

#051

LACUTAMAB IN PATIENTS WITH RELAPSED AND/OR REFRACTORY MYCOSIS FUNGOIDES: LONG TERM FOLLOW-UP AND TRANSLATIONAL DATA FROM THE TELLOMAK PHASE 2 TRIAL

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Clinicaltrials.gov: NCT03902184



TELLOMAK

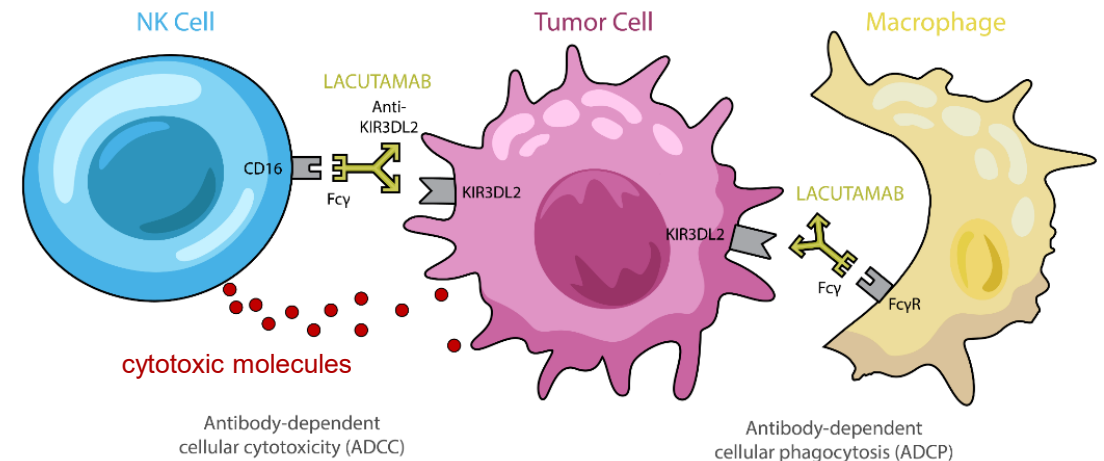


Potential sources of conflict of interest:

Introduction

- **Mycosis fungoides** (MF): most common type (50-60%) of CTCL. About 30% of patients are diagnosed in advanced stage (IIB-IVB), with 5-year survival ~50%¹
- **KIR3DL2** is a killer immunoglobulin-like receptor, **expressed \geq 1% in ~ 50% of MF** (of mononucleated cells in skin biopsy)
- **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 1², lacutamab has been granted key designations:
 - Orphan drug designation for the treatment of CTCL (EMA and FDA)
 - PRIME (EMA) and Fast Track and BTB (FDA) designation for SS patients who have received 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.

We report here long-term follow-up MF 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 MF Cohorts

- Relapsed and/or refractory stage IB-IV MF
- At least 2 prior systemic therapies
- 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

