS

PIERLUIGI PORCU, MD

IPH4102: POTENTIAL FIRST-IN-CLASS MAB TARGETING KIR3DL2 TRIGGERING ANTIBODY DEPENDENT CELLULAR CYTOTOXICITY (ADCC)



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



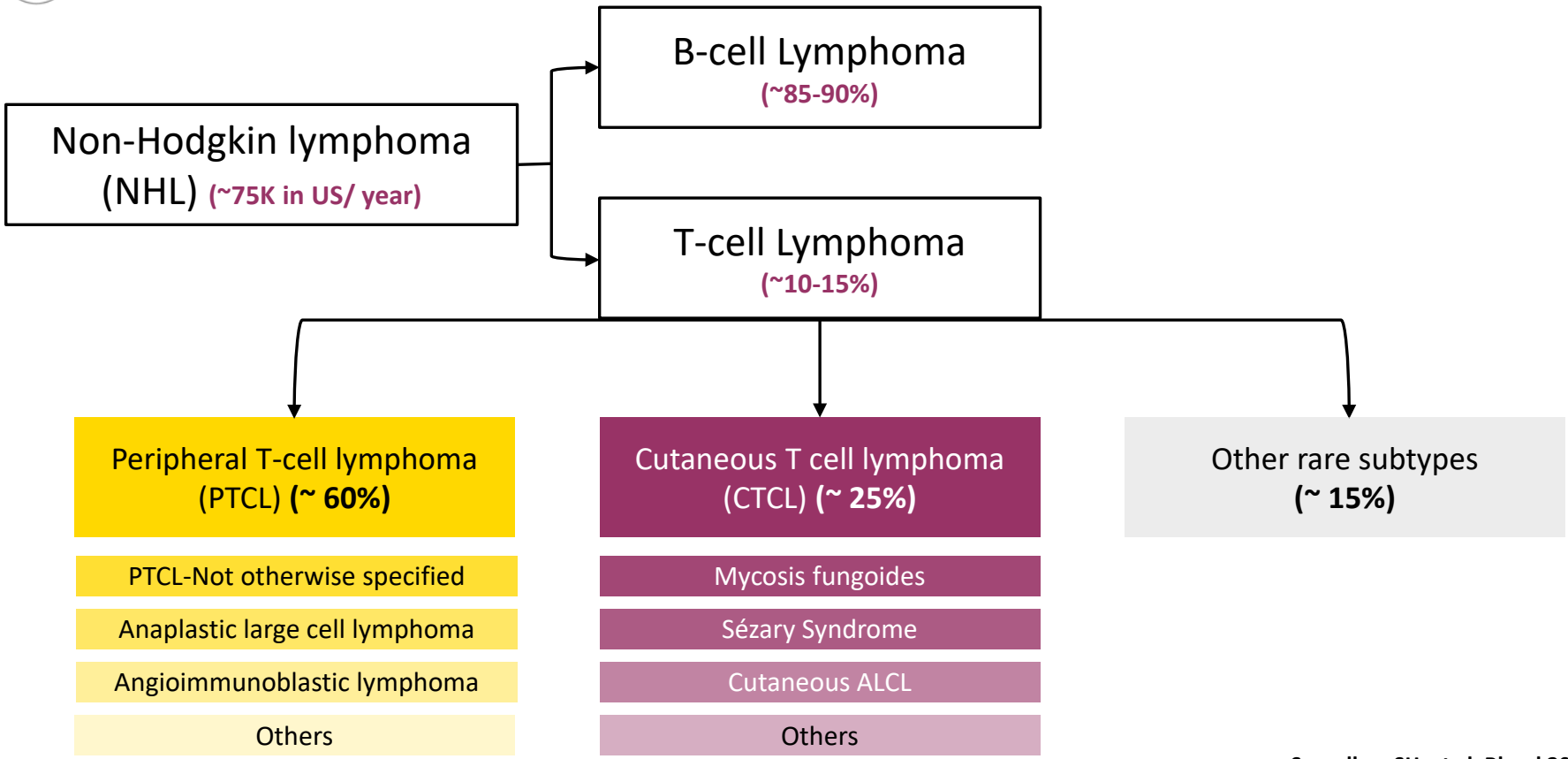
Marie-Cardine A et al, Cancer Res 2014

EXPRESSION OF KIR3DL2

Tissue	Frequency of KIR3DL2 expression
Subsets of T / NK cells	low
Other normal tissues	absent
Sézary syndrome	85-90%
CTCL other than Sézary	~ 65%
PTCL	~ 50%

