3rd International Workshop on Interim PET in Lymphoma
Menton, September 26, 2011
Afternoon Controversies

Pros and Cons:

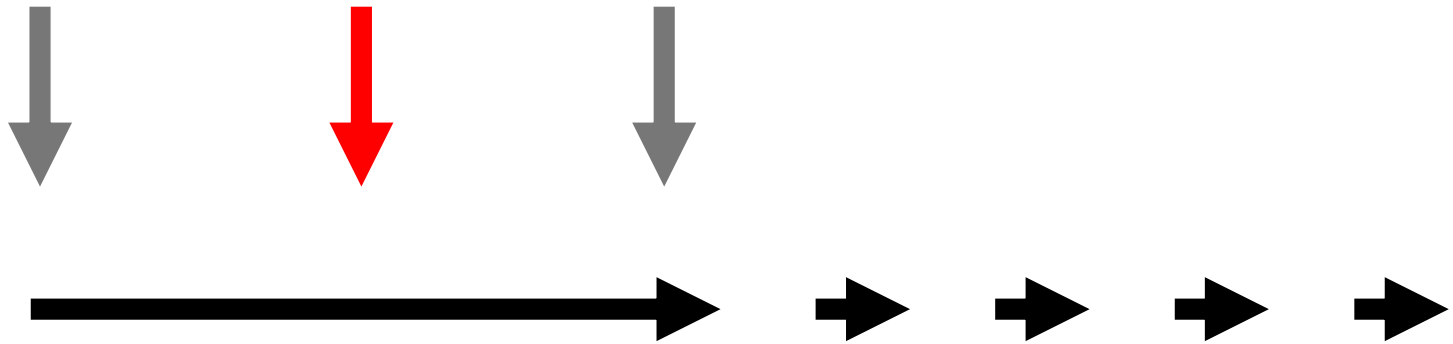
Interim PET in DLBCL

Ulrich Dührsen
Department of Hematology
University Hospital Essen

Pros

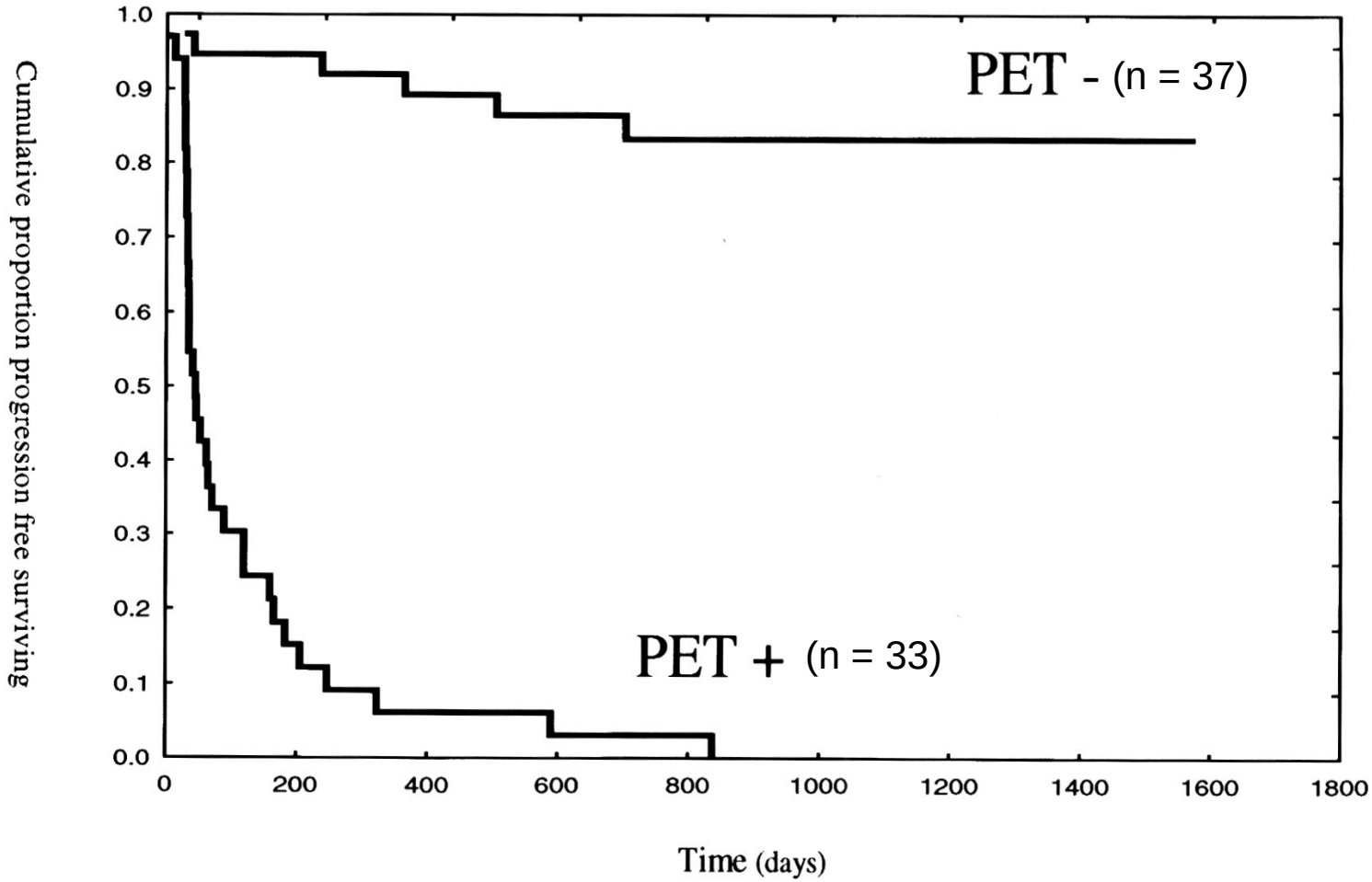
Is there any evidence that early PET (after 1 or 2 cycles) has a prognostic role in DLBCL ?

Should we report early PET qualitatively or quantitatively ?



