

LACUTAMAB IN PATIENTS WITH RELAPSED AND REFRACTORY SEZARY SYNDROME: LONG TERM FOLLOW-UP FROM THE TELLOMAK PHASE 2 TRIAL

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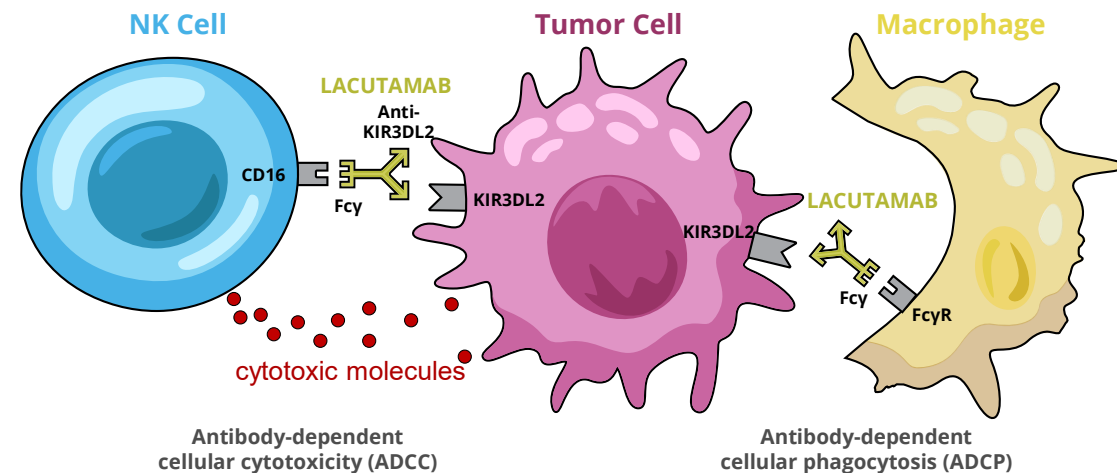
Potential sources of conflict of interest:

- Advisory boards: Innate Pharma, Kyowa Kirin, Helsinn/Recordati

Introduction

- **Sézary syndrome** (SS): rare and aggressive cutaneous T-cell lymphoma (CTCL) with poor prognosis (10-20% 5-year survival), characterized by erythroderma, significant blood involvement, lymphadenopathy
- **KIR3DL2**: a killer immunoglobulin-like receptor, commonly expressed in $\geq 85\%$ of SS patients
- **Lacutamab**: a first-in-class monoclonal antibody designed to specifically deplete KIR3DL2-expressing cells via antibody-dependent cellular cytotoxicity and phagocytosis, in development in CTCL and Peripheral T-cell lymphoma (PTCL)
- In recognition of high-unmet need and early potential demonstrated in phase 1*, lacutamab has been granted key designations:
 - 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 2 prior systemic therapies
 - FDA Breakthrough Therapy Designation (BTD) in relapsed/refractory (R/R) SS after at least 2 prior systemic therapies including mogamulizumab (Feb 2025)

Mechanism of Action of lacutamab first-in-class humanized anti-KIR3DL2 antibody



TELLOMAK Phase 2 Study design (NCT03902184)

evaluating lacutamab in patients with R/R MF or SS after at least 2 prior systemic therapies including mogamulizumab. We report here long-term follow-up SS results

**Sézary Syndrome (N=63)
≥ 2 prior systemic therapies**

Cohort 1 SS

Must include mogamulizumab as prior therapy

**Mycosis Fungoides (N=107)
≥ 2 prior systemic therapies**

Cohorts MF

KIR3DL2 ≥ 1%

KIR3DL2 <1%

Key Eligibility Criteria for SS

- Relapsed and/or refractory stage IVA, IVB SS (blood B2 at screening)
- At least 2 prior systemic therapies including mogamulizumab for SS patients
- No evidence of large cell transformation (LCT), based on central histologic evaluation at screening

Study Endpoints

- Primary endpoint: global ORR (based on the evaluation of 4 compartments: skin, blood, lymph nodes and viscera according to the International Consensus criteria Olsen 2011)
- Secondary endpoints: PFS, OS, DoR, quality of life, safety and tolerability, PK & immunogenicity

Treatment

- Lacutamab iv Q1W for 5 weeks Q2W for 10 administrations then Q4W until disease progression or unacceptable toxicity