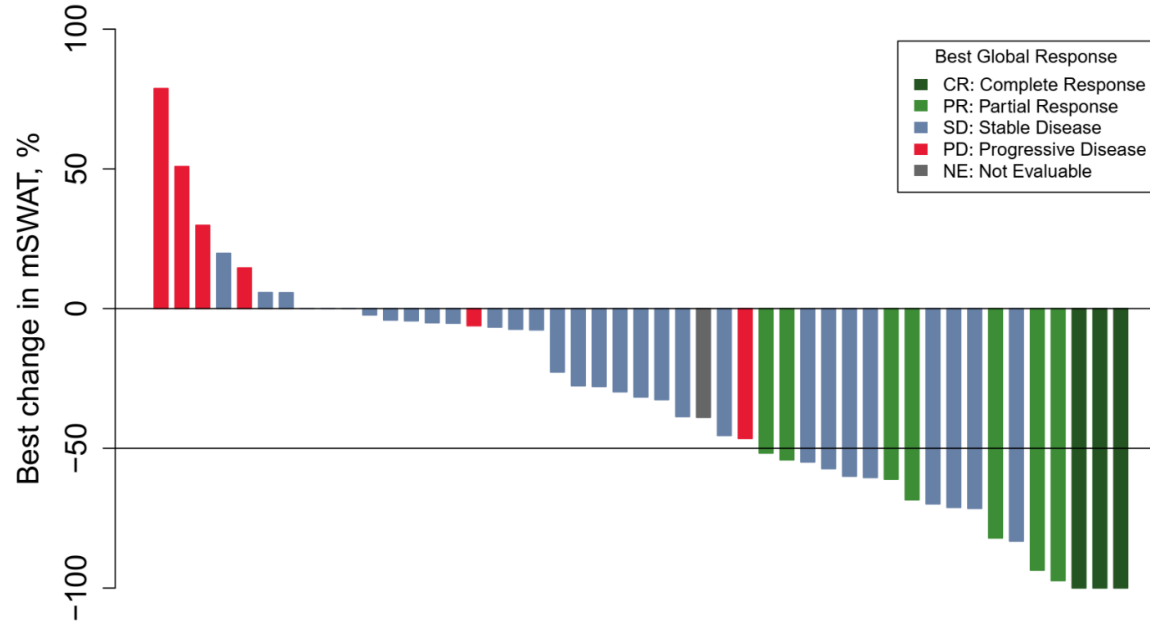
MF	All MF N=107	KIR3DL2 ≥ 1% N=48	KIR3DL2 < 1% N=59
Age in years, Median (range)	62 (19-82)	59 (28-82)	65 (19-81)
Sex, N (%)	<ul style="list-style-type: none"> • Male 72 (67.3) • Female 35 (32.7) 	<ul style="list-style-type: none"> 28 (58.3) 20 (41.7) 	<ul style="list-style-type: none"> 44 (74.6) 15 (25.4)
Stage at baseline, N (%)	<ul style="list-style-type: none"> • IB 45 (42.1) • IIA 27 (25.2) • IIB 12 (11.2) • III 13 (12.1) • IV 10 (9.3) 	<ul style="list-style-type: none"> 20 (41.7) 14 (29.2) 1 (2.1) 9 (18.8) 4 (8.3) 	<ul style="list-style-type: none"> 25 (42.4) 13 (22.0) 11 (18.6) 4 (6.8) 6 (10.2)
Prior systemic lines, median (range)	4.0 (1-14)	4.0 (2-12)	4.0 (1-14)
<ul style="list-style-type: none"> • 2, N (%) 27 (25.2) • 3-4, N (%) 32 (29.9) • >4, N (%) 48 (44.9) 	<ul style="list-style-type: none"> 8 (16.7) 17 (35.4) 23 (47.9) 	<ul style="list-style-type: none"> 19 (32.2) 15 (25.4) 25 (42.4) 	
Prior mogamulizumab, N (%)	34 (31.8)	13 (27.1)	21 (35.6)
Prior brentuximab vedotin, N (%)	33 (30.8)	14 (29.2)	19 (32.2)
Follow-up months, median (95%CI)	22.1 (19.4, 23.6)	23.0 (18.0, 25.8)	20.7 (18.4, 22.5)

Long term efficacy results in MF patients treated with lacutamab

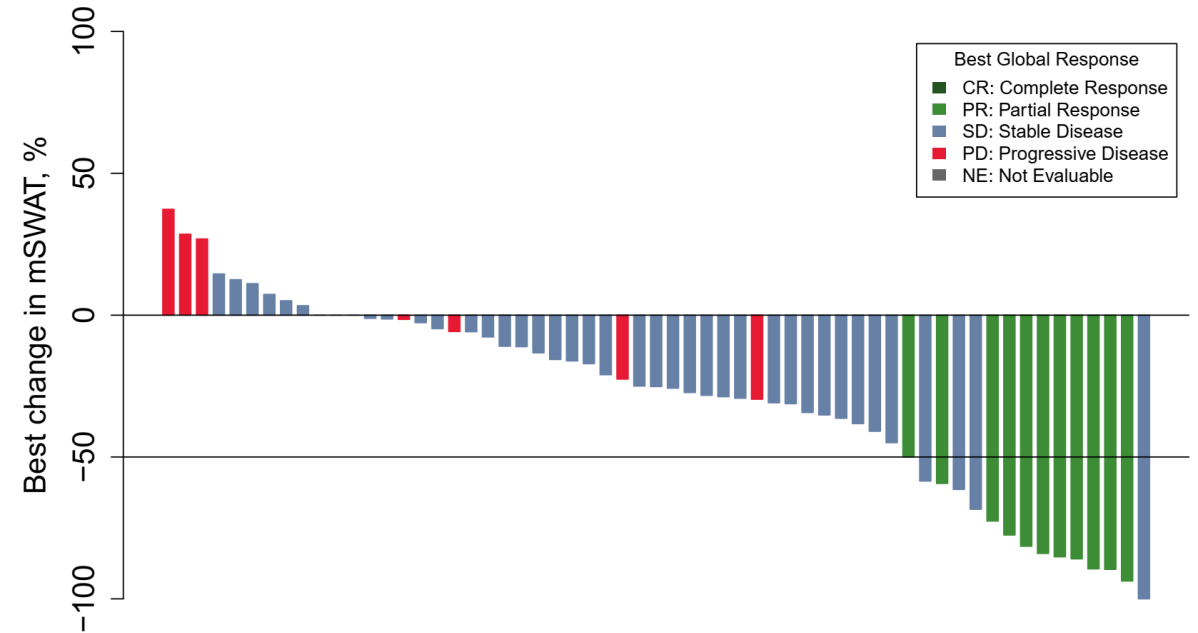
	All MF N=107	KIR3DL2 ≥ 1% N=48	KIR3DL2 <1% N=59
Best response, N (%)			
CR	3 (2.8)	3 (6.3)	0 (0.0)
PR	18 (16.8)	7 (14.6)	11 (18.6)
SD	71 (66.4)	30 (62.5)	41 (69.5)
PD	13 (12.1)	6 (12.5)	7 (11.9)
NE	2 (1.9)	2 (4.2)	0 (0.0)
ORR, % (95%CI) Olsen 2011	19.6 (13.2, 28.1)	20.8 (11.7, 34.3)	18.6 (10.7, 30.4)
ORR, % (95%CI) Olsen 2022	24.3% (17.2, 33.2)	29.2% (18.2, 43.2)	20.3% (12.0, 32.3)
Skin response (n=107), % (95%CI)	29.0% (21.2, 38.2)	33.3% (21.7, 47.5)	25.4% (16.1, 37.8)
Time to response, months, median (range)	2.8 (1-37)	1.0 (1-5)	2.8 (1-37)
DoR, months, median (95% CI)	13.8 (7.4, NE)	13.8 (4.6, NE)	15.7 (5.1, NE)
PFS, months, median (95% CI)	10.2 (8.0, 15.4)	11.8 (5.6, 16.8)	9.5 (6.5, 16.6)

