IPH4102, an anti-KIR3DL2 monoclonal antibody in refractory Sézary Syndrome: Results from a multicenter international phase 1 trial

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CONFLICTS OF INTEREST

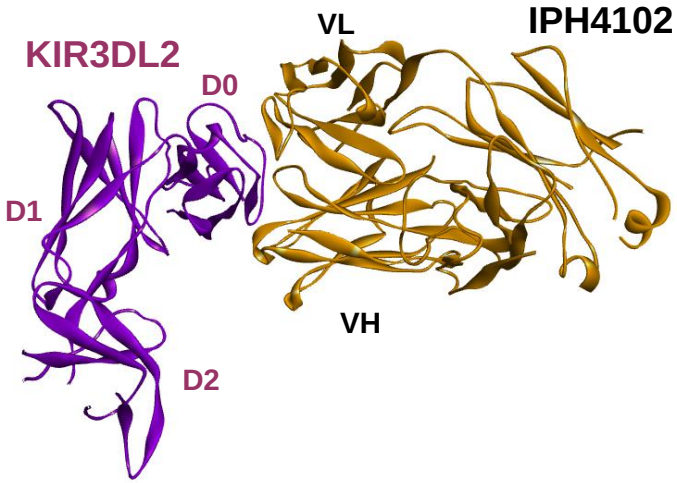
Consultant: Innate Pharma

Advisory committee: Innate Pharma, Actelion, Takeda, Kyowa Kirin

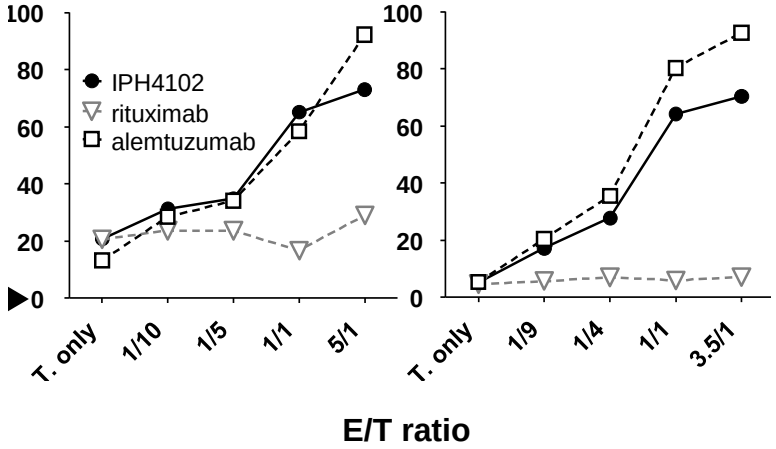
Equity Ownership: Innate Pharma

IPH4102

FIRST IN CLASS mAb DIRECTED AGAINST KIR3DL2

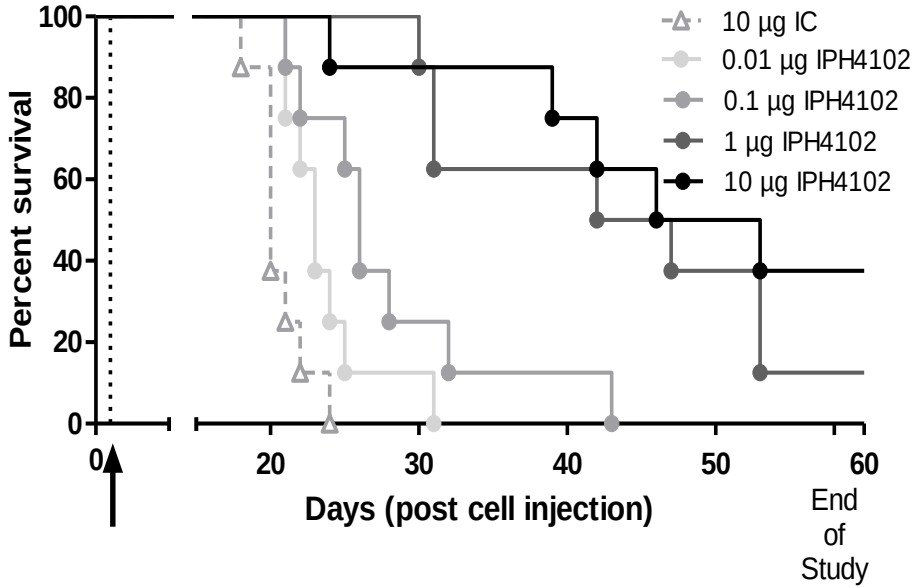


NK cells kill primary Sézary cells in *ex vivo* autologous model through IPH4102-mediated ADCC



