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LACUTAMAB IN PATIENTS WITH MYCOSIS FUNGOIDES (MF): EFFICACY RESULTS ACCORDING TO UPDATED LYMPH NODE (LN) CLASSIFICATION IN THE TELLOMAK STUDY

Youn H Kim[1], Martine Bagot[2], Pablo L Ortiz-Romero[3], Pier Luigi Zinzani[4], Marie Beylot-Barry[5], Stéphane Dalle[6], Eric Jacobsen[7], Andrea Combalia[8], Auris Huen[9], Neha Mehta-Shah[10], Michael S Khodadoust[11], Amitkumar Metha[12], Olivier Dereure[13], Maxime Battistella[14], Alejandro Gru[15], Hélène Moins-Teisserenc [16], Julien Viotti[17], Christine Paiva[17], Agnès Boyer-Chammard[17], **Pierluigi Porcu[18]**.

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PIERLUIGI PORCU DISCLOSURES

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Lacutamab
KIR3DL2 targeted treatment in T-Cell Lymphoma – Phase 1 data

- First-in-class humanized anti-KIR3DL2 cytotoxicity-inducing antibody under development for the treatment of T-cell lymphomas:
  - Cutaneous T-cell lymphoma (CTCL) including Sézary Syndrome (SS)[1] & Mycosis Fungoides (MF)[2]
  - Peripheral T-cell lymphoma (PTCL)
- Phase 1[1] data in SS patients who have been treated by at least two prior systemic therapies:
  - Global Objective Response Rate (ORR): 42.9% (95%CI: 28.0-59.1)
  - Median duration of response (DoR): 13.8 months (95%CI: 7.2-NA)
  - Median progression free survival (PFS): 11.7 months (95%CI: 8.1-NA)
- In recognition of high-unmet need and early potential, 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 received at least 2 prior systemic therapies

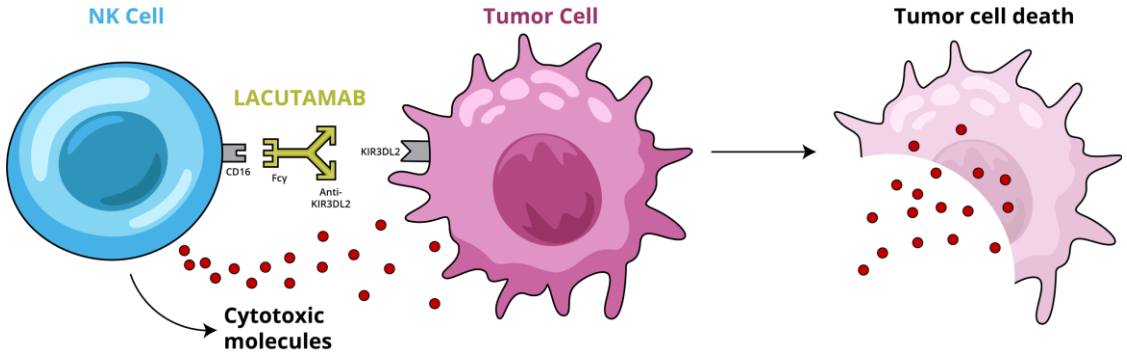

Figure 1: Lacutamab Mechanism of Action

	INDICATION & KIR3DL2 EXPRESSION	INCIDENCE *(US, EU5, Japan),*
	SEZARY SYNDROME • >90% of patients express target* • All tissues involved (skin, blood and lymph nodes)	~80–200 patients[1]
	MYCOSIS FUNGOIDES • ~50% of patients express target*	2,200–4,000 patients[1]

