PET-CT in Peripheral T-cell Lymphoma: To Be or Not To Be

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So What is the Question(s)?

- What is the role for PET-CT in staging of PTCL?
- What is the role of PET-CT in response assessment of PTCL?
- What is the role for interim PET-CT in PTCL?
- What are the new directions for PET-CT in PTCL management?

Histology (patient numbers)	% FDG-avid
Hodgkin lymphoma (489)	97 - 100
Diffuse Large B cell lymphoma (446)	97 - 100
Follicular lymphoma (622)	91 - 100
Mantle cell (83) Burkitt (24) MZL nodal (14) LL (6)	100
Anaplastic large T-cell lymphoma (37)	94 -100 (27% of cutaneous sites)
Natural killer/T-cell lymphoma (80)	83 - 100
Angioimmunoblastic T-cell lymphoma (31)	78 - 100
Peripheral T-cell lymphoma (93)	86 - 98
MALT (227)	54 - 81
Small lymphocytic lymphoma (49)	47 - 83
Enteropathy type T-cell lymphoma (20)	67 - 100
MZL, splenic (13), unspecified (12)	53 - 67
Mycosis fungoides (24) and Sezary (8)	83 -100 (62% of cutaneous sites)
1° cutaneous anaplastic large T-cell (14)	40-60

Modified from Weiler-Sagie et al JNM 51: 25-30, 2010

PET in Staging of PTCL

- Retrospective analysis
- 95 pts - PET-CT at initial/relapse staging
- Histologies –
  - NOS – 35
  - AITL – 17
  - ALCL +/- - 11/12
  - ATLL – 7
  - NK/T – 10
  - EATL - 3

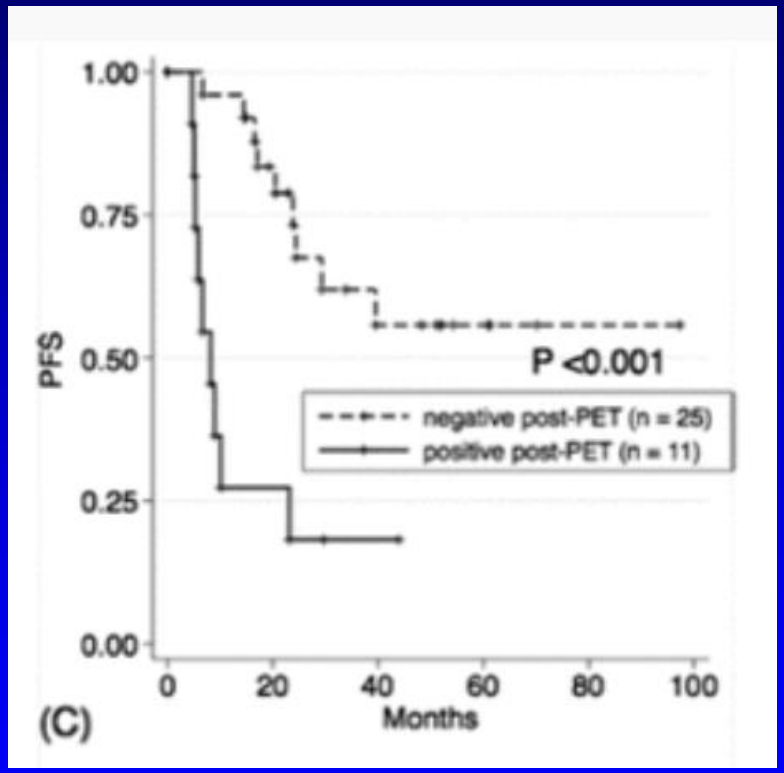
Casulo et al Leuk Lymph 54:2163, 2013

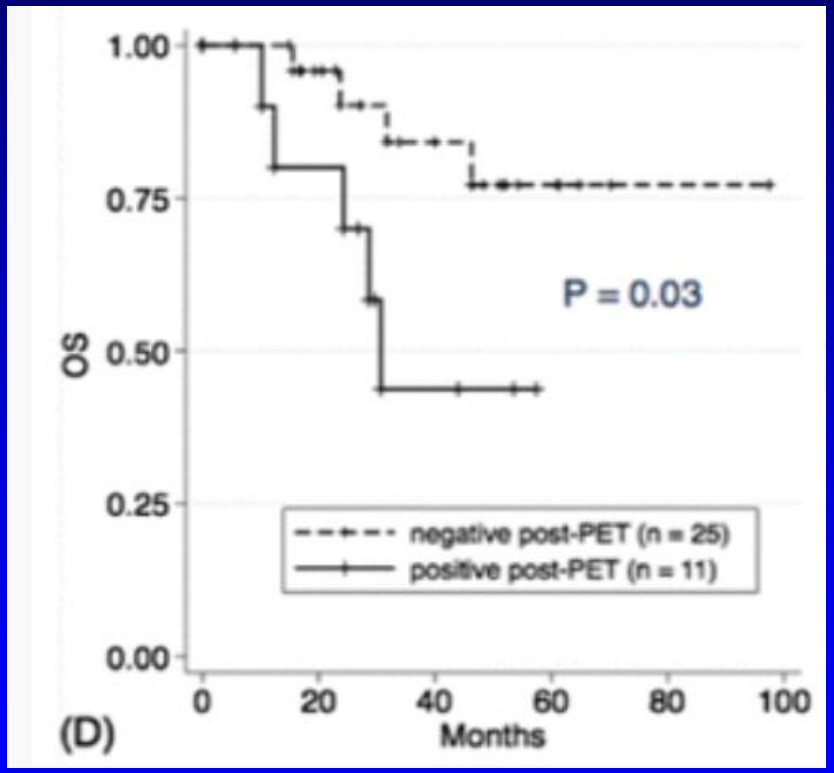
PET in PTCL: Staging

- Pretreatment PET + in 96%
  - PET identified additional sites of disease in 50%
  - Stage changed in only 5.2%
  - PET did not alter treatment plans
- Interim PET after median of 4 cycles
- 29 pts consolidated with BMT or ASCT

Casulo et al Leuk Lymph 54:2163, 2013

Prognosis BY PostTx PET-CT





Tomita et al, Ann Hematol 94:431, 2015

PET in Mature T/NK NHL (n=54)

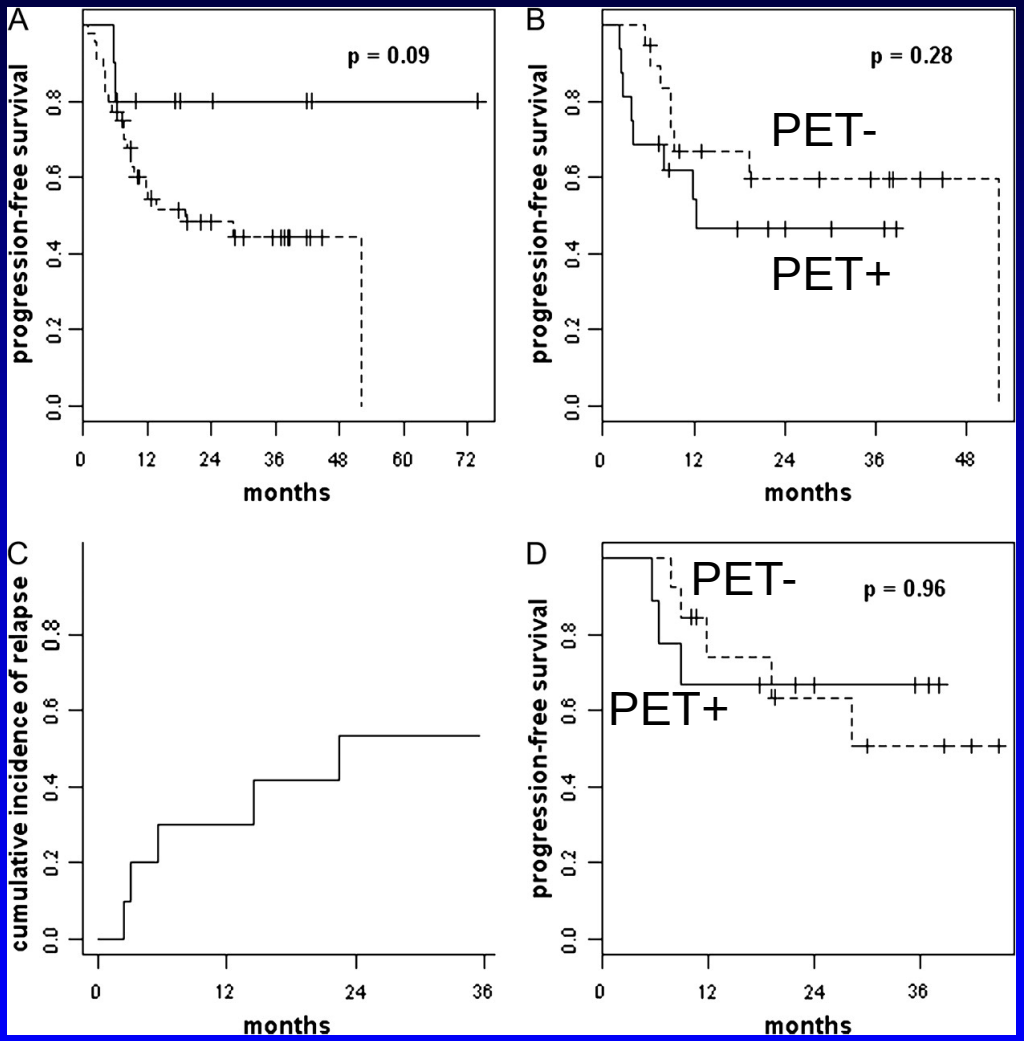
- Initial PET positive in 54/54 pts
- Interim PET negative in 25/44 pts
- Posttreatment 19/31 negative (CR)
- ALK+ ALCL - 4 yr PFS 80%, NPV 83%
- ALK- T/NK – 4 yr PFS 59% for negative interim scan vs 46% with positive scan (NS)
- 4 yr PFS for neg posttreatment scan 51% vs 67% for positive scan (NS)
- 4 yr incidence of relapse 53% with neg scan in ALK-T/NK

