LACUTAMAB IN PATIENTS WITH ADVANCED SEZARY SYNDROME: RESULTS FROM AN INTERIM ANALYSIS OF THE TELLOMAK PHASE 2 TRIAL

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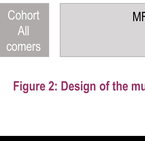
BACKGROUND

Unmet Need in Cutaneous T-cell lymphoma (CTCL)

- CTCL accounts for ~ 4% of all cases of non-Hodgkin lymphoma. Incidence ~ 6 cases per million with average onset between 50-60 years[1,2]
- Sezary syndrome (SS) represents ~5% of all CTCL cases[3], and is associated with poor prognosis and quality of life given a combination of erythroderma (i.e. extensive skin lesions), high blood involvement with malignant SS cells and lymphadenopathy.
- To date, there is no approved treatment option in patients with SS who have received at least two prior systemic therapies, including mogamulizumab, that demonstrates meaningful activity[4].



	5-year Overal Survival Rate	%skin biopsies expressing KIR3DL2+
Mycosis Fungoides (MF)	20 to 95%*	~45%
Sézary syndrome (SS)	~ 10%	> 85%
transformed MF	*≤ 15%*	*> 80%*
CD30+ LPD (ALCL subtype)	76 to 96%	100%
Others (ATL, NK/T, γδ, …)	≤ 20%	~35% to 100%

Figure 1: CTCL subtypes – frequency, outcomes and KIR3DL2 biomarker expression

KIR3DL2 and Lacutamab Development

- KIR3DL2 belongs to the killer immunoglobulin-like receptor (KIRs) family found on a subset of normal NK and T cells and is expressed in all subtypes of CTCL, irrespective of clinical stage, with the highest prevalence in SS.
- Lacutamab (IPH4102) is a potential first-in-class humanized anti-KIR3DL2 cytotoxicity-inducing antibody under development for the treatment of T cell lymphomas including CTCL (SS and MF)[5] and Peripheral T cell lymphoma (PTCL).
- In a Phase 1 study, Lacutamab showed favourable safety profile with no dose limiting toxicities in SS patients who have been treated by at least two prior systemic therapies[5].
- Lacutamab has been granted Orphan Drug Designation for the treatment of CTCL (EMA and FDA); PRIME (EMA) and Fast Track (FDA) designation for SS patients who have been treated by at least two prior systemic therapies.
- TELLOMAK is an open label, multi-cohort and multi-center phase 2 study evaluating Lacutamab as single agent (NCT03902184; Figure 2). The interim analysis for cohort 1 is presented here.

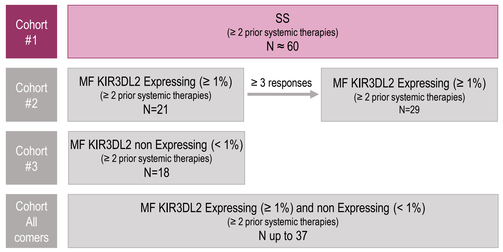


Figure 2: Design of the multi-cohort TELLOMAK study in CTCL (MF and SS specifically)

TELLOMAK TRIAL

Primary Objective:

- To evaluate the global Overall Response Rate (ORR) according to International Consensus criteria[4].

Secondary Objectives:

- To assess the safety and tolerability of lacutamab.
- To assess antitumor activity in terms of duration of response (DoR), Progression free survival (PFS), Overall survival (OS).
- To characterize pharmacokinetics and immunogenicity.

Exploratory Objectives include:

- To evaluate efficacy endpoints in subgroups and disease compartments
- To explore the correlation between the level of KIR3DL2 expression and clinical activity.
- To explore the impact of treatment on KIR3DL2-expressing cells using immunohistochemistry (IHC) and flow cytometry.

Key Inclusion Criteria:

- Stage IVA, IVB (B2 in blood) R/R SS.
- ≥2 prior lines of systemic therapy including mogamulizumab.
- ECOG Performance status ≤ 2.

Key Exclusion Criteria:

- Evidence of large cell transformation
- Life expectancy of less than 3 months.
- Autologous stem cell transplantation less than 3 months prior to enrollment and Prior allogenic transplantation.

