PET in PTCL

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Lysa
THE LYMPHOMA STUDY ASSOCIATION

PET in PTCLs

⇒Role of PET in PTCLs

- What we know
  - Summary of published studies

- Ongoing cooperative LYSA and Danish study (n=142)

⇒Is PET able to give prognostic information to stratify risk patient categories?
  - At baseline
  - After treatment : interim and end of treatment PET.

FDG avidity

Table 2. FDG Avidity According to WHO Classification

Histology	No. of Patients	FDG Avid (%)
Angioimmunoblastic T-cell lymphoma	31	78-100
Peripheral T-cell lymphoma	93	86-98
Anaplastic large T-cell lymphoma	37	94-100*

=161

Barrington S, 2014, J Clin Oncol

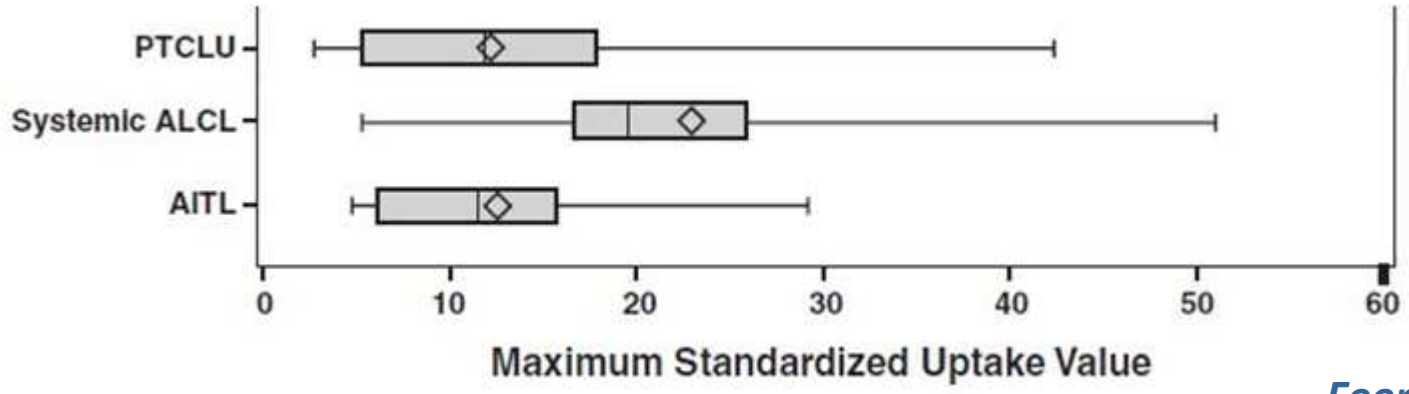
TABLE 1: Summary of PET/CT Findings in All Cases of T-Cell Lymphoma

Type of Lymphoma	No. of Patients	Sex, No. of Patients		PET Scan Positive, No. of Patients/ Total (%)	Type of Disease, No. of Patients/Total			Disease Outside Field of View,[a] No. of Patients	Maximum Standardized Uptake Value, Mean (Range)
		Male	Female		Cutaneous	Nodal	Visceral		
PTCLU	34	24	10	33/34 (97)	8/33	29/33	17/33	7	12.3 (2.8–42.3)
Systemic ALCL	16	11	5	15/16 (94)	4/15	15/15	8/15	3	22.9 (5.3–51.0)
AITL	18	7	11	14/18 (78)	0/14	14/14	7/14	0	12.6 (4.8–29.2)

=68

Feeney J, 2010, AJR

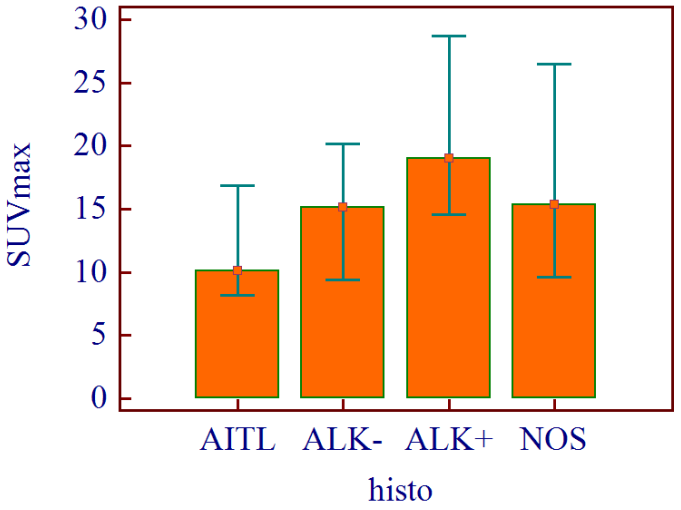
Intensity of uptake



Mean (Range)
12.3 (2.8–42.3)
22.9 (5.3–51.0)
12.6 (4.8–29.2)

Feeney J, 2010, AJR

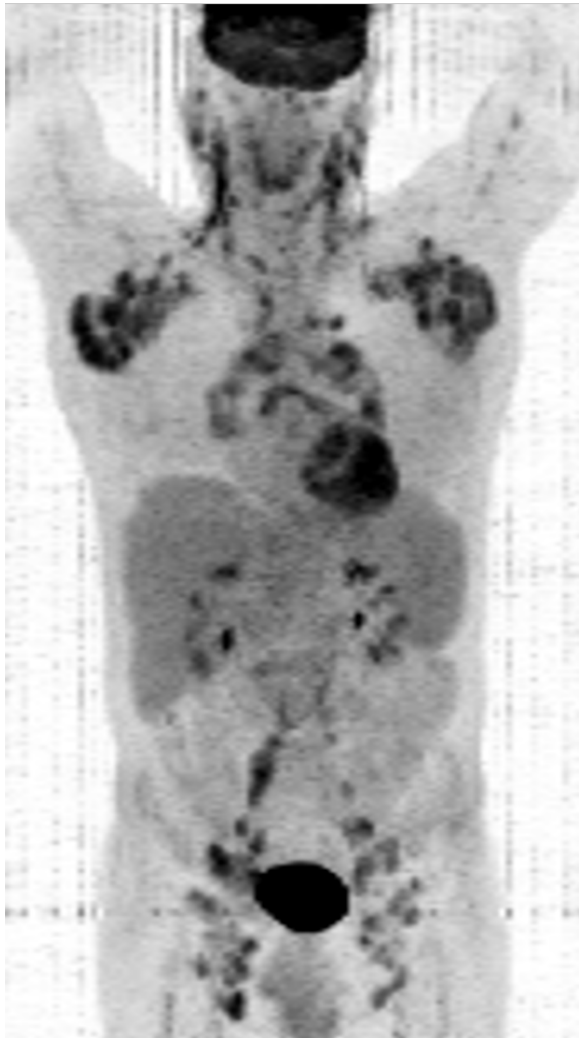
Factor	n	Mean	Median
AITL	54	12,28630	10,15000
ALK-	30	16,54967	15,15000
ALK+	22	21,31364	19,00000
NOS	36	17,55667	15,35000



Cottereau, El Galaly et al. LYSA and Danish groups

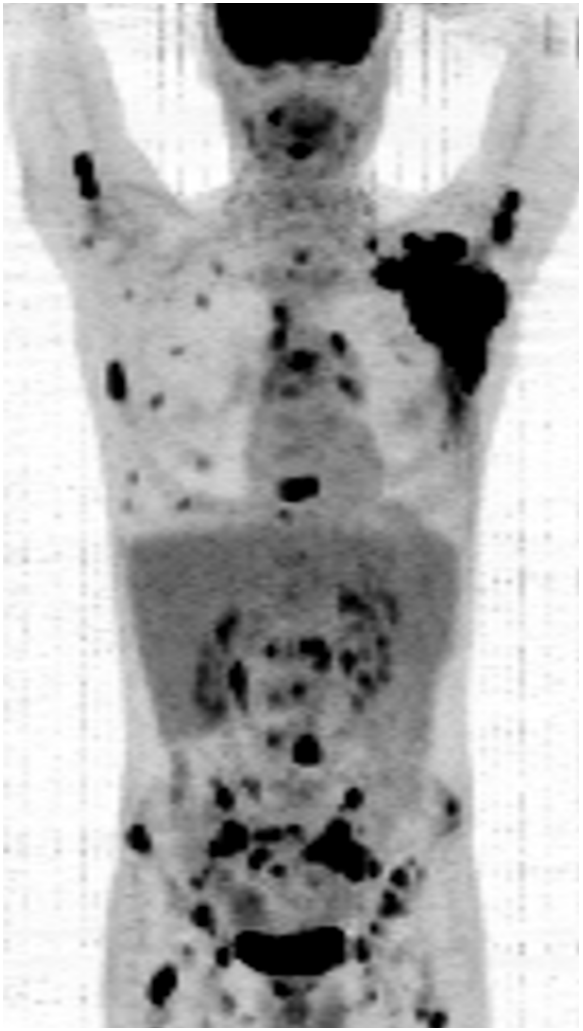
AITL

SUVmax=7.3
TMTV=635 cm^3



ALK + ALCL

SUVmax=39
TMTV=352 cm^3

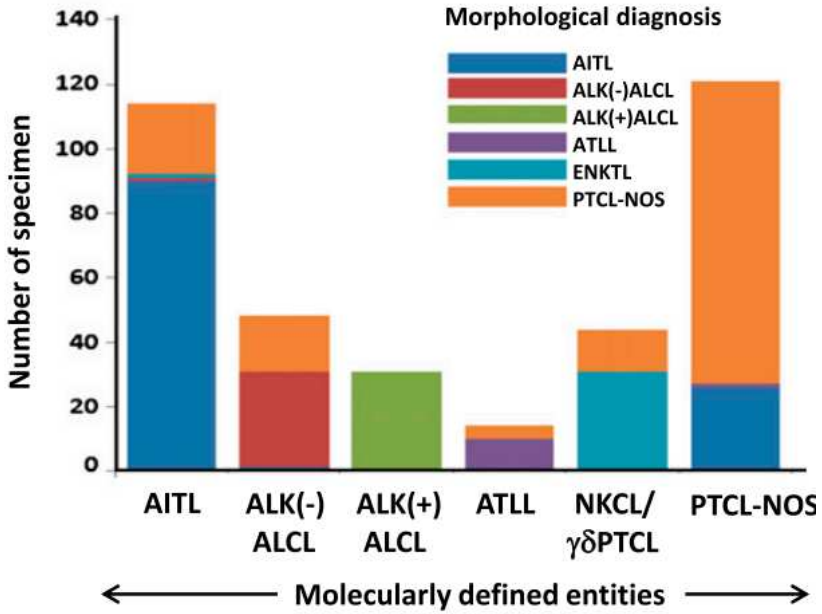


Heterogeneous group of lymphoma

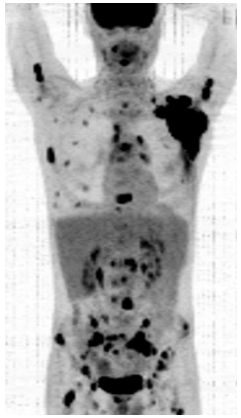
- Uptake not only based on tumor cells but also on microenvironmental cells