Patient baseline characteristics

Patient Characteristics at baseline	Cohort SS, N=63
Age in years, median (range)	69 (42-86)
<ul style="list-style-type: none"> <li data-bbox="129 439 1702 486">- Male, N (%) <li data-bbox="129 486 1702 544">- Female, N (%) 	<ul style="list-style-type: none"> <li data-bbox="1702 439 2412 486">37 (58.7) <li data-bbox="1702 486 2412 544">26 (41.3)
Stage of the disease at baseline, N (%) <ul style="list-style-type: none"> <li data-bbox="129 611 1702 658">- Stage IVA1 <li data-bbox="129 658 1702 715">- Stage IVA2 	<ul style="list-style-type: none"> <li data-bbox="1702 611 2412 658">41 (65.1) <li data-bbox="1702 658 2412 715">22 (34.9)
B2 blood involvement at baseline, N (%)	63 (100.0)
Nodal involvement at baseline, N (%) <ul style="list-style-type: none"> <li data-bbox="129 853 1702 901">- N2 <li data-bbox="129 901 1702 948">- N3 involvement <li data-bbox="129 948 1702 1008">- Nx 	<ul style="list-style-type: none"> <li data-bbox="1702 853 2412 901">6 (9.5) <li data-bbox="1702 901 2412 948">22 (34.9) <li data-bbox="1702 948 2412 1008">17 (27.0)
T4 confluence of erythema covering \geq 80% BSA	40 (63.5)
Number of prior systemic lines, median (range) <ul style="list-style-type: none"> <li data-bbox="129 1146 1702 1193">- 2, N (%) <li data-bbox="129 1193 1702 1240">- 3-4, N (%) <li data-bbox="129 1240 1702 1300">- > 4, N (%) 	<ul style="list-style-type: none"> <li data-bbox="1702 1093 2412 1140">5 (2-13) <li data-bbox="1702 1140 2412 1188">11 (17.5) <li data-bbox="1702 1188 2412 1235">19 (30.2) <li data-bbox="1702 1235 2412 1300">33 (52.4)
Follow-up in months, median (95% CI)	25.1 (21.0-29.4)

Long term efficacy results in SS patients treated with lacutamab

	Global Response N=63	Response in Skin N=63	Response in Blood N=63	Response in LN N=52*
Best Response, N (%)				
CR	6 (9.5)	9 (14.3)	21 (33.3)	9 (17.3)
PR	21 (33.3)	24 (38.1)	11 (17.5)	6 (11.5)
SD	28 (44.4)	27 (42.9)	26 (41.3)	27 (51.9)
PD	8 (12.7)	3 (4.8)	5 (7.9)	6 (11.5)
NE	0	0	0	4 (7.7)
ORR, % (95%CI)	42.9 (31.4-55.1)	52.4 (40.3-64.2)	50.8 (38.8-62.7)	28.8 (18.3-42.3)
TTR, months, median (range)	2.8 (1-10)			
DoR, months, median (95% CI)	25.6 (11.0 – NE)			
PFS, months, median (95% CI)	8.3 (5.1-18.7)			

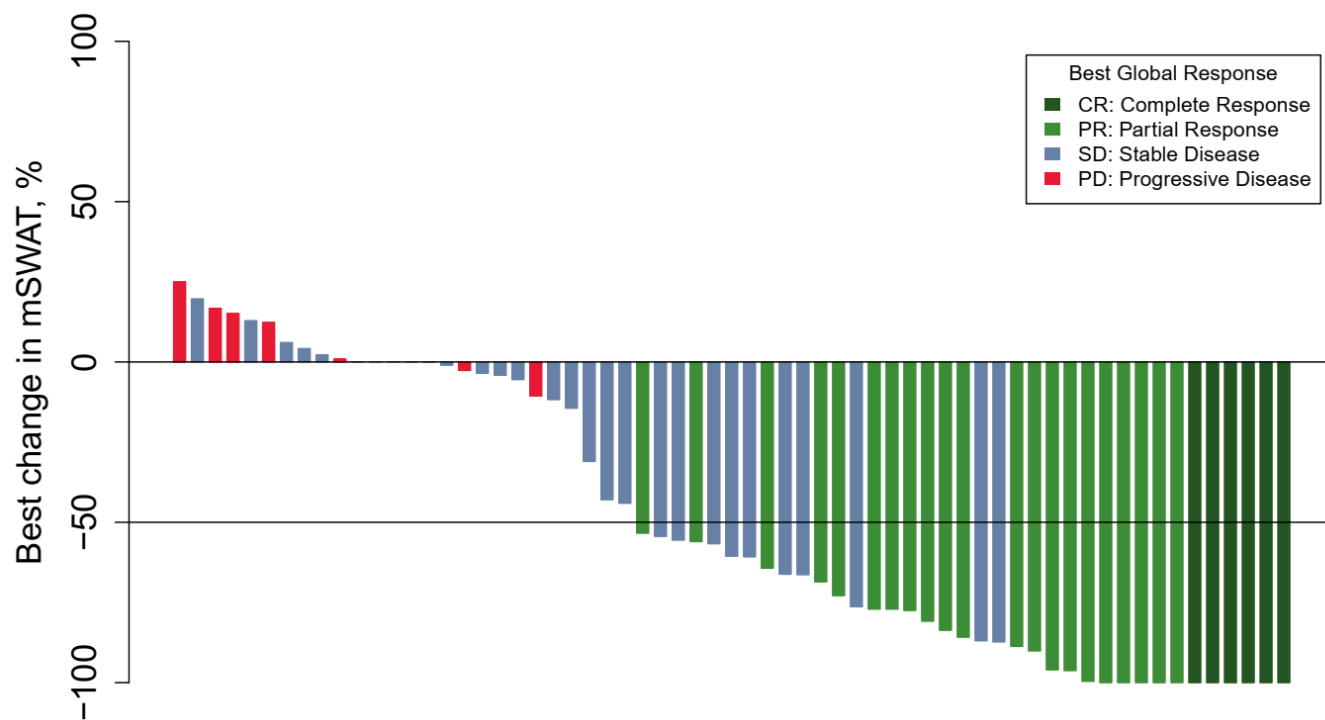
Global Clinical Benefit Rate (CR+PR+SD): 87.3% (95% CI 76.9-93.4)