INTERIM RESULTS

- At the time of DCO, April 29 2022, N=37 patients received treatment (Intent To Treat [ITT]) and N=35 patients were evaluable for efficacy (Efficacy Evaluable Set [EES]).
- The population has advanced (IVA, IVB), highly refractory disease, and was heavily pre-treated, with 6 median number of prior lines including mogamulizumab.

Table 1: Baseline Patient Characteristics of SS patients

	Cohort 1 N=37
Age in years, Median (range)	69 (50-86)
- Female, N (%) - Male, N (%)	15 (40.5) 22 (59.5)
Stage of the disease at screening N (%) - Stage IVA1 - Stage IVA2 - Stage IVB	 22 (59.5) 13 (35.1) 2 (5.4)
Blood involvement (B2), N (%)	37 (100.0)
Nodal involvement, N* (%)	28 (75.7)
N prior lines of systemic therapy, Median (range) - 3-4 N (%) - > 4 N (%)	6 (2 – 11) 10 (27.0) 22 (59.5)
Follow-up (months), Median (range)	10.9 (<1-34)

*Nodal involvement at baseline N2, N3 or Nx

Table 2: ORR observed in Cohort 1 (ITT and EES analysis sets)

		Best Global Response N=37 (ITT) N=35 (EES)	Best Response in Skin N=37 (ITT) N=35 (EES)	Best Response in Blood N=37 (ITT) N=35 (EES)	Best Response in LN N=28 (ITT) N=27 (EES)
Best Response (N)					
CR		**0**	**0**	**8**	**1**
PR		**8**	**13**	**6**	**2**
SD		22	19	18	16
PD		5	3	3	4
NE		2	2	2	5
ORR% [95%CI]	ITT	**21.6%** [11.4-37.2]	**35.1%** [21.8-51.2]	**37.8%** [24.1-53.9]	**10.7%** [3.7-27.2]
	EES	**22.9%** [12.1-39.0]	**37.1%** [23.2-53.7]	**40.0%** [25.6-56.4]	**11.1%** [3.9-28.1]

ITT (Intention to Treat): entered into the study and treated with lacutamab; EES (Efficacy Evaluable Set): treated with lacutamab and have a baseline and at least one post baseline disease assessment; CR: complete response; PR: partial response; SD: Stable Disease

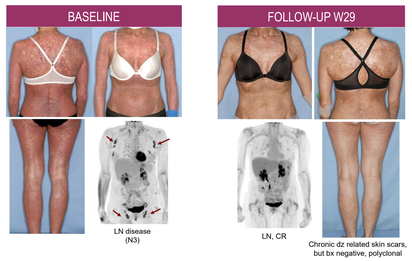
Table 3: Treatment Emergent related Adverse Events[1] Observed

		Total N= 37 n (%)
Any treatment-emergent AEs (TEAEs)		34 (91.9)
Any lacutamab-related TEAEs		18 (48.6)
Most frequent lacutamab-related TEAEs (>5%)	General disorders and administration site conditions	6 (16.2)
	Skin and subcutaneous tissue disorders	5 (13.5)
	Gastrointestinal disorders	3 (8.1)
	Investigations	3 (8.1)
	Vascular disorders	3 (8.1)
Any Serious TEAEs (SAEs)		10 (27.0)
Any Serious lacutamab-related TEAEs		2 (5.4)
Any Grade 3/4/5[2] lacutamab-related TEAEs		6 (16.2)
Any lacutamab-related Death		0 (0)

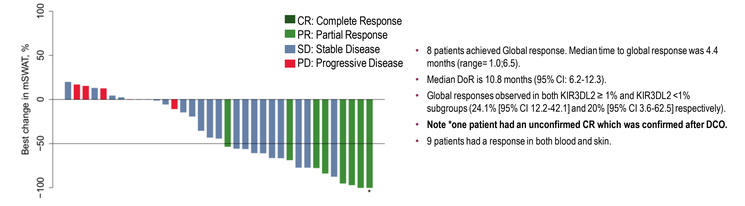
1. Event / as defined by the treating investigator
2. NCI NCI Common Terminology Criteria for Adverse Events (CTCAE)

CASE STUDY

- 58-year-old female. 10 previous lines of therapy. T4N3M0B2 at baseline.
- Response:
  - Skin: PR at W5, CR at W45
  - Blood: CR at W5
  - LN: PR at W5, CR at W13
  - Global: PR at W13, CR at W45