Cahu et al, Ann Oncol, 22:705, 2011

Outcome of patients with T/NK

ALK+ vs -

PET- Post Tx



Interim PET
ALK negatives

PostTx PET
ALK negatives

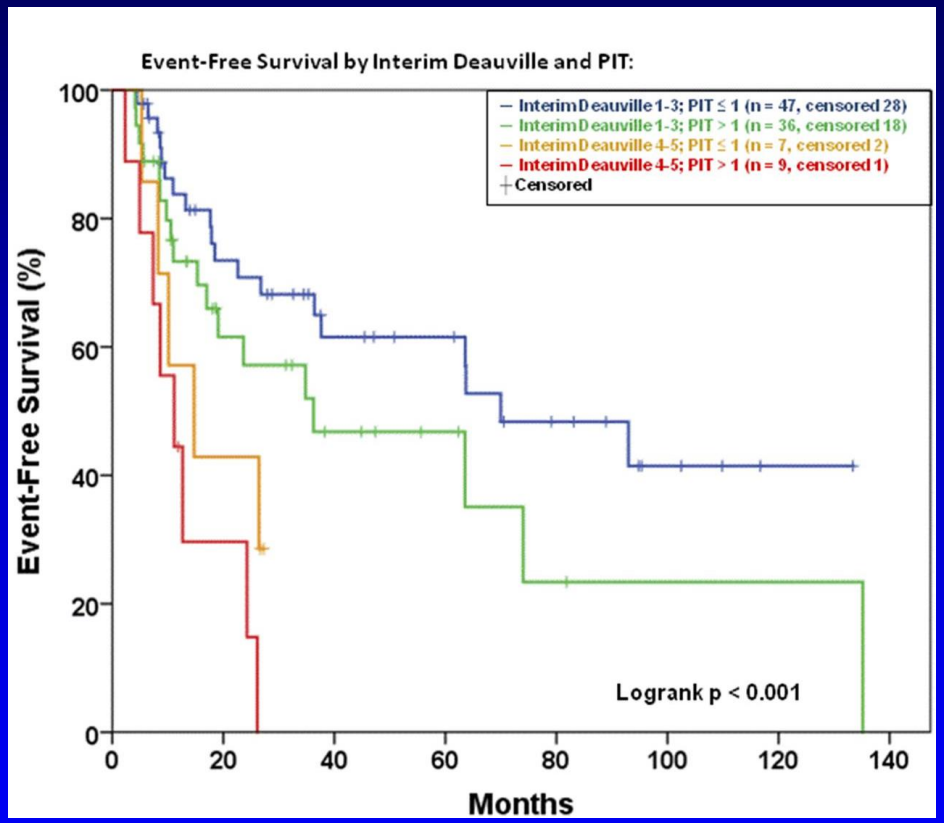
Cahu et al, Ann Oncol, 22:705, 2011

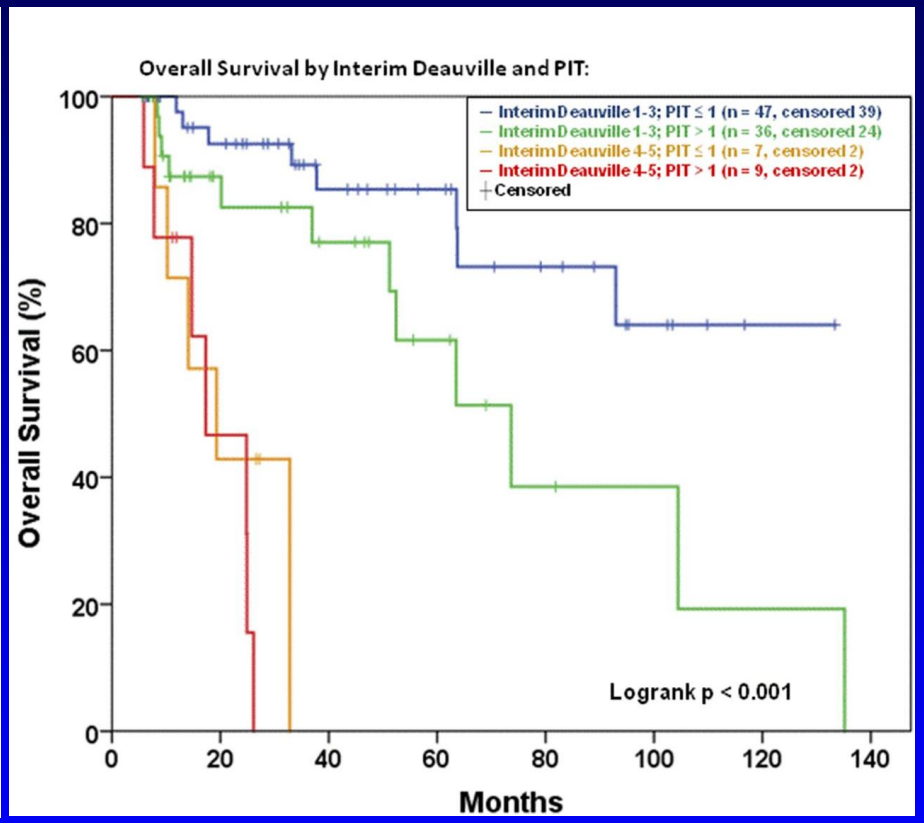
Interim PET in PTCL Using DS

- Retrospective analysis of PTCL treated with CHOP/CHOP-like
- 112 pts in data base: NOS (40), AITL (49), ALK- ALCL (23)
- 99 had interim PET, 90 post cycle 6
- Better predictor compared with PIT score

Mehta-Shah et al. Blood 2016;128:186

Outcome of PTCL by DS and PIT



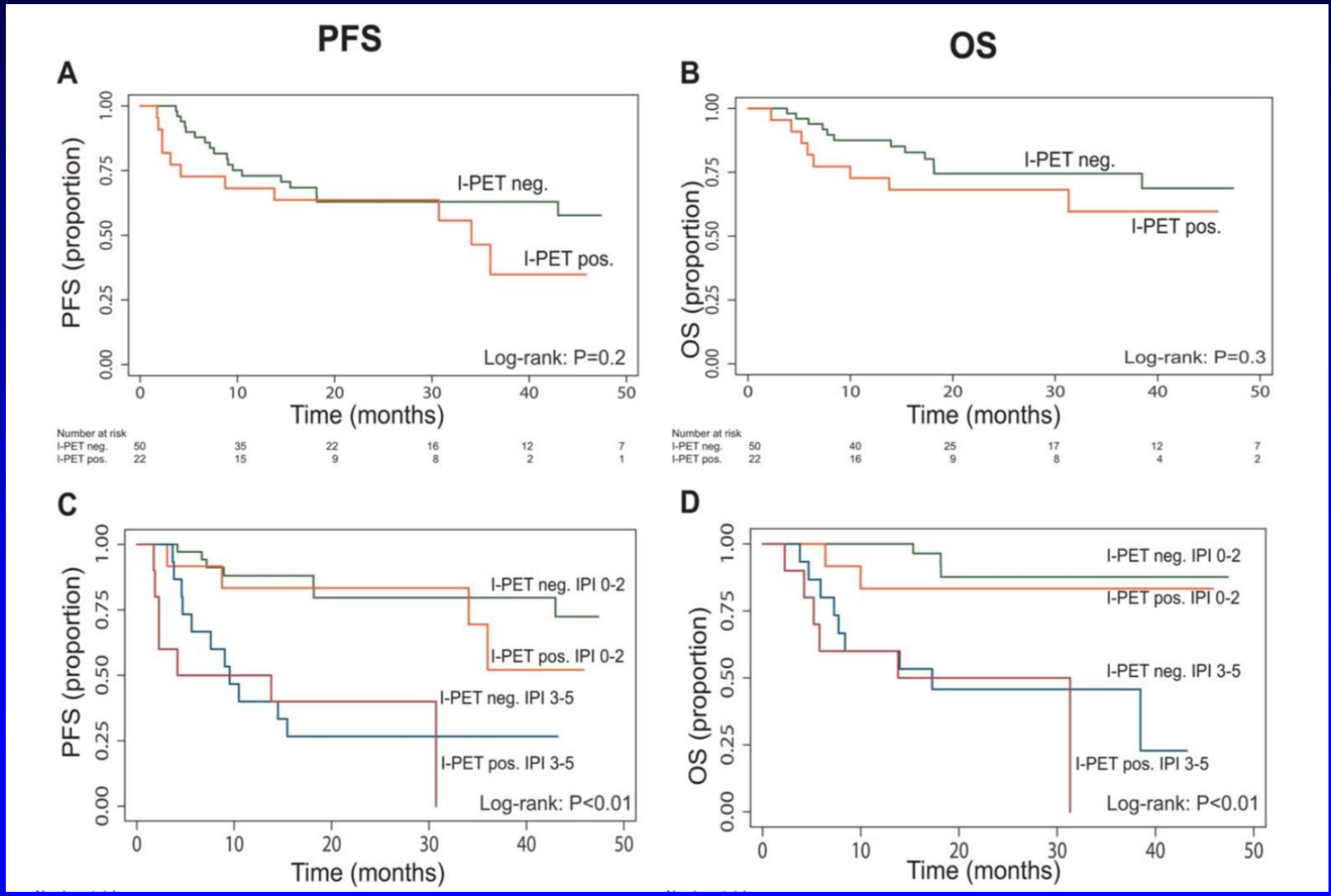


Neha Mehta-Shah et al. Blood 2016;128:186

Interim PET in PTCL

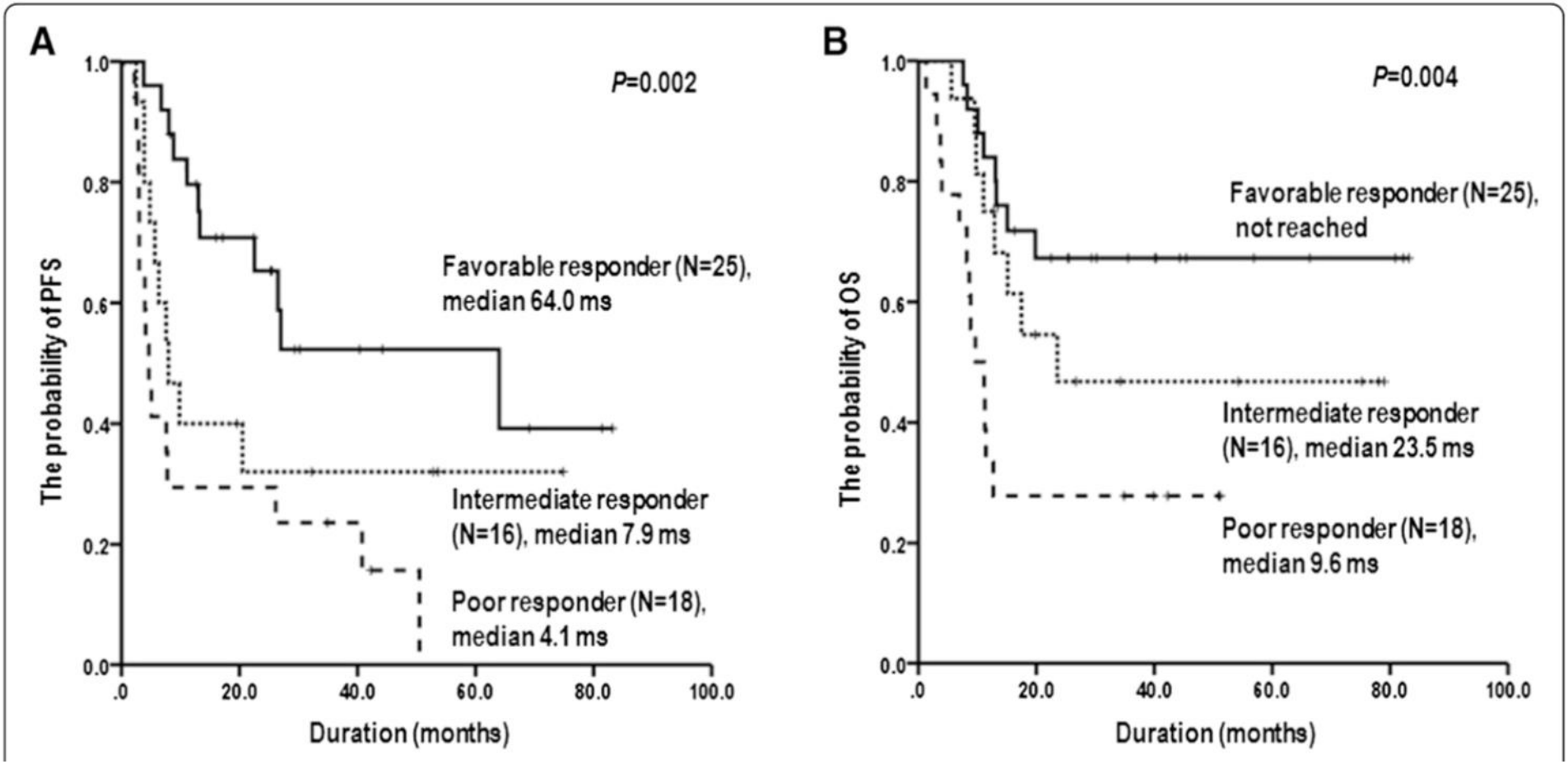
Report	Pts	PFS: I-PET- vs I-PET+	OS: I-PET- vs I-PET+
Cahu (‘11)	54	69% vs 49% (p=.10 @ 4 y)	76% vs 47% (p=.16 @ 4y)
Casulo (‘13)	50	63% vs 25% (p=.03 @ 3 y)	65% vs 48% (p=.17 @ 3y)
Li (‘13)	88	72% vs 21% (p<.001 @ 2 y)	80% vs 47% (p=.02 @ 2y)
Pellegrini (‘14)	34	73% vs 17% (p=.02 @ 3 y)	79% vs 21% (p=.02 @ 3 y)