Interim PET

Predictive value in aggressive lymphomas

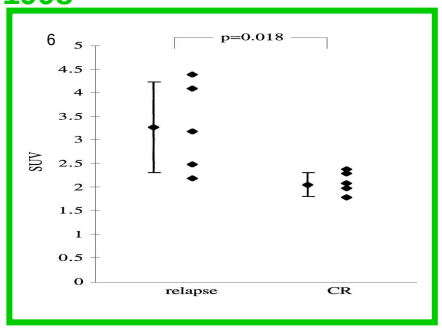


Spaepen et al, Ann Oncol 13: 1356, 2002

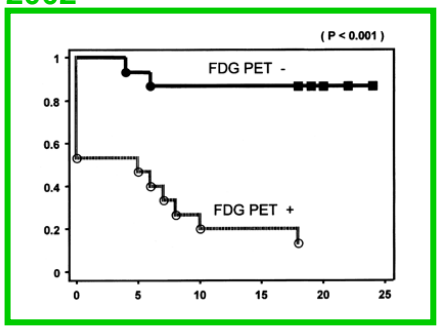
Interim PET

Predictive value in aggressive non-Hodgkin‘s lymphomas

1998



2002



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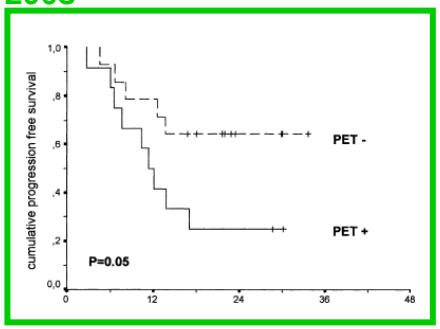

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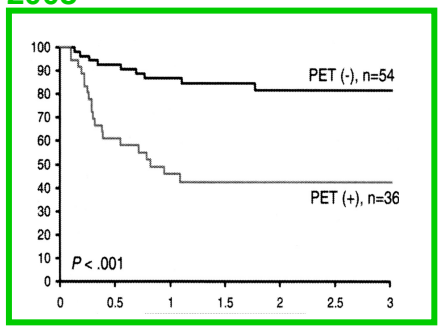
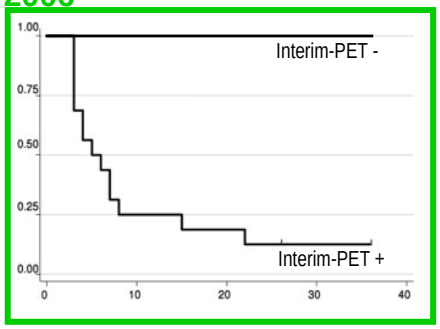
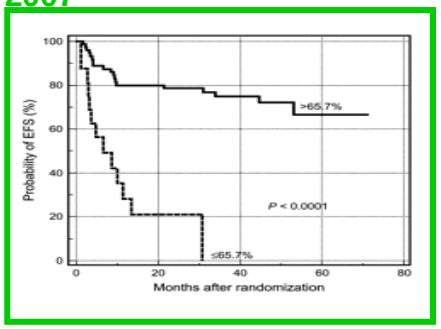


2006



2007



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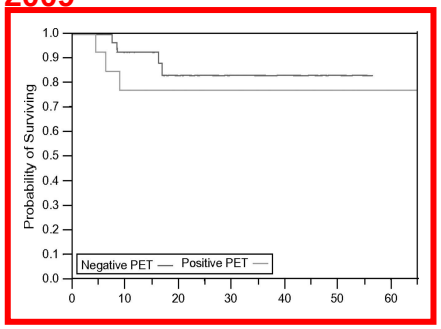

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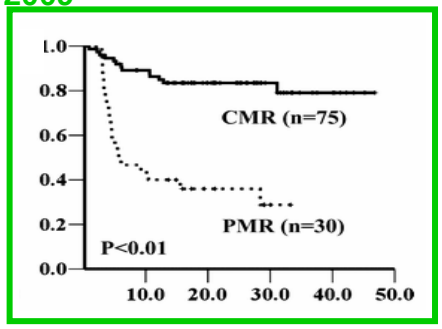

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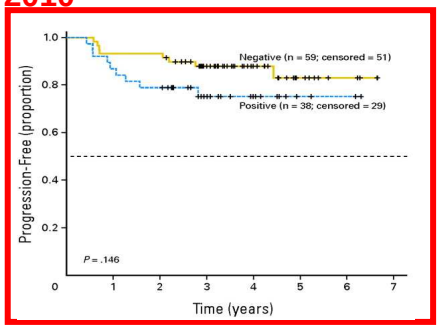
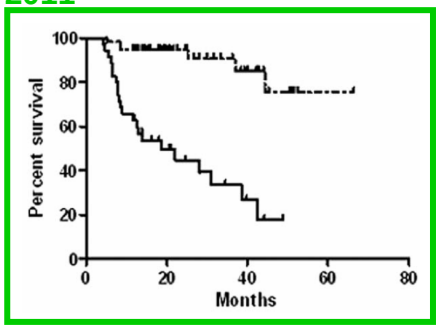


2011



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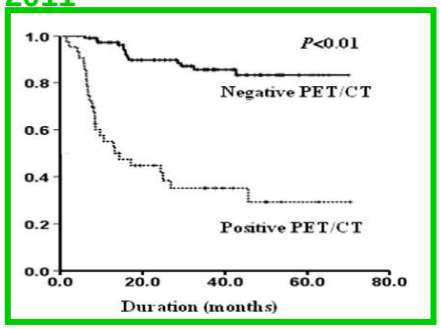
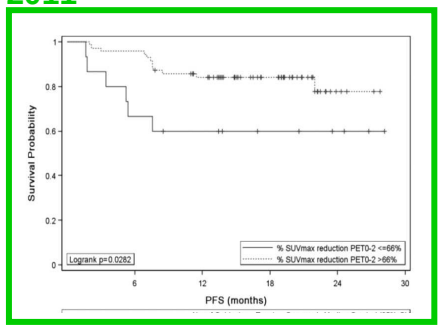