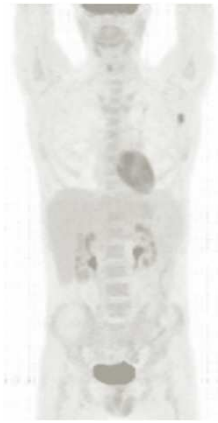
- Different molecular profile
  - AITL
  - ALCL
  - PTCL NOS:

    -> not currently well classified by morphological diagnosis



Iqbal et al, Blood, 2014





1.Baseline PET

2. Interim PET

3. End of treatment PET

C2

C3

C4

C5

FIRST CYCLE

END OF TREATMENT

PET at Staging

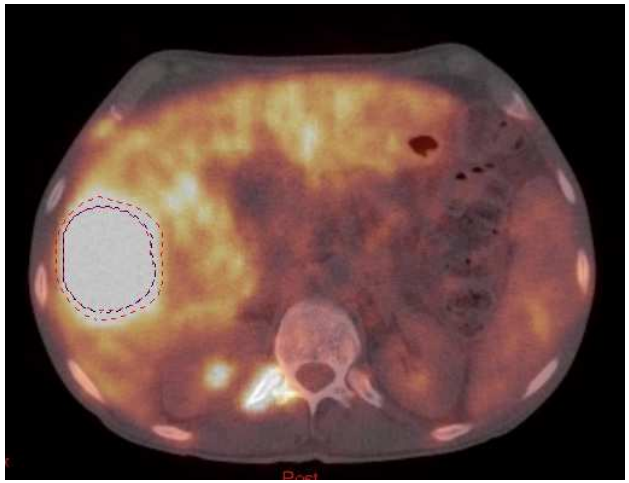
- Detection of additional disease sites
  - 50% of the patients
  - 5% of changing stage

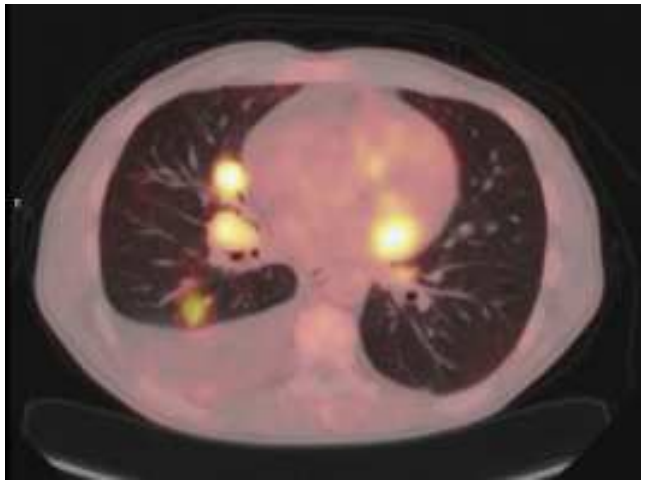
Casulo et al, Leuk lymphoma, 2013

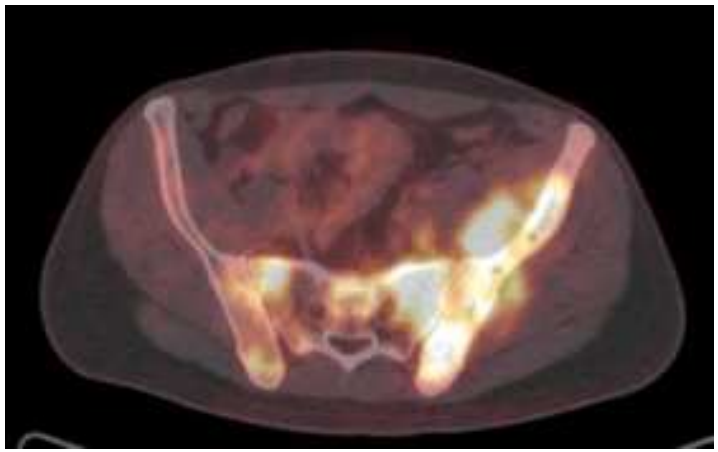
- Extranodal sites
  - Bone marrow, lung, gastro intestinal tract, skin, liver.
  - At least 2 EN sites:
    - predictive of outcome
    - Included in IPI

Broussais et al, Leuk Lymphoma, 2013
Gallamini et al, Blood 2014

Extra nodal disease sites







Bone marrow involvement

- BMI detect by bone marrow biopsy is an adverse factor.
- BMI PET + : defined by at least one focal uptake
- Danish group (124 patients)
  - 11% PET + in bone marrow.
  - Sensitivity of PET to detect positive BMB : Se=19%
  - BMI PET+ : not predictive of outcome

El Galaly, 2015, Am. J.Hematol

- Lysa group
  - 117 patients, from 6 centers
  - 22% PET + in bone marrow.
  - Sensitivity of PET to detect + BMB : Se=29%
  - BMI PET+: Not predictive of outcome

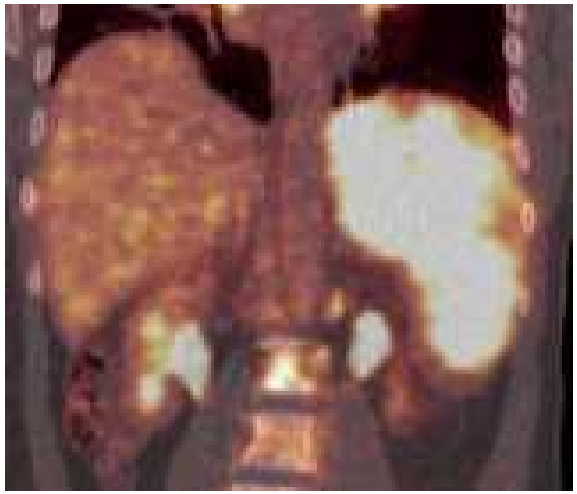
Cottereau et al, abstract, J Nucl Med 2016

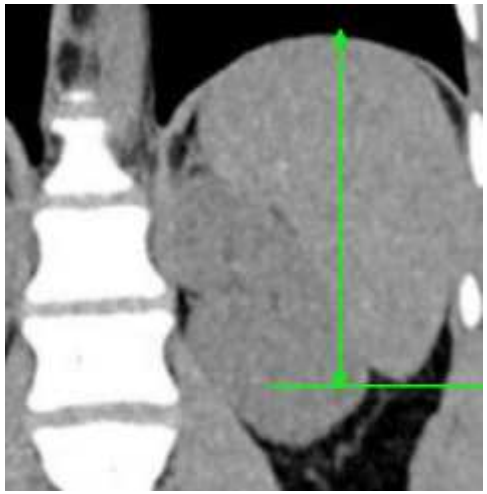
=> PET cannot replace bone marrow biopsy!

Spleen involvement

$\Rightarrow$ SI PET: defined by focal FDG uptake or diffuse FDG uptake higher than the liver.

$\Rightarrow$ SPM: > 13cm in vertical length

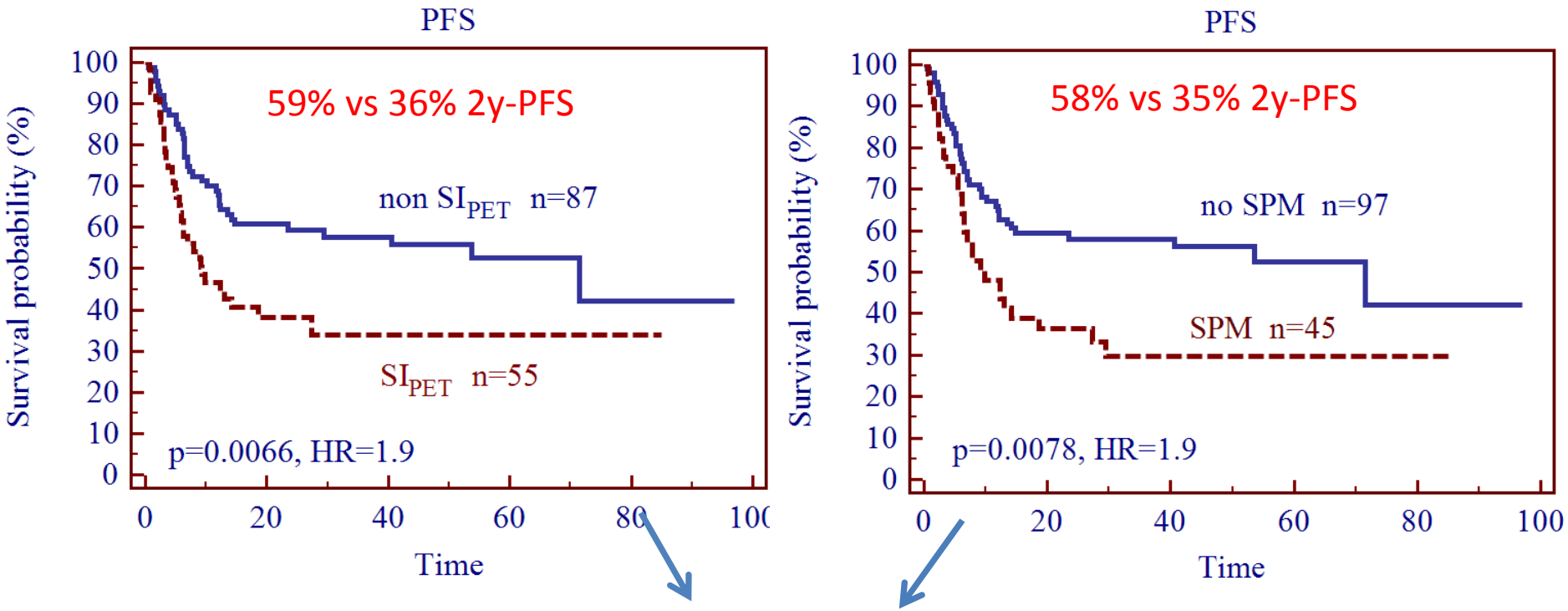




Prognostic value of spleen involvement (SIPET or SPM)