Interim PET Using 5-PS (n=124)



El-Galaly Am J Hematol 90:975, 2015

Prognostic Significance or Interim PET-CT Based on Visual, ΔSUV, ΔMTV*



* Favorable – 0; intermediate – 1,2; poor - 3

Jung et al BMC Cancer 15:198, 2015

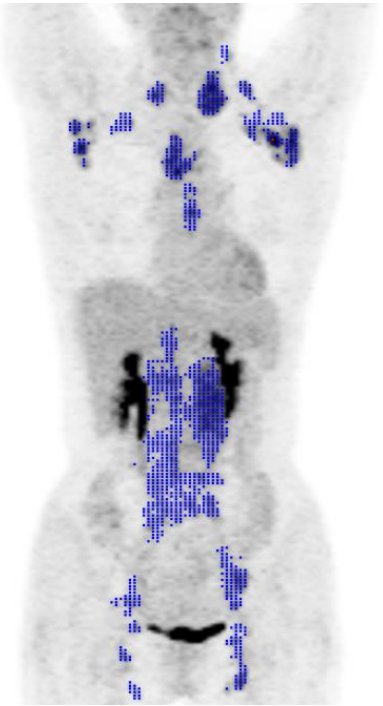
Baseline TMTV in PTCL

- Retrospective analysis of 108 PTCL pts
  - 27 NOS
  - 43 AILT
  - 38 ALCL
- All received anthracycline-based tx
- TMTVo – 41% SUV based threshold
- MVA – only TMTV predicted PFS/OS
- Better when combined with PIT

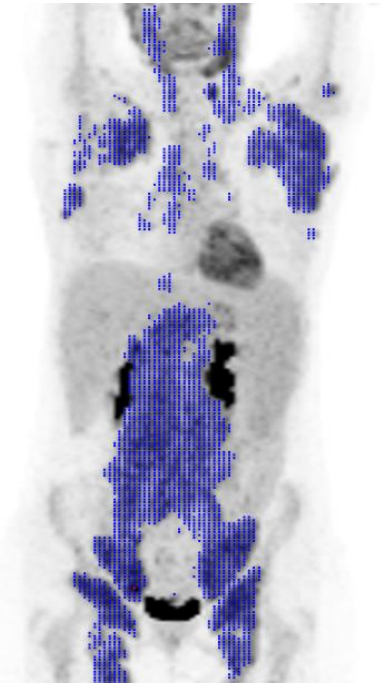
Cottereau et al Ann Oncol 27:719, 2016

Examples of TMTV

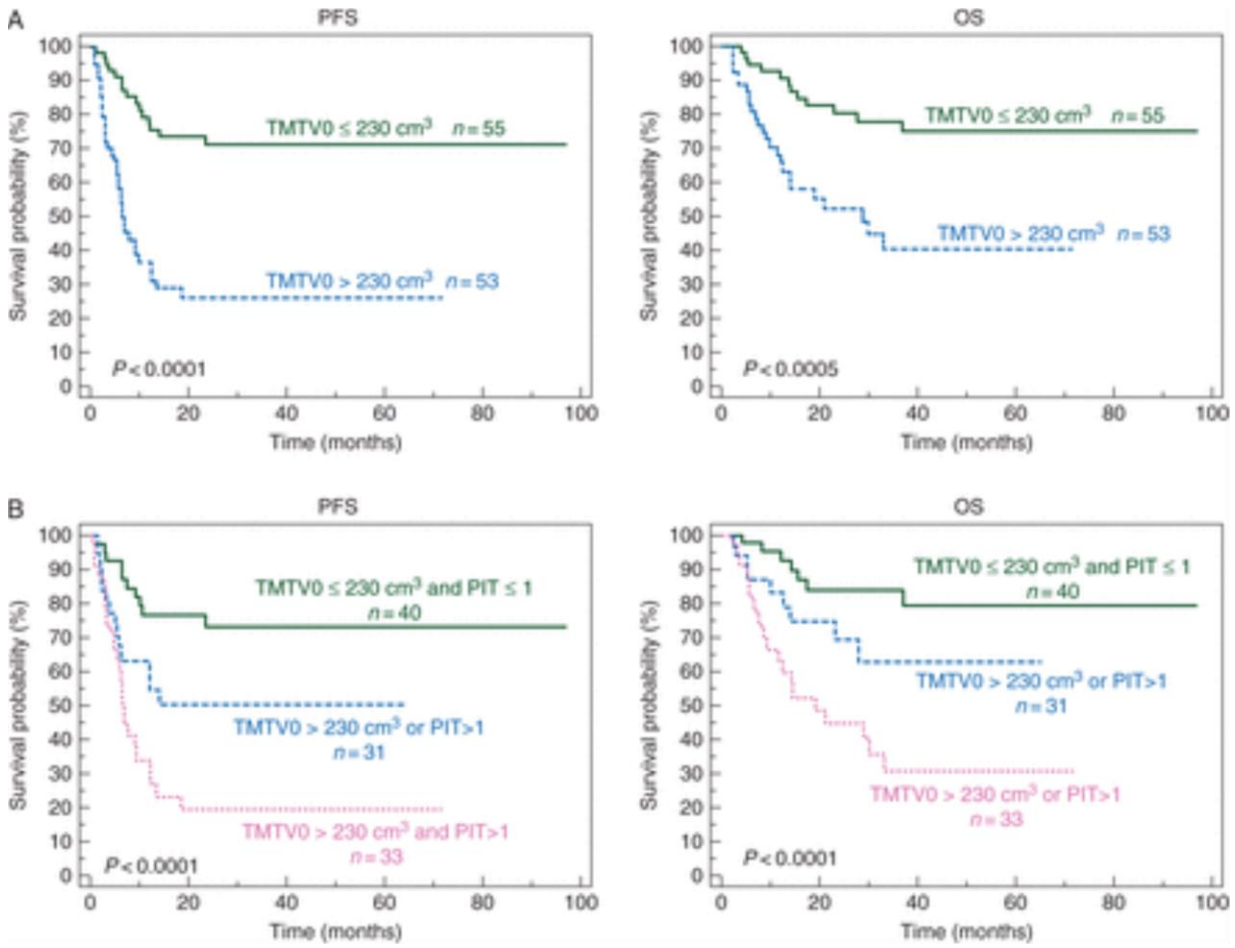
TMTV≤510cm^3



TMTV>510cm^3



Cut off: 510cm^3



Prognostic value of baseline total metabolic tumor volume (TMTV0) measured on FDG-PET/CT in patients with peripheral T-cell lymphoma (PTCL)†

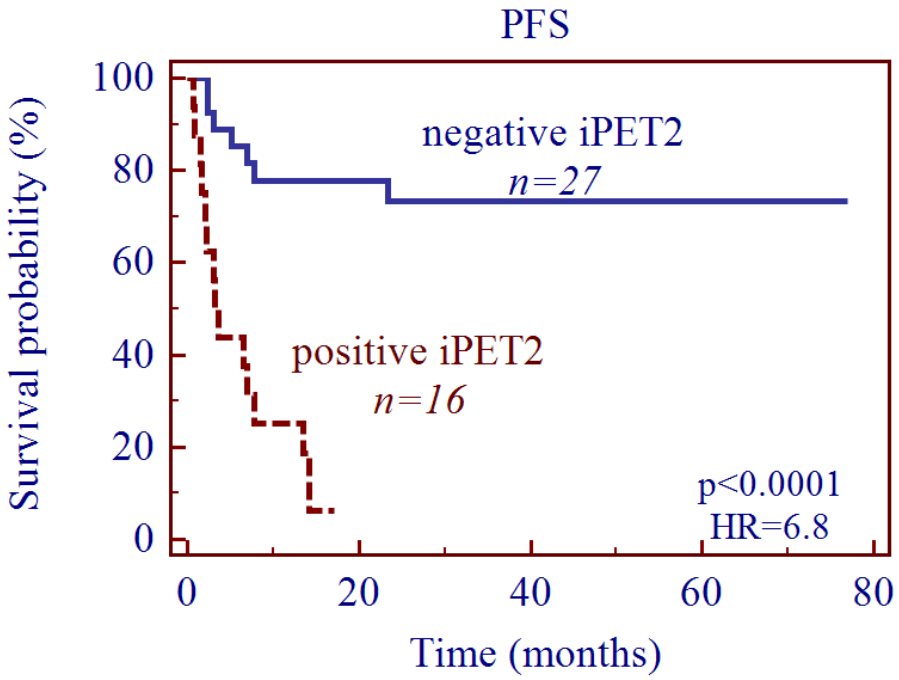
Cottereau et al, Ann Oncol. 2016;27(4):719-724. doi:10.1093/annonc/mdw011

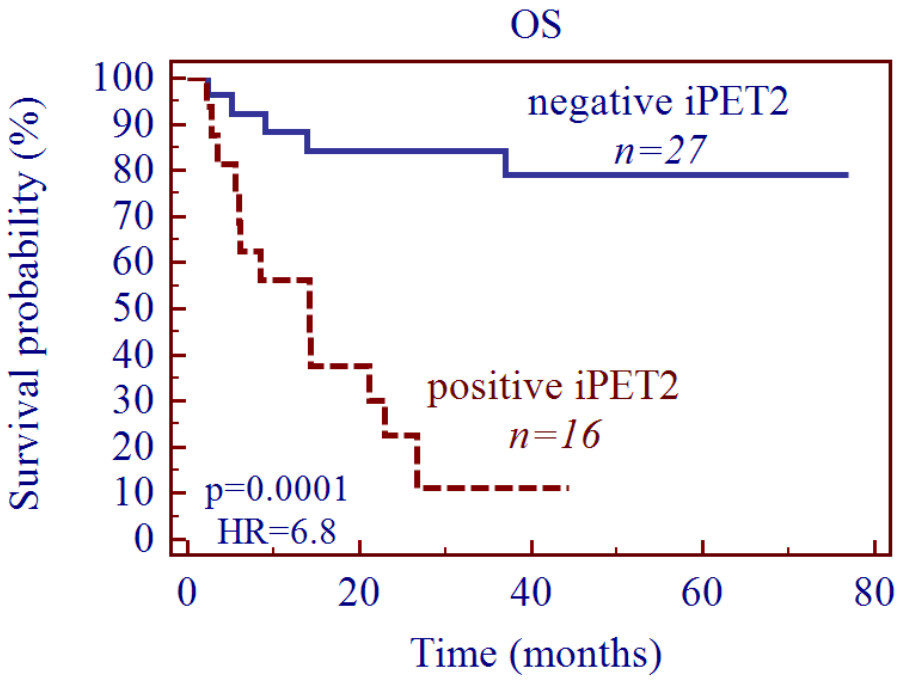
Baseline MTV + PET Response in PTCL

- 142 pts with nodal PTCL + baseline PET-CT
- Treated with CHOP/CHOP-like
- Interim PET-CT
  - 43 after 2 cycles
  - 95 after 3 or 4 cycles
- EOT PET-CT 96 pts
- Response assess by D-5PS
- Median follow-up 43 months