Best global response in MF patients treated with lacutamab

KIR3DL2 $\geq 1\%$



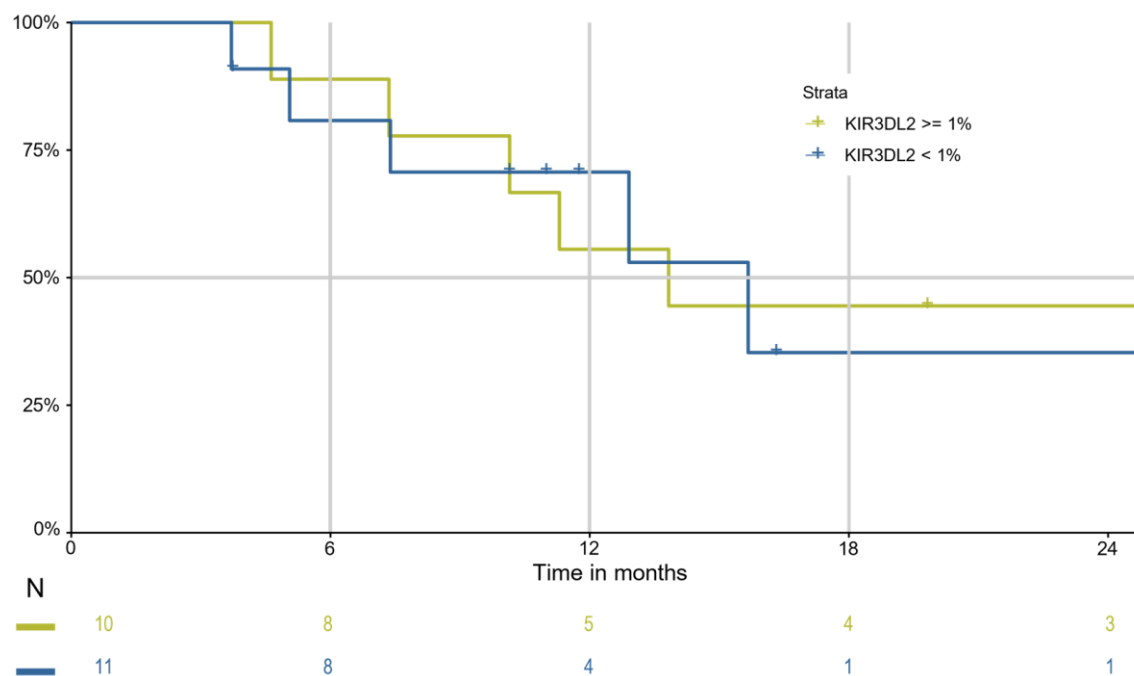
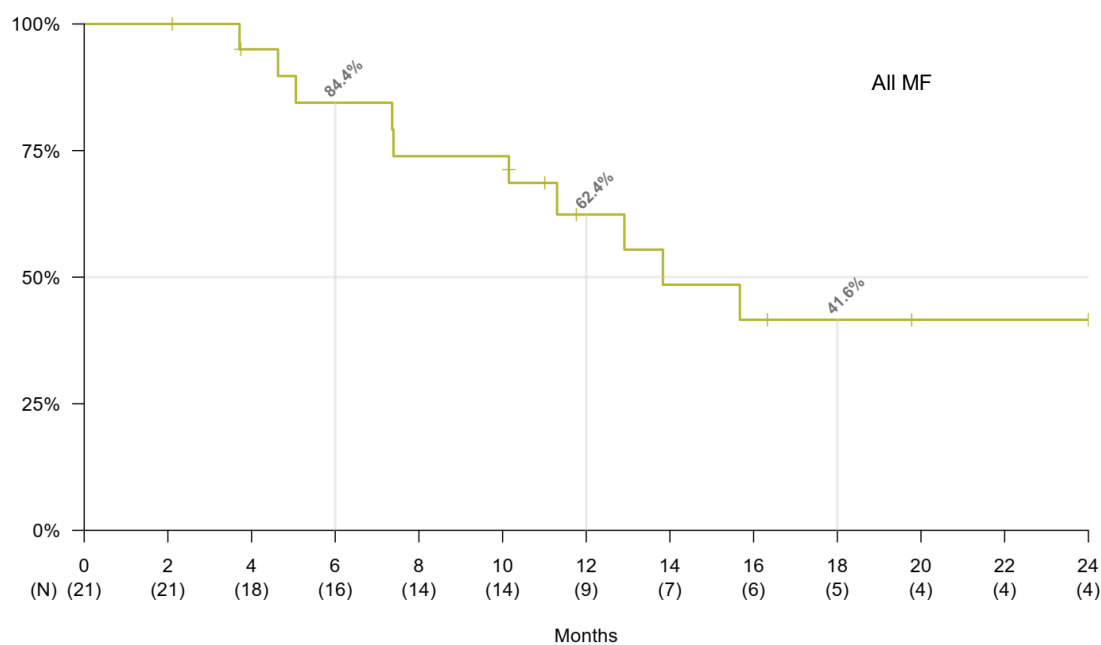
KIR3DL2 $<1\%$