CR: complete response; PR: partial response; SD: Stable Disease; PD: progressive disease; NE: not evaluable; LN: lymph nodes

*includes patients not involved at baseline who progressed in the LN

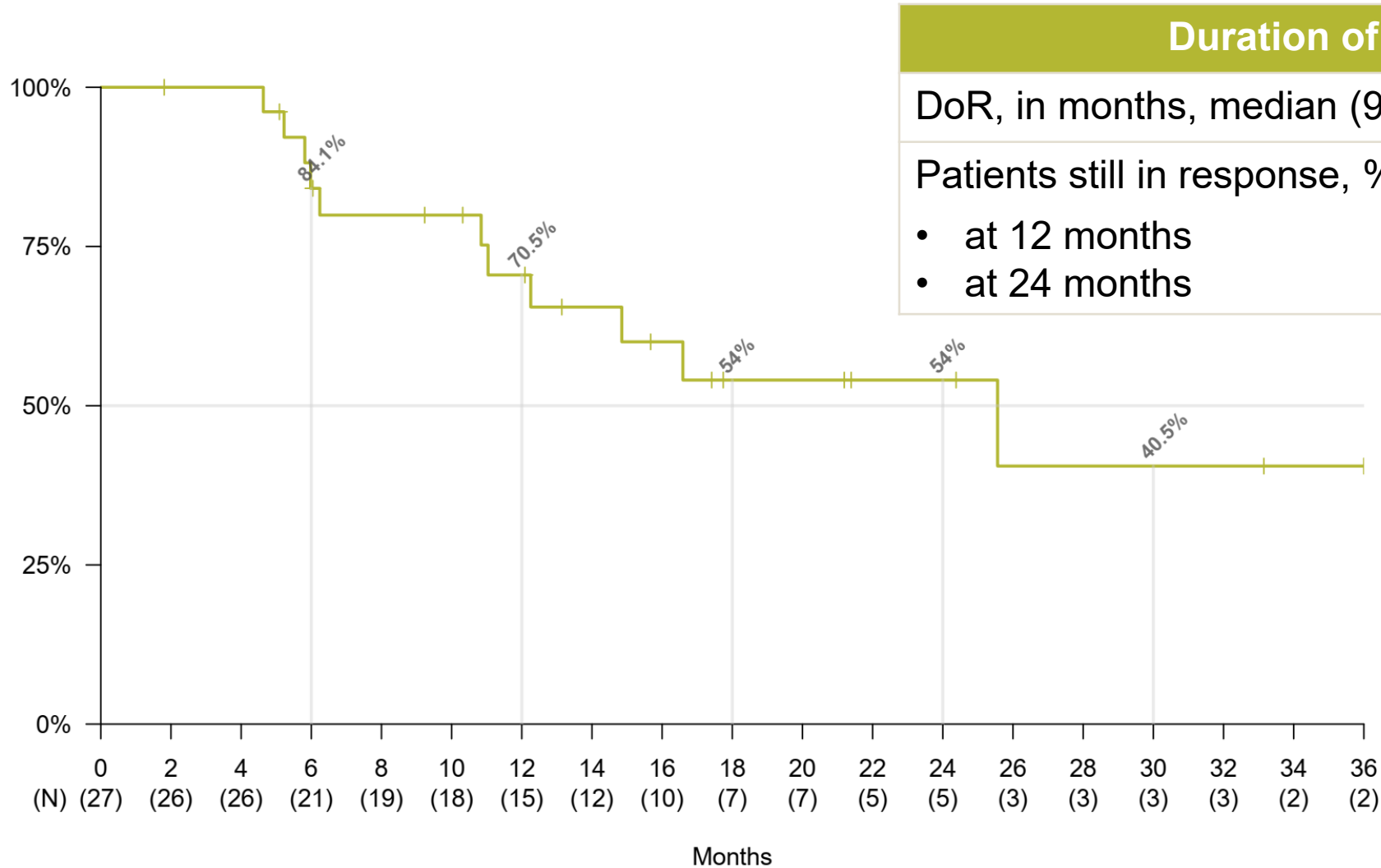
Best Global Response in SS patients treated with lacutamab

