KIR3DL2 expression in cutaneous T-cell lymphomas : a widely-shared target

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INTRODUCTION

KIR3DL2 (CD158k) : killer cell immunoglobulin like receptor normally expressed by 1/3 of NK cells, and about 9% of CD8+ T cells, 25% of γδ T cells, 3% of CD4+ T cells.

- Aberrant expression in clonal malignant cells in Sezary syndrome (SS), transformed MF (tMF) and cutaneous ALCL.
- Enables accurate diagnosis and follow-up of circulating tumor burden in SS (flow cytometric detection)
- Promising target in SS patients: KIR3DL2-directed IPH4102 mAb under development (phase I IPH4102-101 clinical study ongoing)

What about KIR3DL2 expression in all CTCL ? KIR3DL2 prognostic value ?

MATERIAL and METHODS

Monocentric retrospective cohort of 134 CTCL patients

Controls:

- 11 healthy patients,
- 10 erythrodermic inflammatory diseases (EID)

(with available frozen tissue and patient consent)

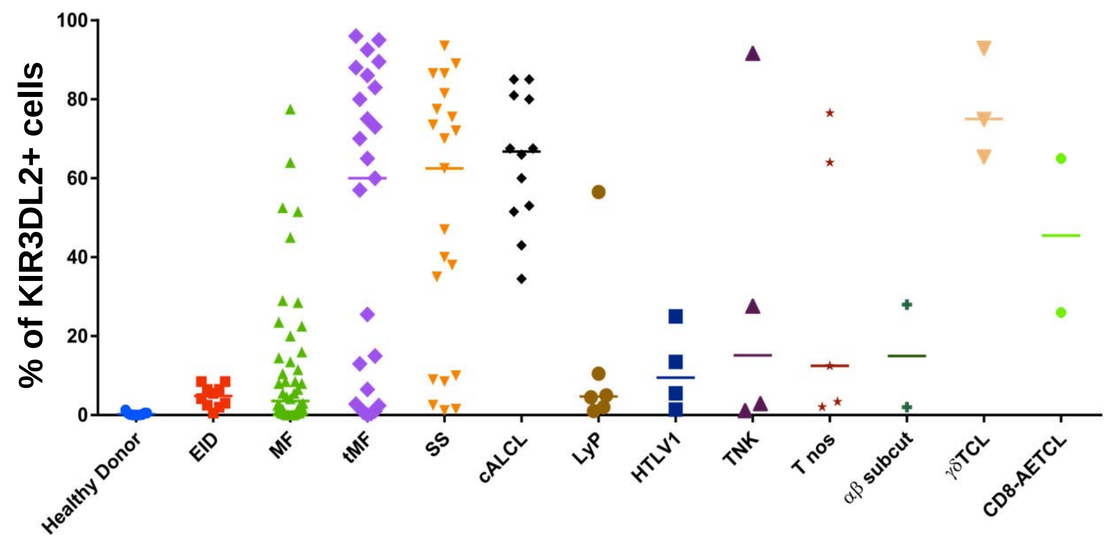
KIR3DL2 immunohistochemistry : monoclonal Ab MOG1-12B11 (Innate Pharma) specific for KIR3DL2 (no cross-detection of KIR3DL1) – independent assessment by 2 pathologists

Other data collected: age, sex, TNMB stage, large cell transformation (LCT), status at last follow-up

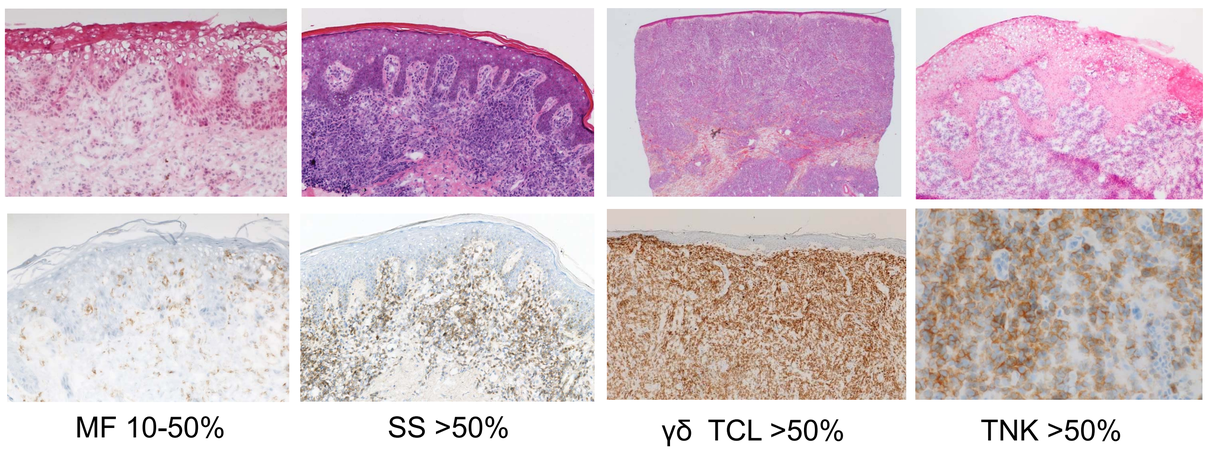
RESULTS

MF (48) Incl. foll MF (6), granulomatous slack skin (2)			tMF (25)		SS (21)
cALCL (12)	LyP (6)	HTLV1 (6)	TNK (4)	T nos (5)	Others * (7)