Early and deep responses observed in MF patients regardless of KIR3DL2 expression level

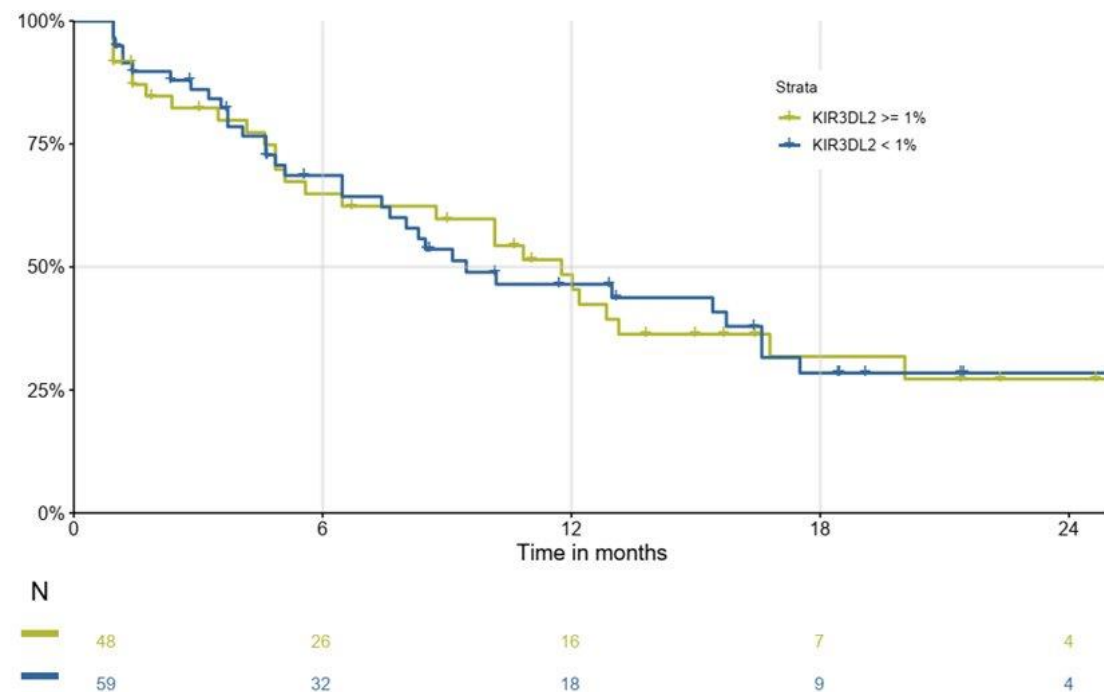
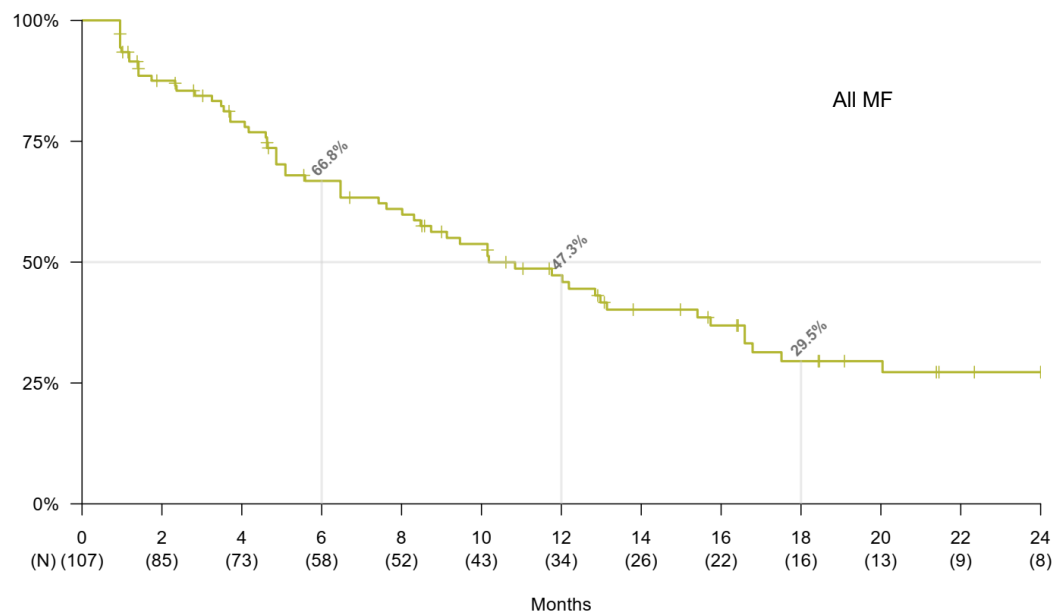
Duration of response in MF patients treated with lacutamab