Best Global Response



- **ORR = 42.9% (31.4-55.1)**
- 27 patients achieved Global Response, including 6 CR and 21 PR
- All patients in CR are still in CR
- Median time to Global Response: 2.8 months (range: 1-10)

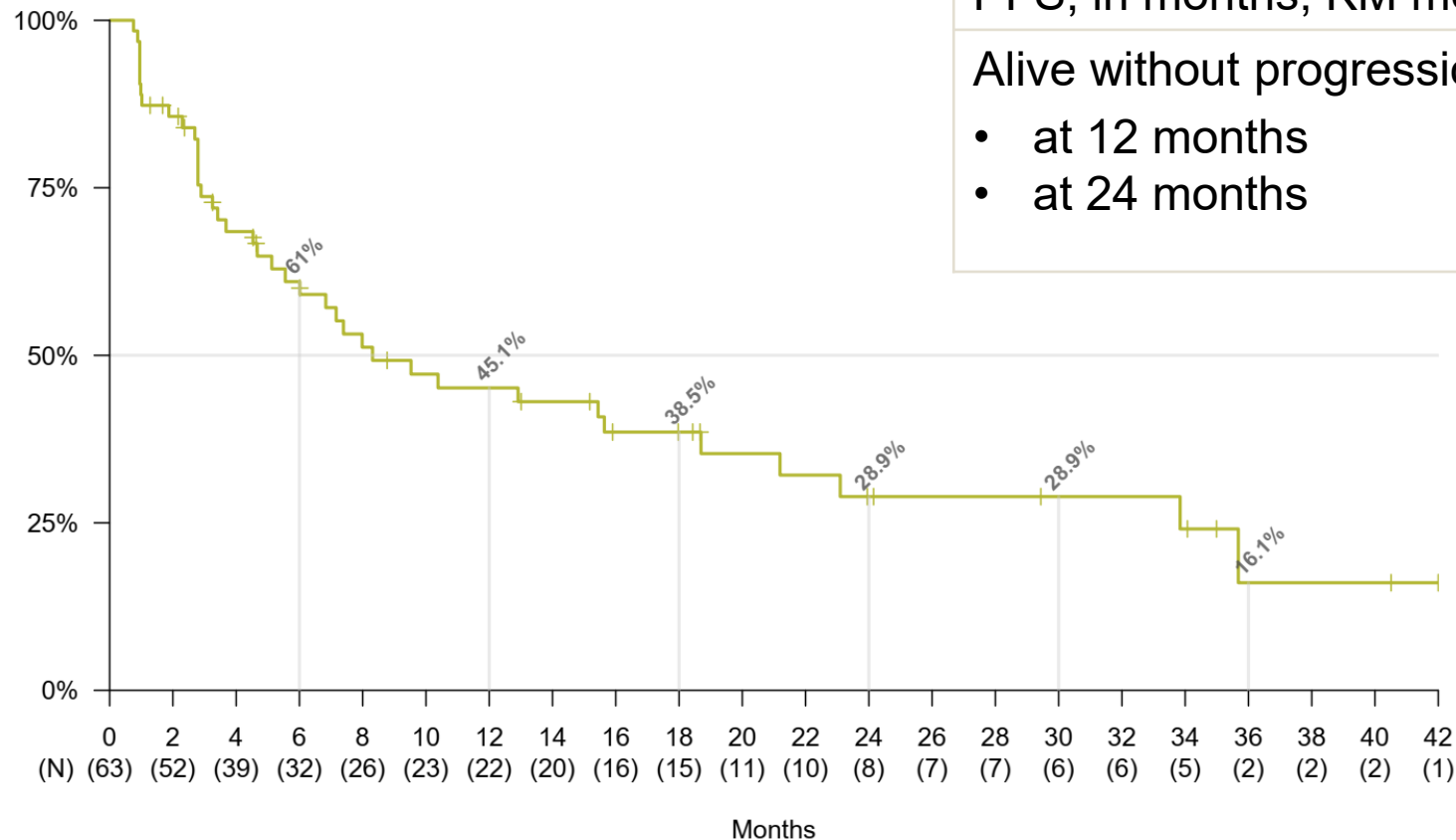
Duration of Response in SS patients treated with lacutamab



Duration of response (DoR)	
DoR, in months, median (95% CI)	25.6 (11.0 - NE)
Patients still in response, % (95%CI)	
• at 12 months	70.5 (47.7-84.8)
• at 24 months	54.0 (30.6-72.6)