Cottereau J Nucl Med 59:589, 2018

Interim PET 2
n=43



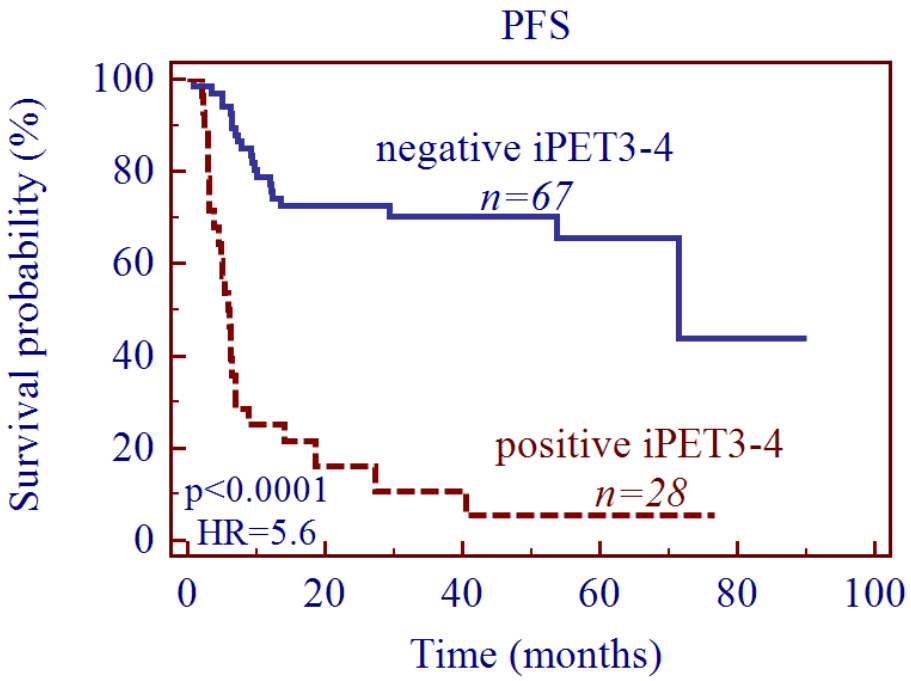


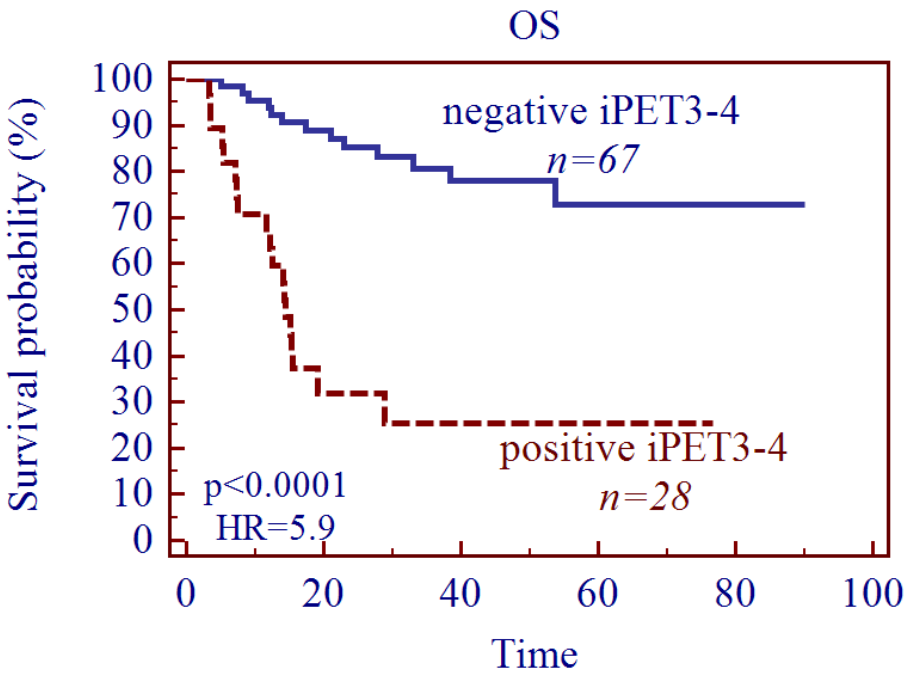
2y-PFS : 73% vs 6%

2y-OS : 83% vs 30%

Interim PET 3-4

n=95 (41 after C3, 54 after C4)