Strong rationale for the exploration of IPH4102 in these diseases

OVERVIEW OF T-CELL LYMPHOMAS



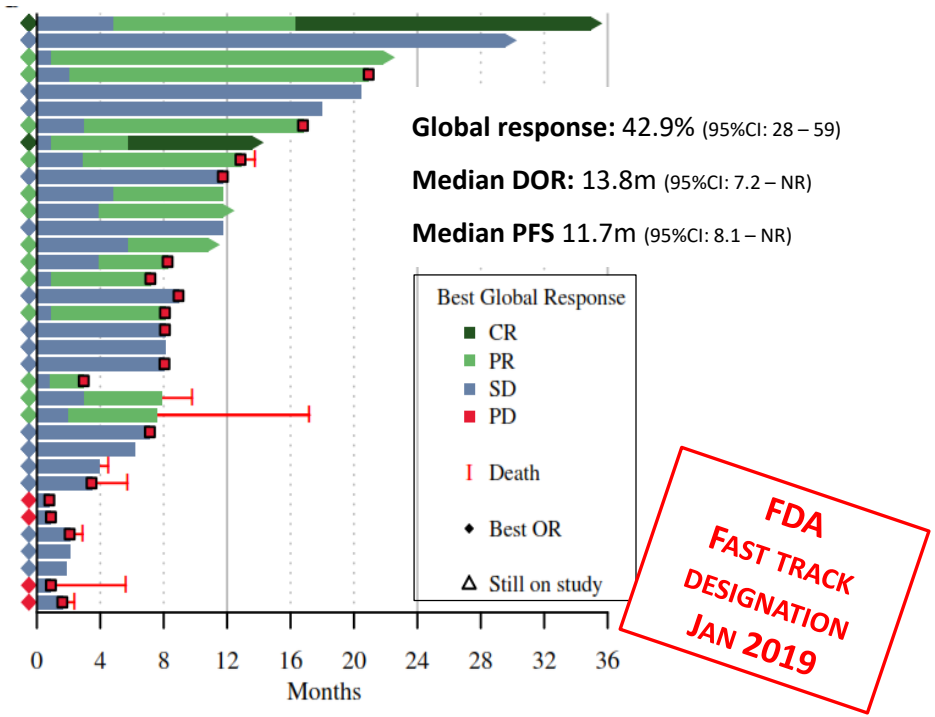
Swerdlow SH et al, Blood 2016



IPH4102 IN SÉZARY SYNDROME

RESULTS OF FIRST-IN-HUMAN PHASE 1 STUDY
FAVORABLE SAFETY PROFILE AND HIGH ACTIVITY OF IPH4102 IN SÉZARY

- Phase 1: N=44 Advanced CTCL
  of which 35 Sézary
- ≥ 2 prior systemic therapies
  39% ≥ 5th line of therapy
  20% previously treated with mogamulizumab
- 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



Bagot M et al, Lancet Oncol 2019

PUTTING IPH4102 PHASE 1 DATA IN CLINICAL CONTEXT
RECENT RESULTS IN MF/SÉZARY PATIENTS

	Mogamulizumab	Vorinostat
Patient population	Patients who received at least **one** systemic therapy Most frequent first line treatments: ECP, Bexarotene ± interferon	
Response rate	MF: 21% Sézary: 37%	MF: 7% Sézary: 2%
Median Progression free survival	MF/Sézary: 7.7 months	MF/Sézary: 3.1 months
Time to next treatment*	MF: 8.8 months Sézary: 12.9 months	MF: 4.1 months Sézary: 3.3 months
FDA label	Patients who received at least **one** prior systemic therapy	Patients who received at least **two** prior systemic therapies

Pro et al, Proc Am Soc Clin Oncol 2019; ^ Kim Y et al, Lancet Oncol 2018

SUMMARY OF RATIONALE FOR IPH4102 IN SÉZARY

- KIR3DL2 highly expressed
- Patients with R/R Sézary, received ≥ 2 prior systemic therapies, including mogamulizumab have a poor outcome
- Significant unmet medical need remains
- IPH4102 Phase 1 data:
  - high and durable responses
  - a favorable safety profile
  - substantial improvement in quality of life (90% of patients)

Strong rationale for cohort #1 of TELLOMAK study

Sézary Syndrome
(N~60)

TELLOMAK : T-CELL LYMPHOMA ANTI-KIR3DL2 THERAPY
A MULTI-COHORT INTERNATIONAL PHASE 2 TRIAL

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

Mycosis Fungoides **(N~90)**
≥ 2 prior systemic therapies including biological agents

Cohort #2: KIR3DL2 expressing, Simon 2 stage

Cohort #3: KIR3DL2 non-expressing, Simon 2 stage

IPH4102 single agent

Peripheral T Cell Lymphoma **(N~100)**
≥ 1 prior systemic therapy including anthracycline-based chemo

Cohort #4: KIR3DL2 expressing, Simon 2 stage

Cohort #5: KIR3DL2 non-expressing, Simon 2 stage

IPH4102 + GEMOX

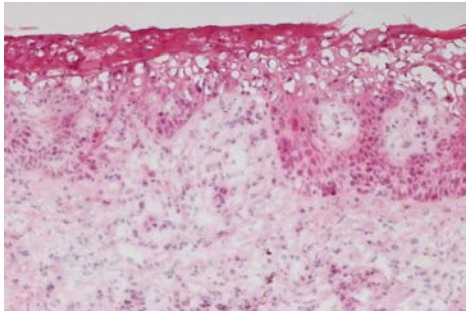
KIR3DL2 expression is defined as ≥1% using central evaluation of KIR3DL2 by immunohistochemistry



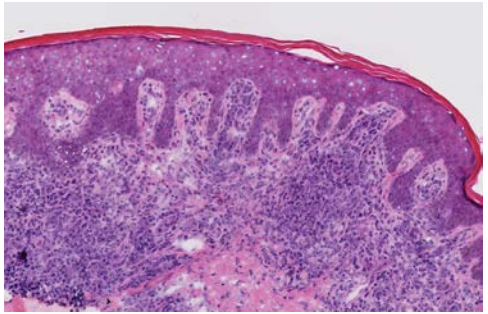
CUTANEOUS T-CELL LYMPHOMA (CTCL)