1. Bagot M et al, Lancet Oncol 2019
2. Lugano 2021, EORTC 2021

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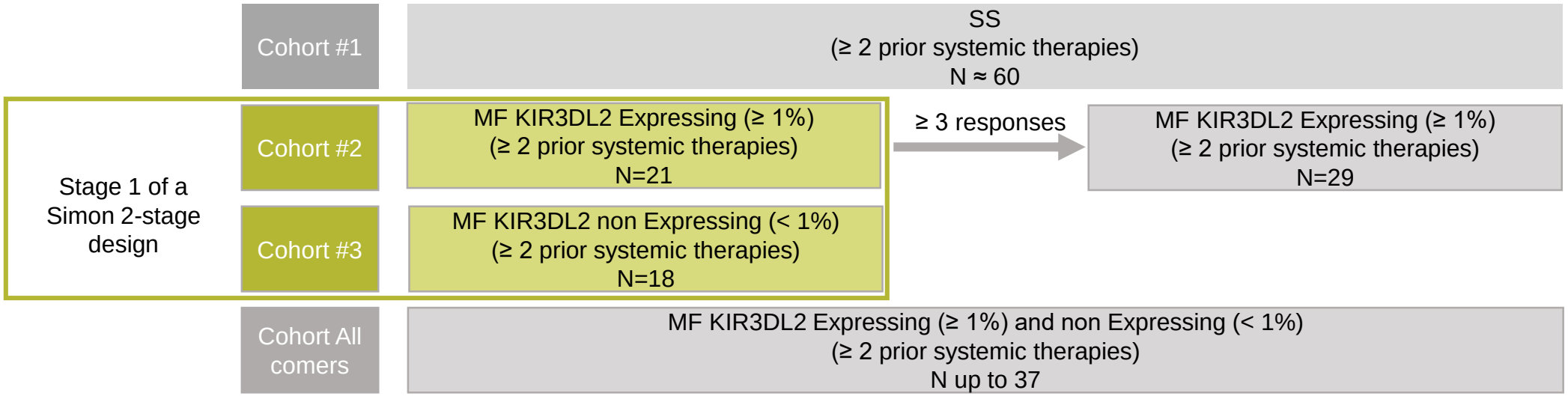
Phase 2 Study in Two CTCL Subtypes (MF and SS) - NCT03902184



Administration
- Lacutamab is administered by intravenous infusion every week for 5 weeks then every 2 weeks for 10 administrations then every 4 weeks, until disease progression or unacceptable toxicity

Study Endpoints
- Primary endpoint: global ORR
- Secondary endpoints: PFS, DoR, quality of life, safety and tolerability, PK & immunogenicity

Key Eligibility Criteria
- Relapsed and/or refractory stage IB-IV; ECOG performance status ≤2
- KIR3DL2 ≥ 1% (Cohort 2) or <1% (Cohort 3) based on central evaluation by immunohistochemistry (IHC)*
- No evidence of large cell transformation (LCT) based on central histologic evaluation at screening

ORR: Objective Response Rate; DoR: duration of response; PFS: progression free survival

* KIR3DL2 expression by IHC assay for use on frozen tissue

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LN Assessment by Updated Response Criteria (Olsen 2022)

- Global Response requires assessment of all compartments (Olsen 2011)
- LN response assessment challenging if:
  - LN clinically abnormal but not biopsy-proven (Nx)
  - LN is enlarged due to inflammation (N1, N2)
- According to updated Olsen 2022 criteria LN involvement with lymphoma requires N3 pathology classification

Skin	Blood, Nodes, Viscera	Global Response
CR	All compartments involved at baseline are now CR	CR
CR	All compartments involved at baseline are now PR or SD.	PR
PR	At least 1 compartment involved at baseline is now CR or PR. No compartment is PD	PR
PR	No compartments involved at baseline is now CR or PR. No compartment is PD	SD

Skin	Blood	LN	Visceral	Global
PR	B0	SD	Not Inv.	SD
PR	B0	Not Inv.	Not Inv.	PR

Olsen et al. Blood 2022, 140 (5):419-437

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Patient characteristics of MF cohorts 2 and 3