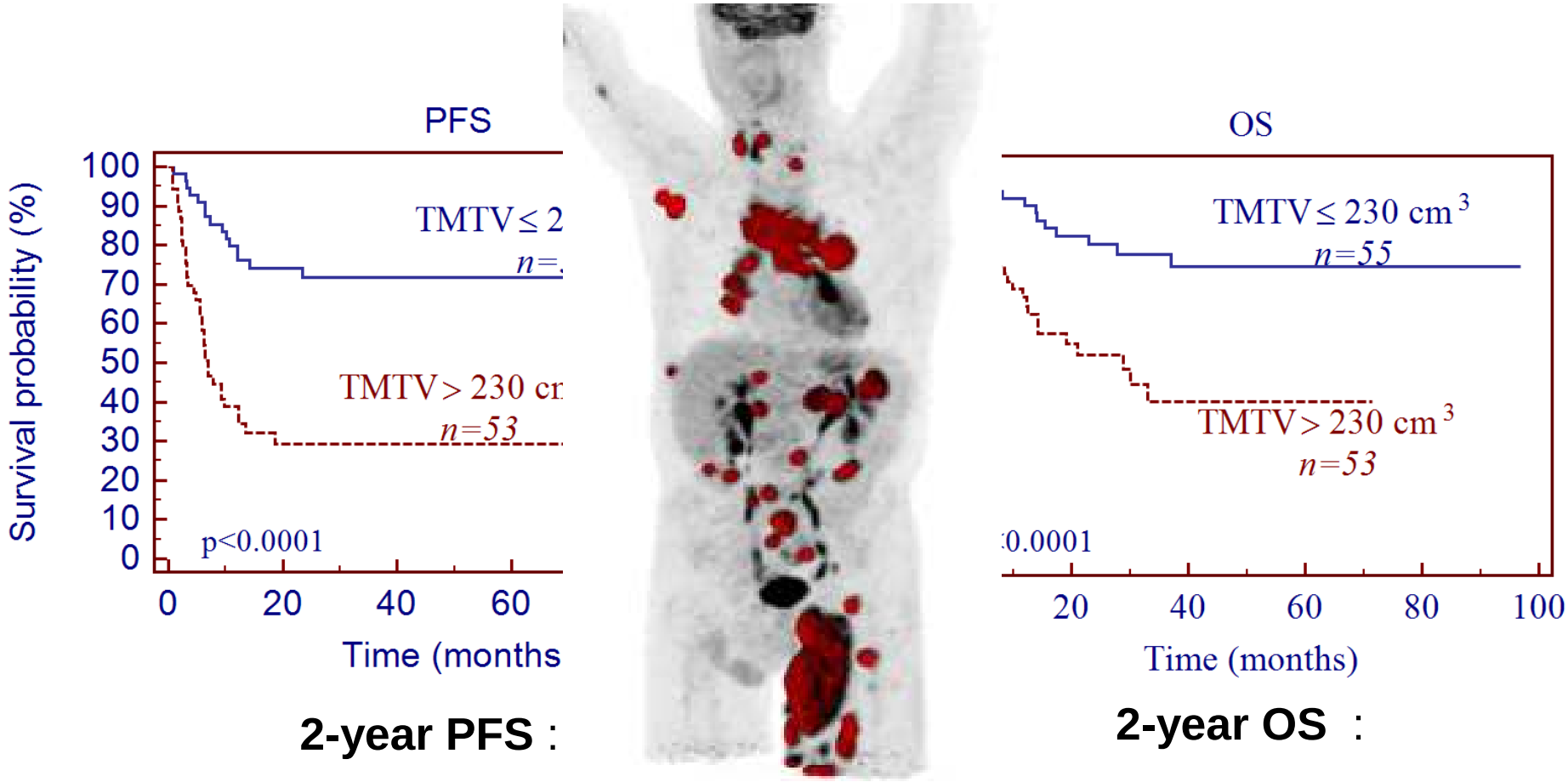
Lysa/Danish groups study (116+26=142)

- SIPET slighly predictive of PFS
- Comparable to SPM (>13cm)



SI and SPM n=32

Total metabolic tumor volume



2-year PFS :

71% (65-77%) ***vs*** **26% (20-32%)**

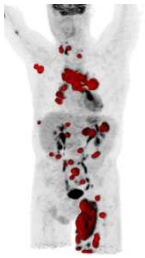
2-year OS :

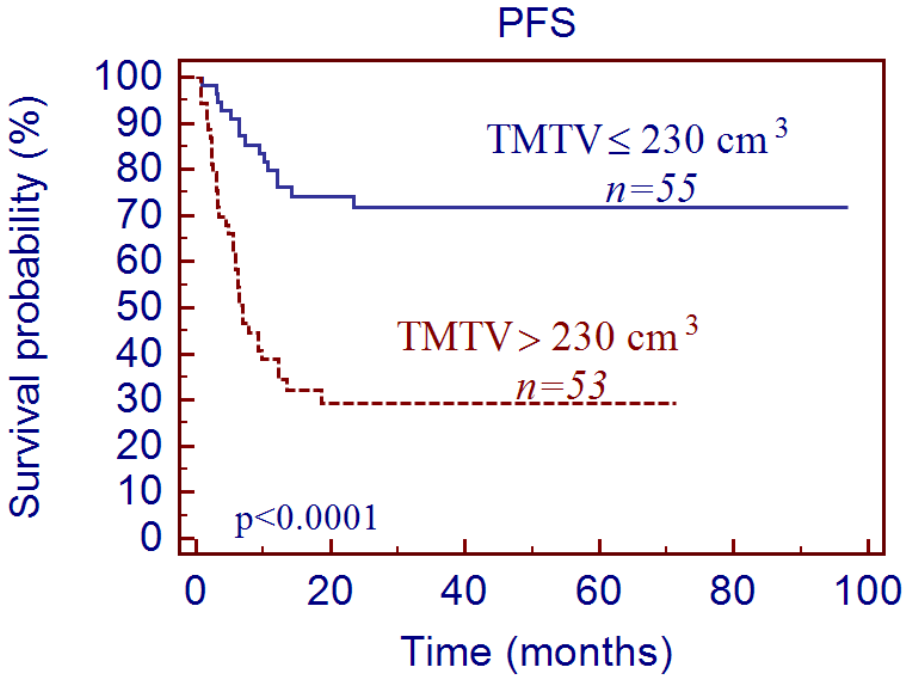
80% (75-85%) ***vs*** **50% (42-58%)**

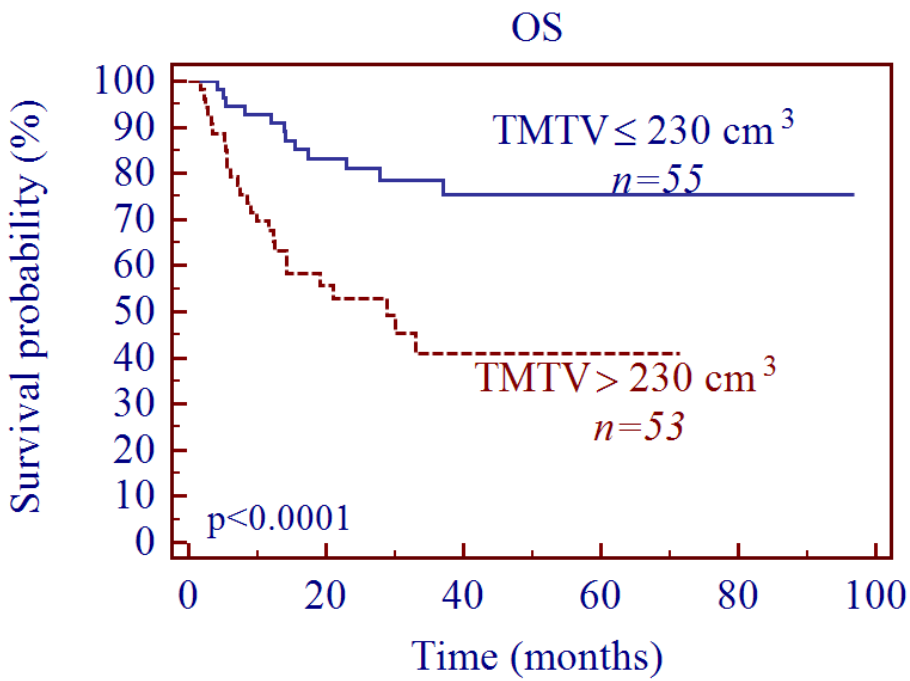
Cottereau et al, Ann Oncol 2016

Annals of Oncology

Total metabolic tumor volume







2-year PFS :

71% (65-77%) *vs* 26% (20-32%)

2-year OS :