2011

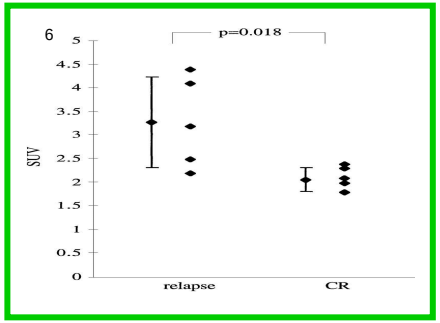


Interim PET

● +/- Rituximab
●● + Rituximab

Predictive value in aggressive non-Hodgkin‘s lymphomas

1998



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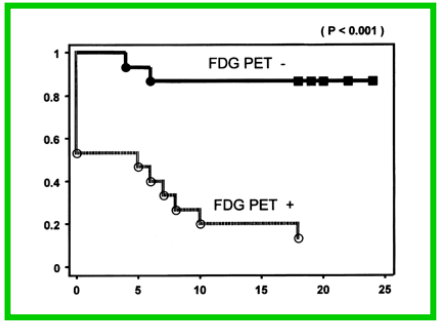

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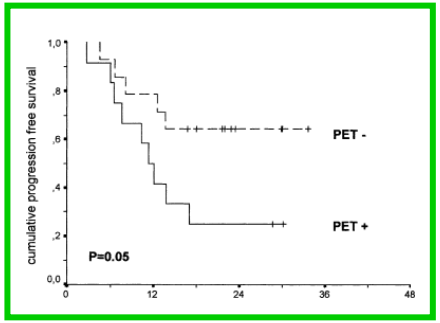

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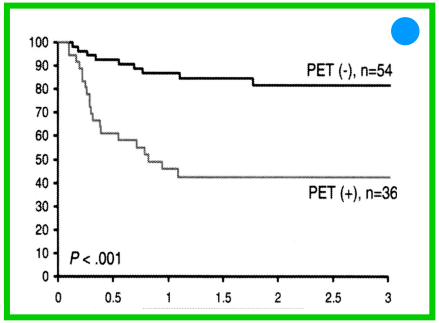

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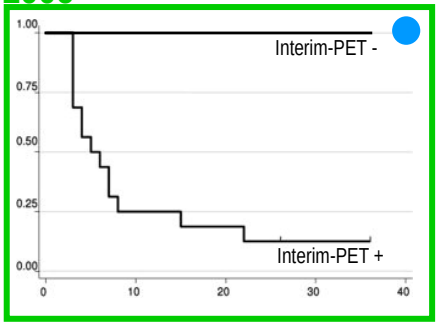

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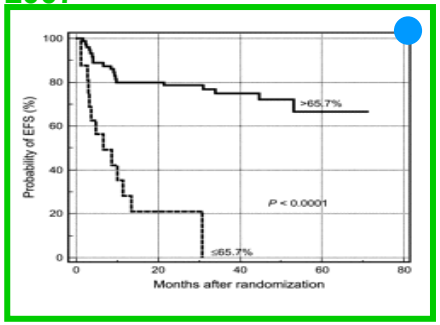

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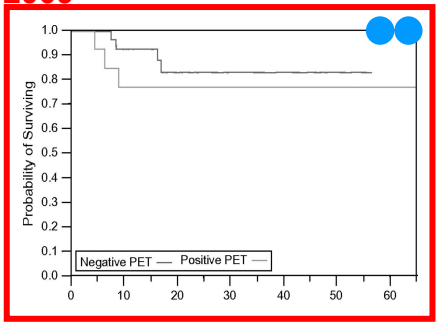

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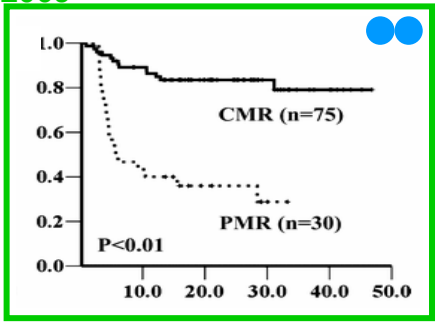

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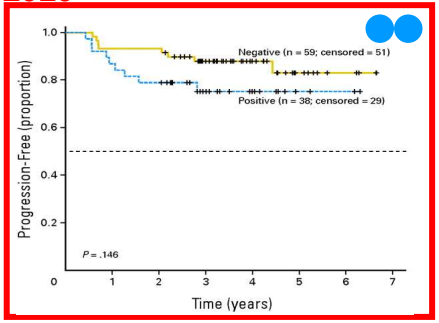

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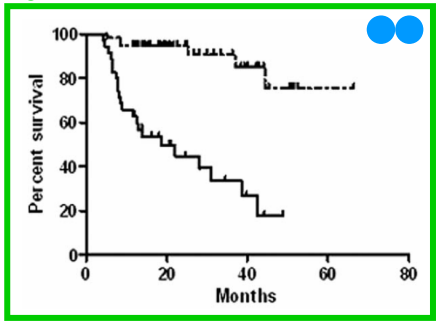

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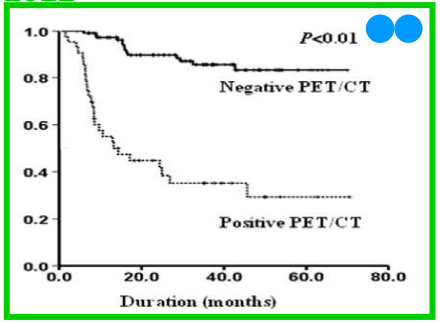