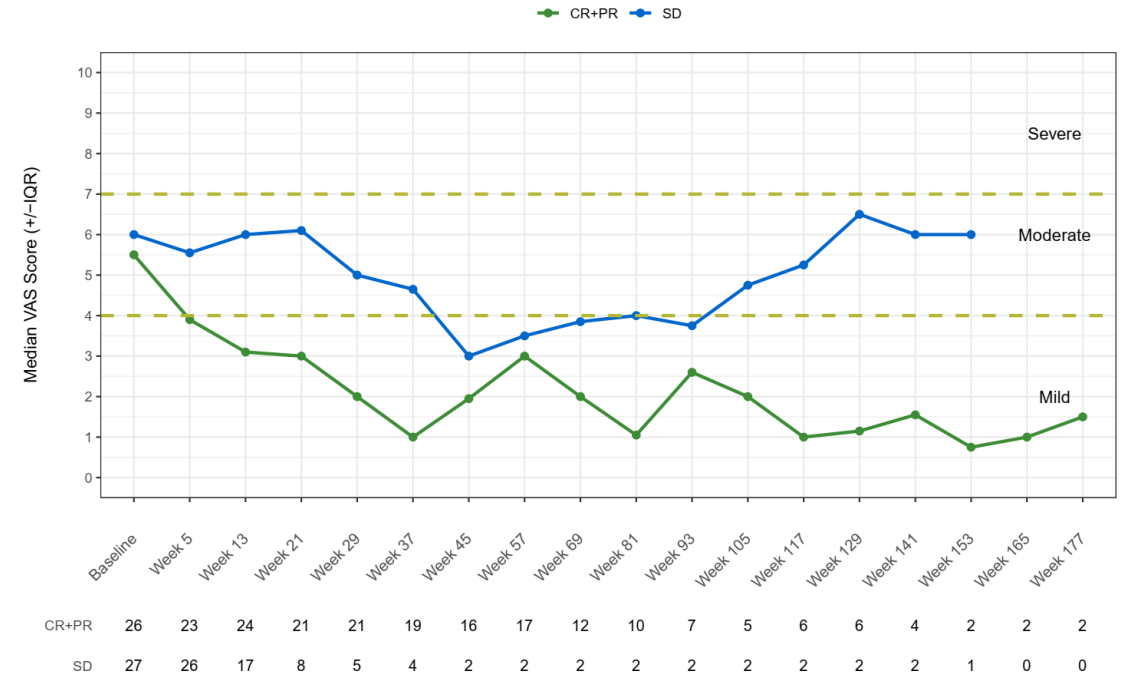
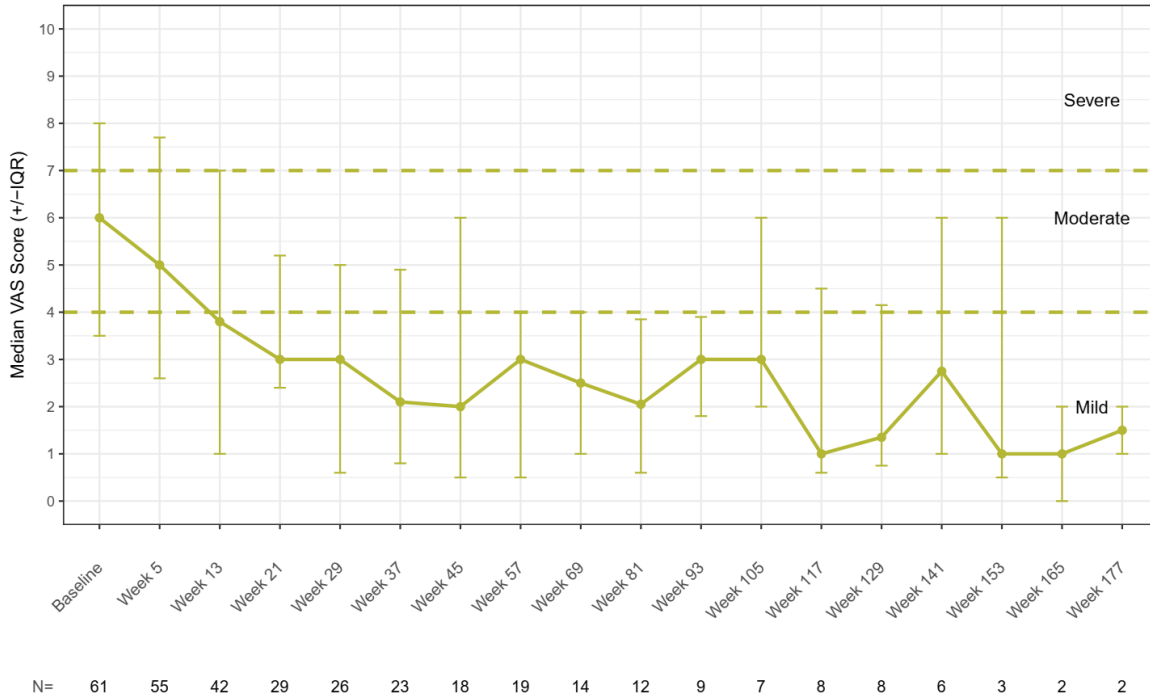
Long lasting response (>24 months) in more than half of the responders

Progression-free Survival in SS patients treated with lacutamab



Progression Free Survival (PFS)	
PFS, in months, KM median (95% CI)	8.3 (5.1-18.7)
Alive without progression, % (95% CI)	
• at 12 months	45.1 (31.6-57.7)
• at 24 months	28.9 (16.2-42.9)