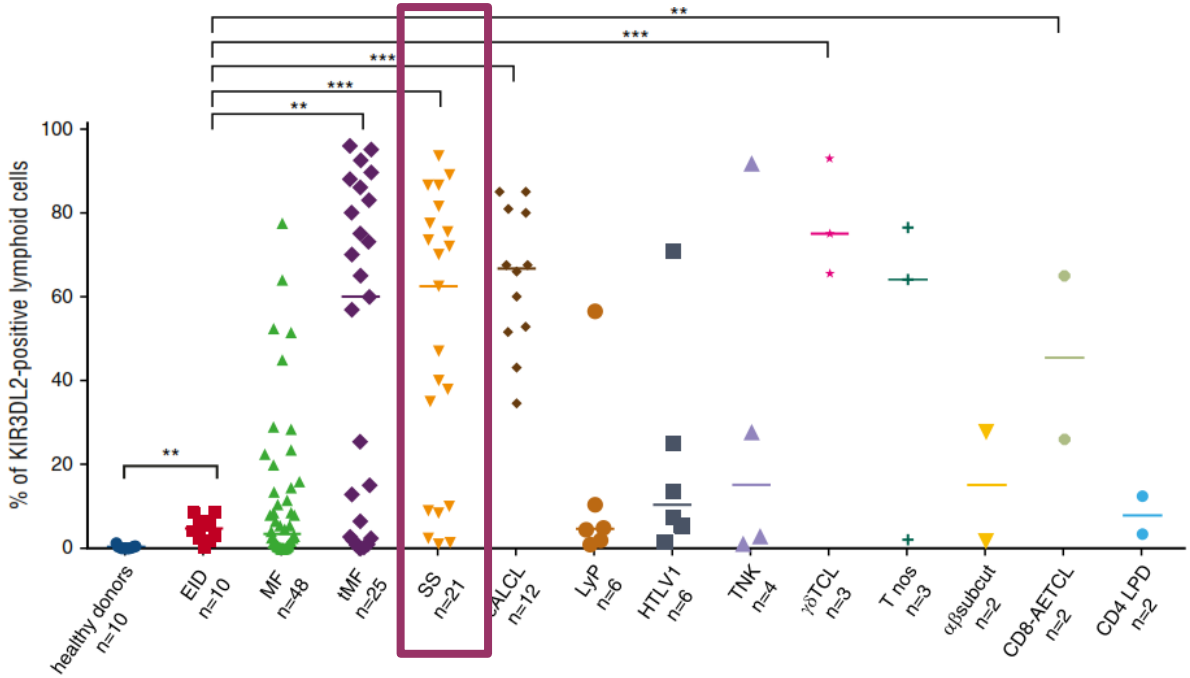
Marie-Cardine A et al, Cancer Res 2014

IPH4102 IMPROVES SURVIVAL IN MOUSE XENOGRAFT MODELS

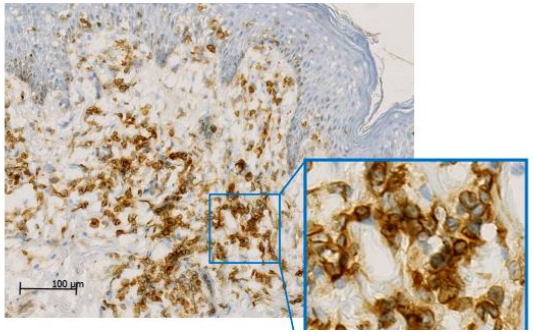


Marie-Cardine A et al, Cancer Res 2014

KIR3DL2 IS EXPRESSED IN CTCL **PARTICULARLY IN SÉZARY SYNDROME**



KIR3DL2 expression by IHC in a SS patient



EID: erythrodermic inflammatory disease, MF: mycosis fungoides, SS: Sézary syndrome, cALCL: cutaneous anaplastic large cell lymphoma, LyP: lymphoid papylosis, HTLV1 Adult T-cell lymphoma, TNKL nasal-type lymphoma, γ δ T-cell lymphoma, T-nos: T cutaneous peripheral T-cell lymphoma non otherwise specified, αβ T celll lymphoma, CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma, LPD: lymphoproliferative disorder

Battistella M et al; Blood 2017

STUDY DESIGN
FIRST IN HUMAN PHASE 1 CLINICAL TRIAL

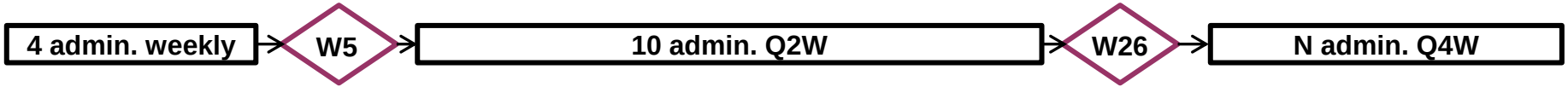
Dose-escalation

- 10 dose levels (up to 10mg/kg) – accelerated 3+3 design
- All CTCL subtypes
- ≥ 2 prior systemic therapies
- KIR3DL2 ≥5% in skin and/or blood (centrally)

Cohort expansion

- Recommended Phase 2 dose (750 mg)
- SS and tMF only
- ≥ 2 prior systemic therapies
- Any KIR3DL2 expression level

- **Dosing regimen**, until progression or unacceptable toxicity



- Intra-patient dose-escalation allowed after Week 5 (W5) in the dose-escalation portion