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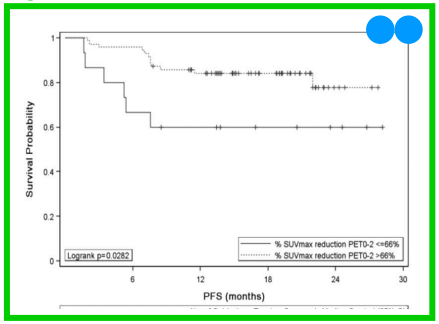
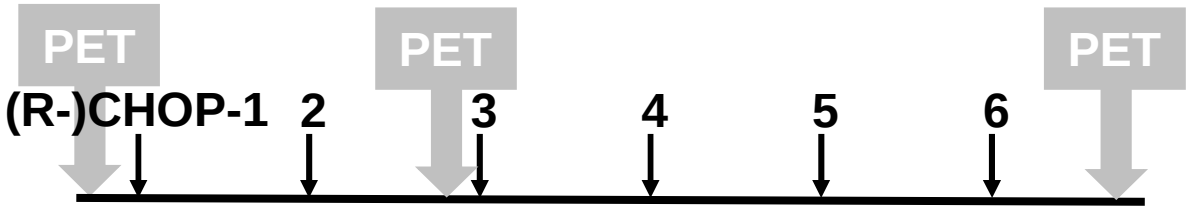
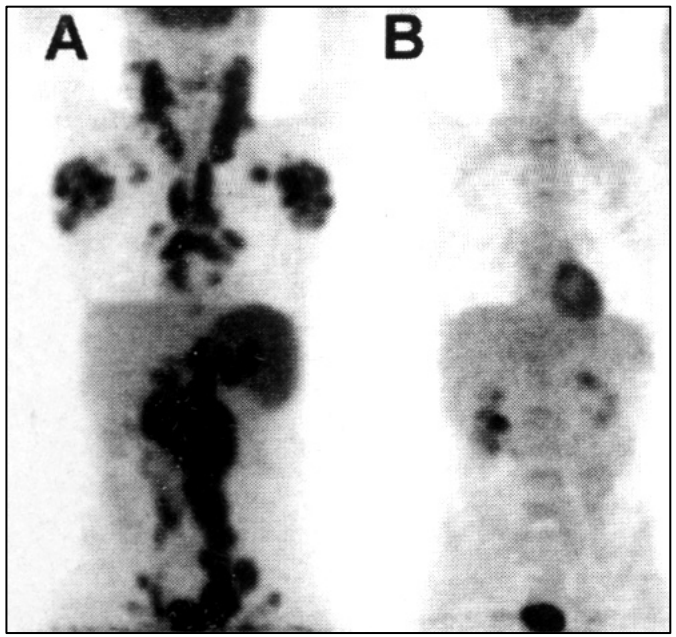


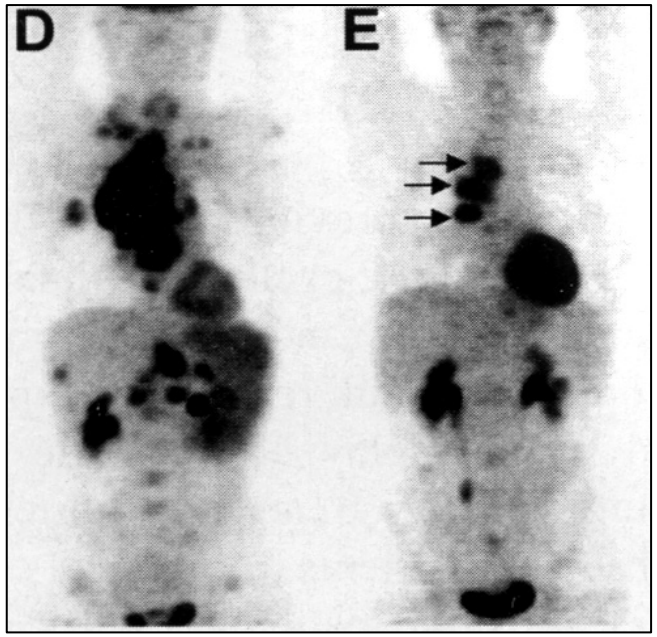
Interim PET

What is a negative PET scan ?





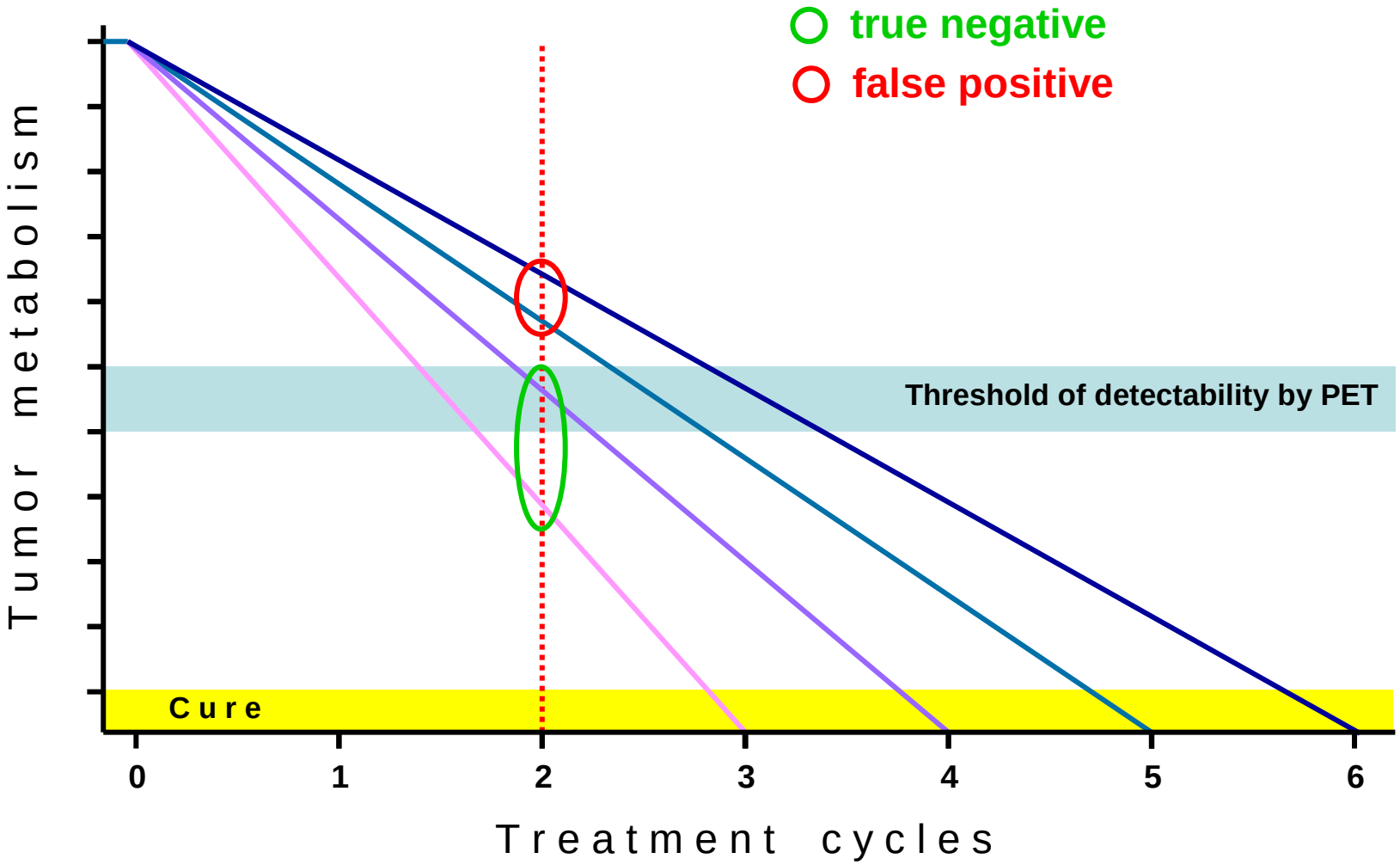
Negative ?