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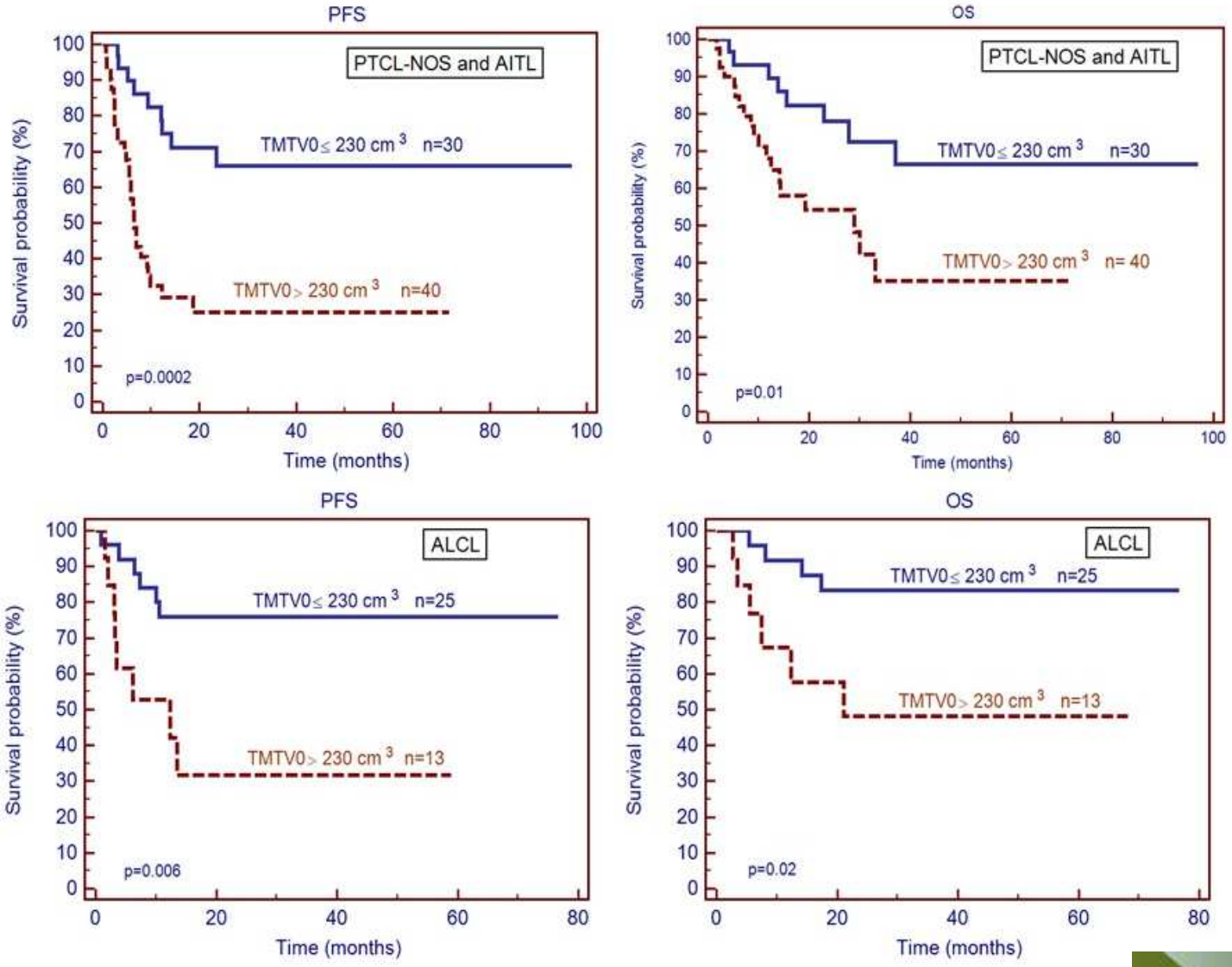
Cottereau et al, Ann Oncol 2016

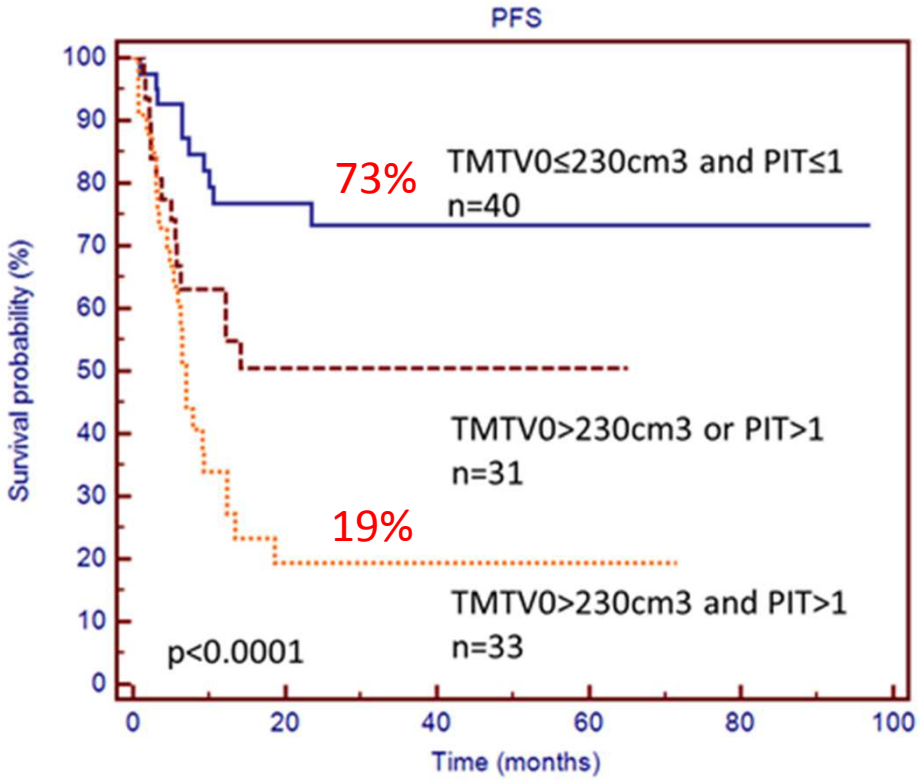
According to each histologic subtypes

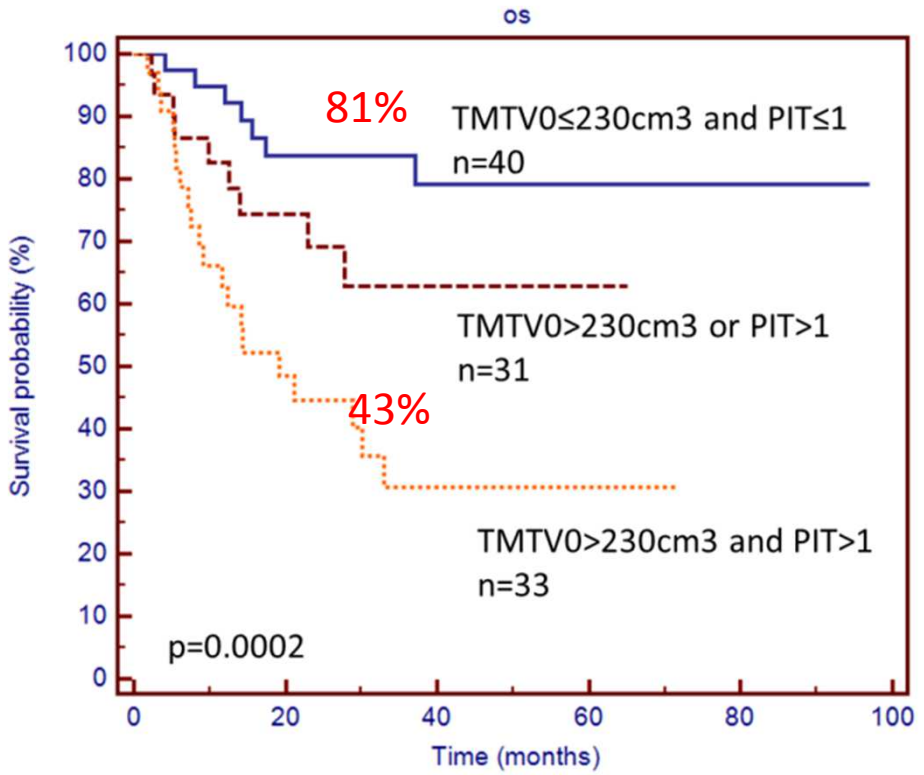


Cottereau et al, Ann Oncol 2016

Annals of Oncology

TMTV combined with PIT





Cottereau et al, Ann Oncol 2016

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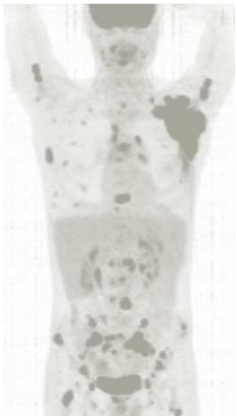
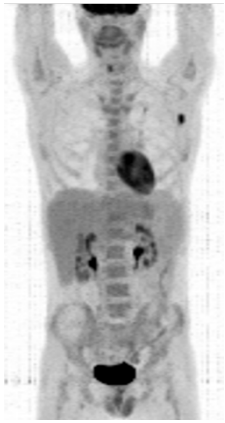
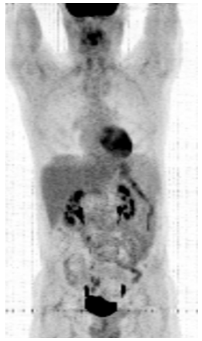






1.Baseline PET

2. Interim PET

3. End of treatment PET

C2

C3

C4

C5

FIRST CYCLE

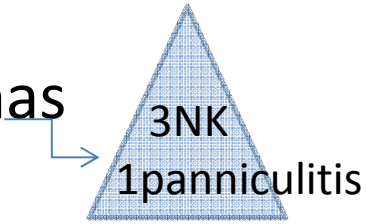
END OF TREATMENT

GOELAMS study

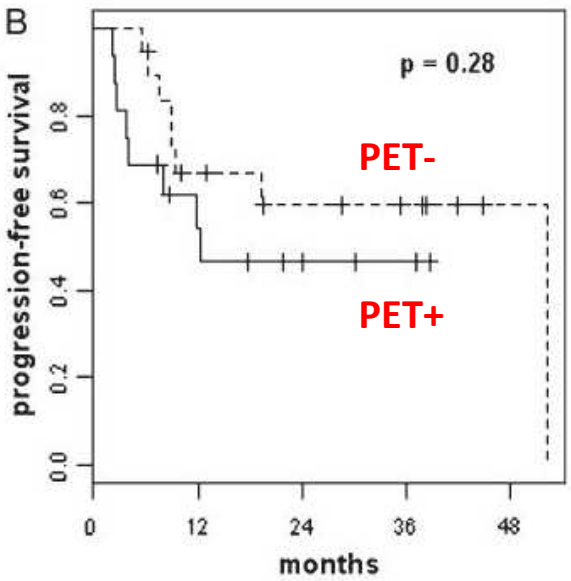
Retrospective study, MFU= 24 months

- 54 patients with Non cutaneous T/NK lymphomas
- CHOP-like regimen
- PET reporting: IHP or 3-point scale (low/moderate/high)