KIR3DL2 IS EXPRESSED IN CUTANEOUS T CELL LYMPHOMA

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



KIR3DL2 expression in **Mycosis Fungoides**

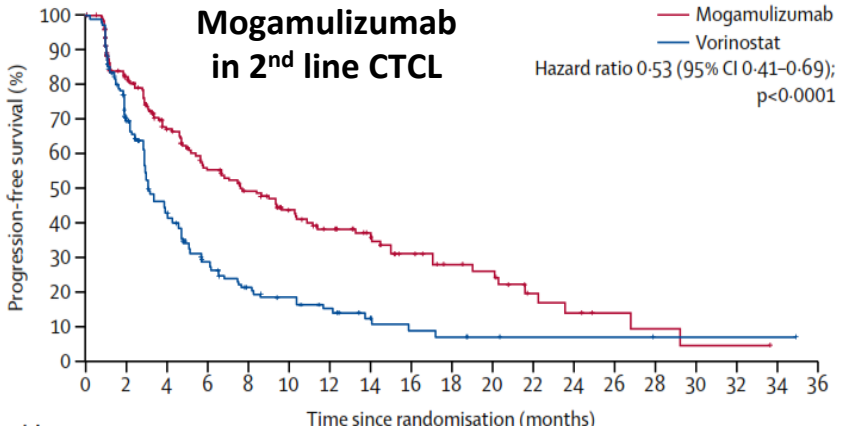


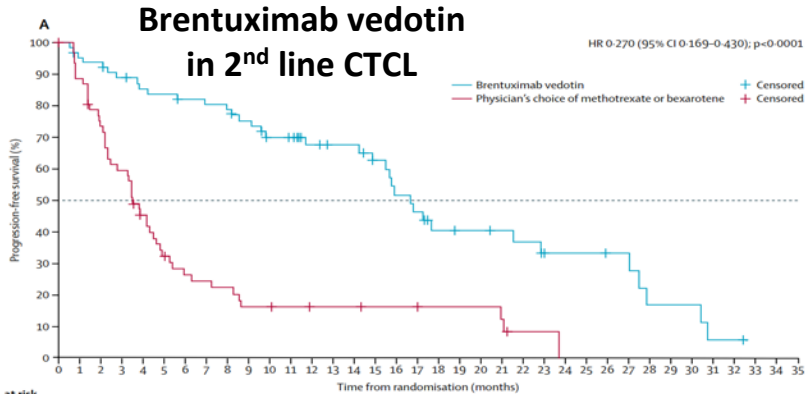
KIR3DL2 expression in **Sézary syndrome**

Battistella M et al, Blood 2017

SYSTEMIC TREATMENT OPTIONS IN MYCOSIS FUNGOIDES

	Mycosis fungoides
1st line	Bexarotene, bexarotene-based combinations
2nd line	Brentuximab / Mogamulizumab
3rd line	Romidepsin / Vorinostat *
4th line	Interferon, methotrexate, gemcitabine, liposomal-doxorubicin





* only available in the US

Kim et al, Lancet Oncol 2018;19: 1192-204; Prince et al, Lancet 2017: 390; 555-66

SUMMARY OF RATIONALE FOR IPH4102 IN MYCOSIS FUNGOIDES

- KIR3DL2 is expressed in ~50% of MF
- Patients with relapsed/refractory MF who have received ≥ 2 prior systemic therapies have a poor outcome and represent a significant unmet medical need
- IPH4102 has shown high and durable responses in Sézary, another malignancy with high KIR3DL2 expression

Strong rationale for cohort #2-3 of TELLOMAK study

Mycosis Fungoides
(N~90)
≥ 2 prior systemic therapies including biological agents

TELLOMAK : T-CELL LYMPHOMA ANTI-KIR3DL2 THERAPY
A MULTI-COHORT INTERNATIONAL PHASE 2 TRIAL

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≥ 1 prior systemic therapy including anthracycline-based chemo

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Cohort #5: KIR3DL2 non-expressing, Simon 2 stage

IPH4102 + GEMOX

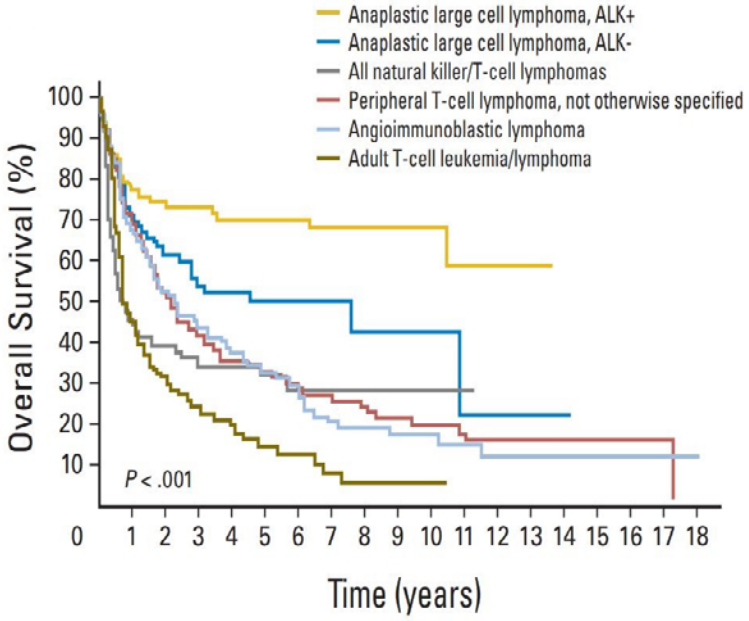
KIR3DL2 expression is defined as ≥1% using central evaluation of KIR3DL2 by immunohistochemistry