Positive ?

Interim PET

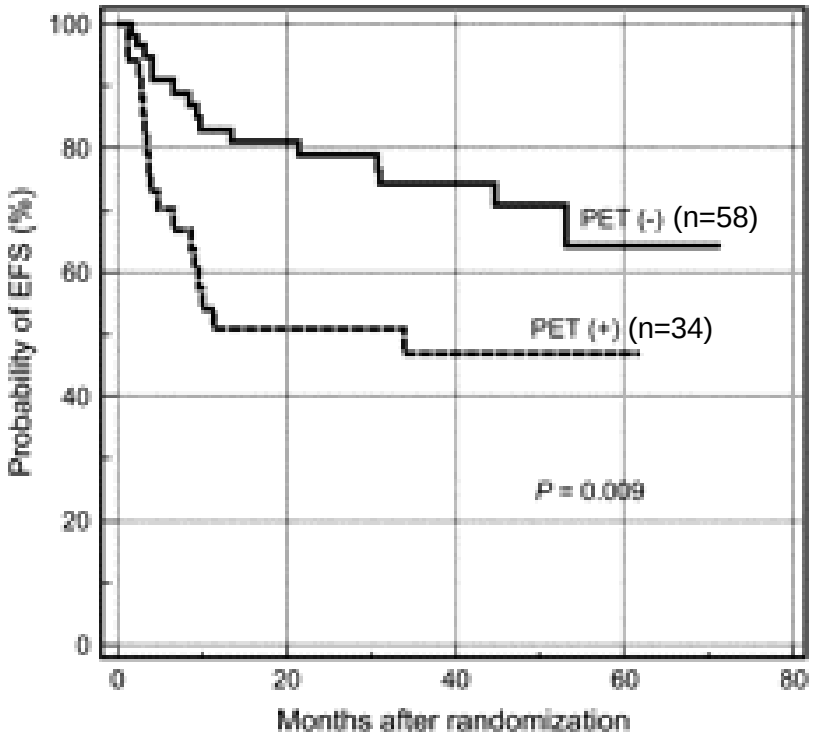
Method of PET evaluation



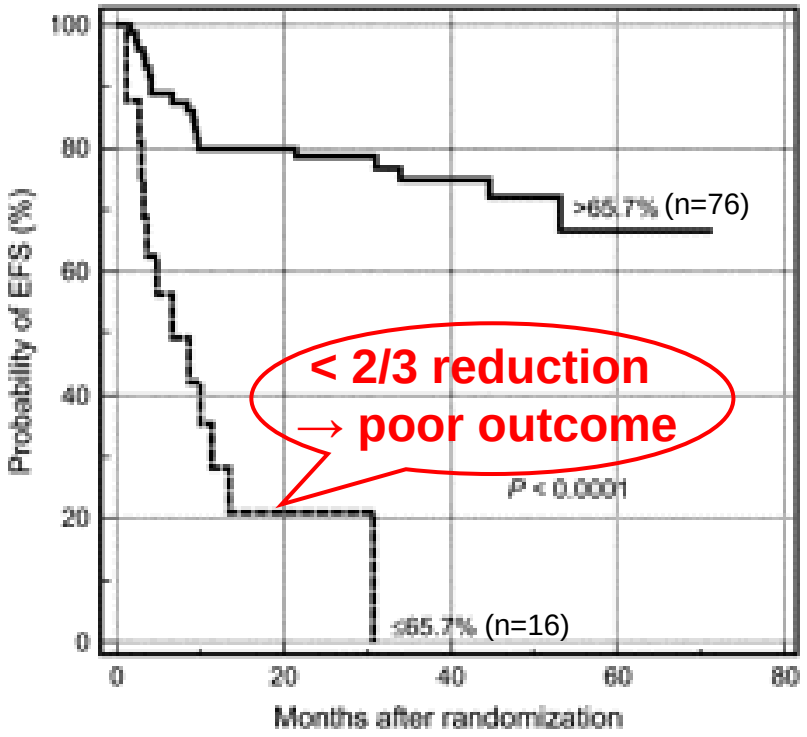
Interim PET

Method of PET evaluation

Visual assessment



SUV-based assessment



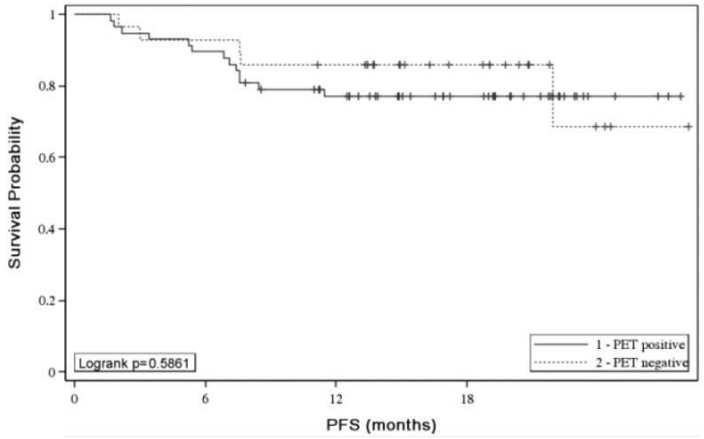
92 DLBCL patients, PET after cycle 2

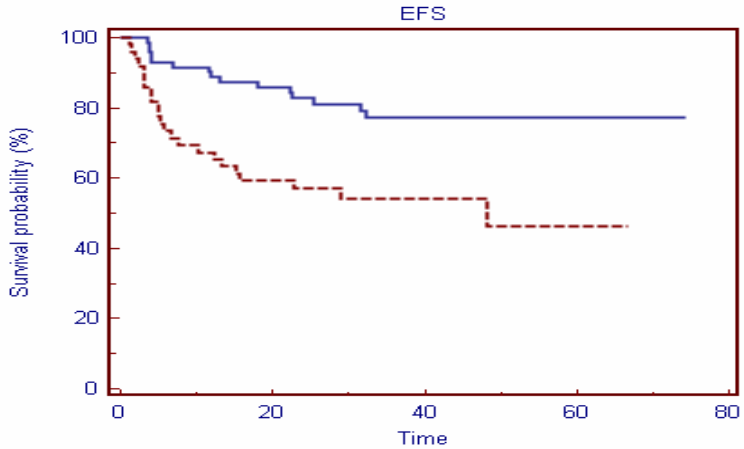
Lin et al, J Nucl Med 48: 1626, 2007

Interim PET

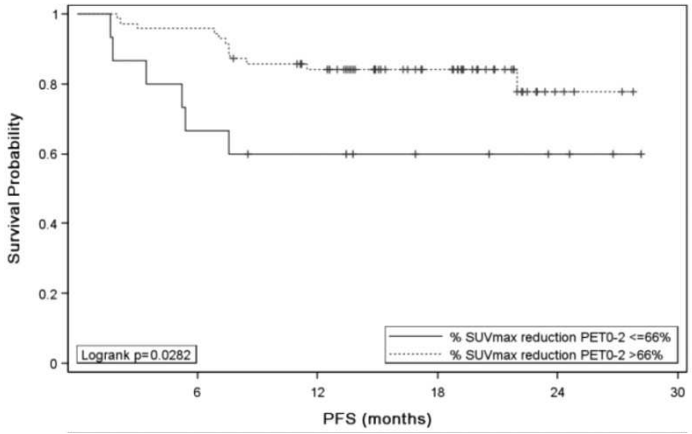
SUV-based PET evaluation: confirmatory studies