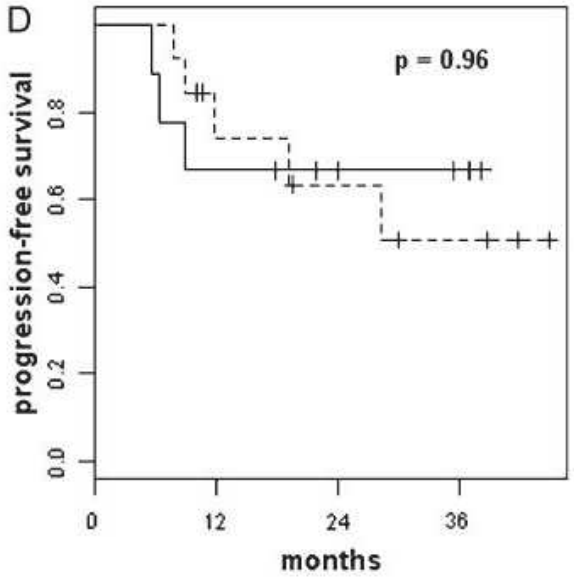
  (negative PET if normal or one lesion grade 1)



interim n=44 (3-4 cycles)



after therapy n=31

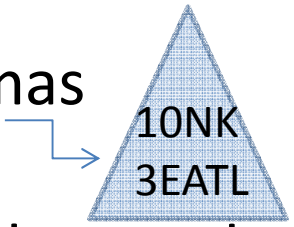


Cahu X, 2011, Ann Oncol

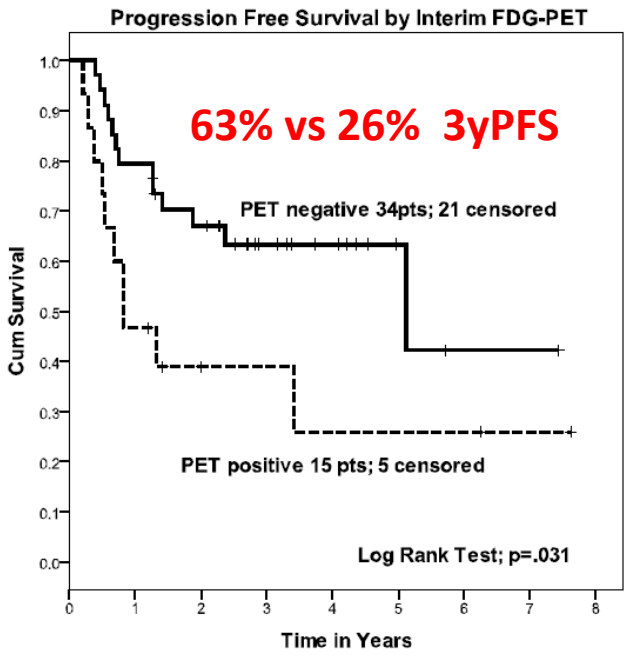
PTCL database of Memorial Sloan-Kettering Cancer

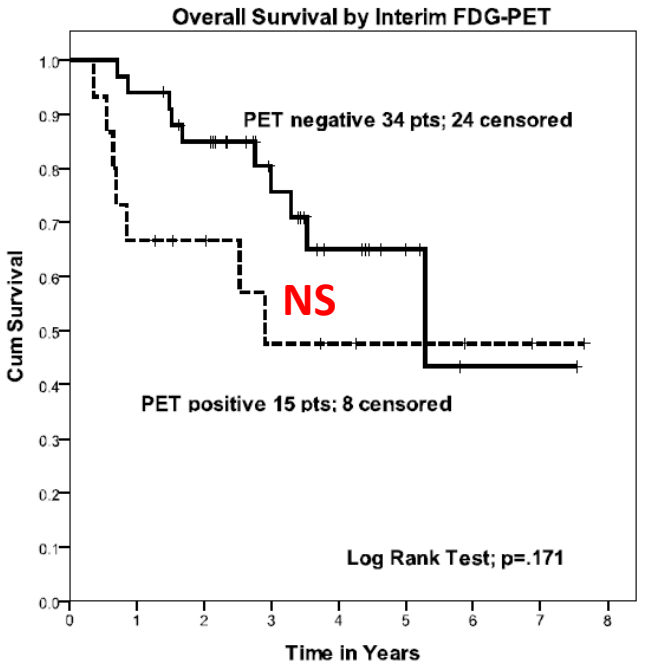
Retrospective study, MFU=40 months

- 95 patients with Non cutaneous T/NK lymphomas
- CHOP-like regimen
- PET reporting : PET+ve =FDG uptake > liver background



interim n=50 (2-10 cycles) with 39 PTCL





Casulo C, 2013, Leuk Lymphoma

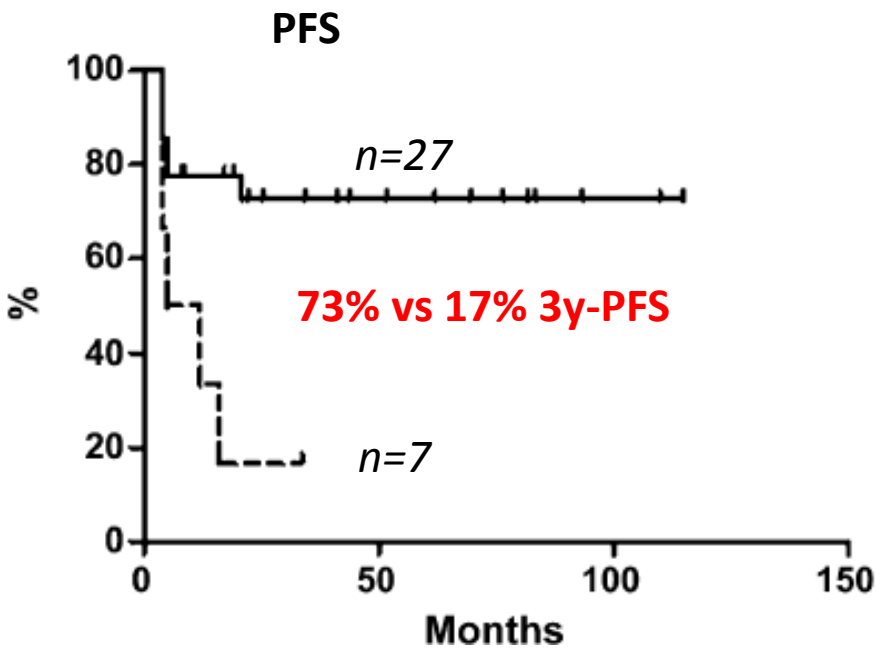
The Oncologist®
2014

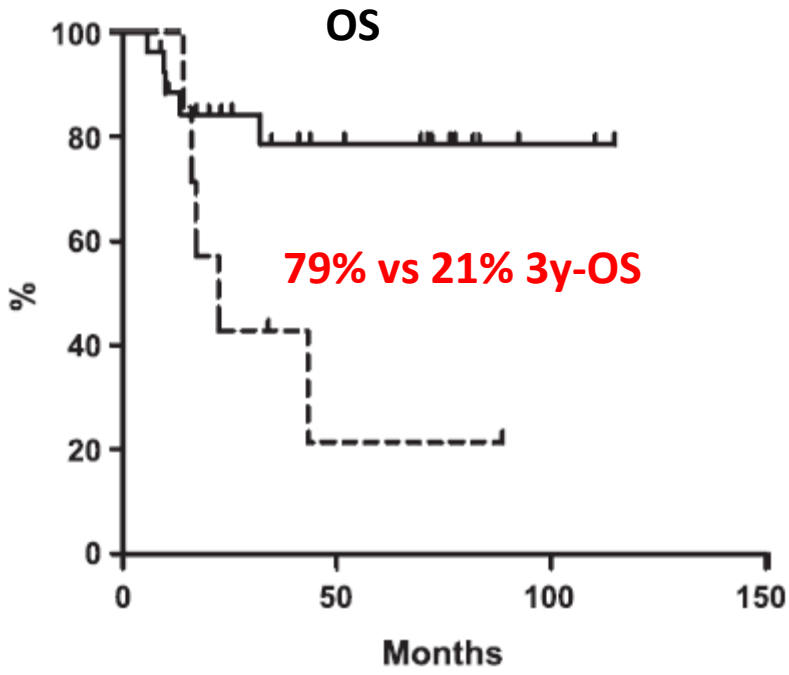
Prognostic Value of Interim Positron Emission Tomography With Peripheral T-Cell Lymphoma

Cinzia Pellegrini, Lisa Argnani, Alessandro Broccoli, Vittorio Stefoni, Enrico Derenzini, Letizia Gandolfi, E
Roberto Maglie, Stefano Pileri, Pier Luigi Zinzani

- Retrospective
- 34 patients (2 NK), treated with CHOP 21

Interim PET (after C3)





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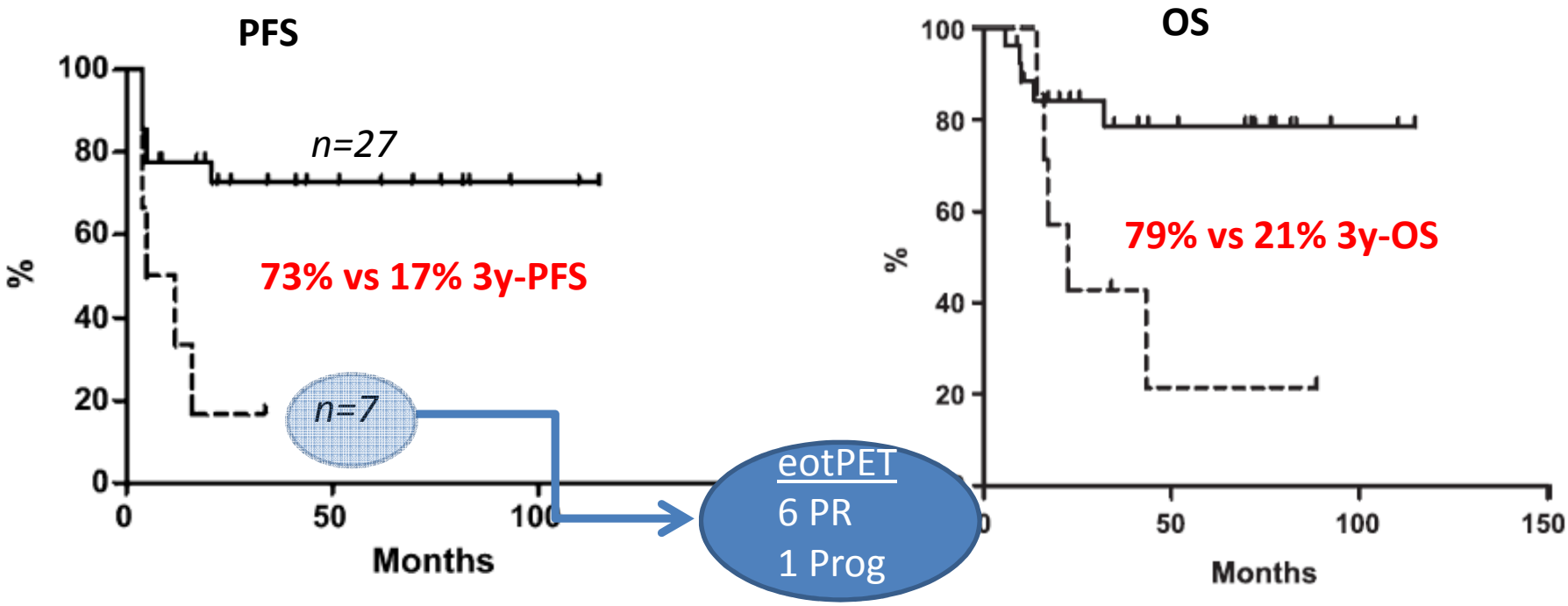