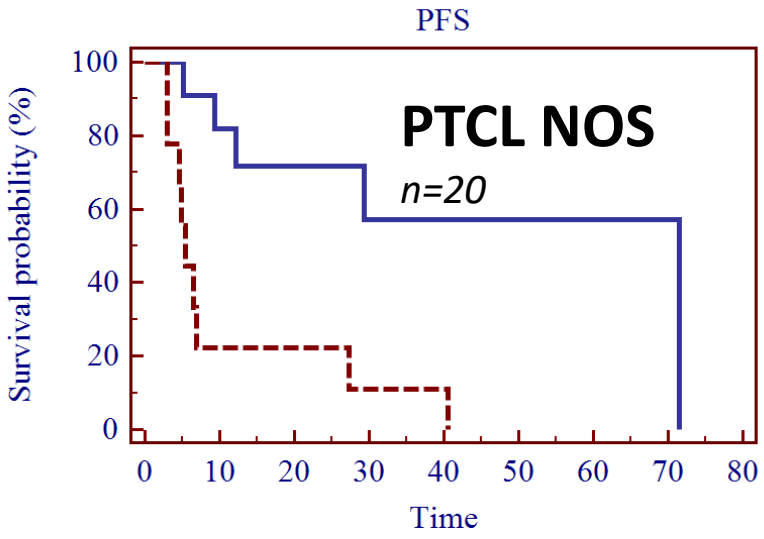


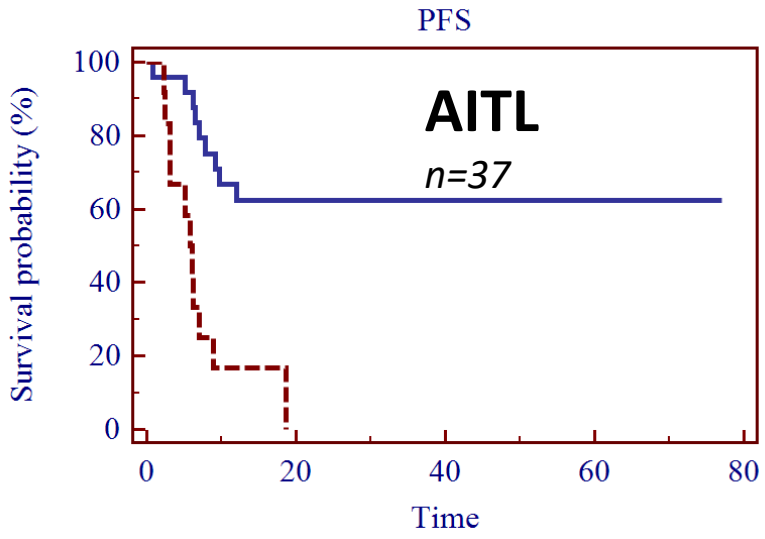


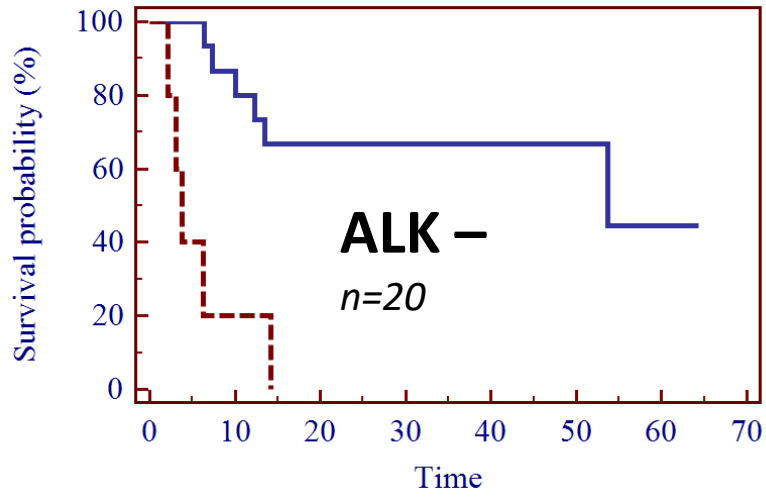
2y-PFS : 72% vs 10%

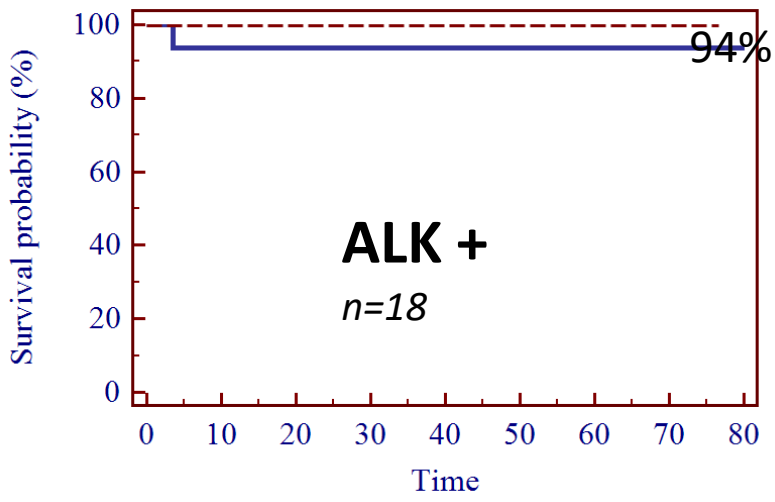
2y-OS : 85% vs 30%

Interim PET prognostic value
According to each histology subtypes

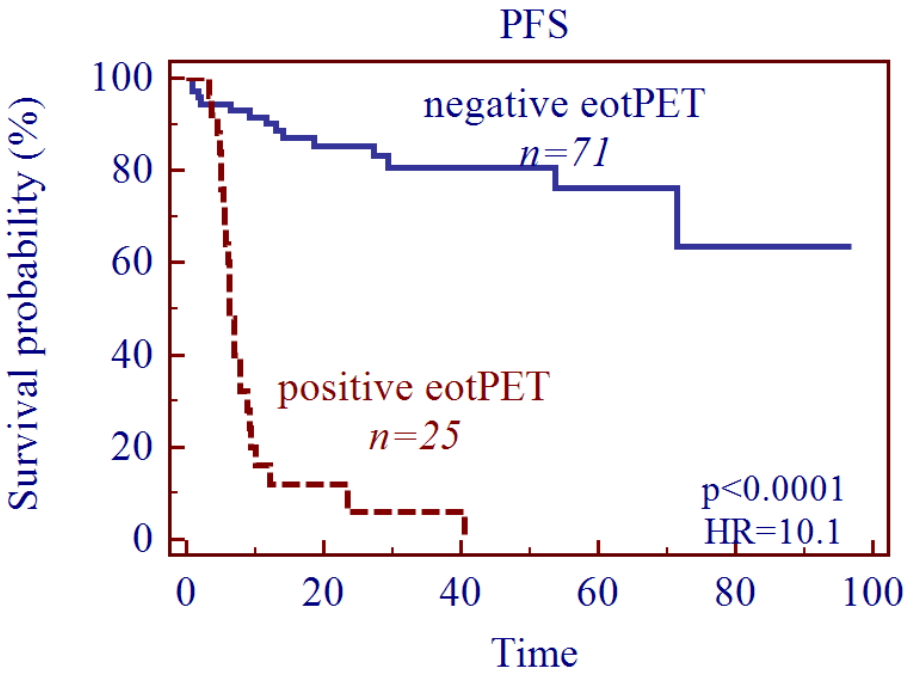


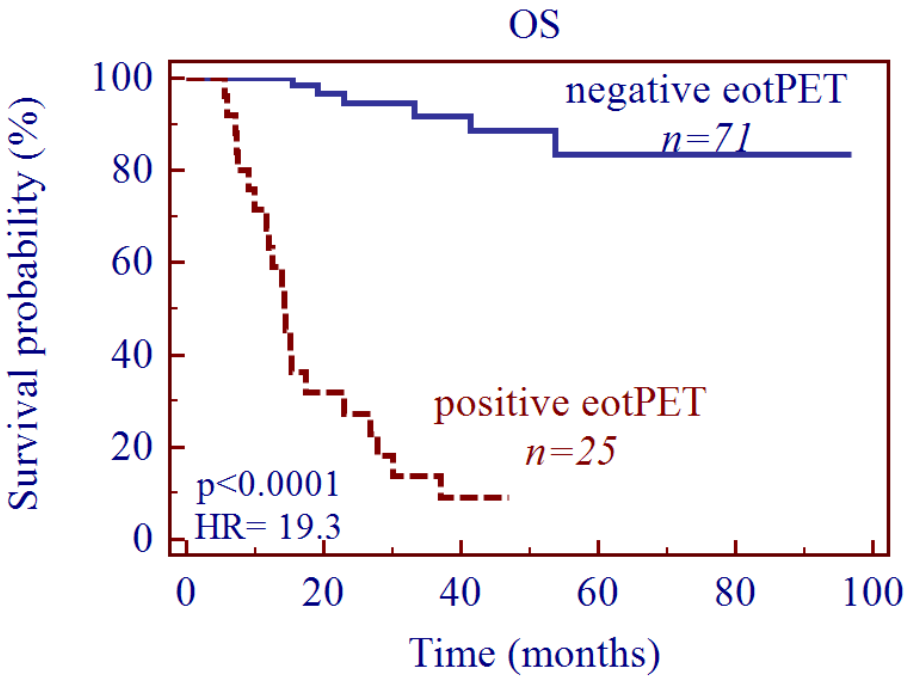






End of Treatment PET
n=96



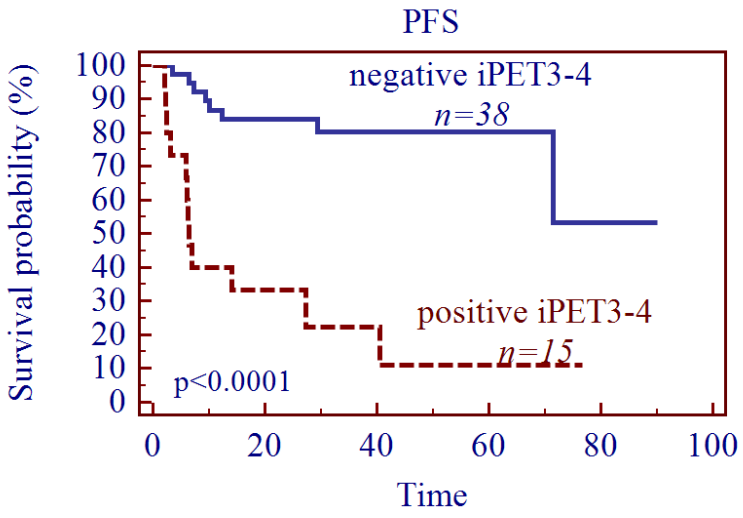


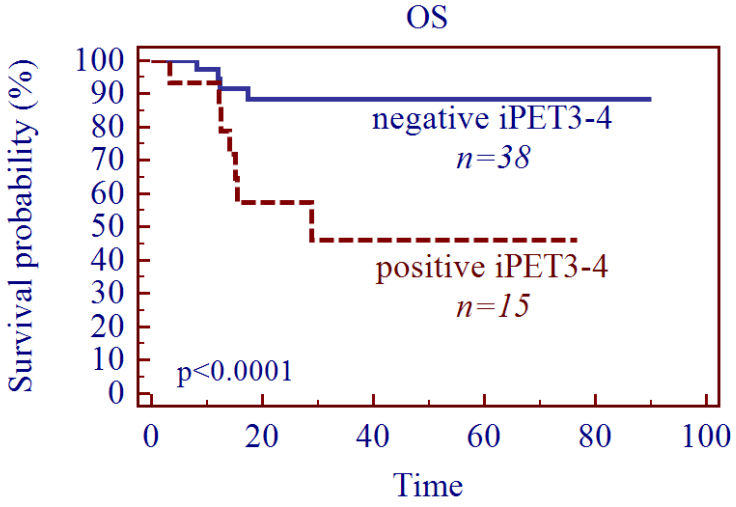
2yPFS : 83% vs 6%

2yOS : 94% vs 27%

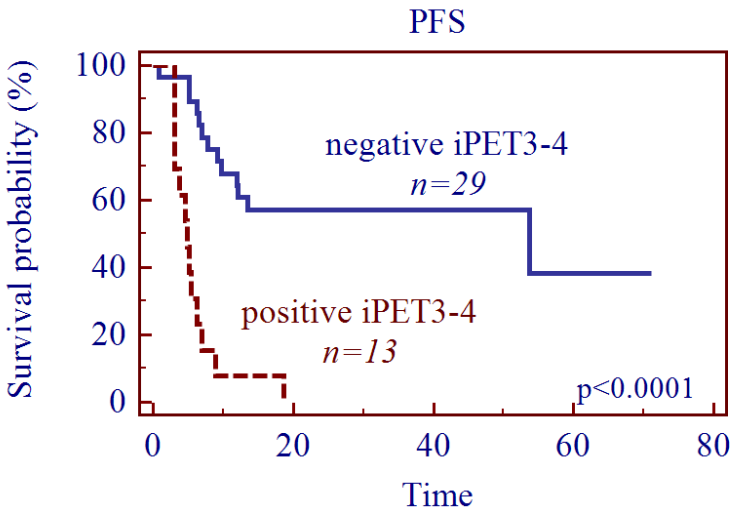
PFS/OS according to IPI and interim PET

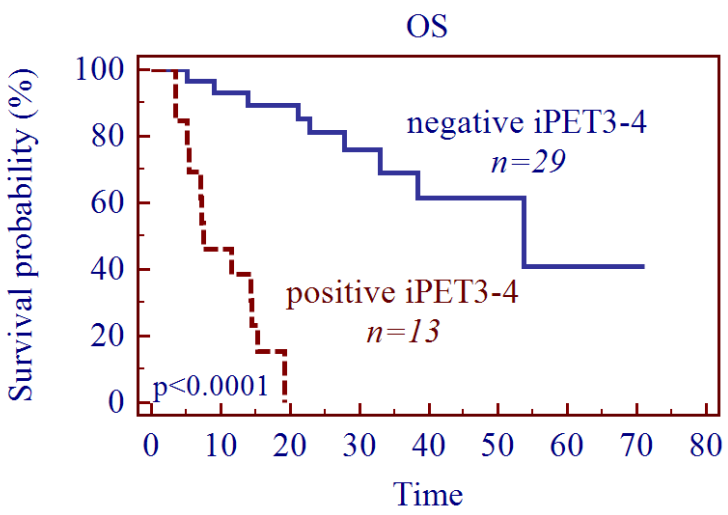
Low IPI (0-1-2)





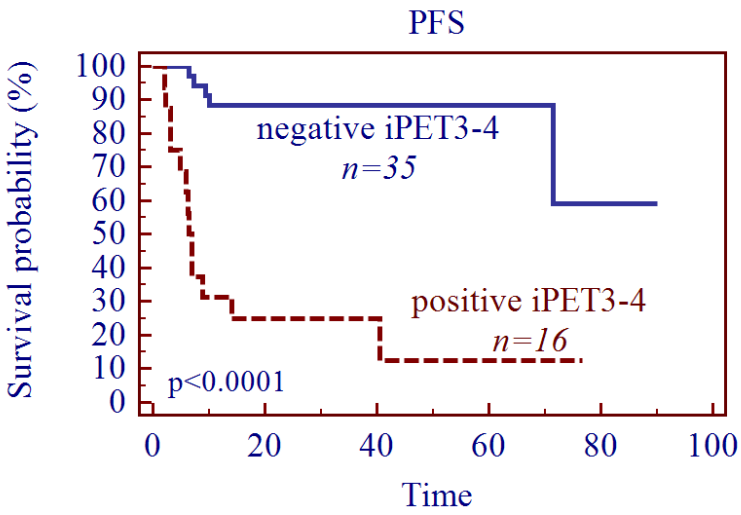
High IPI (3-4-5)

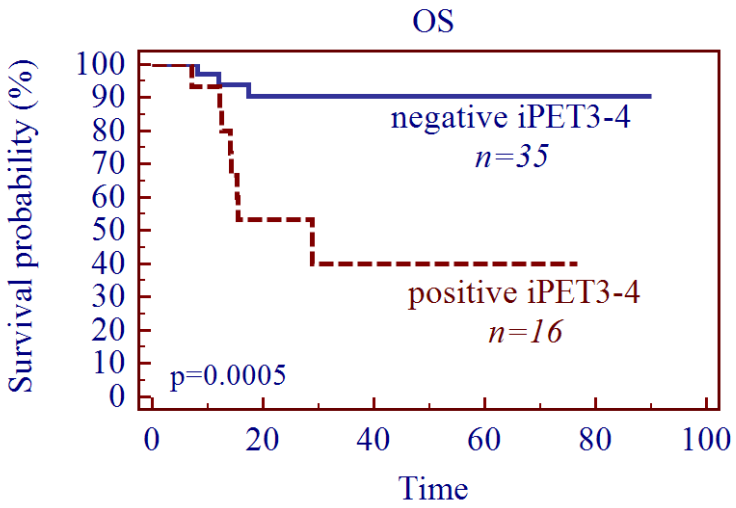




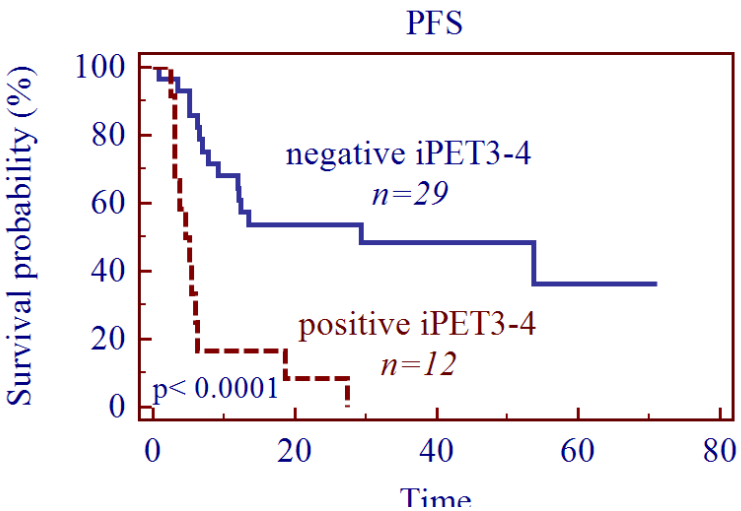
PFS/OS according to PIT and interim PET

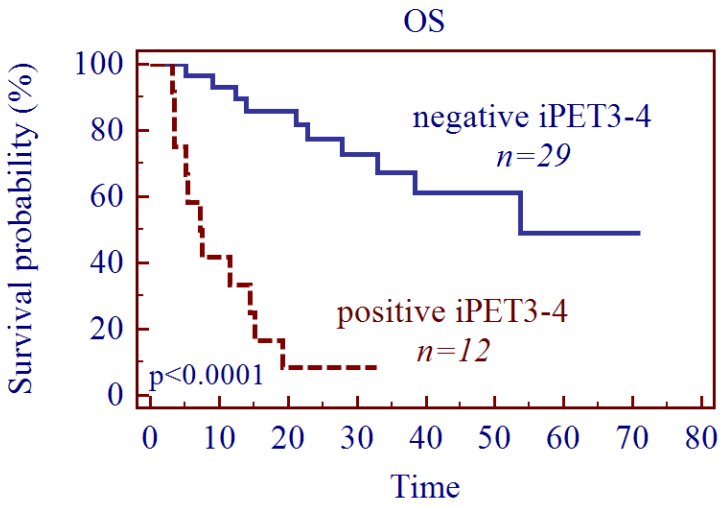
Low PIT (0-1)