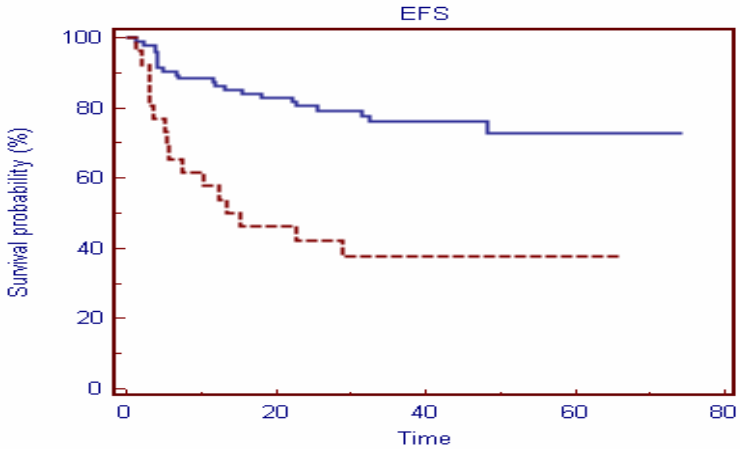
Visual assessment





SUV-based assessment



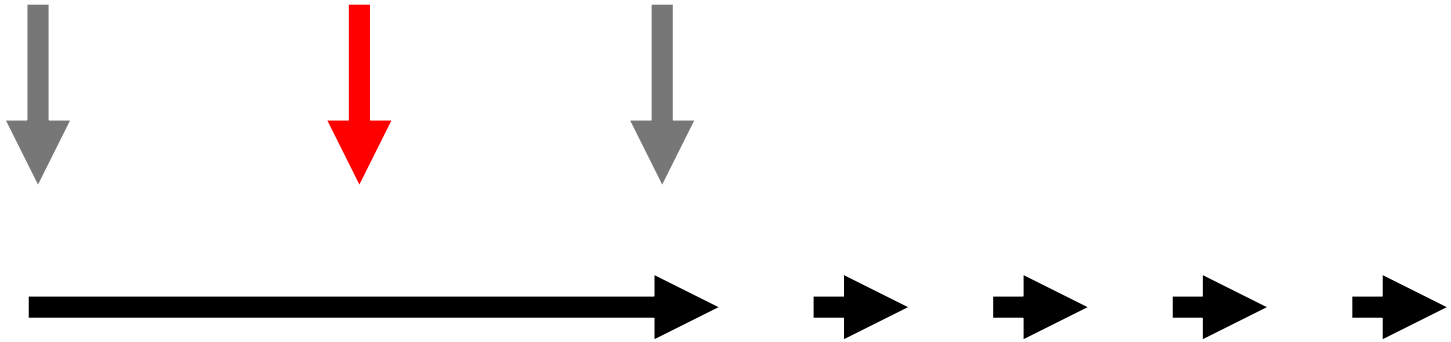


Casasnovas et al, Blood 118: 37, 2011; IVS DLBCL, Menton 2011

Is histological confirmation

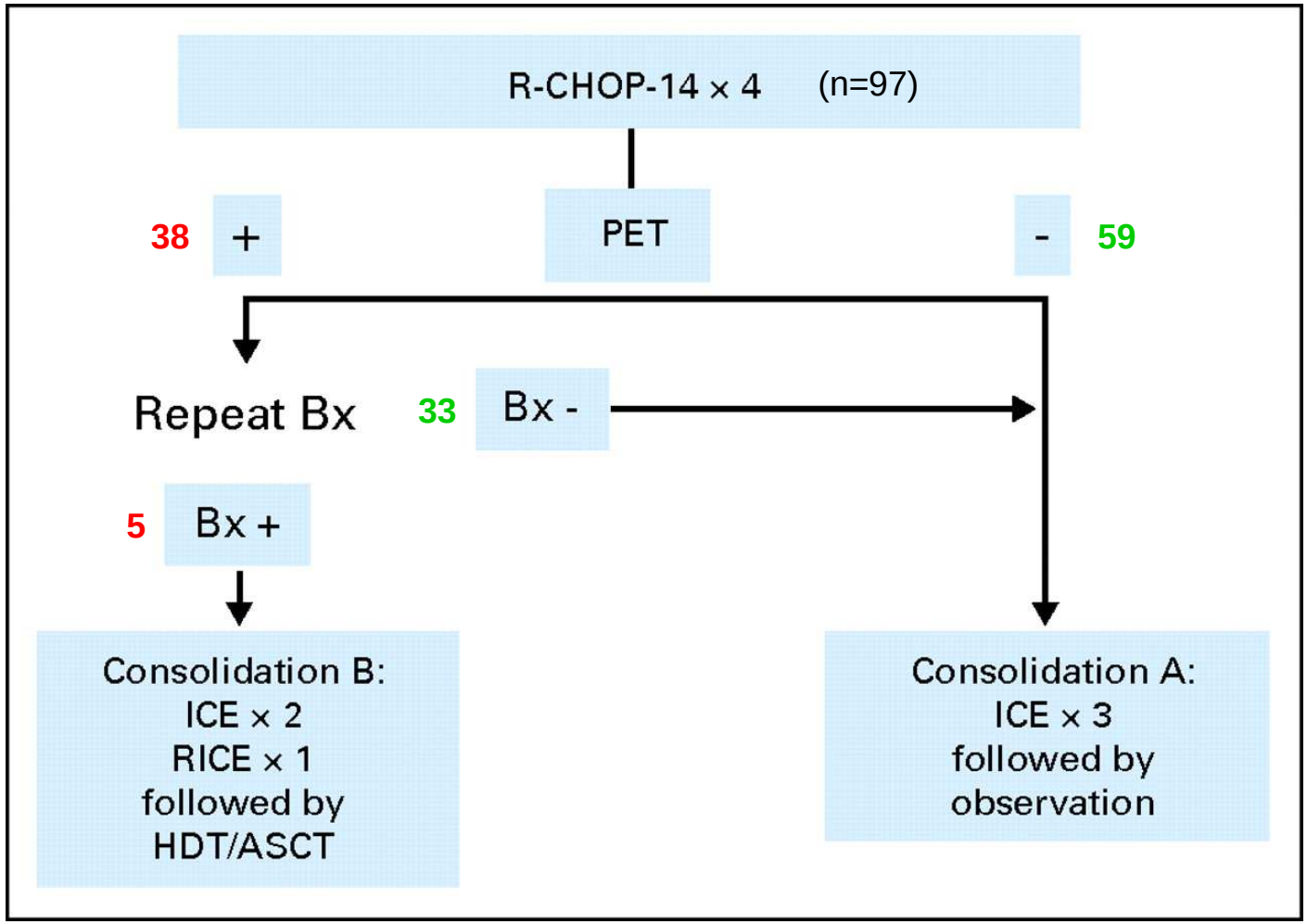
the „gold standard“ reference

for patients with mid-treatment positive PET ?



Interim PET

Histological confirmation in interim PET positive patients



Moskowitz et al, J Clin Oncol 28: 1896, 2010

Interim biopsy

Predictive of treatment failure ?

Method of tissue sampling

Core needle biopsy	**47 %**
Endoscopy	29 %
Open surgery	21 %
Fine needle aspiration	3 %

Prediction of outcome?

Treatment failure	Biopsy: neg.	Biopsy: pos.