STUDY OBJECTIVES

- **Primary objective**: determination of Maximal Tolerated Dose (MTD) and RP2D, overall safety
- **Secondary objectives**:
  - > Overall Response Rate (ORR, Olsen JCO 2011 criteria), duration of response (DOR) and Progression-Free Survival (PFS)
  - > PK and immunogenicity
- **Quality of Life**
  - > Pruritus (Visual Analogue Scale)
  - > SkinDex29
- **Exploratory objectives**:
  - > Early changes (at week 5) in KIR3DL2-positive cells* and molecular residual disease (MRD)** in skin and blood and ORR

TODAY'S PRESENTATION FOCUSES ON SS PATIENTS

* By Immunohistochemitstry (IHC); ** By TCR deep sequencing

BASELINE DISEASE CHARACTERISTICS

SÉZARY SYNDROME (N=35)

	Total N = 35
Median age in years (range)	70 (37 – 90)
Evidence of LCT*, n (%)	7 (20%)
KIR3DL2 expression, n (%) - Skin - Blood - Skin and/or blood	 27 (77%) 33 (94%) 33 (94%)
Median time from diagnosis in months (range)	23 (6 – 268)
Median N. of prior systemic therapy (range) - Treated with IPH4102 as ≥ 5th line of systemic treatment	2 (1 – 9)^ 12 (35%)
Prior treatment with HDAC inhibitors, n (%)	13 (37%)
Prior treatment with Mogamulizumab, n (%)	7 (20%)

* LCT: large cell transformation based on central testing on frozen tissue.
^ One patient had a protocol violation, treated with only one prior line of systemic therapy

SAFETY PROFILE

IPH4102 DISPLAYS A FAVORABLE SAFETY PROFILE

Dose escalation: no DLT / MTD not reached / RP2D = 10mg/kg - 750 mg flat dose

Common AEs	All AEs		Related AEs*	
	All grades	Grade 3-4	All grades	Grade 3-4
Peripheral edema	10 (29%)	0	0	0
Asthenia	9 (26%)	0	5 (14%)	0
Fatigue	8 (23%)	0	3 (9%)	0
Cough	7 (20%)	0	0	0
Pyrexia	7 (20%)	0	3 (9%)	0
Arthralgia	6 (17%)	0	2 (6%)	0
Lymphopenia	5 (14%)	2 (6%)	5 (14%)	2 (6%)
Diarrhea	5 (14%)	0	1 (3%)	0

Only 3 patients (9%) stopped treatment for an AE

Four patients developed 5 possibly related grade ≥ 3 AEs

- grade 5 hepatitis (n=1)**, grade 4 sepsis (n=1), grade 3 lymphopenia (n=3), grade 3 hypotension (n=1).

