

**IPH4102, THE FIRST-IN-CLASS ANTI-KIR3DL2 MAB,
IS SAFE AND CLINICALLY ACTIVE IN ADVANCED
CUTANEOUS T-CELL LYMPHOMA (CTCL) PATIENTS:
RESULTS FROM THE DOSE-ESCALATION PART OF THE
IPH4102-101 PHASE I STUDY**

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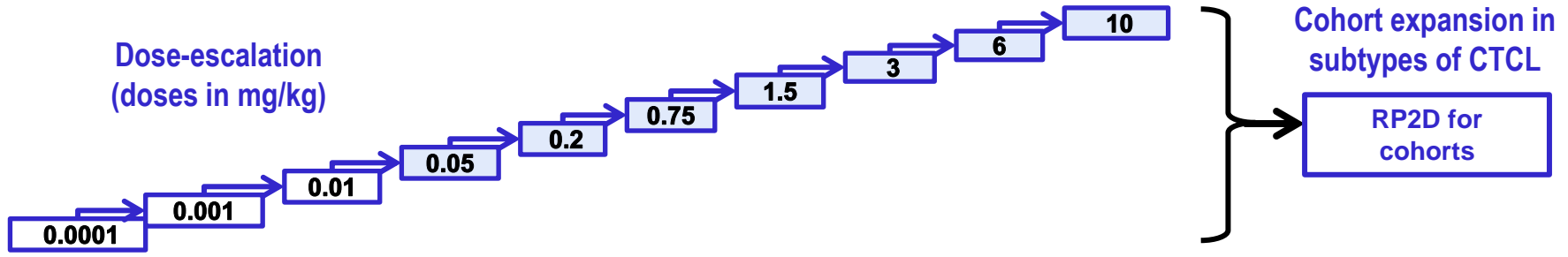
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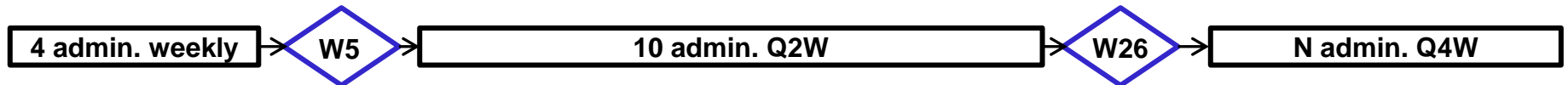
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IPH4102-101

IPH4102-101 PHASE 1 STUDY DESIGN AND OBJECTIVES



- Dose-escalation (10 dose levels – accelerated 3+3 design) followed by cohort expansion
- **Primary objective:** determination of MTD and RP2D, overall safety
- **Secondary objectives:** clinical activity, PK/immunogenicity
- **Exploratory objectives:** changes in KIR3DL2⁺ cells in involved compartments, NK cell function pre-dose
- **Key inclusion criteria:**
 - Any CTCL subtype, ≥ 2 prior lines of systemic therapy, if MF/SS stage \geq IB
 - $> 5\%$ aberrant cells KIR3DL2^{pos} in skin or blood
 - Treatment until progression or unacceptable toxicity
- Intra-patient dose-escalation allowed after W5



BASELINE DISEASE CHARACTERISTICS

	All doses N = 25
Age (years), median (min; max)	71 (42; 90)
MF/SS CTCL type, n (%)	
Mycosis fungoides (MF)	4 (16)
Sézary Syndrome (SS)	20 (80)
Non MF/SS CTCL type, n (%)	
CD4+ T-cell lymphoma, NOS	1 (4)
Clinical stage at study entry (MF/SS), n (%)	
IB	1 (4)
IIB	3 (12)
IVA1	20 (80)
No. of regimen (systemic) received, median (min; max)	4 (2; 10)

PATIENT EXPOSURE

	All doses N = 25
Duration of exposure, days median (min; max)	218 (22; 610)
No. of administrations received per patient median (min; max)	16 (4; 30)
No. of patients receiving increased doses, n (%) No Increased Dose Increased dose ≥ Three times	6 (24) 19 (76) 10 (40)
No. of patients who received IPH4102, n (%) ≤ 4 times (QW) 5-14 times (QW & Q2W) > 14 times (QW, Q2W & Q4W)	2 (8) 7 (28) 16 (64)

SUMMARY OF ADVERSE EVENTS (AE)

N = 25	Total	Grade 3	Grade 4
DLT	0	-	-
AE	23 (92%)	6 (24%)	2 (8%) [†]
Related AE	13 (52%)	2 (8%)	-
SAE	8 (32%)	2 (8%)	2 (8%)
Related SAE	2 (8%) ^{††}	-	-
AE causing treatment discontinuation	1 (4%)	1 (4%)*	-
Fatal AE	2 (8%)**		

n is the number of subjects having the given event, or an event in the given category at least once

DLT: Dose limiting Toxicity; (S)AE: (Serious) Adverse Event

[†] Two patients had grade 4 AE: (i) one 69 year-old patient with grade 4 confusion attributed to viral meningitis, (ii) one other patient with *S. aureus* sepsis before going into CR.