no	26	3
yes	7	2

Fisher's Exact Test: p = 0.338

Moskowitz et al, J Clin Oncol 28: 1896, 2010

Success rate of core needle biopsy

Aggressive NHL (Pappa et al. 1996)[1]

Posttreatment evaluation	**60 %**
Suspected progression	**83 %**

All lymphomas (de Kerviler et al. 2000)[2]

Suspected progression or recurrence	**89 %**

All lymphomas (Goldschmidt et al. 2003)[3]

Suspected progression	**75 %**

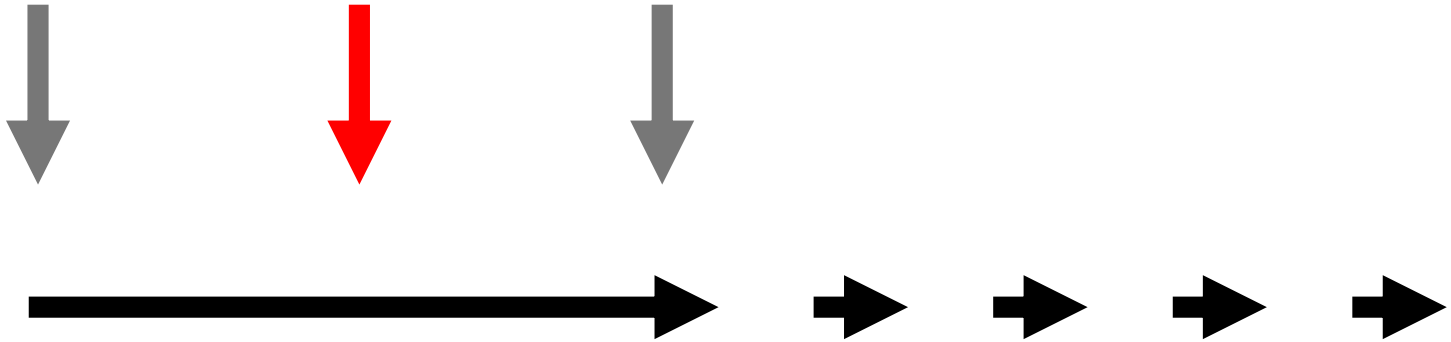
Average success rate **77 %**

[1] Pappa et al, J Clin Oncol 14: 2427, 1996

[2] De Kerviler et al, Cancer 89: 647, 2000

[3] Goldschmidt et al, Ann Oncol 14: 1438, 2003

Is interim PET feasible in multicenter clinical trials ?