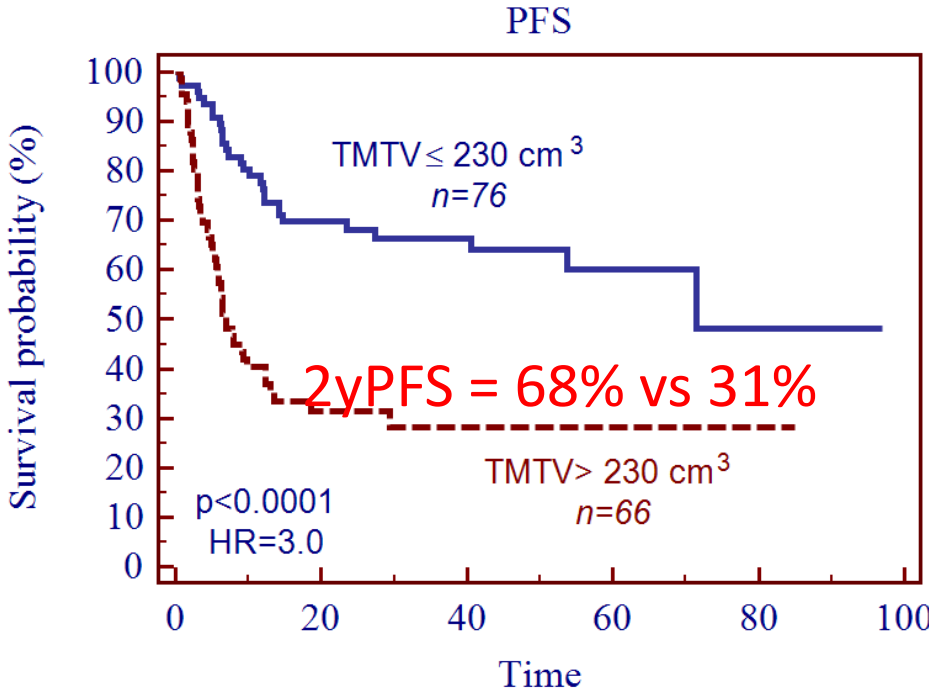


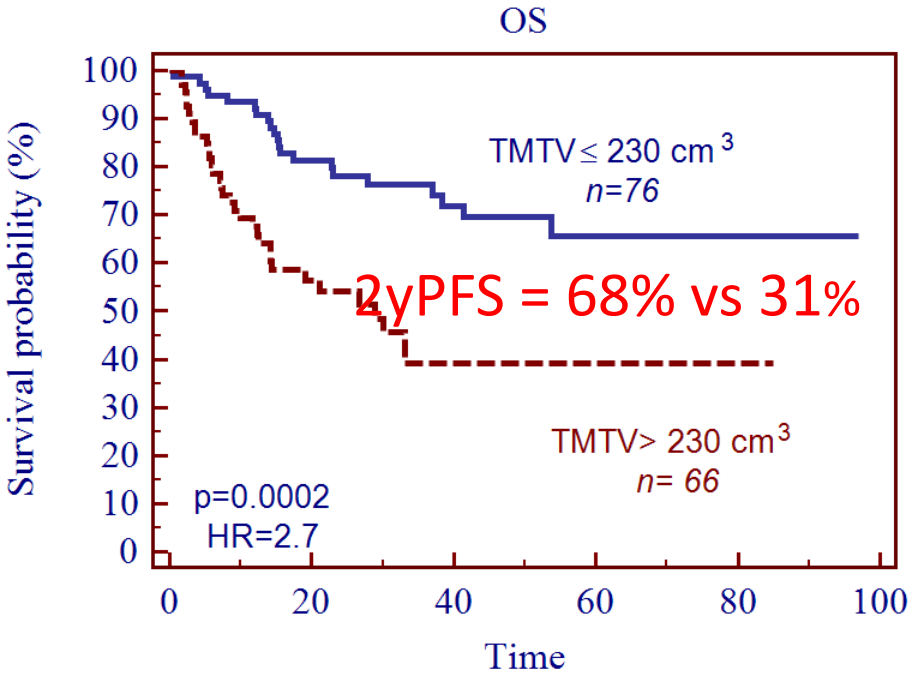
High PIT (2-3-4)





Total metabolic tumor volume





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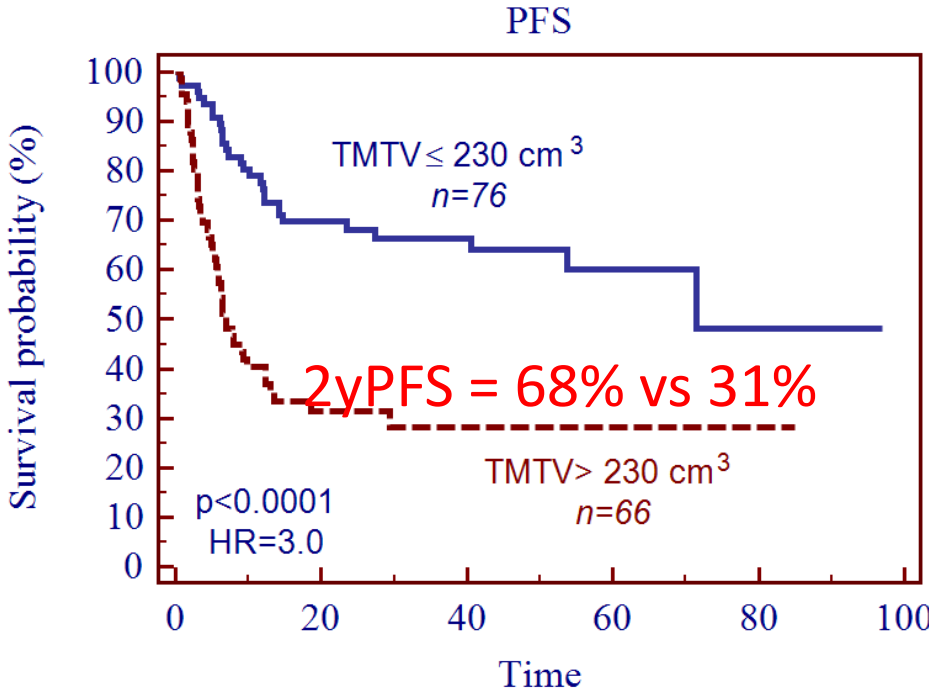
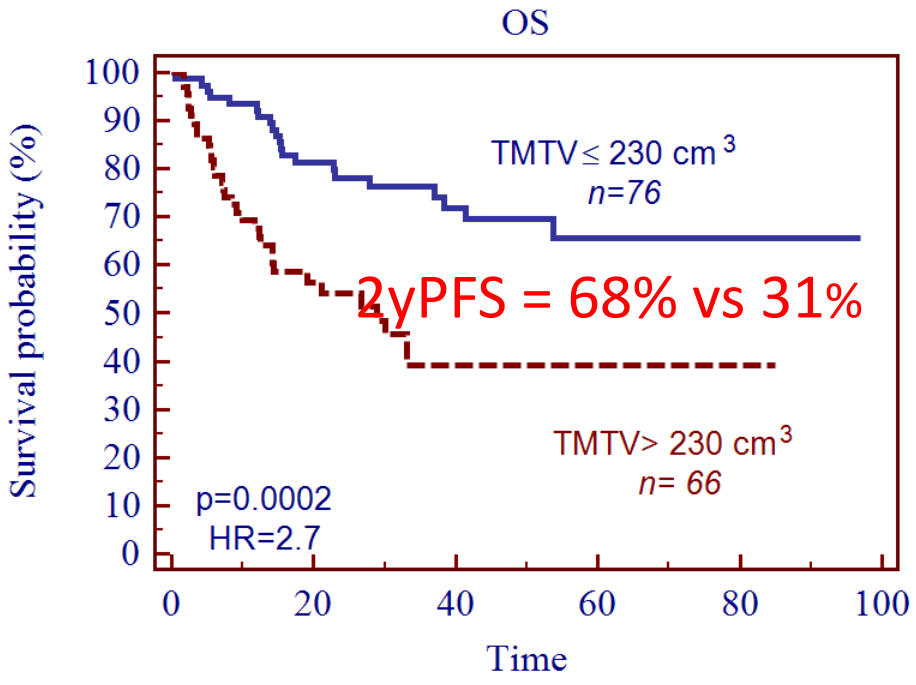
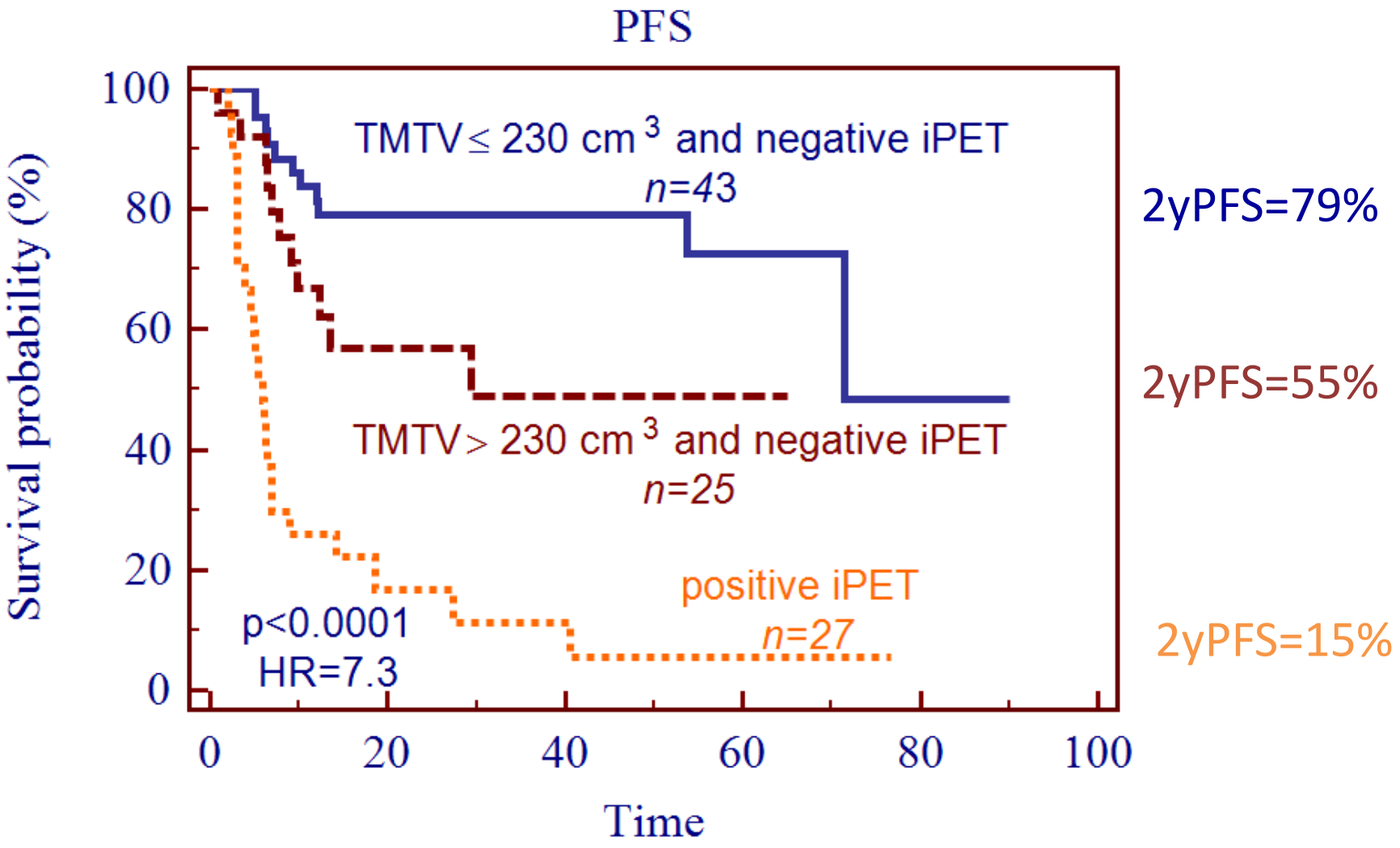