	Cohort 2 MF KIR3DL2 ≥ 1%* (N= 21)	Cohort 3 MF KIR3DL2 < 1%* (N=18)
Age in years, Median (range)	59 (33-77)	58 (19-81)
• Female, N (%) • Male, N (%)	7 (33%) 14 (67%)	3 (17%) 15 (83%)
• Stage IB / II, N (%) • Stage III[1], N (%)	16 (76%) 5 (24%)	15 (83%) 3 (17%)
Blood involvement[2], N (%)	8 (38%)	4 (22%)
Nodal Stage at Baseline, N (%) • N0 • N1 • N2 • **N3** • Nx	 10 (47.6%) 2 (9.5%) 2 (9.5%) **0 (0%)** 7 (33.3%)	 9 (50%) 3 (16.7%) 1 (5.5%) **0 (0%)** 5 (27.8%)
Prior systemic therapies, Median N (range)	4 (2-8)	4.5 (2-15)
Follow-up (months), Median (range)	12.2 (3-25)	13.8 (1-24)

1. Stage IV, SS not included
2. Blood involvement at baseline: B1
* KIR3DL2 expression by IHC assay for use on frozen tissue

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Preliminary Efficacy Results in Cohort 2 MF (KIR3DL2 ≥ 1%)

Cohort 2 MF KIR3DL2 ≥ 1%	Best Skin Response N=21	Best Blood Response N=8	Best Global Response by LN assessment N=21		
			All N categories N1-2 (n=4), Nx (n=7), N3 (n=0)	Only Nx and N3 Nx (n=7) N3 (n=0)	Only N3 (n=0)
N (%)					
CR	2 (9.5%)	5 (62.5%)	2 (9.5%)	2 (9.5%)	**2 (9.5%)**
PR	10 (47.6%)	0 (0%)	4 (19%)	6 (28.6%)	**7 (33.3%)**
SD	7 (33.3%)	3 (37.5%)	13 (61.9%)	11 (52.4%)	**10 (47.6%)**
PD	2 (9.5%)	0 (0%)	2 (9.5%)	2 (9.5%)	**2 (9.5%)**
NE	-	-	-	-	**-**
ORR % [95%CI]	**57.1% [36.5-75.5]**	**62.5% [30.6-86.3]**	**28.6%** [13.8-50.0]	**38.1%** [20.8-59.1]	**42.9% [24.5-63.5]**

DCO:04Mar2022
Per Olsen 2011

Data Presented @ EORTC-CL 2022

DCO:04Mar2022
Per Olsen 2022

Global Clinical Benefit Rate (CBR) 90.5% [95% CI 71.1-97.3]

CR: complete response, PR: partial response, SD stable disease, PD Progressive disease; N: number, CBR: Clinical benefit Rate (CR+PR+SD), ORR: Overall Response Rate,