^{††} Two patients had possibly related SAE: (i) one had grade 2 atrial flutter diagnosed by mandatory ECG without clinical symptoms one hour after end of the first administration. The patient was known for cardiac arrhythmia. She was hospitalized for cardiac work-up, received amiodarone and arrhythmia resolved. The patient received 15 more administrations without reoccurrence of atrial flutter, (ii) one other patient had hepatitis occurring 6 weeks after last administration and treatment discontinuation due to PD. The patient had global PR, received treatment for 1 year, and had normal liver function until 4 weeks after treatment discontinuation. Work-up could not identify a clear cause before death; liver biopsy was suspicious of either viral infection or drug-induced liver injury in presence of HHV-6B in the liver and blood.

* One patient discontinued treatment due to not related general malaise in context of disease progression.

** Two patients had fatal AE: (i) one unrelated death to *S. aureus* sepsis, (ii) one death caused by possibly related SAE of hepatitis (see ^{††}).

ADVERSE EVENTS AT LEAST POSSIBLY RELATED TO DRUG (REPORTED BY ≥ 2 PATIENTS)

	Related AE (N = 25)		
	All grades* n (%)	Grade 3 n (%)	Grade 4 n (%)
Lymphopenia	4 (16)	2 (8)	0
Asthenia	3 (12)	0	0
Nausea	2 (8)	0	0
Chills	2 (8)	0	0
Pyrexia	2 (8)	0	0
Arthralgia	2 (8)	0	0
Muscle spasm	2 (8)	0	0

n is the number of subjects having the given events, or an event in the given category at least once