PERIPHERAL T-CELL LYMPHOMA (PTCL)

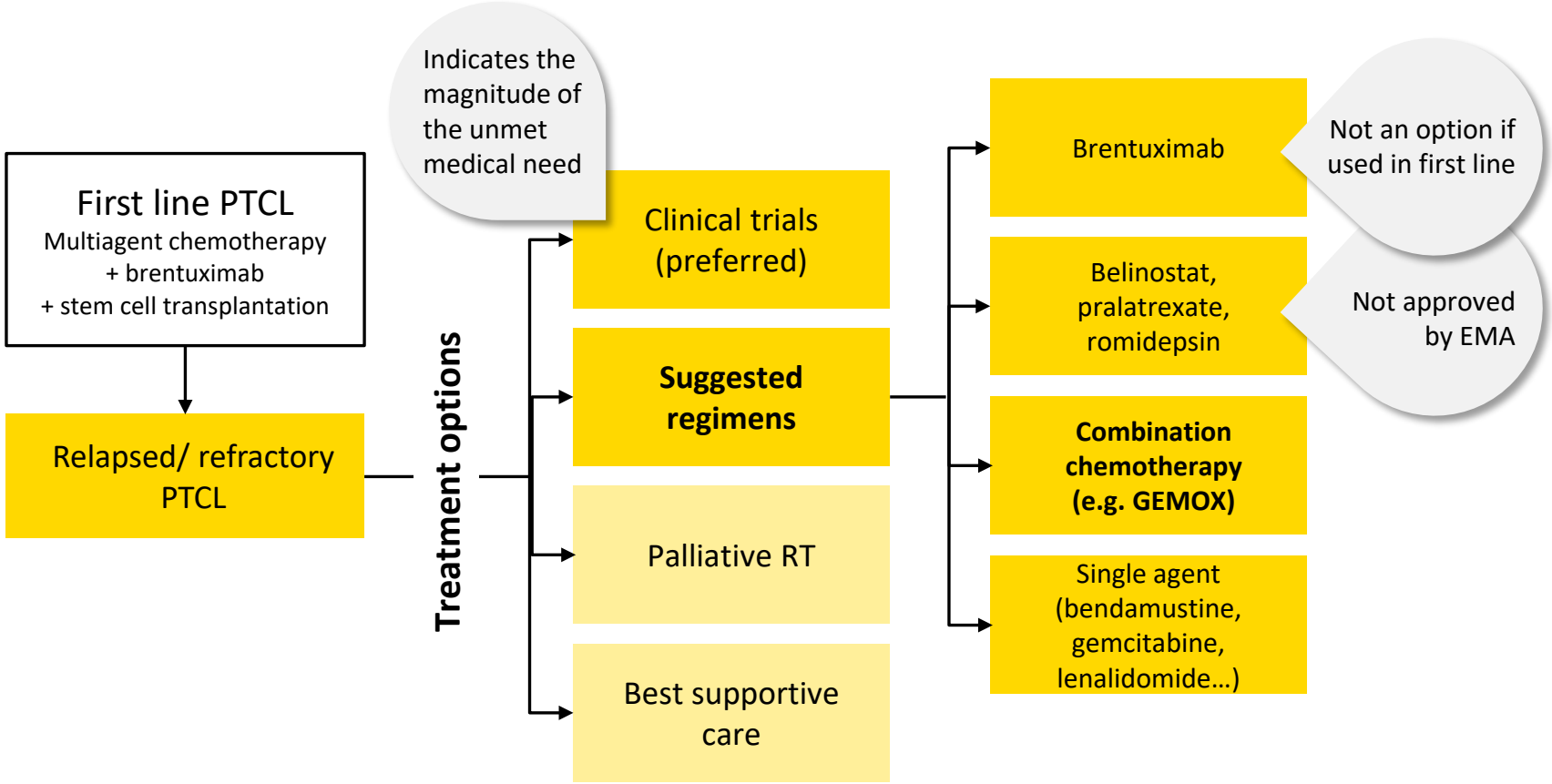
PERIPHERAL T CELL LYMPHOMA SURVIVAL BY KEY SUBTYPES

PTCL Type	Frequency (%) Europe & US	5-y overall survival (%)
PTCL not otherwise specified	34	32
Angioimmunoblastic	16-28	32
Anaplastic large cell lymphoma (ALCL) ALK+	6-16	70
Anaplastic large cell lymphoma, ALK -	8-9	49