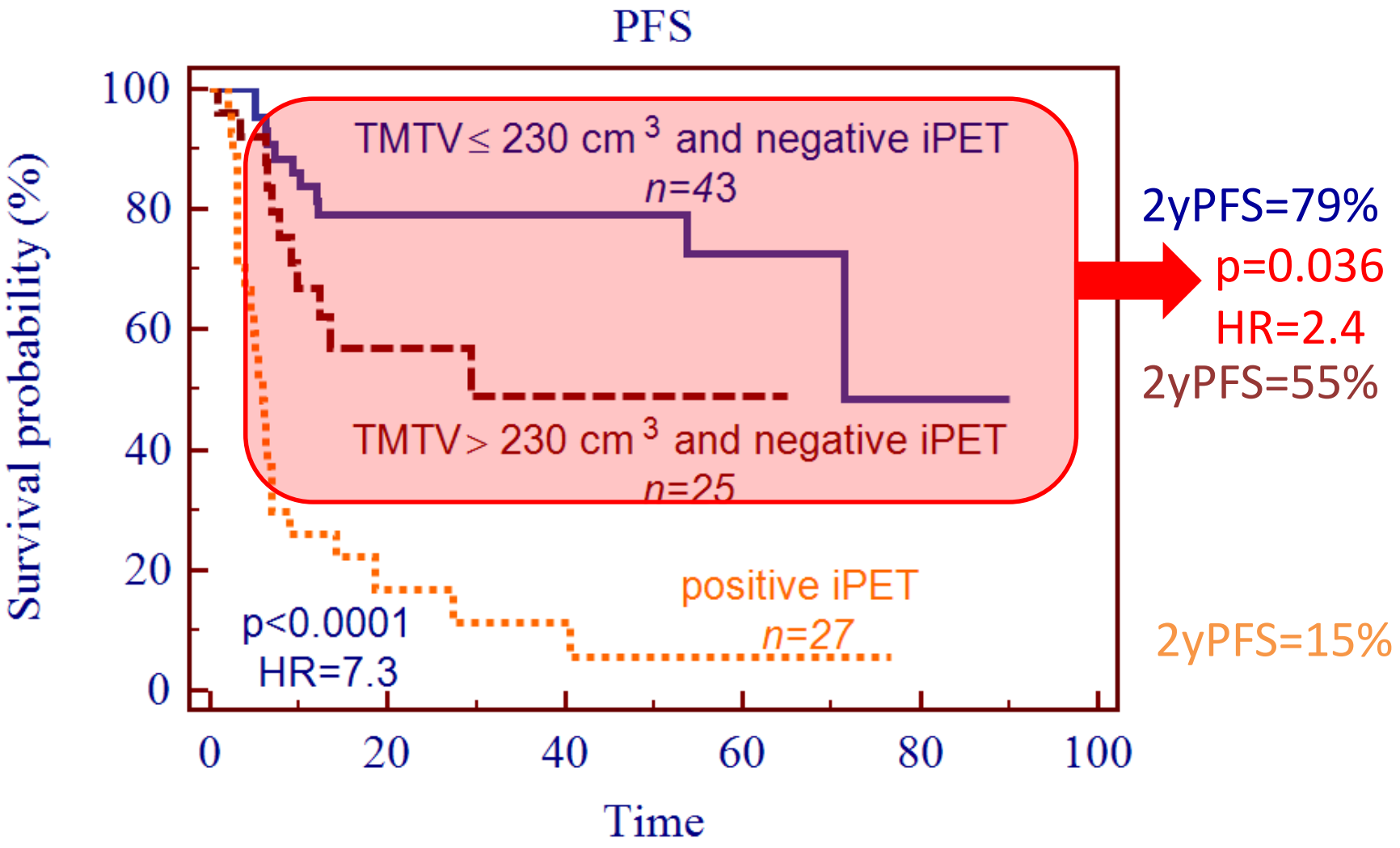


	PFS			OS		
	HR	95% CI	p	HR	95% CI	p
TMTV	3.3	1,8-6,1	0,0001	1.9	0,9-3,8	0,07
iPET 3-4	6.7	3,6-12,3	<0,0001	6.1	2,9-12,6	<0,0001
TMTV	2.2	1,1-4,4	0,0197	1.7	0,8-3,6	0,1942
eotPET	15.2	7,0-33,0	<0,0001	23.9	8,9-64,3	<0,0001

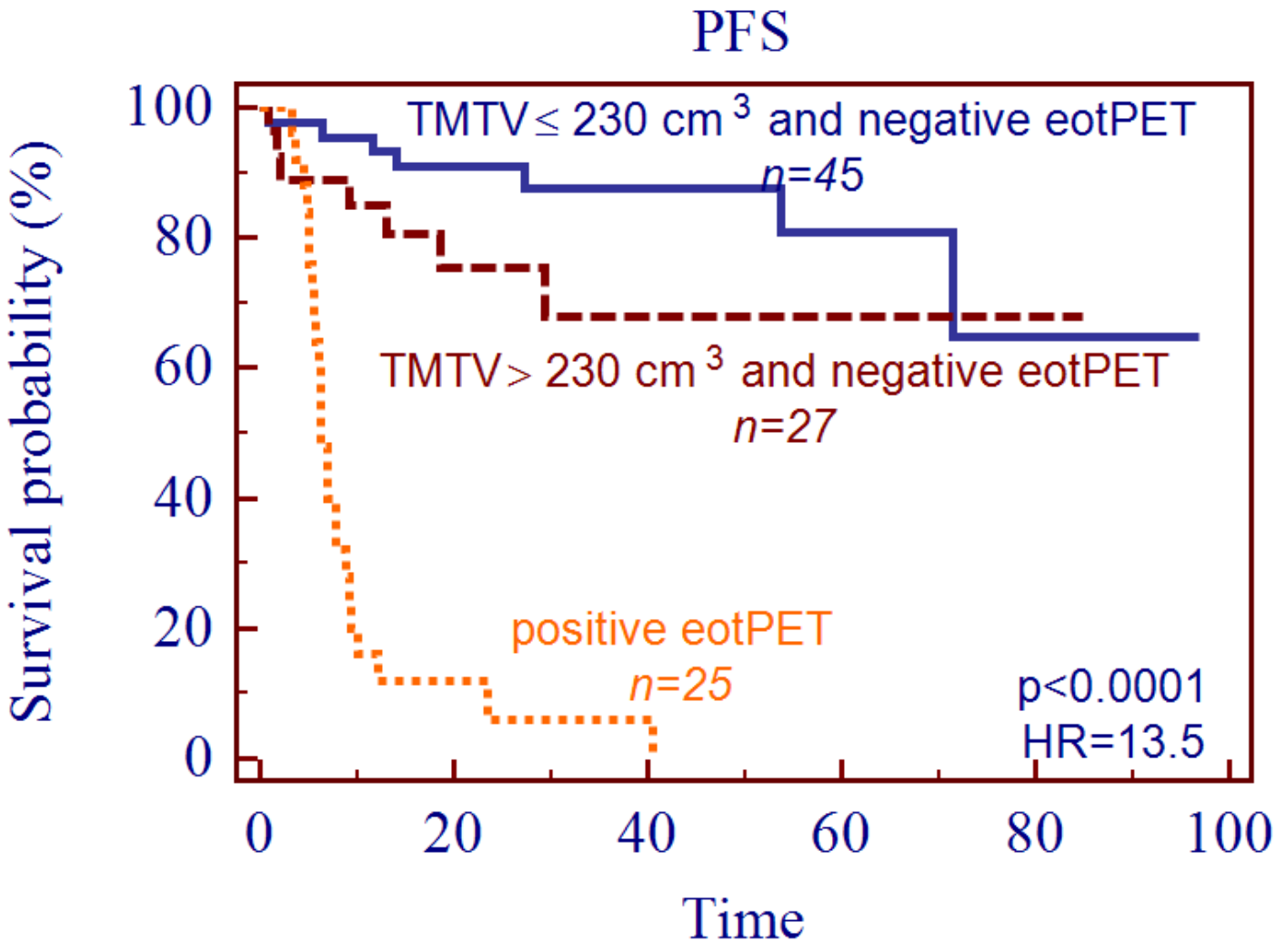
TMTV and iPET3-4 response



TMTV and iPET3-4 response



TMTV and eot PET

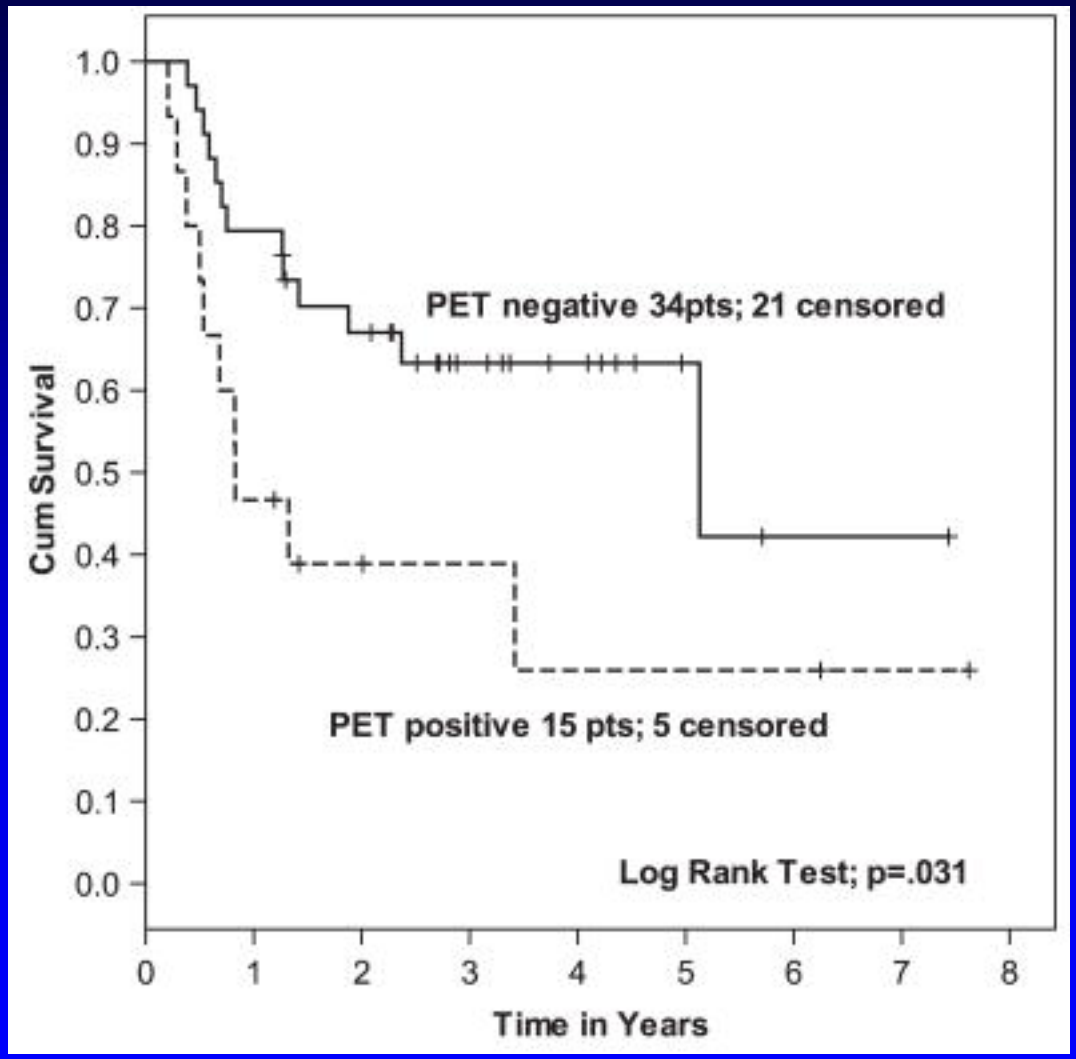


Treatment Based on i-PET in PTCL

- Interim PET after median of 4 cycles – 5PS
- No difference in PFS if iPET <4 or ≥ 4 cycles
- 29 pts consolidated with BMT or ASCT
- 8 of 15 pts with iPET+ remained alive following additional therapy
  - 3 alloBMT
  - 1 ABMT
  - 2 salvage chemo
- Only 2 iPET+ A&W without disease