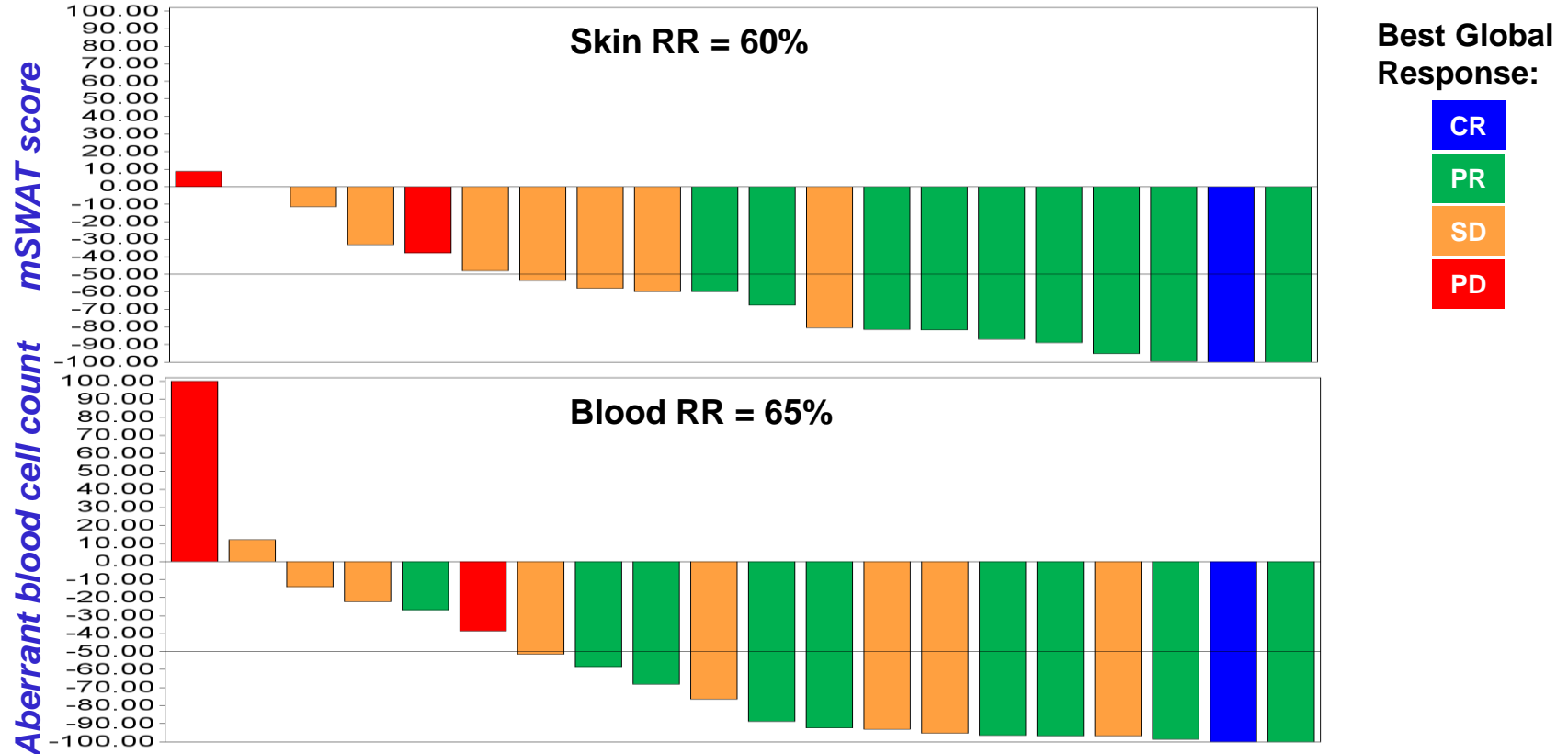
PRELIMINARY CLINICAL RESPONSE RESULTS

	Best Response in all patients		Best Response in Sézary Syndrome patients		
	Global N=25	Global	Skin	Blood	
		n=20	n=20	n=20	
Best Response (n)					
CR	1	1	2	5	
PR	10	9	10	8	
SD	12	8	8	6	
PD	2	2	0	1	
ORR	44 %	50 %	60 %	65 %	
ORR4, n (%)	9 (36%)	8 (40%)			
DOR (days) - median (min – max)	251 (8.2 months) (64 – 519+)	302 (9.9 months) (64 – 519+)			
PFS (days) - median (min – max)	299 (9.8 months) (28 – 610+)	329 (10.8 months) (28 – 610+)			

ORR: Overall Response Rate
 ORR4: Rate of responses lasting ≥4 mo
 PFS: Progression-Free Survival
 DOR: Duration of Response

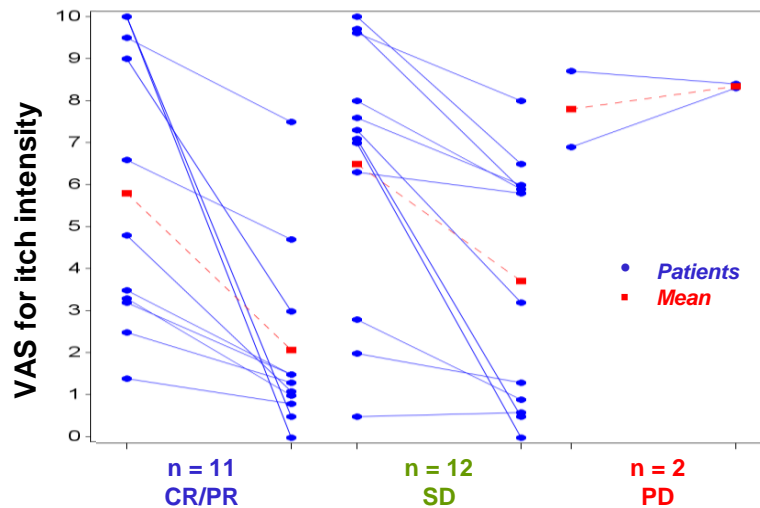
- Results for 25 patients (20 SS) treated with doses ranging from 0.0001 to 10 mg/kg
- All clinical responses are confirmed; 4 responses ongoing (DOR range 104 – 519 days)
- 2 patients reached “near CR” skin response, ie >90% reduction in mSWAT