International T cell lymphoma Project, J Clin Oncol 2008

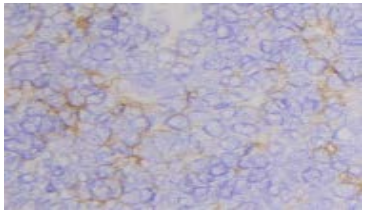
TREATMENT OF RELAPSED PTCL
BASED ON THE NCCN GUIDELINES VERSION 2.2019



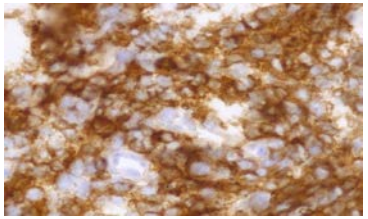
IPH4102 IN PERIPHERAL T-CELL LYMPHOMA
RATIONALE

Expression of KIR3DL2 in PTCL subtypes

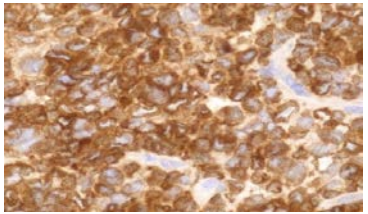
AITL (9/25, 36%)



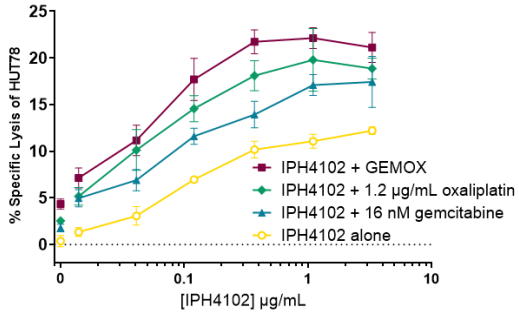
PTCL-NOS (7/20, 35%)



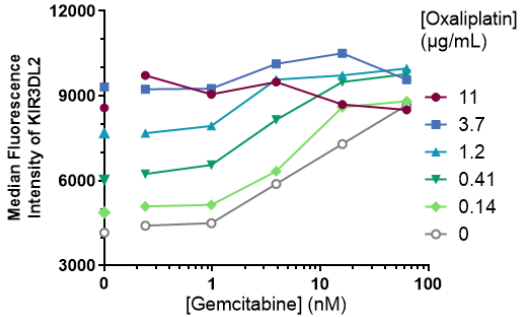
ALCL (8/14, 57%)



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

SUMMARY OF RATIONALE FOR IPH4102 IN PTCL

- KIR3DL2 is expressed in ~50% of PTCL
- Patients with relapsed/refractory PTCL who have received 1 prior systemic therapy have a poor outcome and represent a significant unmet medical need
- IPH4102 has shown high and durable responses in Sézary, another malignancy with high KIR3DL2 expression

Strong rationale for cohorts #4-5 of Tellomak study

Peripheral T Cell Lymphoma
(N~100)
≥ 1 prior systemic therapy including anthracycline-based chemo

TELLOMAK : T-CELL LYMPHOMA ANTI-KIR3DL2 THERAPY
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IPH4102 single agent

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Cohort #4: KIR3DL2 expressing, Simon 2 stage

Cohort #5: KIR3DL2 non-expressing, Simon 2 stage

IPH4102 + GEMOX

KIR3DL2 expression is defined as ≥1% using central evaluation of KIR3DL2 by immunohistochemistry

Clinicaltrials.gov: NCT03902184

KEY ELIGIBILITY CRITERIA

TELLOMAK

Sézary Syndrome	Mycosis Fungoides	Peripheral T Cell Lymphoma
• Relapsed/refractory Sézary	• 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

*LCT: Large Cell Transformation

Clinicaltrials.gov: NCT03902184

STUDY ENDPOINTS

TELLOMAK

- **Primary endpoint**
  - > Overall response rate
    - Cohort 1-3 (International consensus criteria, Olsen 2011)
    - Cohort 4-5 (Lugano criteria, Cheson 2014)
- **Key secondary endpoints**
  - > Toxicity: incidence of TEAEs
  - > Duration of response, PFS, OS at 1 and 2 years
  - > Quality of life (QoL) measured by Skindex29 questionnaire, pruritus as measured by the Visual Analog Scale
  - > PK and immunogenicity