JNM The Journal of NUCLEAR MEDICINE 2013

Prognostic Value of Interim and Posttherapy ^{18}F-FDG PET/CT in Patients with Mature T-Cell and Natural Killer Cell Lymphomas

Ya-Jun Li, Zhi-Ming Li, Xi-Ya Xia, Hui-Qiang Huang, Zhong-Jun Xia, Tong-Yu Lin, Su Li, Yi Xia, Xiu-Yu Cai and Wen-Qi Jiang

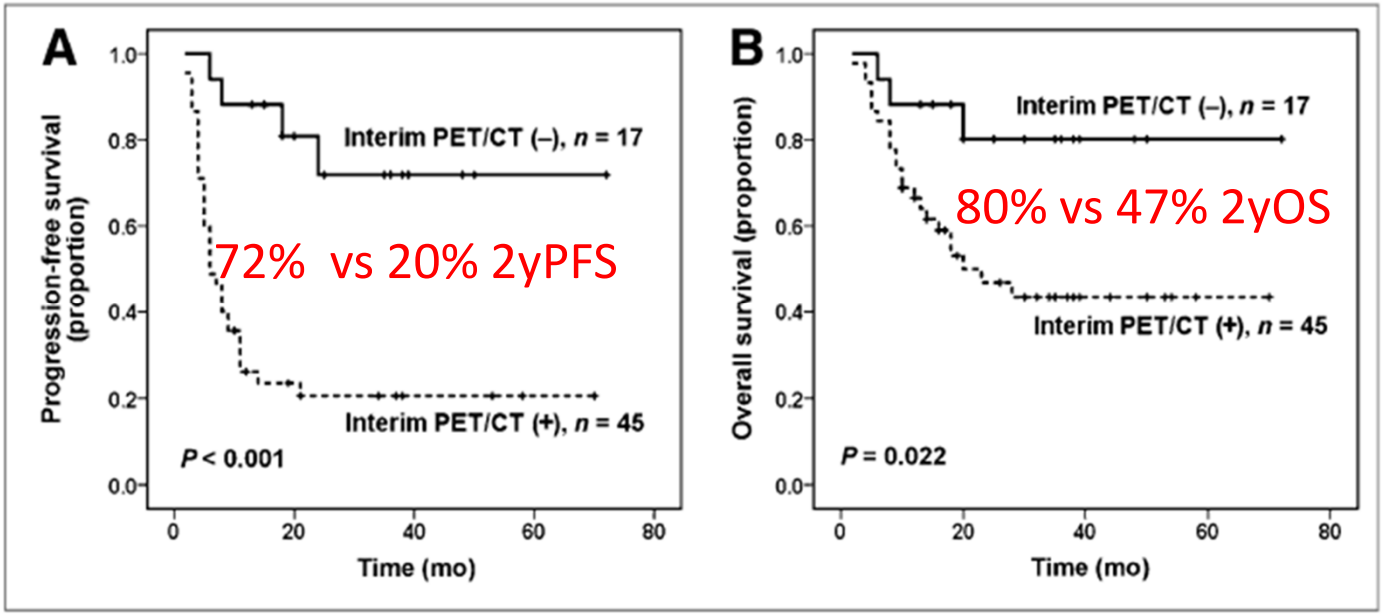
Retrospective study, MFU= 19.5months

- 88 patients with T/NK lymphomas

44NK
3EATL

- CHOP, EPOCH, triple therapy (CHOP-B, IMVP-16,DHAP) or GEMOX
- PET reporting: IHP

interim n=62 (1-4cycles) with 28 non ENKL



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- 88 patients with T/NK lymphomas

44NK
3EATL

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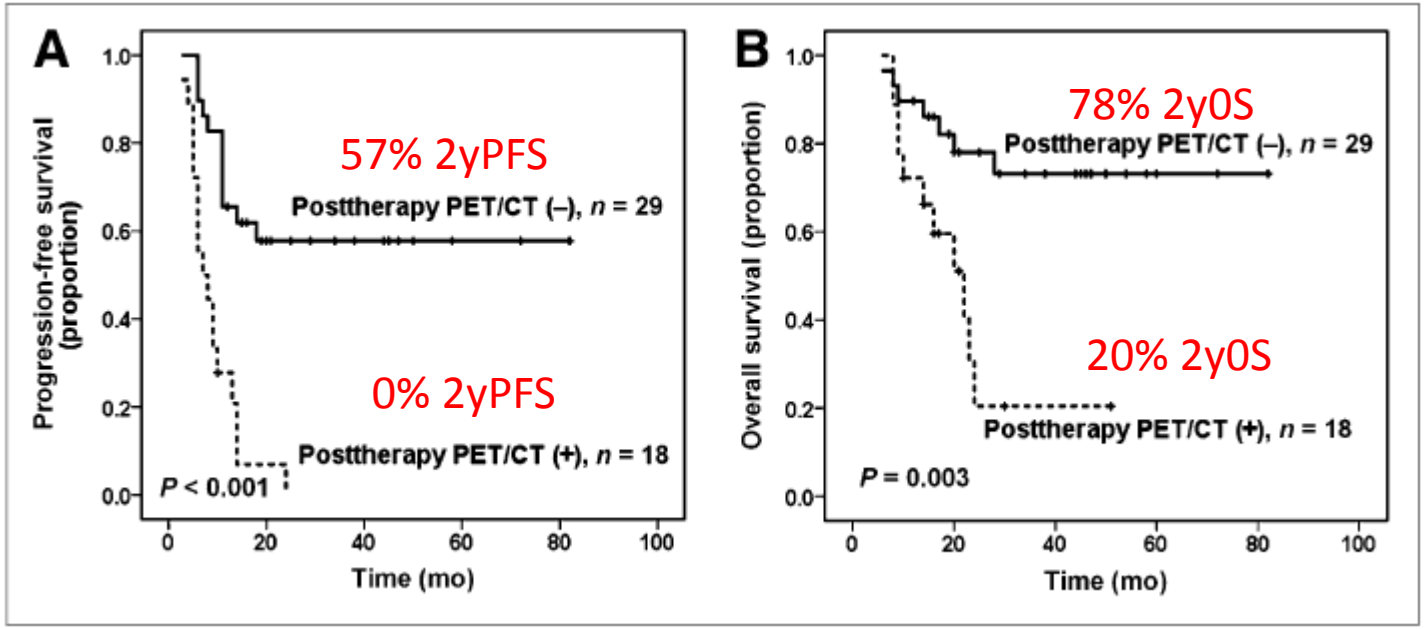
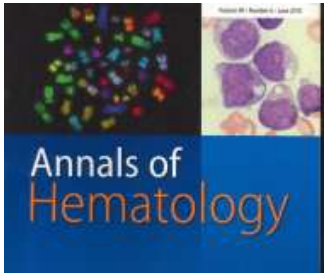
- PET reporting: IHP **Eot PET n=57** (with 30 non ENKL)



Post-therapy ^{18}F-fluorodeoxyglucose positron emission tomography for predicting outcome in patients with peripheral T cell lymphoma

2015

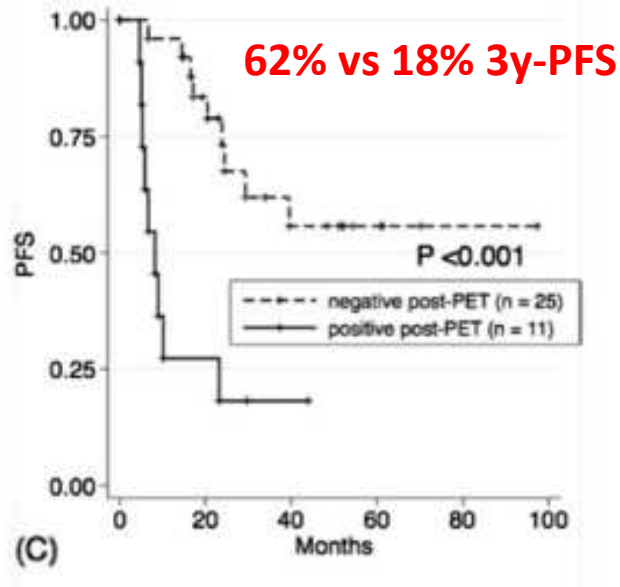


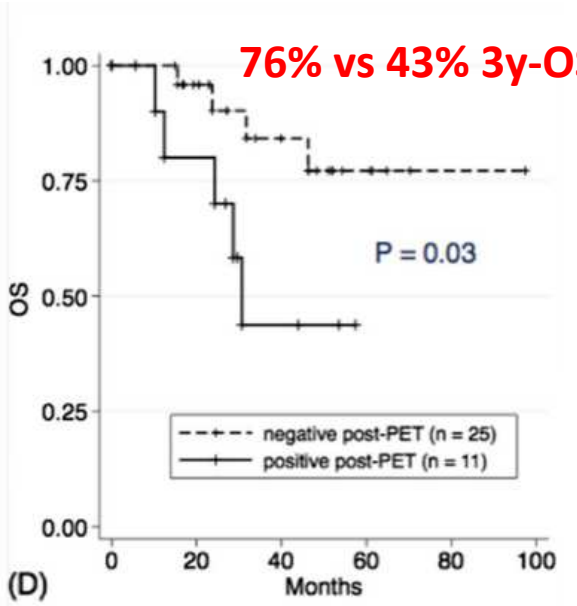
Naoto Tomita · Yukako Hattori · Shin Fujisawa · Chizuko Hashimoto · Jun Taguchi · Hirotaka Takasaki · Rika Sakai · Ukihide Tateishi · Yoshiaki Ishigatsubo