MAXIMUM PERCENT CHANGE IN mSWAT SCORE AND ABERRANT BLOOD CELL COUNTS IN SEZARY PATIENTS

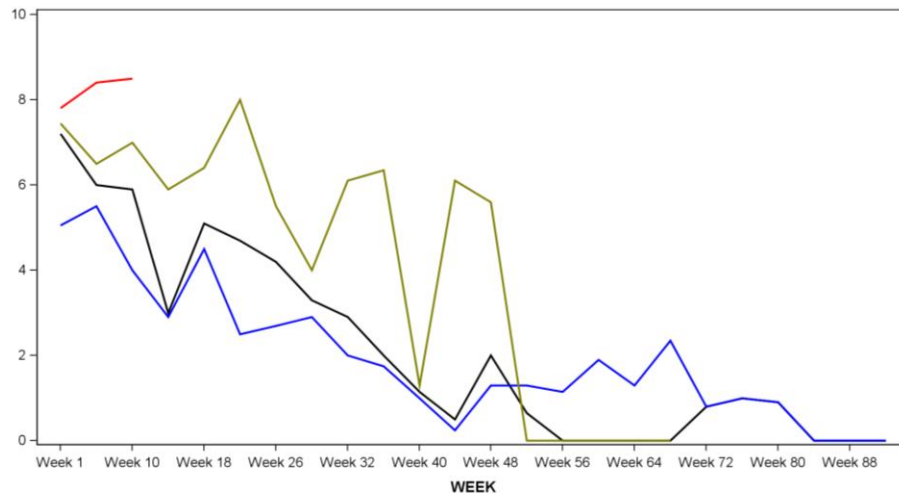


PRURITUS IMPROVEMENT BY VAS SCORE

Baseline vs Best change in VAS



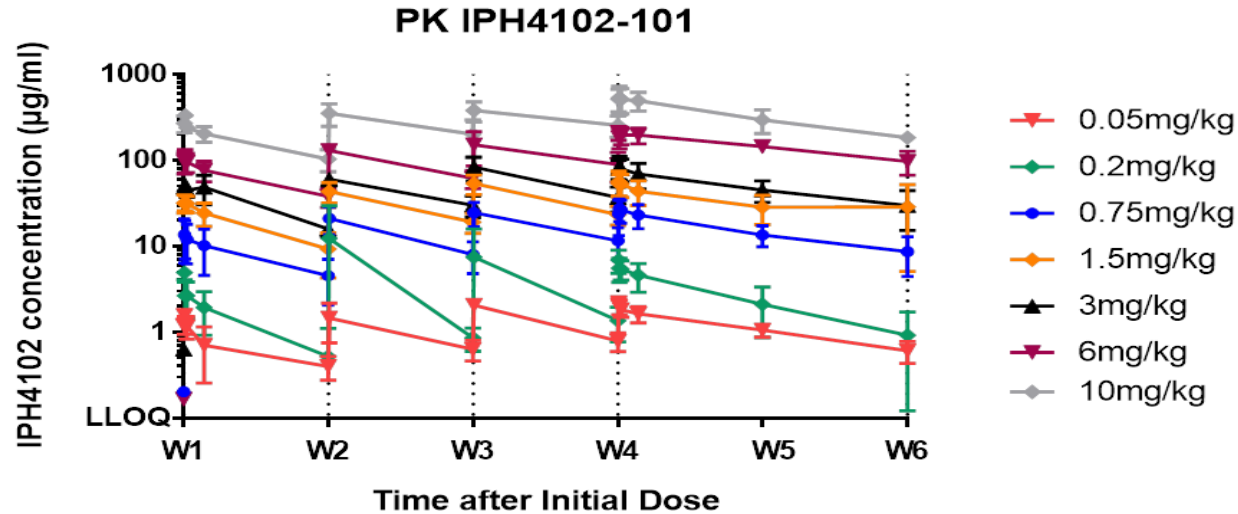
Median VAS change over time



	Week 1	Week 10	Week 18	Week 26	Week 32	Week 40	Week 48	Week 56	Week 64	Week 72	Week 80	Week 88														
overall	20	18	18	16	17	15	15	15	15	10	6	5	6	4	3	3	3	3	2	2	2	2	1	1	1	
CR/PR	10	10	9	9	9	8	9	9	9	6	3	2	3	3	2	2	2	2	2	2	2	2	2	1	1	1
obs SD	8	7	8	7	8	7	6	6	6	4	3	3	3	3	1	1	1	1	1							
obs PD	2	1	1																							

VAS: Visual Analogue Scale

IPH4102 PK RESULTS



- IPH4102 PK is dose-proportional from 0.75 to 10 mg/kg
- Only slight (and expected) accumulation during the QW regimen (predicted half-life 14-21 days)
- Disease burden can influence exposure: Target-Mediated Drug Disposition (TMDD) was seen in pts with high mSWAT treated at 0.2 mg/kg
- ...but no TMDD observed at higher doses in other patients with high disease burden
- Only 1 patient was found positive for Anti-Drug Antibodies (ADA)

IPH4102-101 HIGHLIGHTS

SAFETY, CLINICAL ACTIVITY AND PK

- IPH4102 MTD was not reached, RP2D is 10 mg/kg
- IPH4102 is safe and well tolerated by heavily pretreated advanced CTCL patients
- Best global ORR is 44% in the overall population and 50% in Sezary patients
- In the Sezary population, median Duration of Response is 9.9 months
- Pruritus is substantially improved in patients having global response or stable disease
- IPH4102 PK is dose-proportional from 0.75 to 10 mg/kg; 1 patient developed ADA
- Biomarker results were presented by M. Battistella *et al.*, Abstract O-27
- **Expansion cohorts started accruing in July 2017 at the flat dose of 750 mg**
- **As of today, 12 patients started treatment in the cohort expansion part**

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All our patients and their families...