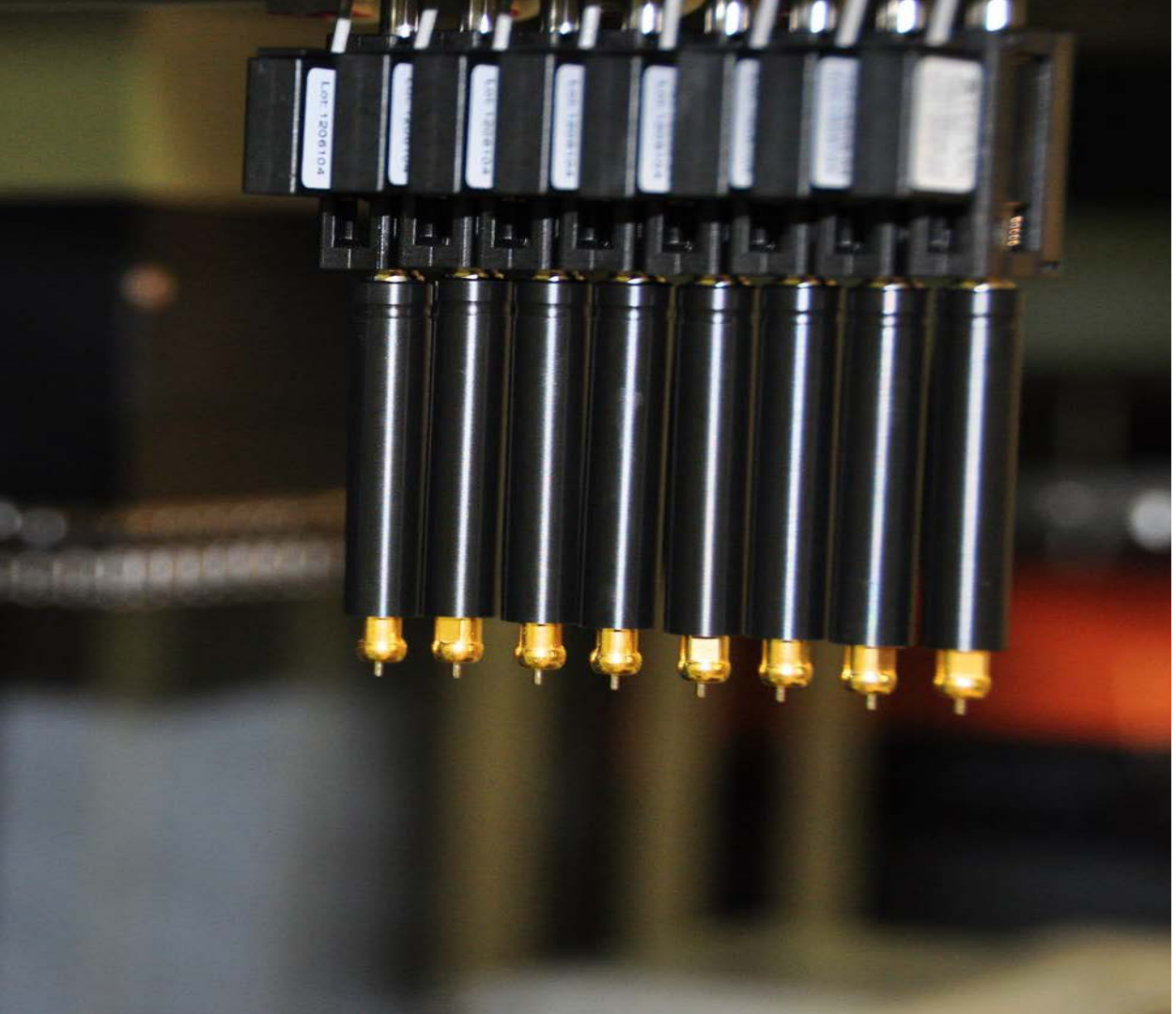
Clinicaltrials.gov: NCT03902184

STUDY FACTS

TELLOMAK

- Open in US, France, Italy, UK, Germany and Spain with target activation of around 40 centers
- Recruitment ongoing
- 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

Clinicaltrials.gov: NCT03902184



IPH4102 TELLOMAK KOL CALL

PERSPECTIVES AND COMMENTS

PIERRE DODION, MD

CHIEF MEDICAL OFFICER
INNATE PHARMA

TELLOMAK STRATEGY

- As illustrated by Dr. Porcu in his presentation, TELLOMAK is an ambitious trial, with an innovative design that allows to simultaneously:
  - > To further assess the safety and efficacy of IPH4102 in R/R Sézary syndrome, an orphan indication in the US and EU
    - This cohort could enable the registration of IPH4102 in this indication for patients who have received > 2 prior systemic therapies including mogamulizumab
    - and may provide quicker market access
  - > To explore the safety and efficacy of IPH4102 in MF and PTCL
    - Expansion of the target population