	All MF	KIR3DL2 ≥ 1%	KIR3DL2 <1%
DoR in months, Median, (95%CI)	13.8 (7.4, NE)	13.8 (4.6, NE)	15.7 (5.1, NE)
Patients still in response, % (95% CI) at 12 months	62.4 (36.6, 80.1)		
at 24 months	41.6 (18.2, 63.7)		

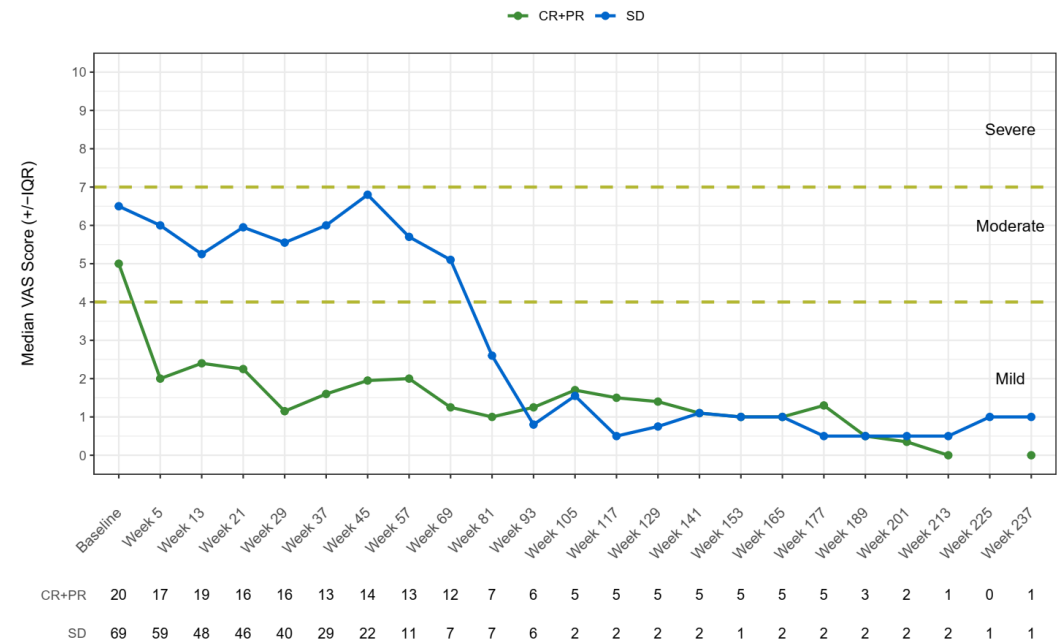
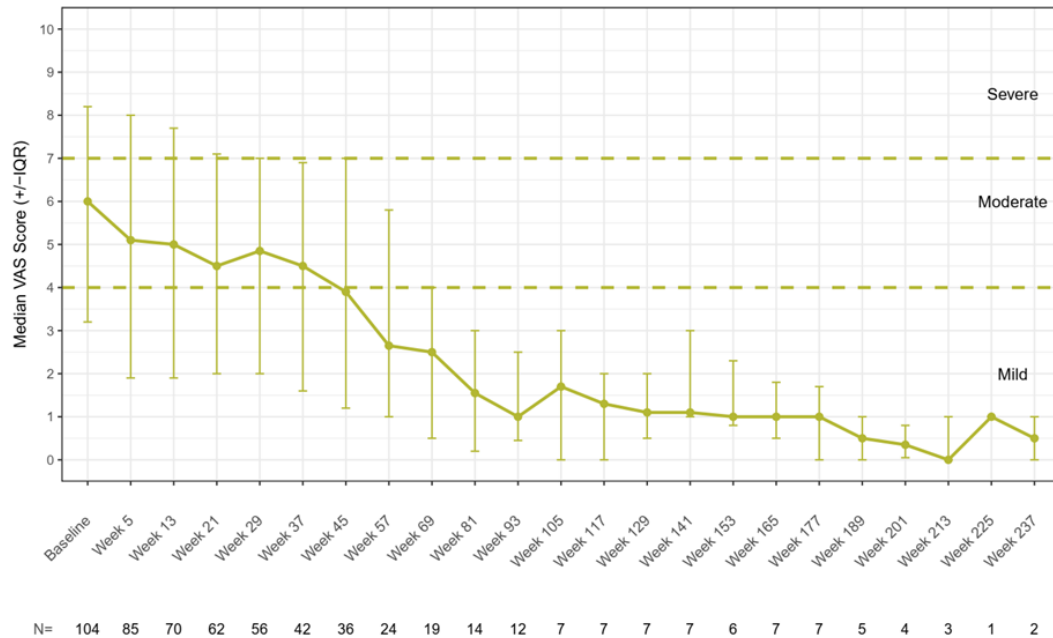