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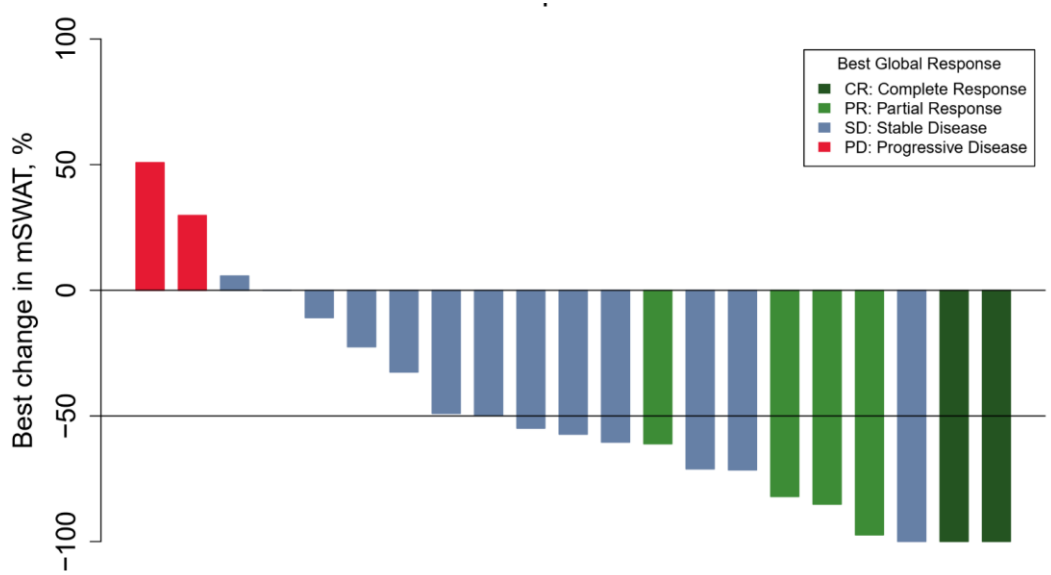
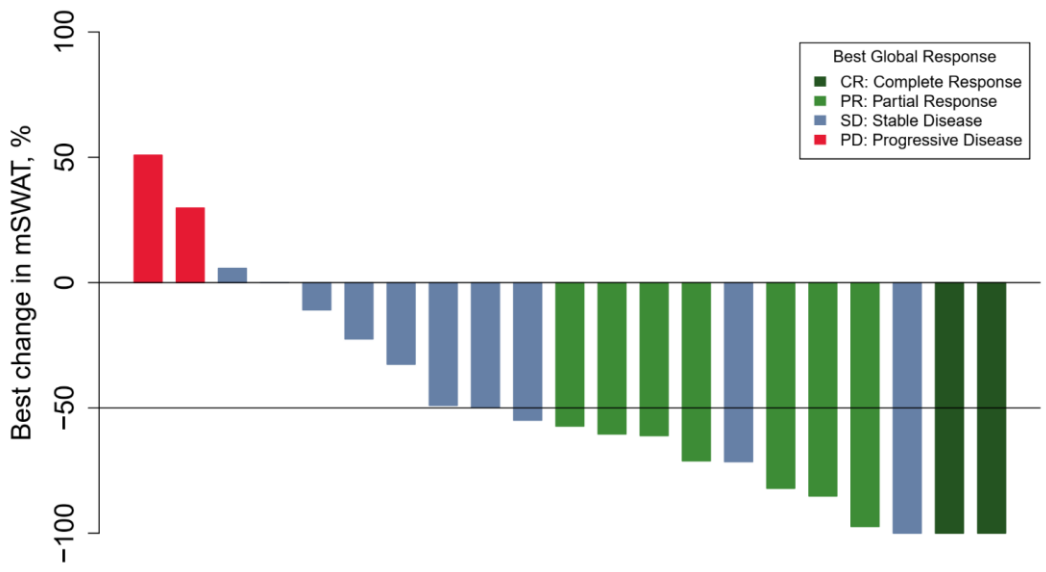
Preliminary Efficacy Results in Cohort 2 MF (KIR3DL2 ≥ 1%)

Best Overall Response
Olsen 2011 (N1, N2, N3, Nx involvement)



- 6 patients achieved Global Response (GR)
- Median time to GR: 1 month (range: 1.0-3.0)
- Median DoR: 10.2 months (95% CI: 4.6-N.A)

Best Overall Response
Olsen 2022 (N3 involvement)



- 9 patients achieved Global Response (GR)
- Median time to GR: 1 month (range: 0.9-4.7)
- Median DoR: 7.4 months (95% CI: 3.7-N.A)

- Median time to Skin Response: 1.0 month (range: 0.9-4.7)
- Median time to Blood Response: 1.0 month (range: 1.0-3.0)

DoR: duration of Response

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Preliminary Efficacy Results in Cohort 3 MF (KIR3DL2 < 1%)