Clinicaltrials.gov: NCT03902184

TELLOMAK EXPECTED TIMELINES

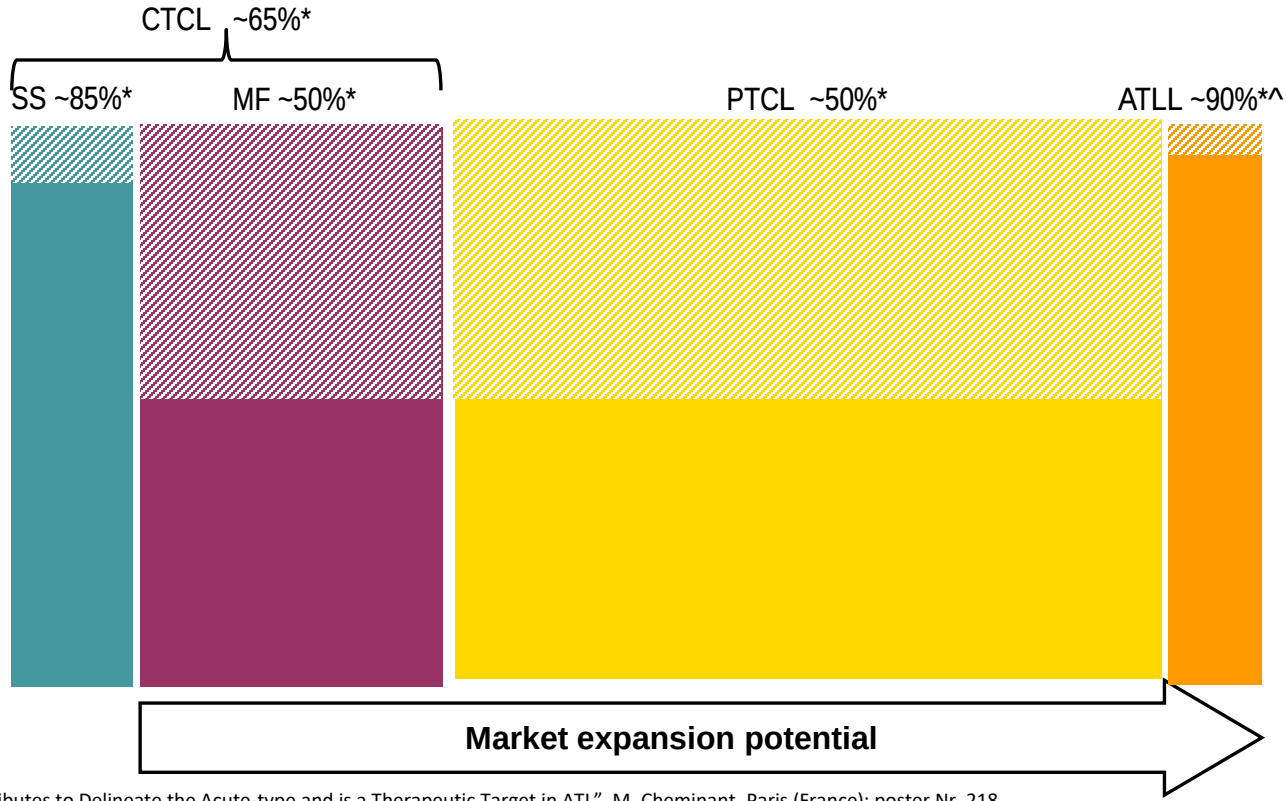
- We expect to announce the outcome **of the first stage** of the **MF and PTCL cohorts** in the **second half of 2020** and report initial efficacy data for the different cohorts starting in 2021
- The results of the dedicated **Sézary syndrome cohort** may support a future **BLA submission to the FDA**

Clinicaltrials.gov: NCT03902184

IPH4102 – COMMERCIAL OPPORTUNITY
SIGNIFICANT POTENTIAL BEYOND SÉZARY

- 15% of all NHL
- Highly heterogeneous
- MF most common form CTCL
- SS most aggressive form CTCL
- ^Acute-type ATLL, the most aggressive form of ATLL
- Medical need in late lines

- Differentiated profile
- Biomarker driven stratification
- Premium pricing strategy
- LCM options

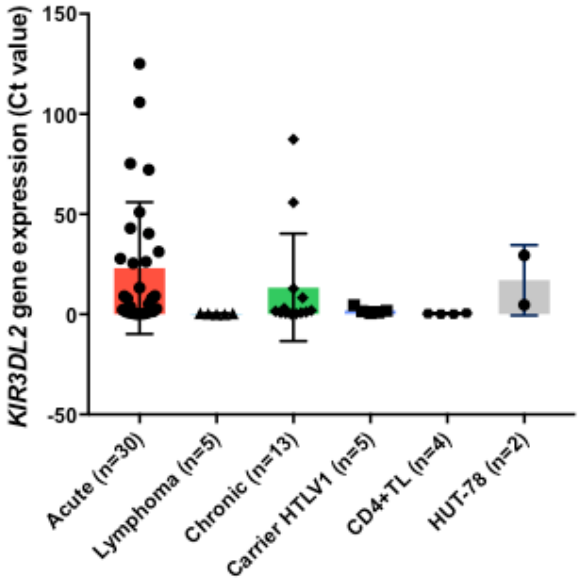


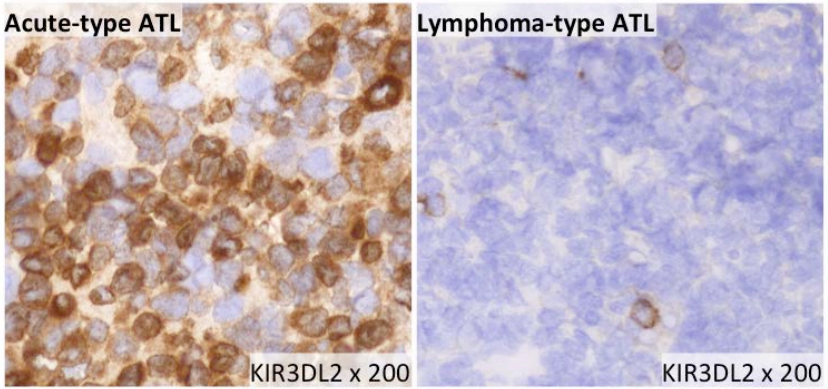
^Membrane Expression of NK Receptor KIR3DL2 Contributes to Delineate the Acute-type and is a Therapeutic Target in ATL", M. Cheminant, Paris (France); poster Nr. 218

Boxes' width reflects approximation of subpopulation sizes based on external research and best Internal current estimates

IPH4102 IN ACUTE-TYPE ADULT T-CELL LEUKEMIA
RATIONALE

KIR3DL2 is expressed in almost all acute-type ATL patients (n=28/30, 93%).
In contrast, lymphoma and chronic/smoldering cases were often negative for KIR3DL2 (n=2/8 and n=2/12 respectively; p=0.001).