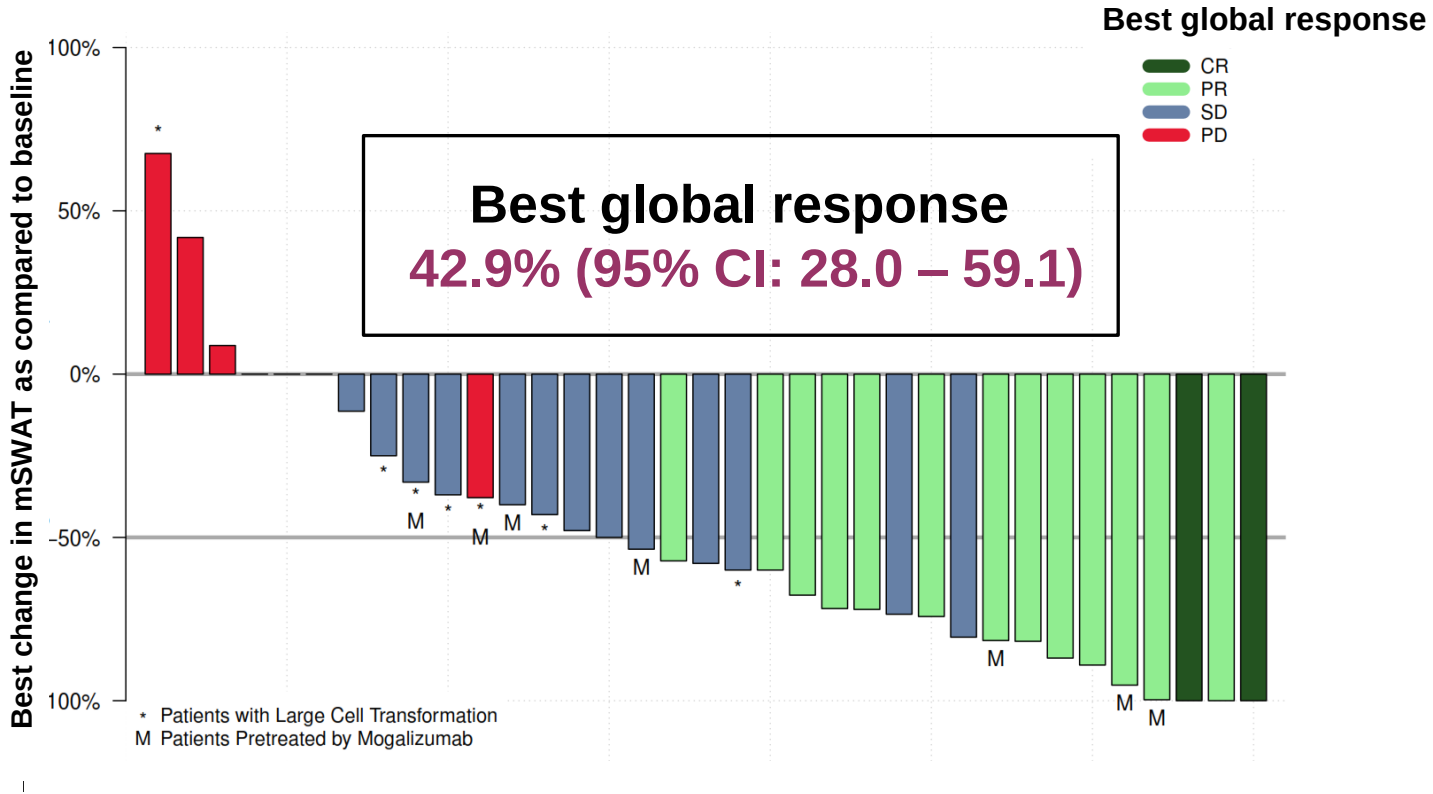
Data Cut-off: October 15, 2018

* According to investigator assessment

** 6 weeks after stopping IPH4102, evidence of HHV-6B infection

CLINICAL EFFICACY RESULTS

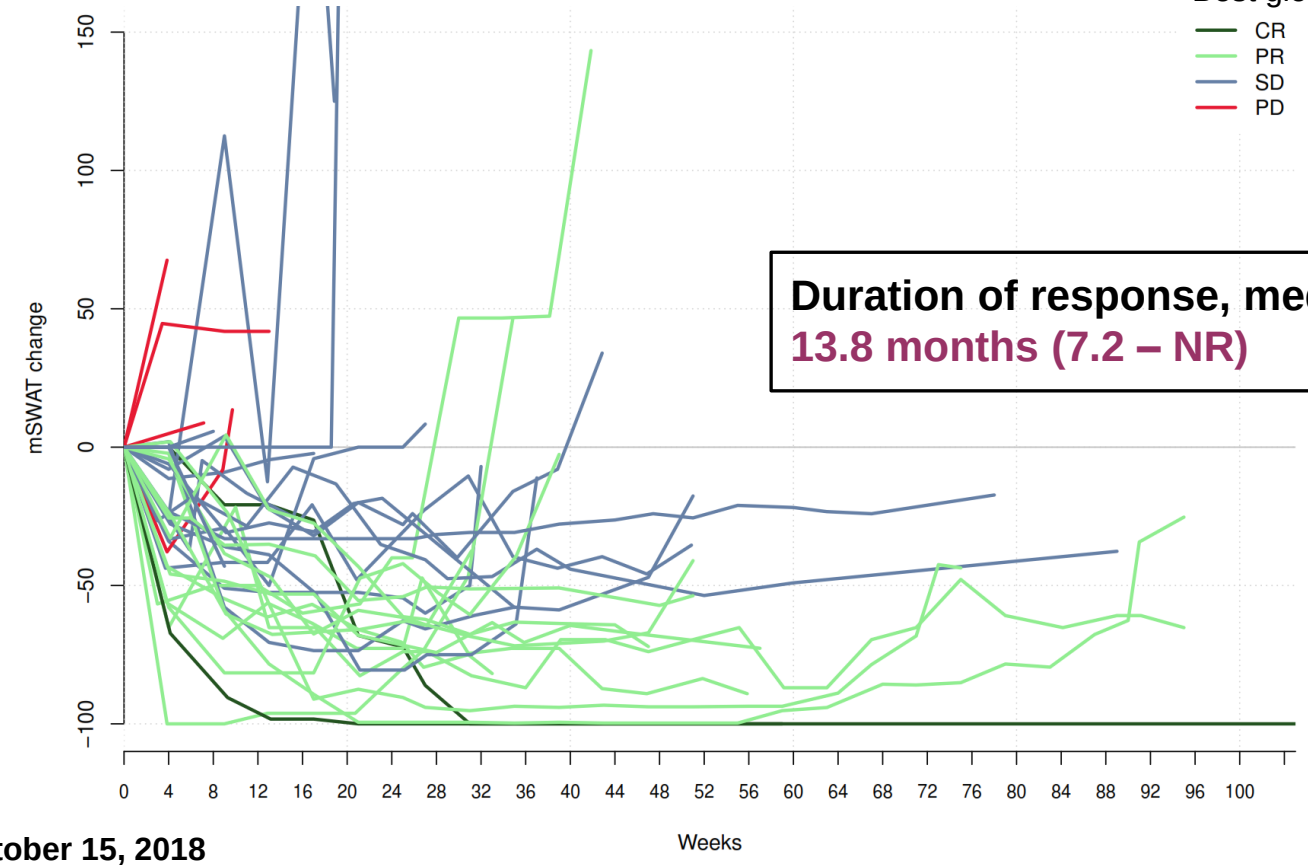
HIGH OVERALL RESPONSE RATE



Data Cut-off: October 15, 2018

CLINICAL EFFICACY RESULTS

DURABLE RESPONSES

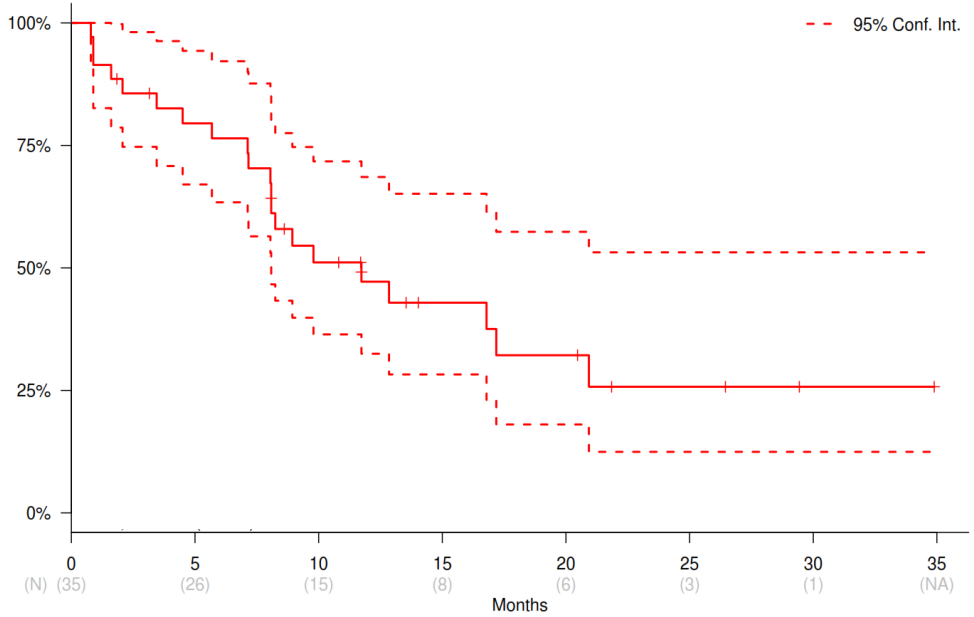


Duration of response, median (95% CI)
13.8 months (7.2 – NR)

Data Cut-off: October 15, 2018

NR: Not Reached

CLINICAL EFFICACY RESULTS
LONG PROGRESSION FREE SURVIVAL



PFS, median (95% CI)
11.7 months (8.1 – NR)