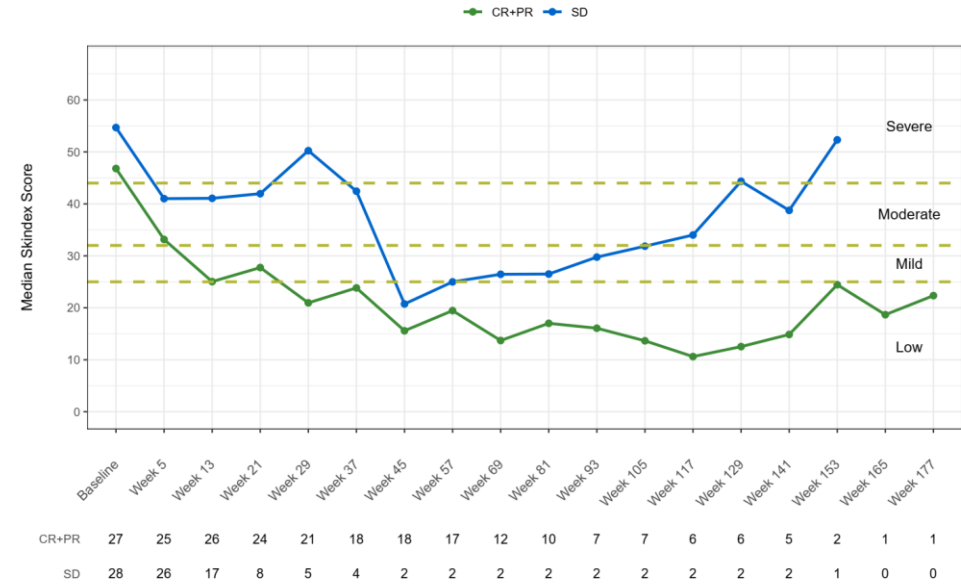
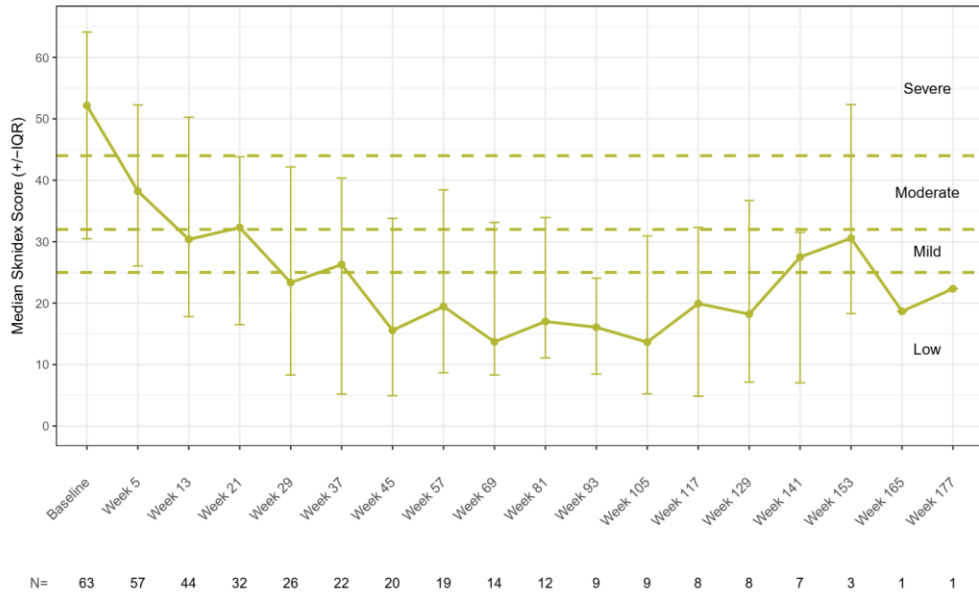
Visual Analog Scale for Itch Intensity Score Over Time in SS patients



The presence and severity of pruritus was assessed using a 10 point visual analogue scale (VAS) ranging from 0 (no itch) to 10 (worst imaginable itch)

- At baseline, median VAS 6.0, 25% of patients had VAS>8 (severe score)
- Early decrease of pruritus intensity starting from W5
- Clinically meaningful decrease of >2 points in VAS scale to mild pruritus from W13 (median VAS<4) maintained over time