* γδ T-cell lymphoma (3), panniculitis-like subcutaneous αβ T-cell lymphoma (2), CD8+ agressive epidermotropicT-cell lymphoma (2)

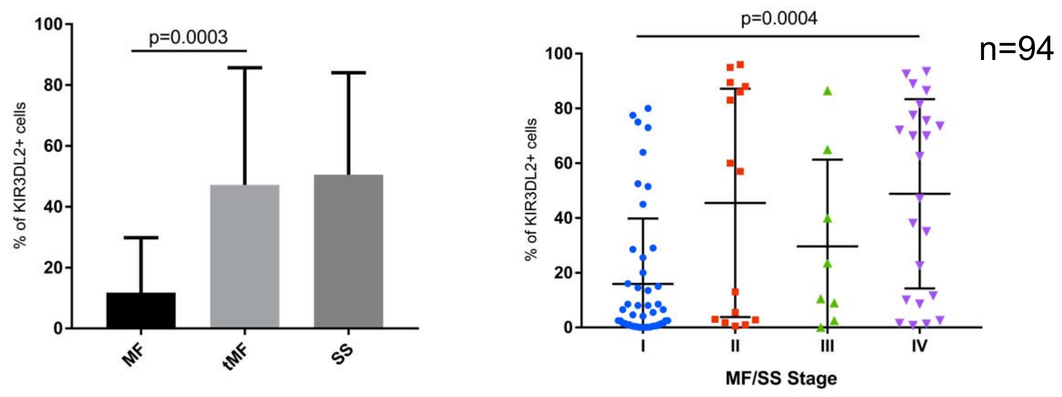


KIR3 DL2	HD	EID	MF	tMF	SS	cALCL	LyP	HTLV1	TNK	T NOS	αβ subcut	γδ TCL	CD8+ AETCL
>5%	0	5 (50%)	22 (46%)	18 (72%)	18 (86%)	12 (100%)	2 (33%)	5 (83%)	2 (50%)	3 (60%)	1 (50%)	3 (100%)	2 (100%)
>10%	0	0	15 (31%)	17 (68%)	16 (76%)	12 (100%)	2 (33%)	3 (50%)	2 (50%)	3 (60%)	1 (50%)	3 (100%)	2 (100%)
>50%	0	0	4 (8%)	**14 (56%)**	**11 (53%)**	**10 (83%)**	1 (17%)	1 (17%)	1 (25%)	2 (40%)	0	**3 (100%)**	**1 (50%)**



MF 10-50% | SS >50% | γδ TCL >50% | TNK >50%

KIR3DL2, stage and LCT in MF/SS



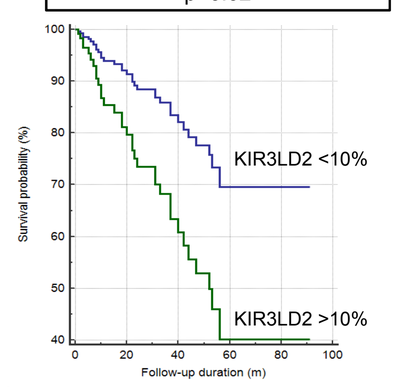
n=94

KIR3DL2 expression increases with cytological transformation and disease extent in MF/SS patients.

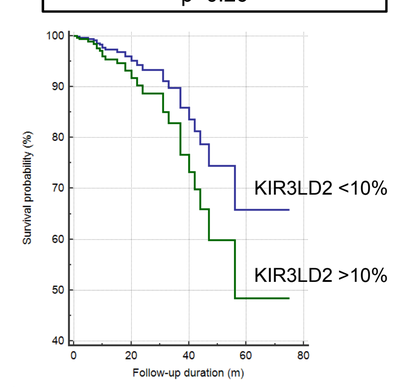
KIR3DL2>10%: independent prognostic factor of OS

	Univariate analysis		Multivariate analysis
	Median OS (95% CI)	P-value	P-value
Age>60	44 (37-56) *vs* 91 (52-nr)	**0.022**	**0.02**
Male	52 (37-91) *vs* nr	0.099	0.38
Extracutaneous involvement (N or M)	22 (10-53) *vs* nr	**0.0004**	**0.0007**
KIR3DL2>50%	53 (18-56) *vs* 91 (10-53)	0.010	
KIR3DL2>10%	53 (24-56) *vs* 52 (44-91)	**0.028**	**0.02**
KIR3DL2>5%	56 (31-56) *vs* 52 (44-91)	0.114	

All CTCL cohort
Cox multivariate analysis
p=0.02



MF/SS patients
Cox multivariate analysis
p=0.26



NEW CHALLENGES

- Test practicability: for the moment test using frozen material only. FFPE KIR3DL2-specific test still under research
- KIR3DL2 prognostic value : need for larger prospective validation cohorts (especially for MF/SS)

KIR3DL2 is expressed in >5% cells in 66% of CTCL.

High KIR3DL2 expression (>50%) is characteristic of tMF, SS, cALCL, CD8+ AETCL, γδ T-cell lymphoma, and some MF, TNK lymphoma, T nos lymphoma.

KIR3DL2 is associated with disease progression in MF/SS and a putative independent factor of OS in CTCL.