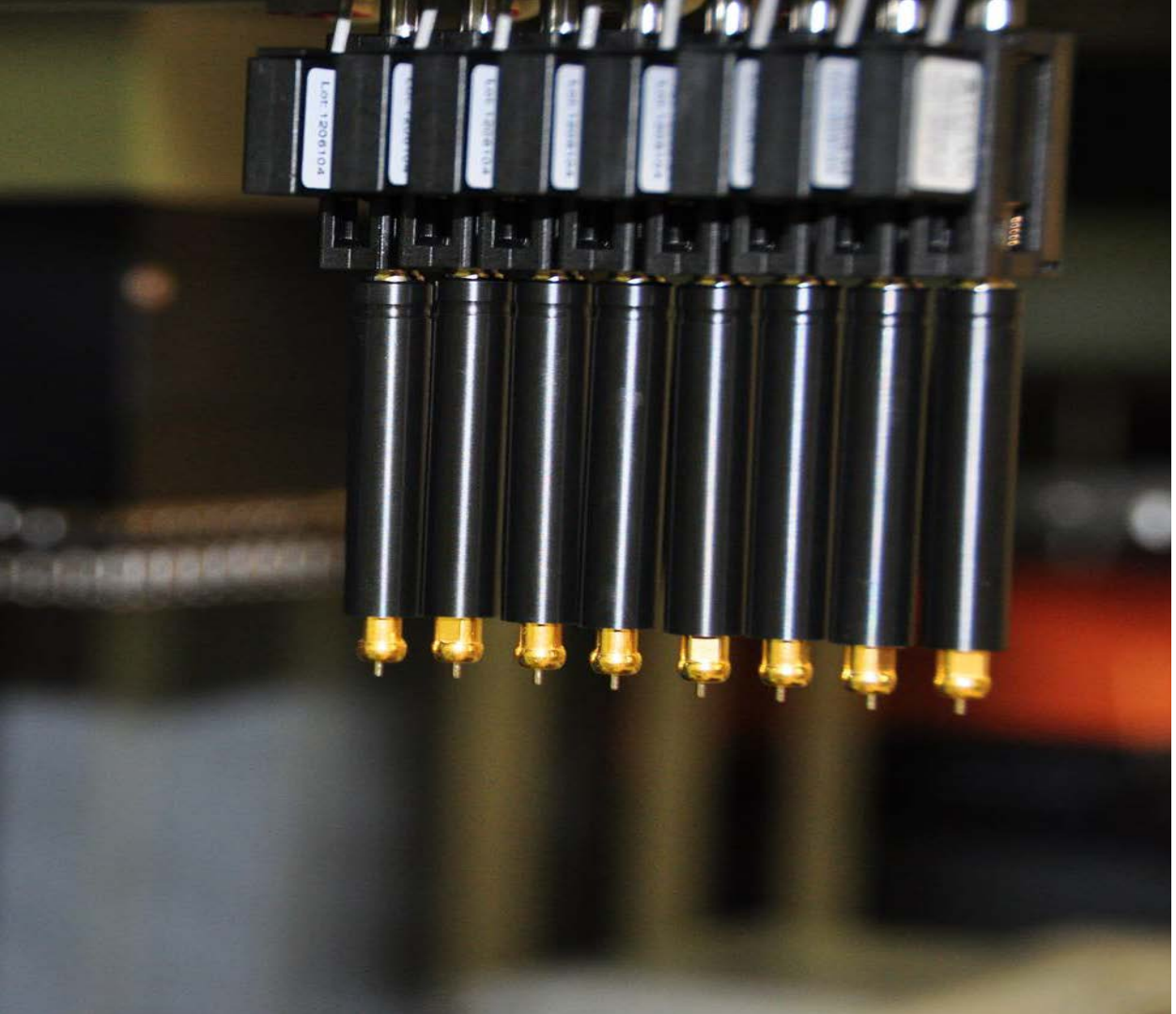


Membrane Expression of NK Receptor KIR3DL2 Contributes to Delineate the Acute-type and is a Therapeutic Target in ATL", M. Cheminant, Paris (France); poster Nr. 218, poster discussion



IPH4102 TELLOMAK KOL CALL

QUESTIONS AND ANSWERS



IPH4102 TELLOMAK KOL CALL

BACKUPS

SCHEDULE OF ADMINISTRATION & DISEASE EVALUATION

TELLOMAK

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

Clinicaltrials.gov: NCT03902184

FREQUENCY AND OPPORTUNITY

Most common CTCL types, their frequency as a percentage of all cases of CTCL, and prognosis

CTCL Type	Frequency (%)	5-year disease-specific survival (%)
Mycosis fungoides	39	88
Primary cutaneous CD30+ lymphoproliferative disorders (LPD)	20	95-99
Primary cutaneous CD4+ small/medium T-cell LPD	6	100
Mycosis fungoides variants	5	75
Sézary syndrome	2	36

Various PTCL types, their frequency as a percentage of all TCL cases, and prognosis

PTCL Type	Frequency (%) Europe & U.S.	5-year overall survival (%)
PTCL not otherwise specified	34	32
Angioimmunoblastic	16-28	32
Anaplastic large cell lymphoma, or ALCL, ALK+	6-16	70
Anaplastic large cell lymphoma, ALK-	8-9	49