Median follow-up:
14.2 months (95% Ci: 11.8 – 20.5)

Data Cut-off: October 15, 2018

CLINICAL EFFICACY RESULTS
SUBGROUP ANALYSIS

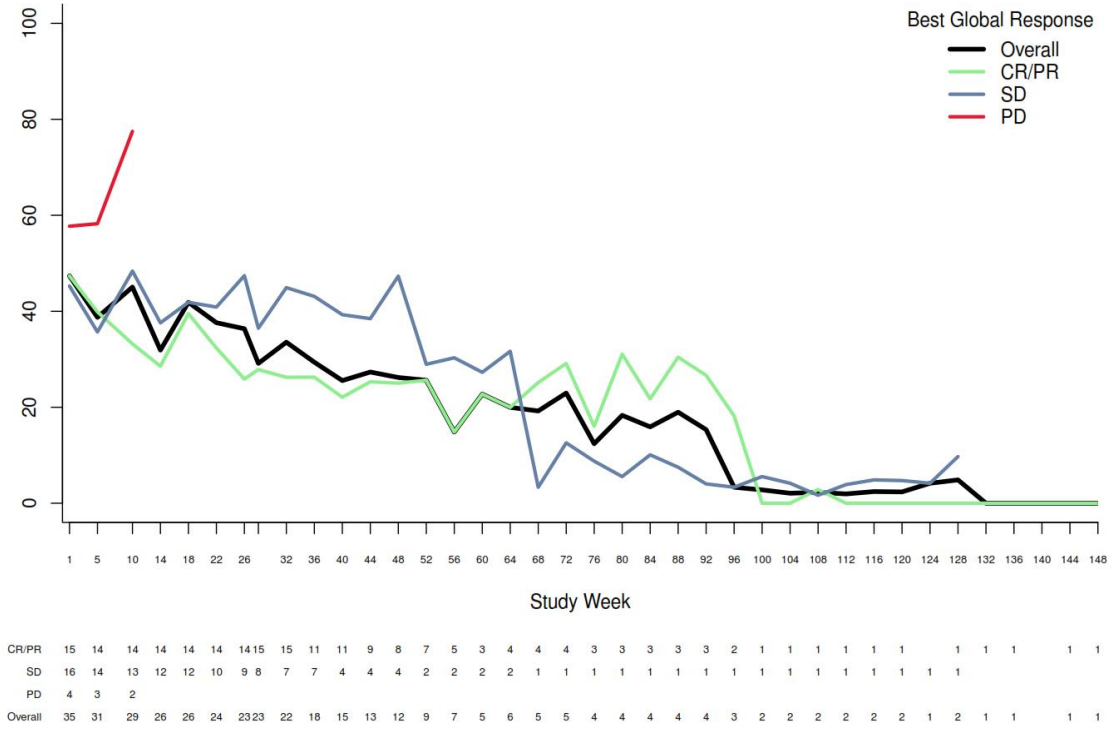
	All SS N=35	SS without LCT N=28	Prior treatment with mogamulizumab N=7
Best global response - CR - PR - SD - PD	**42.9% (28.0 – 59.1)** 2 (5.7%) 13 (37.2%) 16 (45.7%) 4 (11.4%)	**53.6% (35.8 – 70.5)** 2 (7.1%) 13 (46.5%) 11 (39.3%) 2 (7.1%)	**42.9% (15.8 – 75.0)** 0 3 (42.9%) 3 (42.9%) 1 (14.2%)
Duration of Response*	13.8 (7.2 – NR)	13.8 (7.2 – NR)	13.8 (7.2 – NR)
Progression Free Survival*	11.7 (8.1 – NR)	12.8 (8.2 – NR)	16.8 (8.1 – NR)