Skindex-29 Total Score Over Time in SS patients

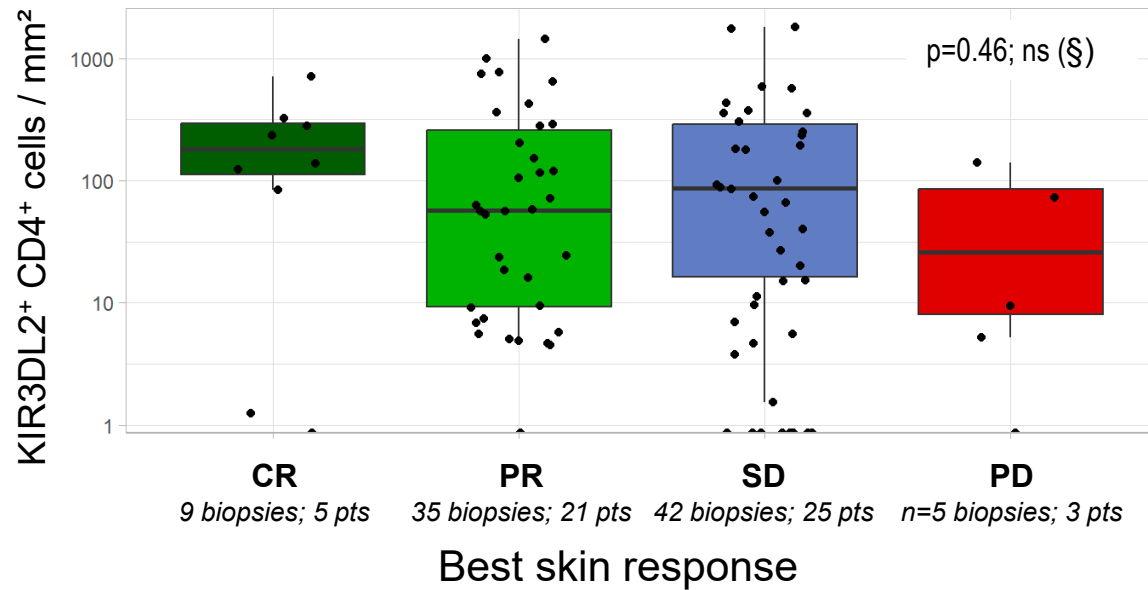


Skindex-29 questionnaire inquiries about how often (Never, Rarely, Sometimes, Often, All the time) during the previous 4 weeks the pt experienced the effect described in each item. Overall score are expressed on a 100-point scale, higher scores indicating lower levels of quality of life

- At baseline, median Skindex-29 global score was severe (52.2)
- Early decrease of global score starting from W5 to moderate score
- Continuous and deep decrease to low score maintained over time

Main translational results

- Response to lacutamab in skin occurs irrespective of baseline density of KIR3DL2⁺ CD4⁺ T cells

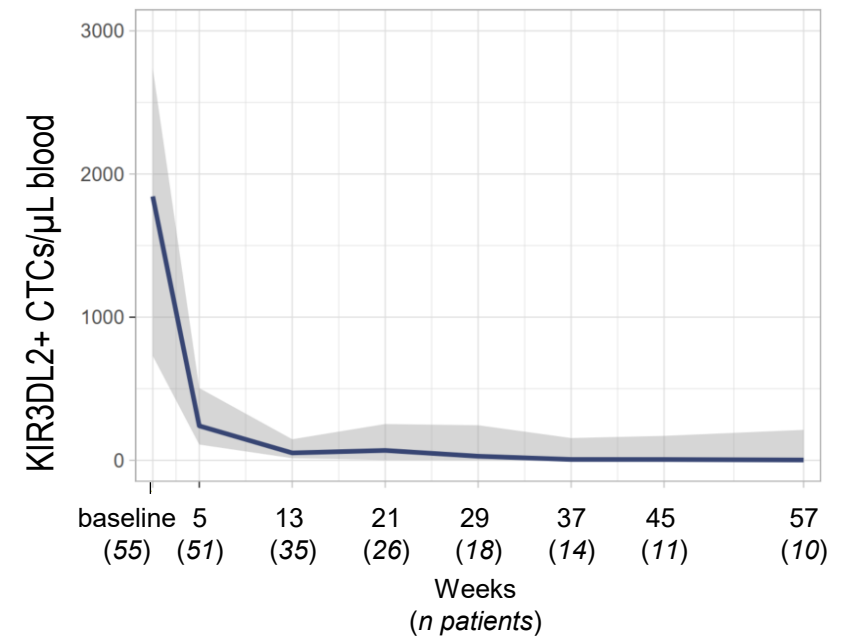


ORR in skin = 52.4% (95% CI: 40.3-64.2)

KIR3DL2⁺ CD4⁺ cell density in skin biopsies was determined by multiplex immunofluorescence.
n=54 patients

§: Kruskal-Wallis test; ns: non significant

- In blood, lacutamab induces an early and deep depletion of KIR3DL2⁺ circulating tumor cells (CTCs)



KIR3DL2⁺ CTCs/μL blood was determined by flow cytometry.
n=55 patients

Safety profile

Nb and (%) of pts with at least one		Total N= 63
Treatment-emergent adverse events (TEAEs)		61 (96.8)
Related TEAEs		36 (57.1)
Most frequent (>5%) related TEAEs	Fatigue	12 (19.0)
	Asthenia	6 (9.5)
	Diarrhea	5 (7.9)
	Arthralgia	4 (6.3)
Serious TEAEs		21 (33.3)
Serious related TEAEs		6 (9.5)
Related Grade \geq 3 TEAEs		13 (20.6)
Related TEAEs leading to discontinuation*		4 (6.3)
AEs leading to death**		5 (7.9)
Related AEs leading to death		1 (1.6)