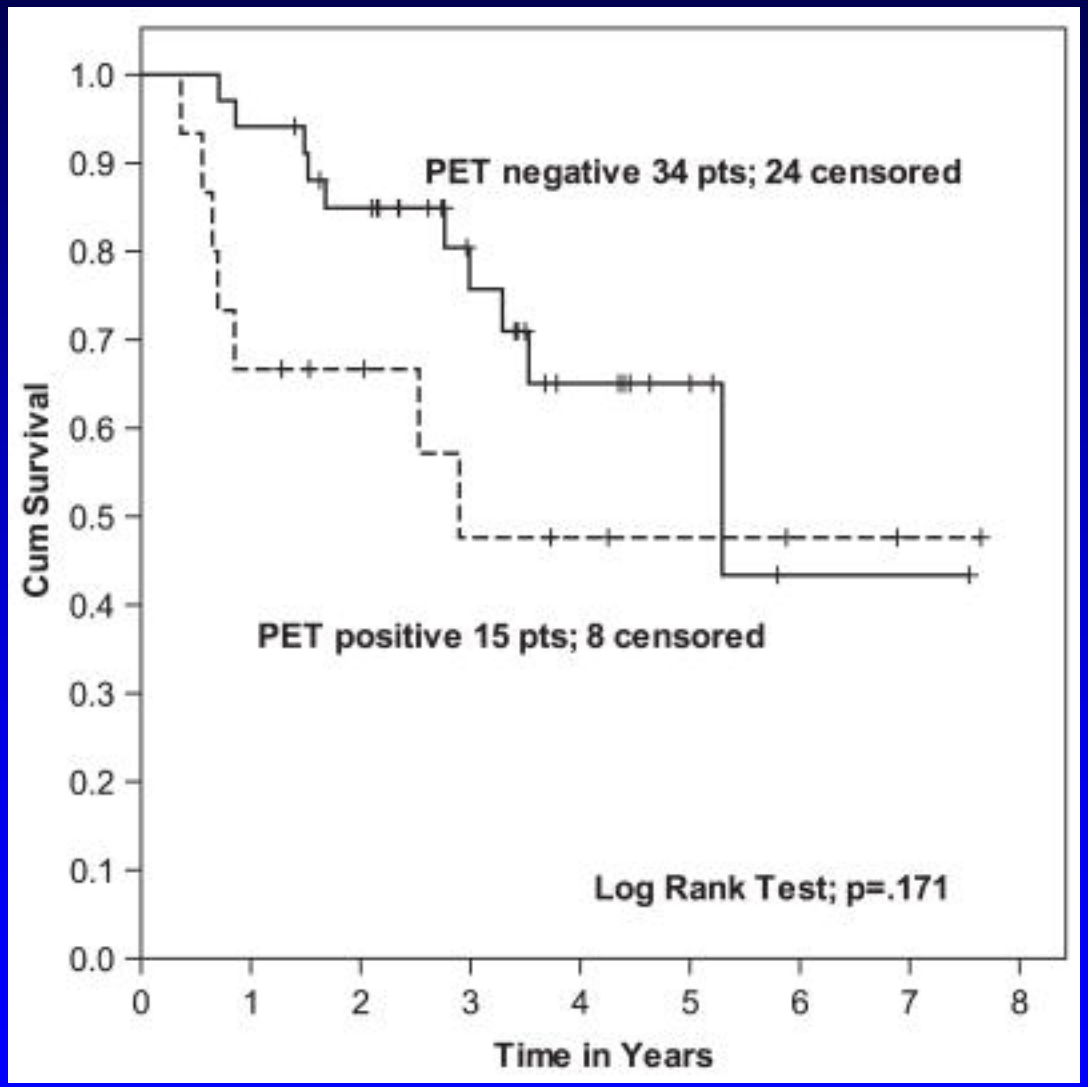
Casulo et al Leuk Lymph 54:2163, 2013

Interim PET in PTCL:PFS



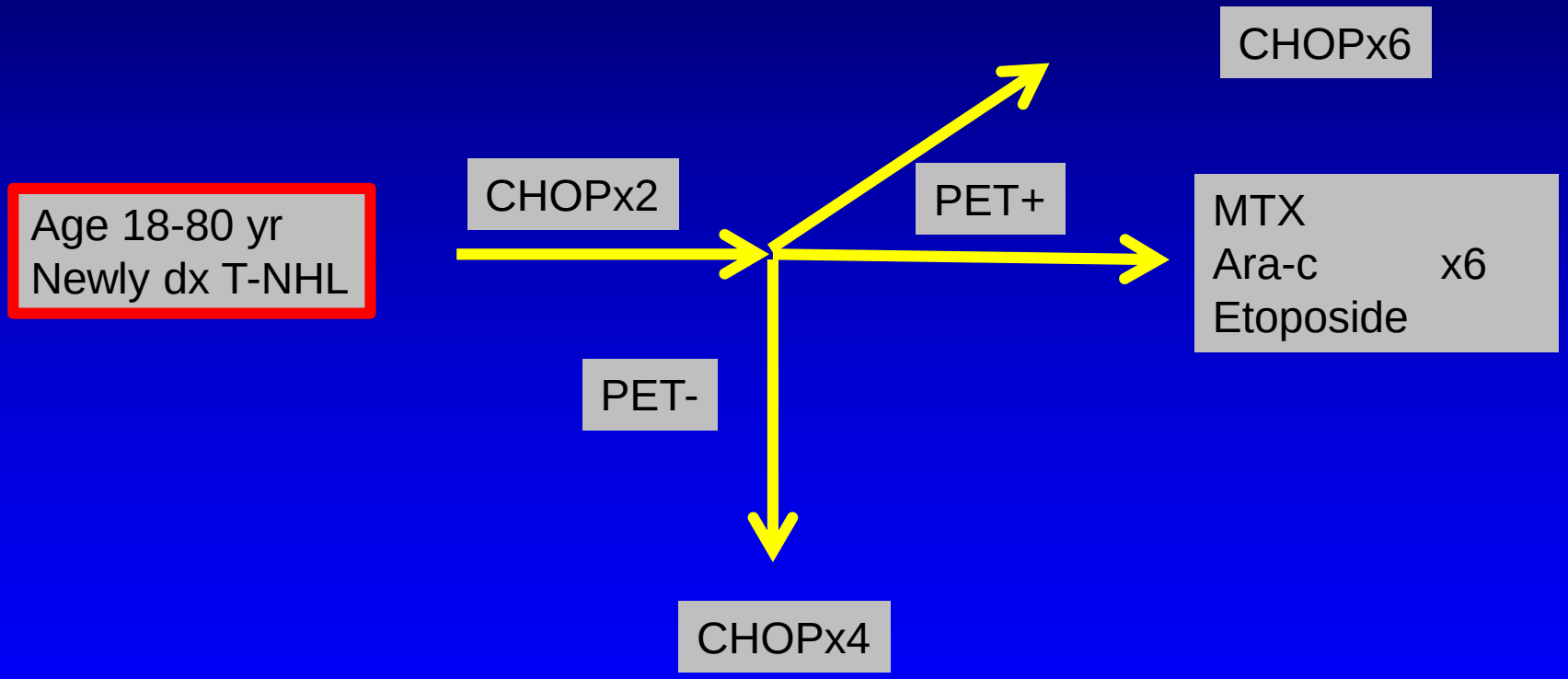
Casulo et al Leuk Lymph 54:2163, 2013

Interim PET in PTCL:OS



Casulo et al Leuk Lymph 54:2163, 2013

PETAL Study (PTCL) (n=76/862)



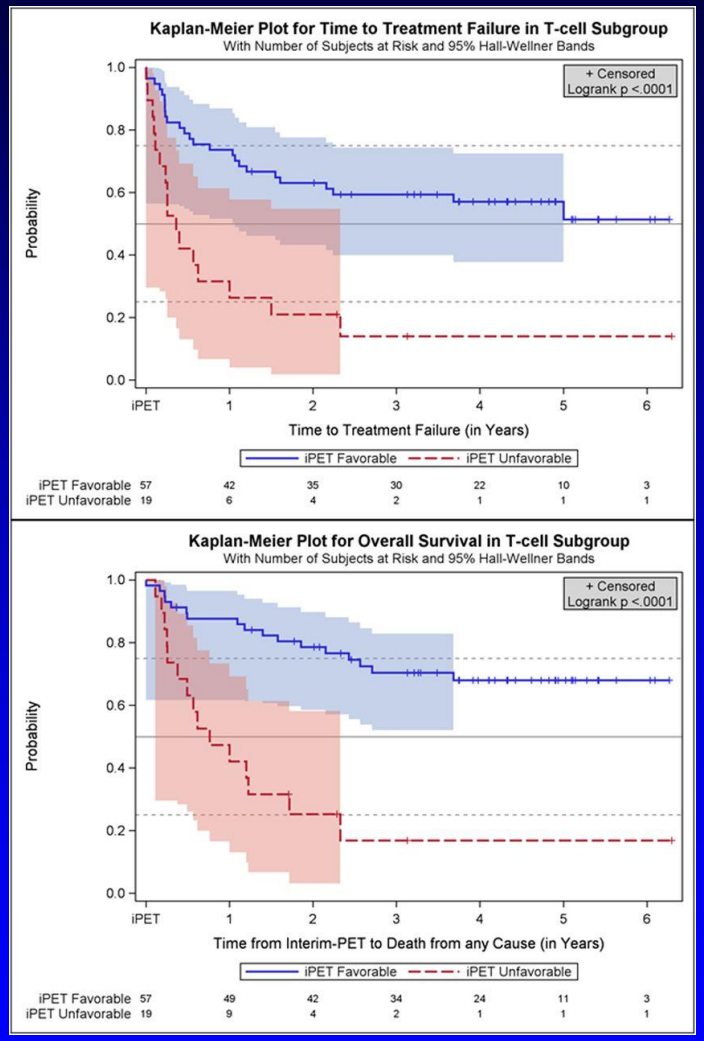
Hüttmann et al. Blood 2016;128:185

PETAL Study

- Of 1072 newly diagnosed B- and T-cell registered, 862 PET+
- 76 (8.8%) PTCL: 21 ALK+ ALCL; 13 ALK- ALCL, 18 AITL, 20 NOS
- Interim PET before cycle 3
- Favorable: > 66% decrease in SUV
- iPET – negative in 57 (75%); + 19 (25%)

Hüttmann et al. Blood 2016;128:185

PETAL Study Outcome



Hüttmann et al. Blood 2016;128:185

PETAL Trial Results

- Change of treatment resulted in more gr 3-4
  - Neutropenia
  - Thrombocytopenia
  - Infections
  - Mucositis
- ***No benefit in TTTF or OS from changing to intensive therapy!!!***

Conclusions: PET-To Be? (or Not)

- PET-CT improves accuracy of staging of PTCL as per Lugano Classification
- Change of stage/treatment infrequent
- End of treatment PET variably prognostic because of poor outcome
- Interim scan results variable
  - DS cut-off
  - PIT
  - MTV
  - Others

Conclusions 2: PET-To Be? (or Not)

- No data to support altering treatment on basis of interim scan
- Better techniques in development to improve PET prediction
- *Better treatments required to improve patient outcome*