* Median (95% CI)
NR: Not Reached
LCT: Large Cell Transformation tested centrally on frozen tissue

Data Cut-off: October 15, 2018

QUALITY OF LIFE

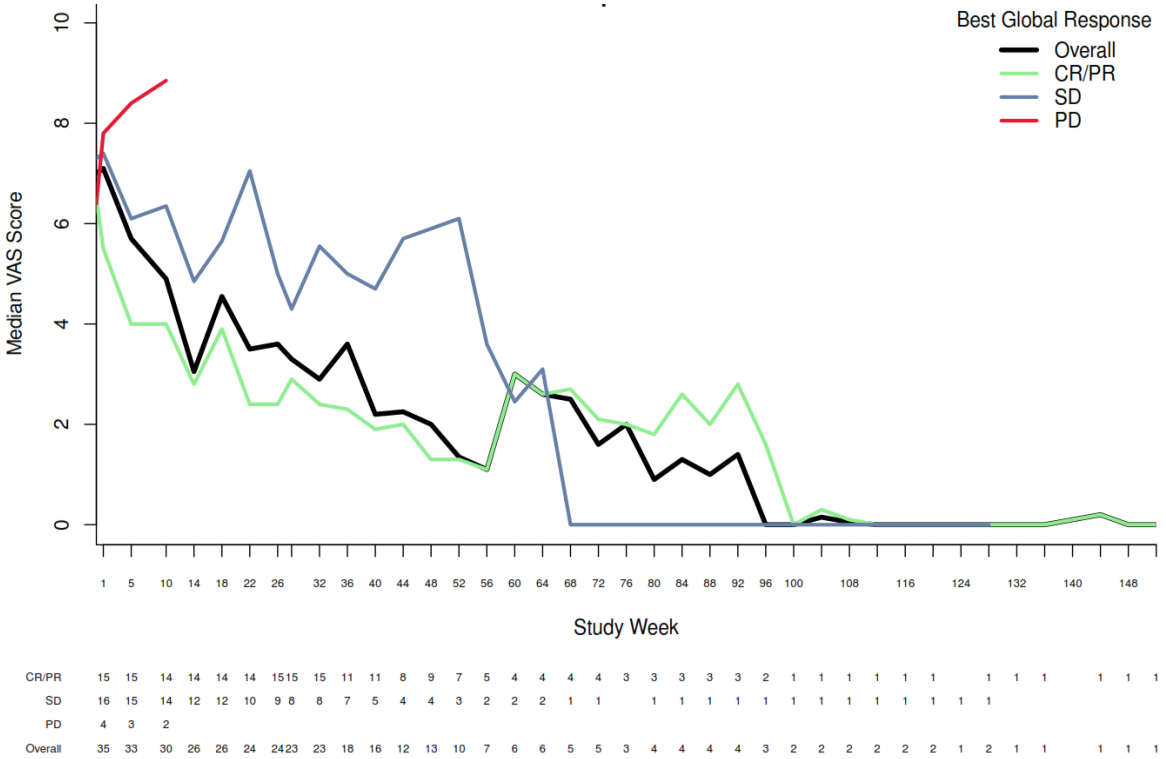
SKINDEX29 (N = 35)



Data Cut-off: October 15, 2018

QUALITY OF LIFE

PRURITUS VISUAL ANALOGUE SCALE SCORE (N = 35)



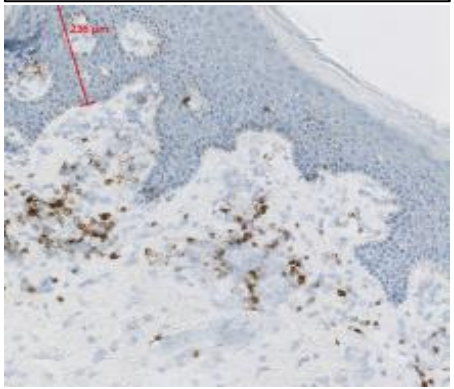
Data Cut-off: October 15, 2018

EXPLORATORY BIOMARKERS

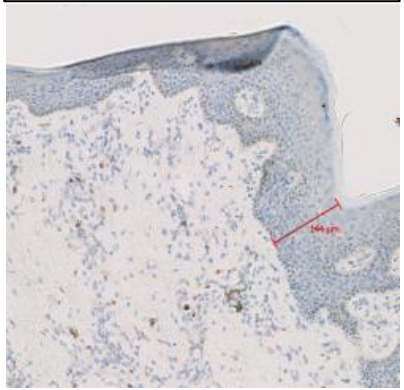
CHANGES IN KIR3DL2 EXPRESSING CELLS IN SKIN