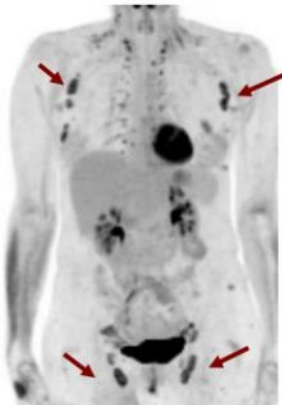
*Toxic skin eruption, Skin fissures, Pruritus and AST elevation, Haemophagocytic lymphohistiocytosis (HLH)

**Sepsis, Acute respiratory failure, Infection, cardiac arrest all Not related to lacutamab and one patient died with transformed cell lymphoma/HLH considered as related as per investigator (related to the disease as per sponsor). Relatedness as defined by the treating investigator; Grade as per NCI Common Terminology Criteria for Adverse Events (CTCAE) DCO 17 Oct 2024

Patient Case #1, ongoing

- 58-year-old female
- 10 previous lines of therapy
- Stage IVA2 (N3) at baseline
- Response ongoing sustained at W189:
 - Skin: PR at W13, CR at W45
 - Blood: CR at W5
 - LN: PR at W5, CR at W13
 - Global: PR at W13, CR at W45

Baseline

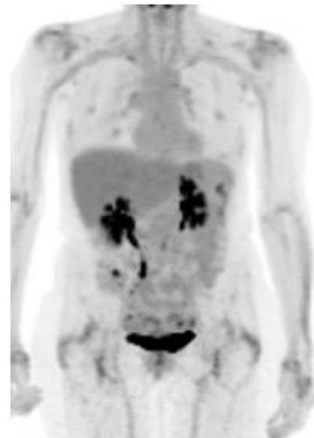


Sézary cells
1473 (B2)

mSWAT 95

LN N3

W45 global CR, ongoing & sustained at W189



Sézary cells
44 (B0)

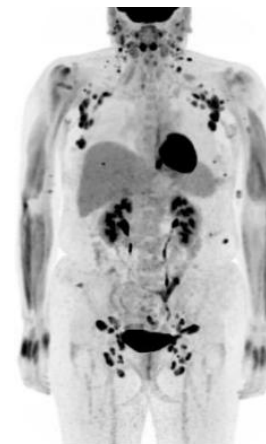
mSWAT 0

LN CR

Patient Case #2, ongoing

- 51-year-old female
- 6 previous systemic lines of therapy
- Stage IVA2 (N3) at baseline
- Response ongoing sustained at W93:
 - Skin: PR at W5, CR at W13
 - Blood: CR at W5
 - LN: CR at W5
 - Global: PR at W5, CR at W13

Baseline

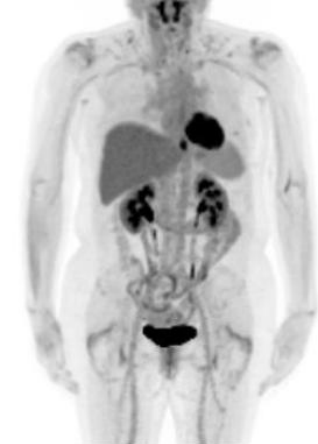


Sézary cells
5526 (B2)

mSWAT 83

LN N3

W13 global CR, ongoing & sustained at W93



Sézary cells
78 (B0)

mSWAT 0

LN CR

Conclusion

- TELLOMAK is a Phase 2 study evaluating lacutamab monotherapy in Cutaneous T-cell lymphoma.
- Cohort 1 enrolled relapsed and/or refractory **SS patients with ≥ 2 prior systemic therapies** including mogamulizumab, a high unmet medical need population with no approved therapy.
- Lacutamab demonstrated a robust clinical activity in heavily pretreated (median 5 prior systemic therapies) SS patients with a **favorable safety profile** and a meaningful **improvement in quality of life and pruritus**.
- Long-term follow-up data from TELLOMAK confirm the meaningful clinical activity with **global ORR 42.9%** (95%CI 31.4-55.1) and an impressive median **duration of response of 25.6 months** (95%CI 11.0, NE).
- These promising results generated in a heavily pretreated population with no available standard therapy, strongly support the development of lacutamab for SS and MF (see #051).
- Moreover, the excellent tolerability of lacutamab in addition to preclinical data, strongly support further investigation in combination with other anti-lymphoma agents beyond CTCL.

Long-term follow-up data demonstrated the high response rate and long-lasting response with lacutamab in SS patients

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- **USA (17 sites)**

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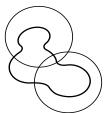
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