Retrospective study, MFU= 19.5months

- 36 patients : 16 PTCL NOS and 20 AITL
- THP-ADR (83%), THP-COP
- PET reporting: IHP

EoT PET





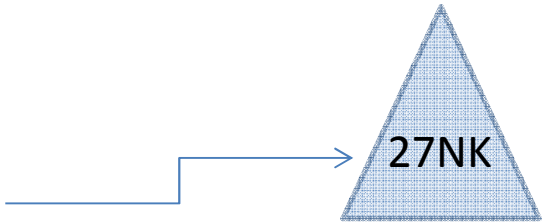
Prognostic significance of interim PET/CT based on visual, SUV-based, and MTV-based assessment in the treatment of peripheral T-cell lymphoma

BMC Cancer

Jung et al, 2015

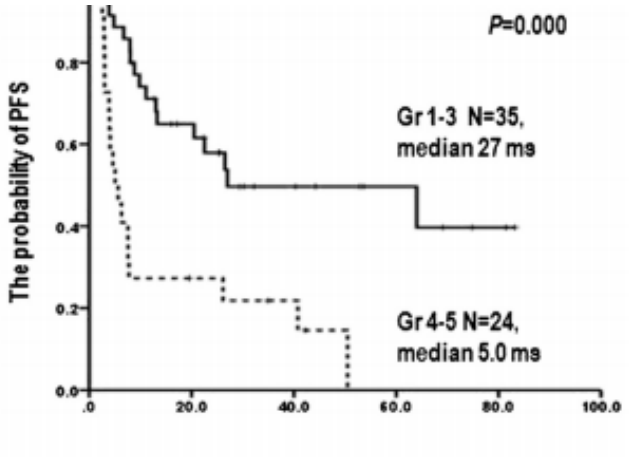
Prospective study, MFU= 40.3months

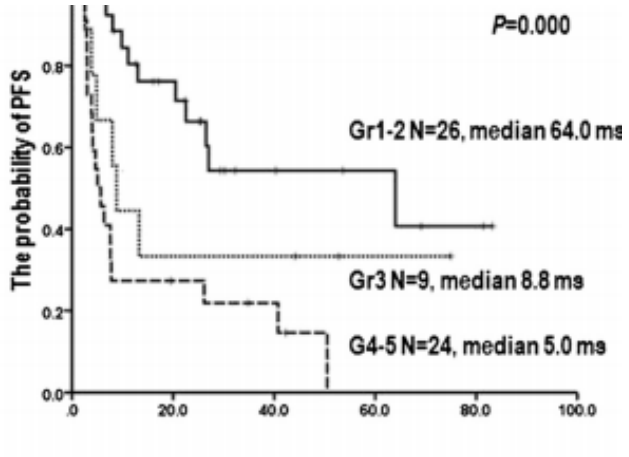
- 63 patients with NK/PTCL
- CHOP/CHOP like regimen
- PET reporting: Deauville 5-PS



interim n=63 (3-4cycles)

median PFS 27 vs 5 months





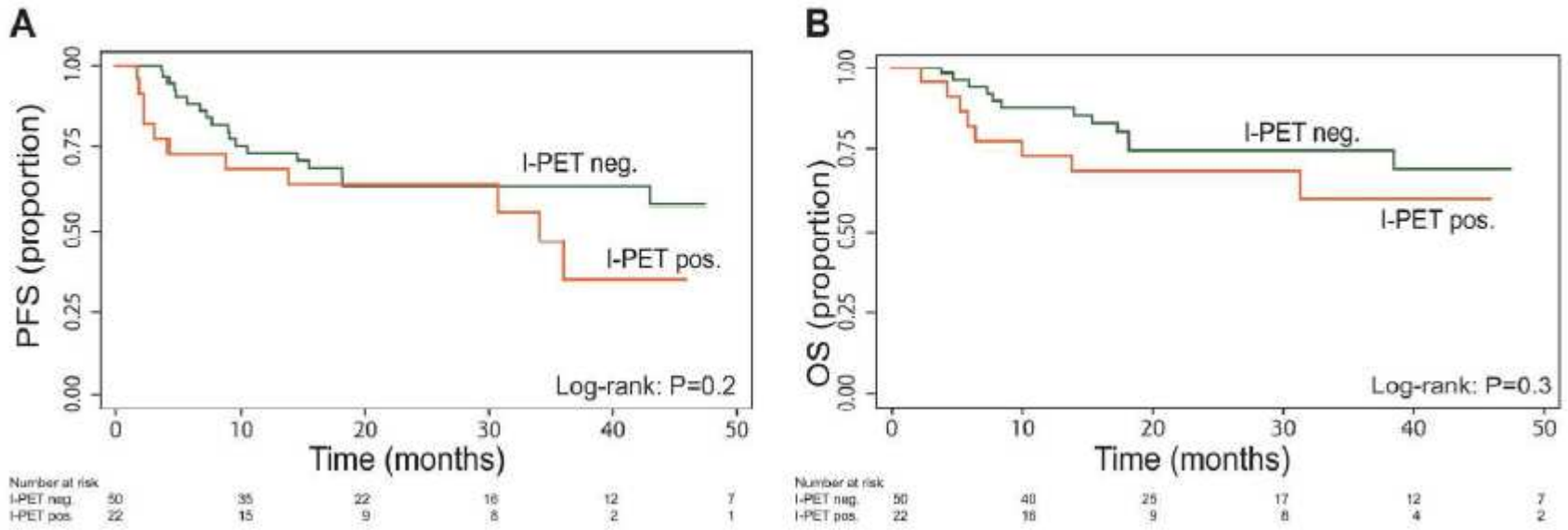
American Journal of Hematology AJH

Utility of interim and end-of-treatment PET/CT in peripheral T-cell lymphomas: A review of 124 patients

Tarec Christoffer El-Galaly ✉, Martin Bjerregård Pedersen, Martin Hutchings, Karen Juul Mylam, Jakob Madsen, Anne Ortved Gang, Martin Bøgsted, Peter de Nully Brown, Annika Loft, Anne Lerberg Nielsen, Helle Westergreen Hendel, Victor Iyer, Lars Christian Gormsen

- 72 PTCL patients; interim PET (2-4 cycles)
- PET reporting: 5 DS

PFS **OS**



Utility of ^{18}fluoro-deoxyglucose positron emission tomography for prognosis and response assessments in a phase 2 study of romidepsin in patients with relapsed or refractory peripheral T-cell lymphoma

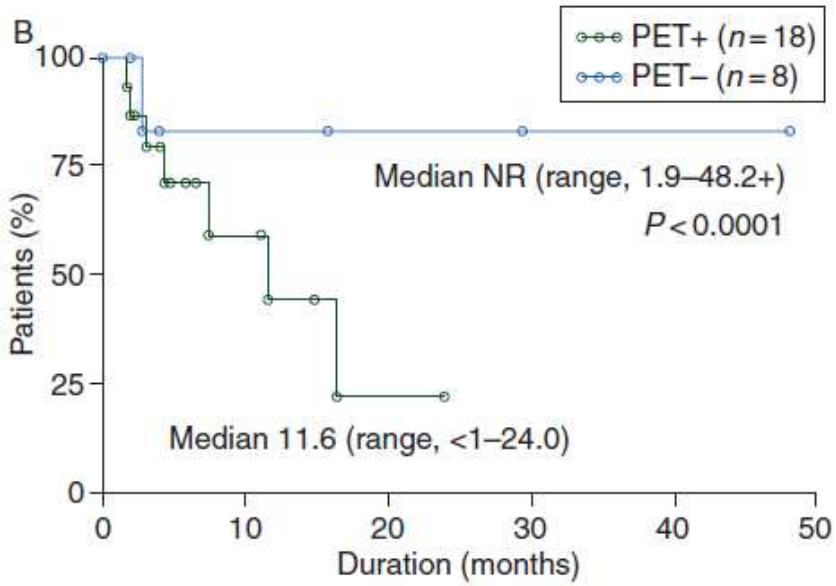
Annals of Oncology
January 2015
Horwtiz *et al.*

Prospective phase 2 study, MFU= 22months

- 130 patients with relapsed/refractory PTCL
- PET reporting :IHP

CT responders:
CR/Cru/PR

PET End of treatment n=26



Year	Study	Treatment	PET criteria	Nb of PTCL	Interim PET	Nb of PTCL	EOT PET
2011	*Cahu et al.* Ann Oncol	100% CHOP	IHP	44	*3-4 cycles* NS	31	NS
2013	*Li et al.* JNM	64% CHOP	IHP	62	*1-4 cycles* PFS, OS	57	PFS ,OS
2013	*Casulo et al.* Leuk Lymphoma	38% CHOP 48% CHOP/ICE	+ if> liver	50	*2-10 cycles* PFS		
2014	*Pellegrini et al.* The oncologist	100% CHOP 21	IHP	36	*3 cycles* PFS,OS		
2015	*Horwitz et al*. Ann Oncol	Relapse/refractory romidepsine	IHP			26	Duration of response
2015	*Jung et al.* BMC	84% CHOP/ CHOP like	5 DS	63	*3-4 cycles* PFS		
2015	*Tomita et al.* Ann Hem	CHOP THP-COP	IHP			36	PFS, OS
2015	*El Galaly et al.* Am. J. Hematol	88% CHOP/ CHOP like	5 DS	72	*2-4 cycles* NS		
2016	*Cordoba et al.* Menton	CHOP/CHOEP	5 DS			29	**PFS, OS**

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2016	*Cordoba et al.* Menton	?	5 DS			50	PFS, OS

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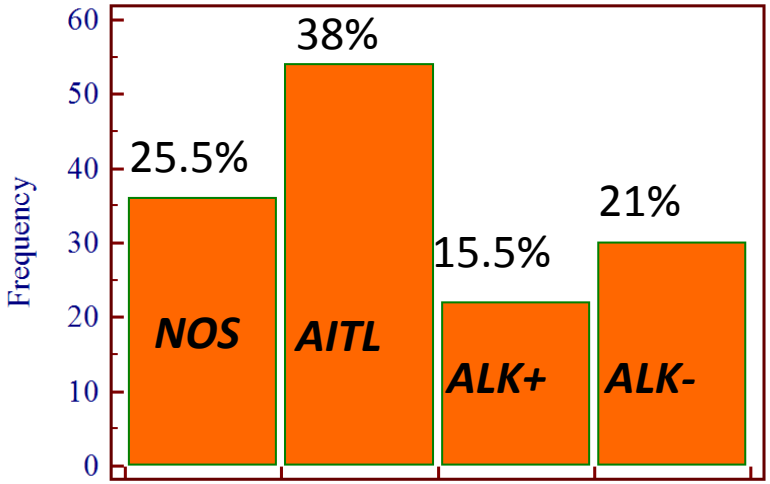
LYSA and Danish cooperative study preliminary results