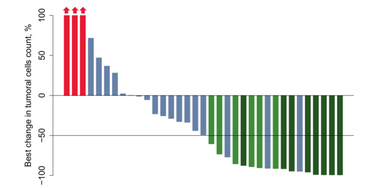


Best Global Response



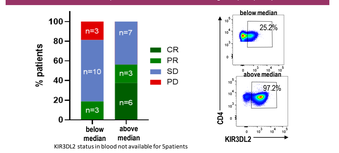
- 8 patients achieved Global response. Median time to global response was 4.4 months (range= 1.0;6.5).
- Median DoR is 10.8 months (95% CI: 6.2-12.3).
- Global responses observed in both KIR3DL2 ≥ 1% and KIR3DL2 <1% subgroups (24.1% [95% CI 12.2-42.1] and 20% [95% CI 3.6-62.5] respectively).
- **Note *one patient had an unconfirmed CR which was confirmed after DCO.**
- 9 patients had a response in both blood and skin.

Best Blood Response



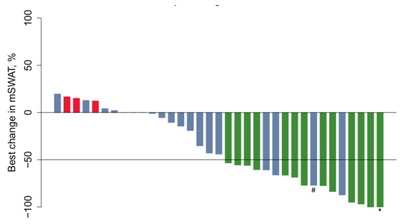
Note that y axis was limited to +100%; the three progressive patients (identified with arrows at the end of the bar) have a change in best tumoural cells count of respectively +1168%, +906% and +253%

Blood Response in KIR3DL2 subgroups (ITT)

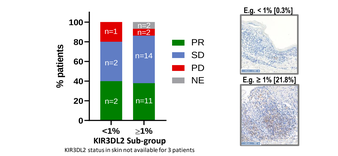


- 14 patients achieved a blood response; Median time to blood response was 1.0 month (range= 1.0;6.5).
- KIR3DL2 is expressed on CD4 T-cells of all patients at baseline; Median frequency of KIR3DL2 expressing CD4 T-cells is 88.1%; Best blood response rate is 56.3% (95% CI 33.2-76.9) in the above median group and 18.8% (95% CI 6.6-43.0) in the below median group, respectively; In this small dataset, all CRs are found in the above median group

Best Skin Response



Skin Response in KIR3DL2 subgroups (ITT)



- 13 patients achieved a skin response; Median time to skin response was 2.8 months (range= 0.9;10.2).
- **Note *one patient had an unconfirmed CR which was confirmed after DCO; #one patient who had an unconfirmed PR at DCO was confirmed after DCO**
- KIR3DL2 is expressed in the skin of 85.3% SS patients, consistent with literature; Skin responses are observed in both KIR3DL2 ≥ 1% and KIR3DL2 <1% subgroups (37.9% [95% CI 22.7-56] and 40% [95% CI 11.8-76.9] respectively)

CONCLUSIONS

- TELLOMAK is a Phase 2 study evaluating lacutamab monotherapy in CTCL. Cohort 1 enrolls a relapsed/refractory SS population pretreated with ≥ 2 prior systemic therapies including mogamulizumab. In this interim analysis, lacutamab demonstrates clinical activity with favorable safety.
  - The study population has advanced (IVA, IVB), highly refractory disease, and was heavily pre-treated, with a median of 6 prior lines of therapy.
  - Responses, including CRs, were observed in multiple compartments:
    - Blood ORR: 37.8% (95% CI: 24.1-53.9) in ITT population with CR in 21.6% (8/37)
      40.0% (95% CI: 25.6-56.4) in EES population with CR in 22.9% (8/35)
    - Skin ORR: 35.1% (95% CI: 21.8-51.2) in ITT population
      37.1% (95% CI: 23.2-53.7) in EES population
  - Within the subgroup of patients that achieved a global response, mDoR is 10.8 months (95% CI: 6.2-12.3) with median time to global response of 4.4 months (range =1.0;6.5); median time to blood and skin response was 1.0 months (range = 1.0;6.5) and 2.8 months (range= 0.9;10.2) respectively.
- Enrollment to TELLOMAK continues. Final data with long-term follow-up will provide more mature conclusions.

ACKNOWLEDGEMENTS

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