Patient 11-005, global partial response since W10 lasting 1 year and 8 months

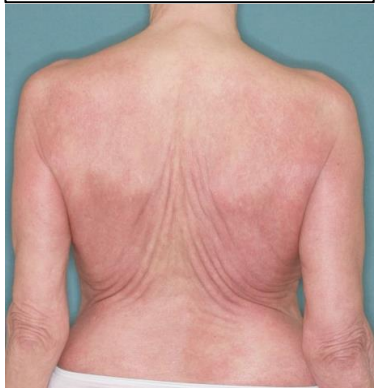
Baseline
KIR3DL2: 52%



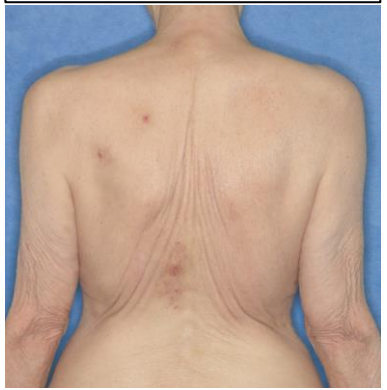
Week 5
KIR3DL2: 4.4%



Baseline
mSWAT: 80.5/1/0



Week 64
mSWAT = 5.2/0/0

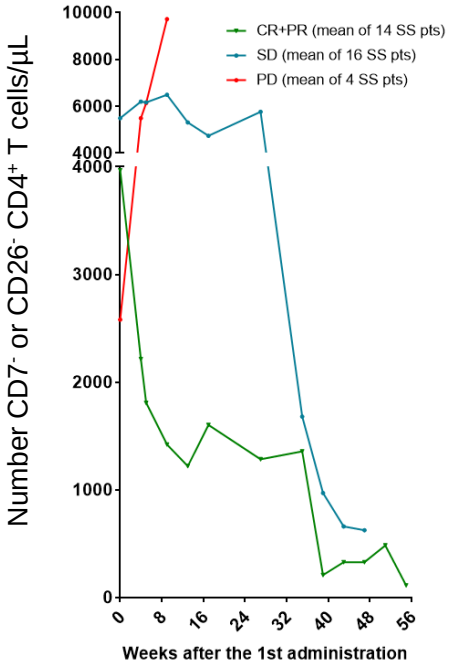


^ 77 y old woman, received 6 prior lines of systemic therapies including Bex, IFN, HDAC and Mogamulizumab
Global PR since week 10 (starting dose : 0.05 mg/kg)