Progression Free Survival in MF patients treated with lacutamab

	All MF	KIR3DL2 ≥ 1%	KIR3DL2 <1%
PFS in months, median, (95%CI)	10.2 (8.0, 15.4)	11.8 (5.6, 16.8)	9.5 (6.5, 16.6)
Alive without PD, % (95% CI) at 12 months	47.3 (36.5, 57.3)	48.4 (32.2, 62.9)	46.5 (32.0, 59.8)
at 24 months	27.2 (17.2, 38.3)		



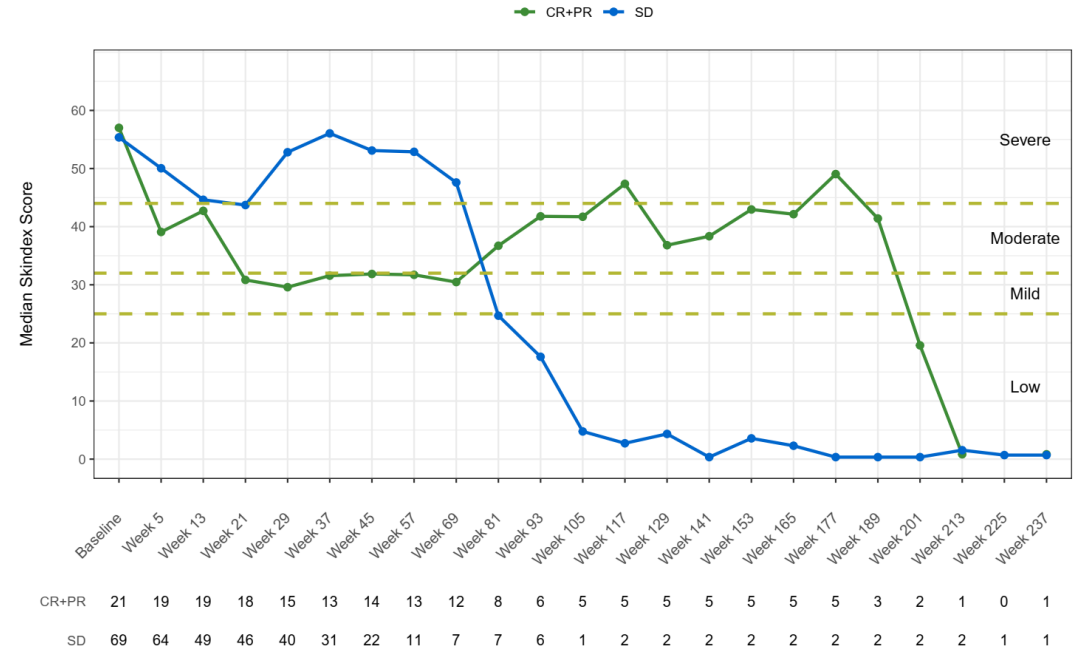
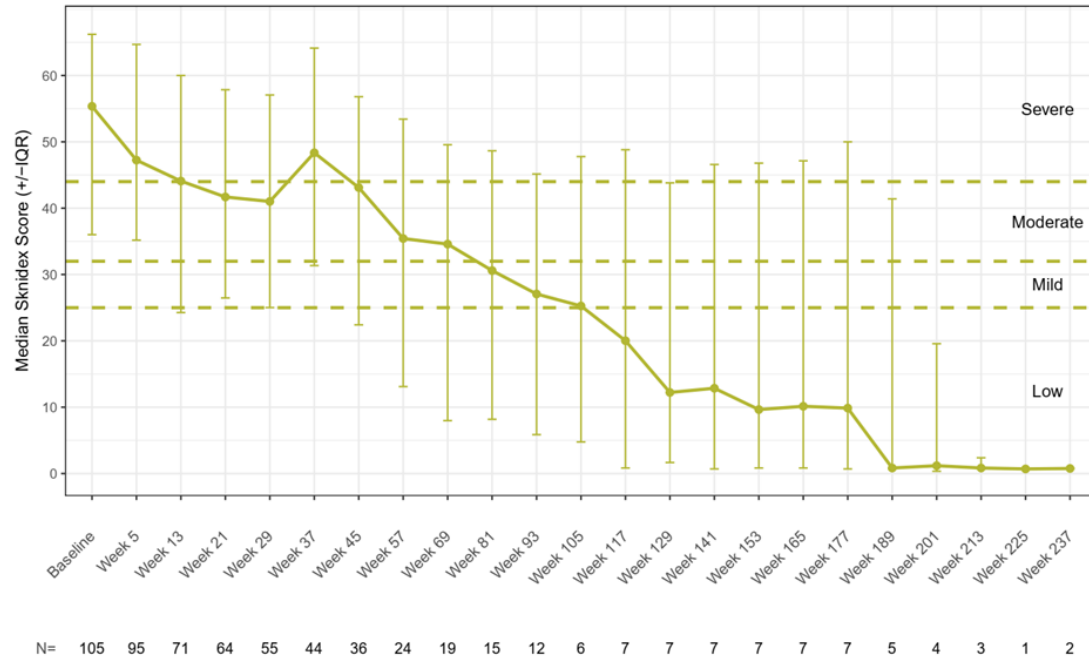
Visual Analog Scale (VAS) for Itch Intensity Score Over Time in MF