- 142patients
  - 116 from 6 LYSA centers
  - 26 from the Danish group



- 84% CHOP/CHOP like regimen
- 22% ASCT
- 87% stage 3-4

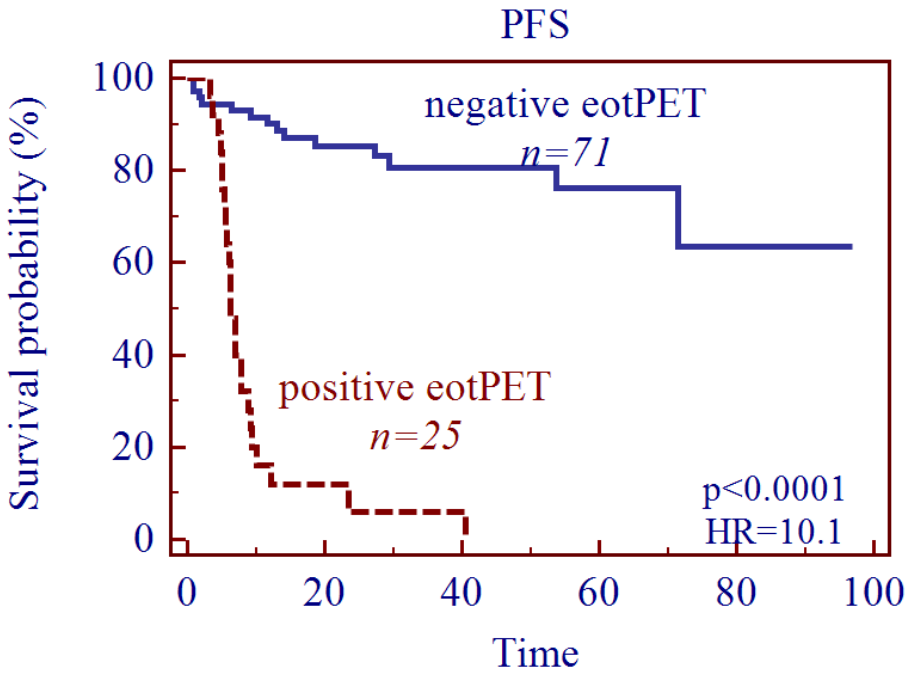
- 32% positive BMB
- 49% IPI 3- 5 ; 47% PIT 2-4

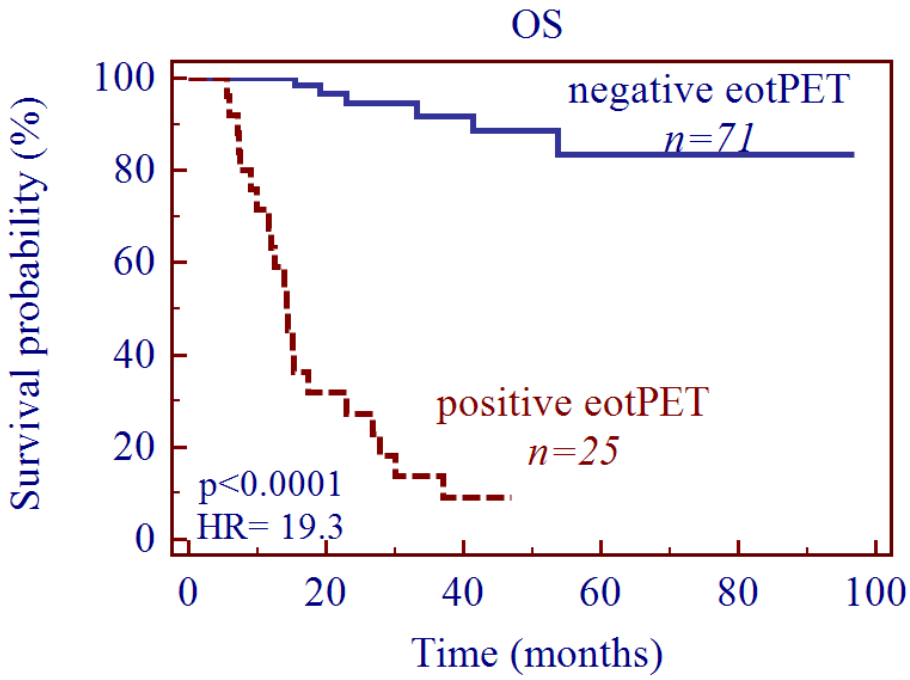
- Median follow up: 2 years
- 51% 2y-PFS, 67% 2y-OS

PET evaluation

- All patients had a baseline PET (n=142)
- Interim PET
  - After 2cycles (n=43)
  - After 3 or 4 cycles (n=95)
- End of treatment PET (n=96)
  - after first line of chemotherapy
- PET reporting: Deauville scale (4-5 = positive)

End of Treatment PET
n=96

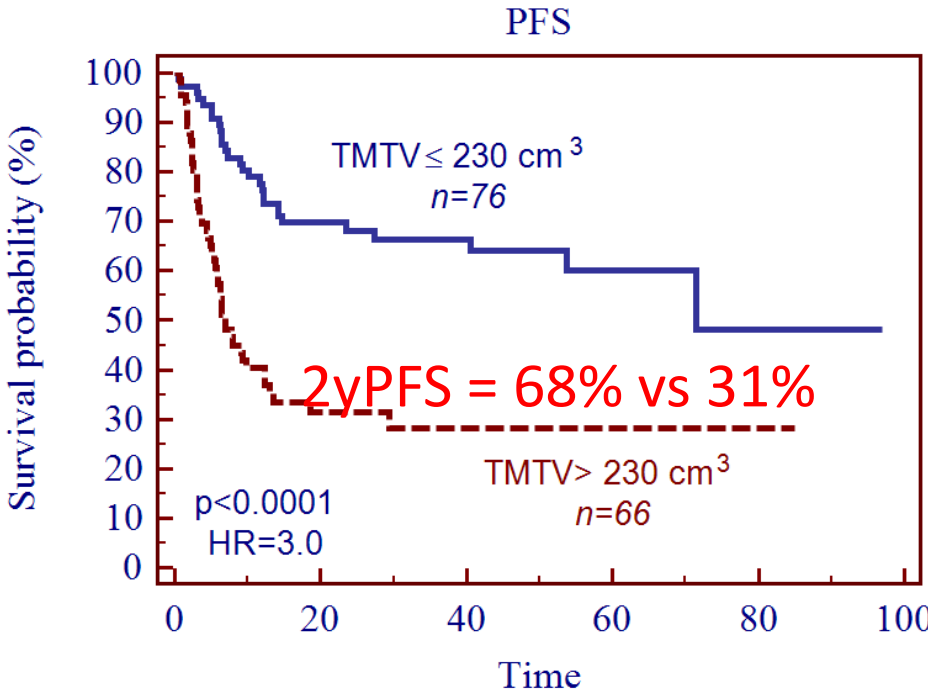


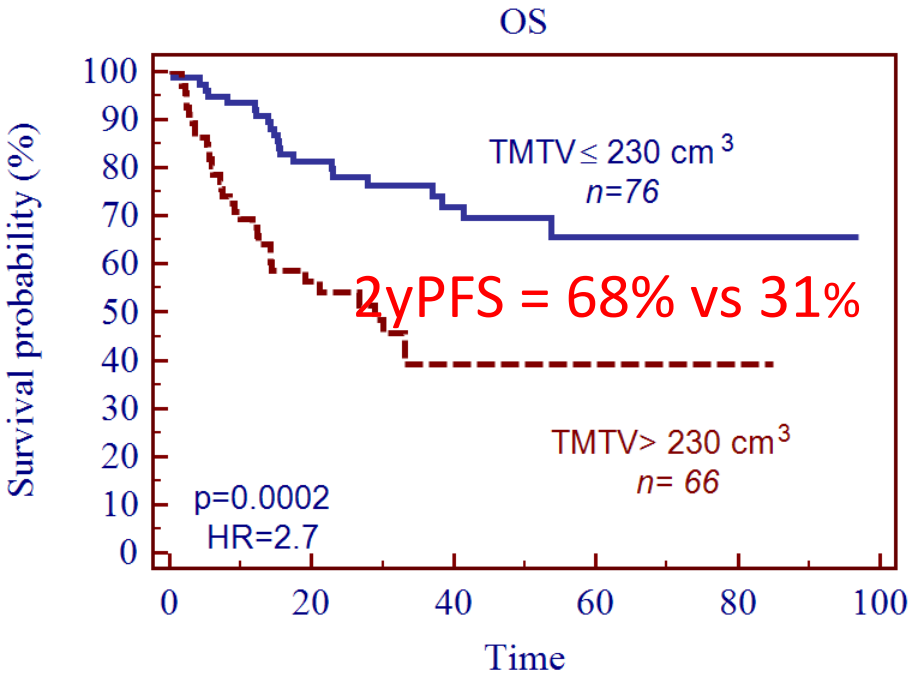


2yPFS : 83% vs 6%

2yOS : 94% vs 27%

Total metabolic tumor volume





Conclusions

- PET/CT is useful **at baseline** for PTCL
  - Staging
  - Prediction of prognostic : TMVT is a promising tool.
    - need to be confirmed on a prospective cohort
    - Validate the TMTV optimal threshold

- Response assessment by PET/CT
  - interim and end of treatment
  - predictive of outcome, as others aggressive lymphoma.
  - independent from IPI or PIT score
  - in all PTCL subtypes except ALCL ALK+

Conclusion

- To be further investigated
  - From retrospective data, increasing the number of patients available (from the different groups participating of the meeting?)
  - From prospective studies with homogenous treatment
    - LYSA trials (Revail, Rochop).

- Mix of different histologies with different microenvironnement
  - Need to explore each subtypes separately
  - To understand the link between
    - FDG uptake and histology
    - PET parameters and molecular bio markers :

    Ex: TMTV and IDH2 in AITL patients.

Thank you for your attention

Acknowledgement : Lars Jelstrup and Johan Lofgren

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CHU
Centre Hospitalier Universitaire
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