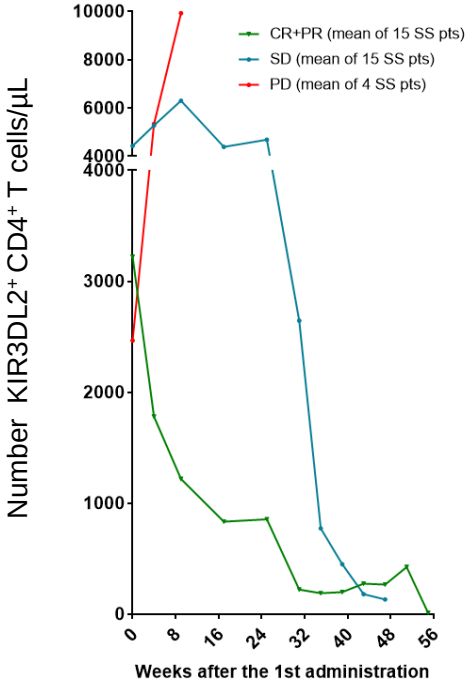
EXPLORATORY BIOMARKERS

CHANGES IN TUMOR CELLS AND KIR3DL2 IN BLOOD

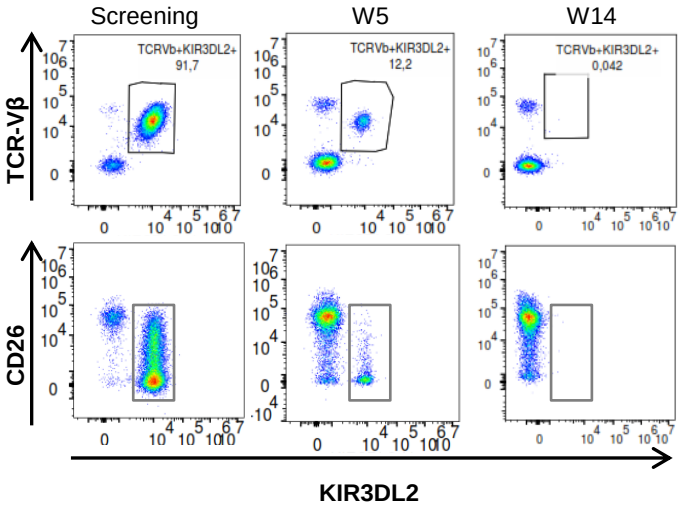
Aberrant cells



KIR3DL2+ CD4+ T cells

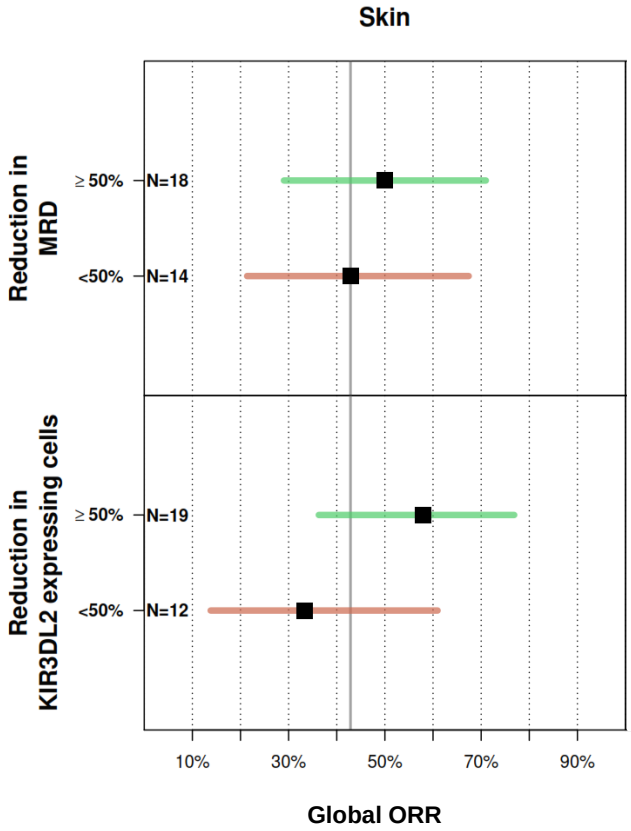


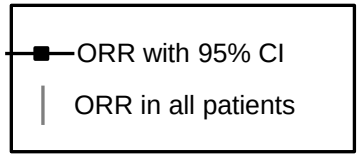
Patient 01-036, ongoing complete response > 1 year

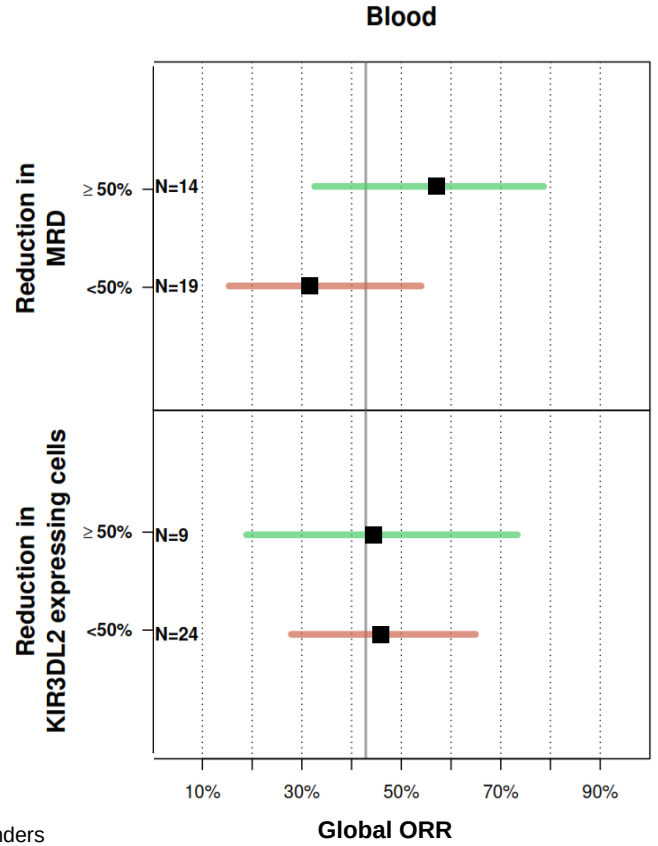


EXPLORATORY BIOMARKERS

REDUCTION IN KIR3DL2 / MRD AT WEEK 5 AND GLOBAL RESPONSE







Exploratory analysis unadjusted for possible confounders

CONCLUSIONS

- IPH4102 is **safe and well tolerated** in heavily pretreated relapsed/refractory SS.
- IPH4102 shows impressive clinical activity, demonstrated by **high and durable response** rate and **long PFS.**
- IPH4102 **substantially improved QOL** even in patients with stable disease.
- Exploratory biomarker analyses show **relevant pharmacodynamics effects of IPH4102 in skin and in blood**. These results will be further evaluated in future studies.

PHASE 2 STUDY (N≈250)
TELLOMAK : T-CELL LYMPHOMA ANTI-KIR3DL2 THERAPY

TELLOMAK

Sézary Syndrome
≥ 2 prior systemic therapies that must include mogamulizumab

Mycosis Fungoides
≥ 2 prior systemic therapies

IPH4102 single agent

Peripheral T Cell Lymphoma
≥ 1 prior systemic therapy including anthracycline-based chemo

IPH4102 + GEMOX

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Hatem Azim

All our patients and their families…