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 was 6.0, with 25% of patients having VAS>8 (severe score)
- Early decrease of itch intensity over time starting from W5
- Significant improvement ≥ 2 points decrease in itch intensity in VAS scale to mild pruritus with median VAS<4 from W45 maintained over time

Skindex-29 Total Score Over Time in MF

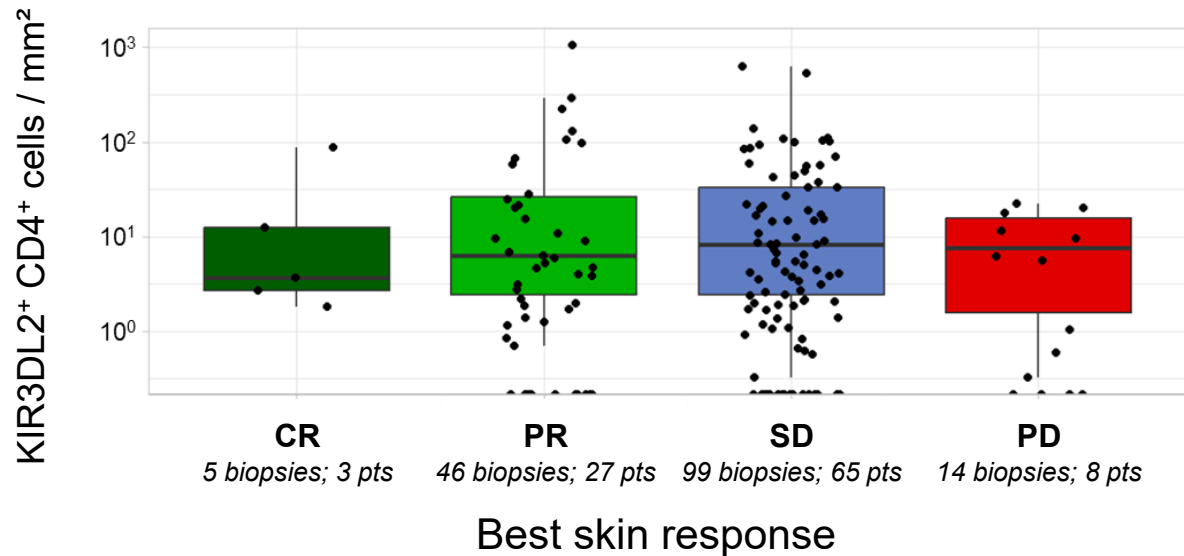


Skindex-29 questionnaire inquiries about how often (Never, Rarely, Sometimes, Often, All the time) during the previous 4 weeks the pt experienced the effect described in each item

- Overall score are expressed on a 100-point scale, with higher scores indicating lower levels of quality of life
- At baseline, median Skindex-29 global score was severe (55.4)
- Early and sustained decrease to moderate then mild and low score of Skindex-29 over time