Cohort 3 MF KIR3DL2< 1%	Best Skin Response N=18	Best Blood Response N=4	Best Global Response by LN assessment N=18		
			All N categories N1-2 (n=4), Nx (n=5), N3 (n=0)	Only Nx and N3 Nx (n=5) N3 (n=0)	Only N3 (n=0)
n (%)					
CR	0 (0%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
PR	3 (16.7%)	0 (0%)	2 (11.1%)	2 (11.1%)	2 (11.1%)
SD	13 (72.2%)	2 (50%)	14 (77.8%)	14 (77.8%)	14 (77.8%)
PD	1 (5.6%)	0 (0%)	1 (5.6%)	1 (5.6%)	1 (5.6%)
NE	1 (5.6%)	1 (25%)	1 (5.6%)	1 (5.6%)	1 (5.6%)
ORR % [95%CI]	**16.7% [5.8-39.2]**	**25% [4.6-69.9]**	**11.1 % [3.1-32.8]**	**11.1 % [3.1-32.8]**	**11.1 % [3.1-32.8]**

Global Clinical Benefit Rate (CBR) 88.9 % [95% CI 67.2-96.9]

DCO:04Mar2022
Per Olsen 2011

Data Presented @ EORTC-CL 2022

DCO:04Mar2022
Per Olsen 2022

CR: complete response, PR: partial response, SD stable disease, PD Progressive disease; N: number, CBR: Clinical benefit Rate, ORR: Overall Response Rate

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Preliminary Safety Results in Cohorts 2&3 (N=39)

		Total N=39 n (%)
Any treatment-emergent AEs (TEAEs)[1]		36 (92.3)
Any Lacutamab-related TEAEs[1]		23 (59.0)
Most frequent Lacutamab-related TEAEs	• Asthenia	5 (12.8)
	• Arthralgia	4 (10.3)
	• Nausea	3 (7.7)
Any Serious TEAEs (SAEs)		7 (17.9)
Any Serious Lacutamab-related TEAEs		2 (5.1)
Any Grade 3/4/5[2] Lacutamab-related TEAEs		2 (5.1)
Any Lacutamab-related Death[3]		1 (2.6)

1. Event / as defined by the treating investigator
2. NCI Common Terminology Criteria for Adverse Events (CTCAE)
3. 24Nov2020 Interstitial lung disease, Gr3 probably related, 11Nov2020 discontinued study treatment. Mar2022 Interstitial lung disease, Gr5 probably related

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Conclusions

- TELLOMAK is a Phase 2 study evaluating lacutamab monotherapy in CTCL. Cohort 2 and 3 enroll R/R MF patients with ≥ 2 prior systemic therapies who express KIR3DL2 at the ≥ 1% and <1% level.
- Lymph Node assessment is an important component of staging and response assessment in CTCL. The recent update to the consensus guidelines (Olsen 2022) states that LN involvement requires pathology fulfilling N3 criteria. Based on updated LN criteria:
  - In Cohort 2 (KIR3DL2 ≥1%, N=21)
    - Global ORR 42.9% (95% CI [24.5; 63.5]) (Only N3) and 28.6% (95% CI [13.8-50.0]) (N1,N2, Nx, N3)
    - Blood ORR 62.5% (95% CI: 30.6-86.3)
    - Skin ORR 57.1% (95% CI: 36.5-75.5)
    - Clinical Benefit Rate 90.5% [95% CI 71.1-97.3]
  - in Cohort 3 (KIR3DL2 < 1%, N=18)
    - Findings remain consistent
- In this preliminary analysis of cohort 2 and 3 (N=39), lacutamab has clinical activity with favorable safety.
- Updated assessment of LN status results in a higher global response, highlighting the impact of the adoption of the 2022 criteria on clinical trial design and outcome.

Olsen et al. Blood 2022, 140 (5):419-437.

Acknowledgments

In total 53 active sites

- France (10)
- Germany (8)
- Spain (6)
- Italy (4)
- Belgium (3)
- Austria (2)
- Poland (3)

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