Main translational results

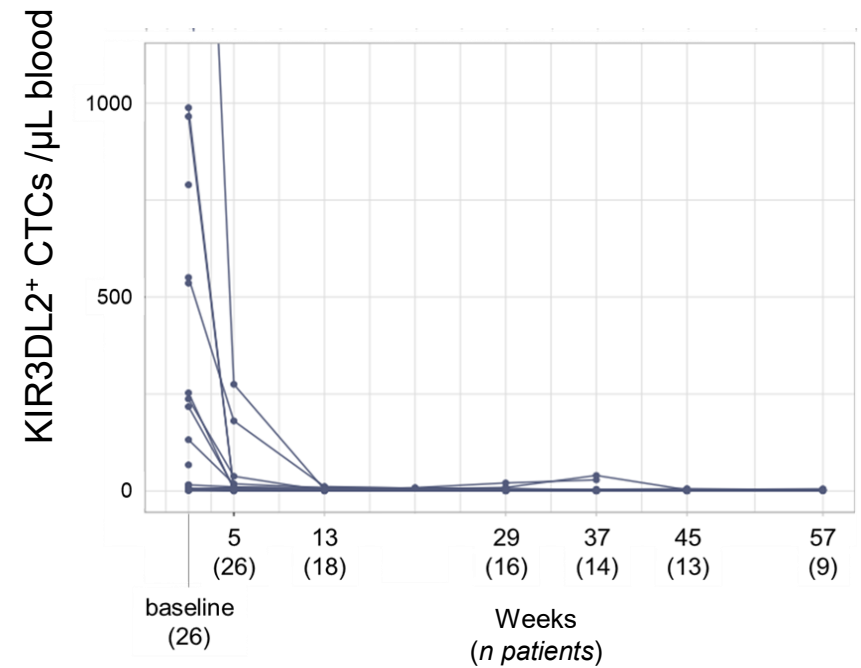
- Response to lacutamab in skin occurs irrespective of baseline density of KIR3DL2⁺ CD4⁺ T cells



ORR in skin = 29% (95% CI: 21.2, 38.2)

KIR3DL2⁺ CD4⁺ cell density in skin biopsies was determined by multiplex immunofluorescence

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



KIR3DL2⁺ CTCs/μL blood was determined by flow cytometry

Safety profile

Nb and (%) of pts with at least one		All MF N=107	KIR3DL2 ≥ 1% N=48	KIR3DL2 <1% N=59
Treatment-emergent adverse events (TEAEs)		98 (91.6)	43 (89.6)	55 (93.2)
Related TEAEs		64 (59.8)	31 (64.6)	33 (55.9)
Most frequent (>10%) related TEAEs	Nausea	14 (13.1)	4 (8.3)	10 (16.9)
	Fatigue	13 (12.1)	7 (14.6)	6 (10.2)
	Asthenia	12 (11.2)	5 (10.4)	7 (11.9)
	Arthralgia	12 (11.2)	6 (12.5)	6 (10.2)
Serious TEAEs		26 (24.3)	13 (27.1)	13 (22.0)
Serious related TEAEs		4 (3.7)	2 (4.2)	2 (3.4)
Grade ≥3 TEAEs		30 (28.0)	14 (29.2)	16 (27.1)
Related Grade ≥3*		5 (4.7)	2 (4.2)	3 (5.1)
TEAEs leading to discontinuation		6 (5.6)	2 (4.2)	4 (6.8)
Related TEAEs leading to discontinuation**		3 (2.8)	1 (2.1)	2 (3.4)
AEs leading to death***		3 (2.8)	1 (2.1)	2 (3.4)

Relatedness as defined by the treating investigator. Grade as per NCI Common Terminology Criteria for Adverse Events (CTCAE)

Asthenia; Oedema peripheral; Hypothermia; pneumonia pseudomonal; Sepsis (n=3); Systemic candida; Hypoglycemia; ILD; Acute kidney injury; **pneumonia pseudomonal, arthralgia, interstitial lung disease; *pseudomonas pneumonia, possibly related; ILD assessed as probably related per investigator, not related per sponsor; Sepsis, not related*

Patient Case

Patient characteristics

- 68-year-old female
- MF diagnosed in 2016
- 4 previous lines of therapy (PUVA therapy, bexarotene, interferon, methotrexate)
- T2N0M0B1 at baseline
- Response still ongoing after 3.5 yrs
- Skin: PR from W5, CR from W37
- Blood: CR from W5
- LN: Not involved (N0 at baseline)
- Global response: PR from W5 then CR from W37, still ongoing at W201 (Jan 2025)

BASELINE
October 05, 2020



Week 57
March 29, 2022



Conclusions

- TELLOMAK is a Phase 2 study evaluating lacutamab monotherapy in Cutaneous T-cell lymphoma (CTCL).
- The study enrolled relapsed and/or refractory **MF patients with ≥ 2 prior systemic therapies**.
- Lacutamab treatment induced **early and durable responses** and **improvement in pruritus and quality of life** in heavily pretreated patients with MF.
- The long-term follow-up data from TELLOMAK study confirm promising activity in heavily pretreated MF patients with a **median PFS of 10.2 months** (8.0, 15.4) and confirm that anti-tumor **activity is observed in all patients** (KIR3DL2 $\geq 1\%$ or $< 1\%$ at baseline)
- Importantly, **no safety concerns** nor delayed toxicities were identified and lacutamab was very well tolerated.
- These highly promising data, in a population with multiple prior systemic treatments and no available standard therapy, strongly support the development of lacutamab for MF and CTCL (see #052).
- Moreover, the excellent tolerability of lacutamab confort the strong rationale for further investigations in combination, beyond CTCL, with other anti-lymphoma agents in peripheral T-cell lymphomas (PTCL).

Acknowledgment

- **USA (17 sites)**

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