Interim PET

Requirements in multicenter clinical trials

Standardization of the procedure

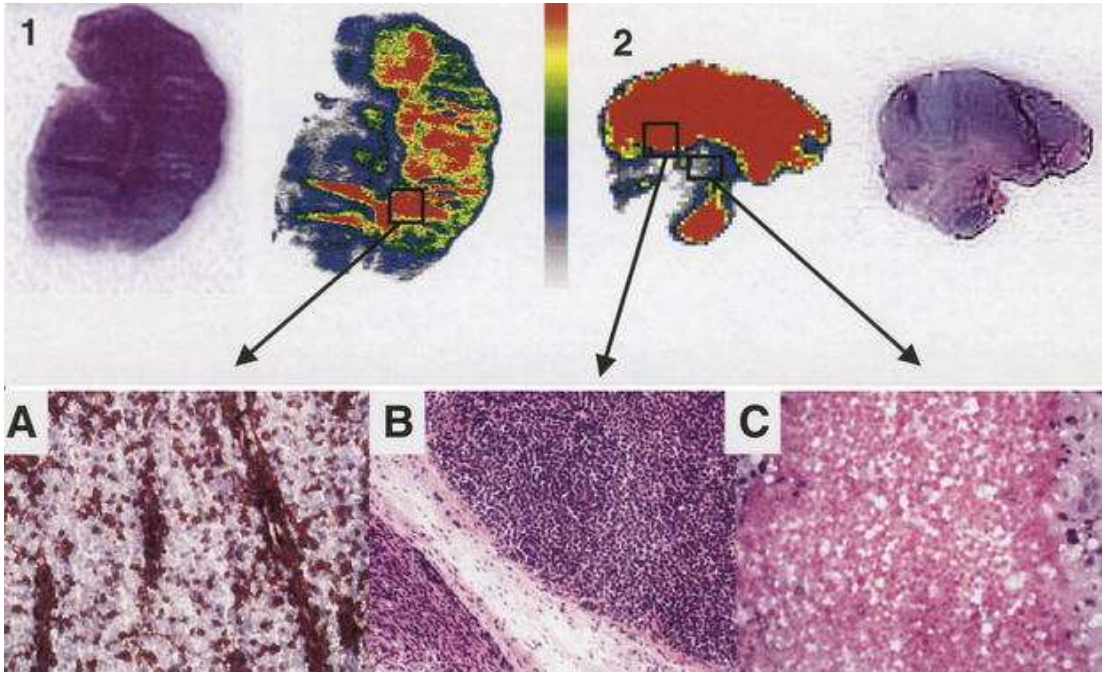
- timing in relation to chemotherapy
- control of comedication
- preparation of the patient
- scanning conditions

Standardized, reproducible, easy-to-use method of evaluation

Interim PET

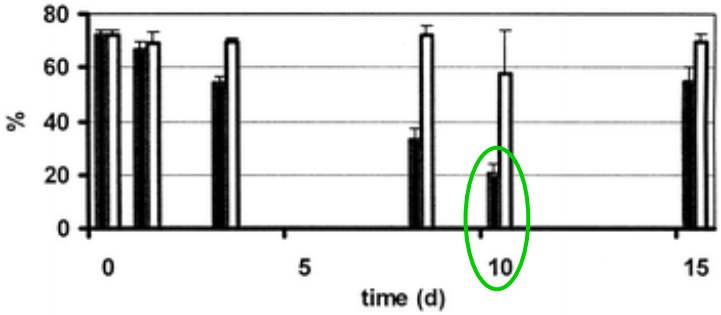
Interval between chemotherapy and PET

Day 10 Day 15

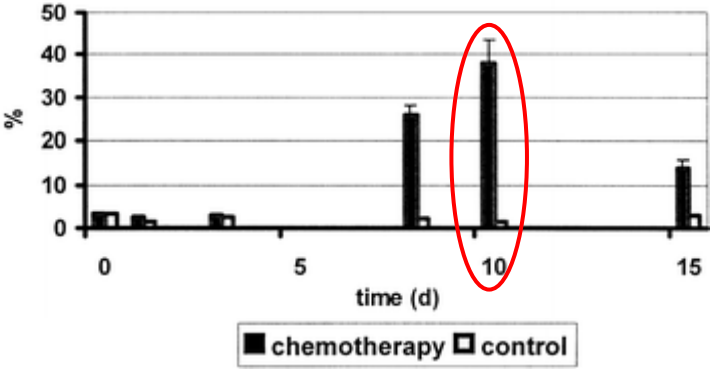


Macrophages Lymphoma cells Necrosis

Viable tumor cells



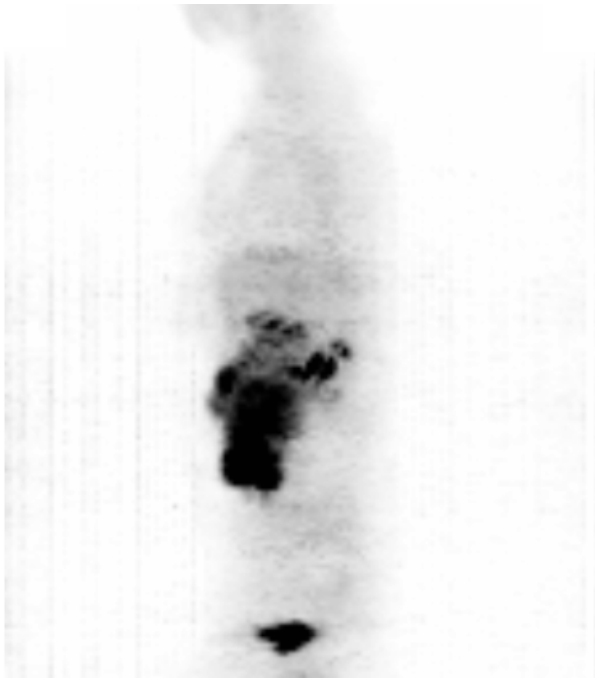
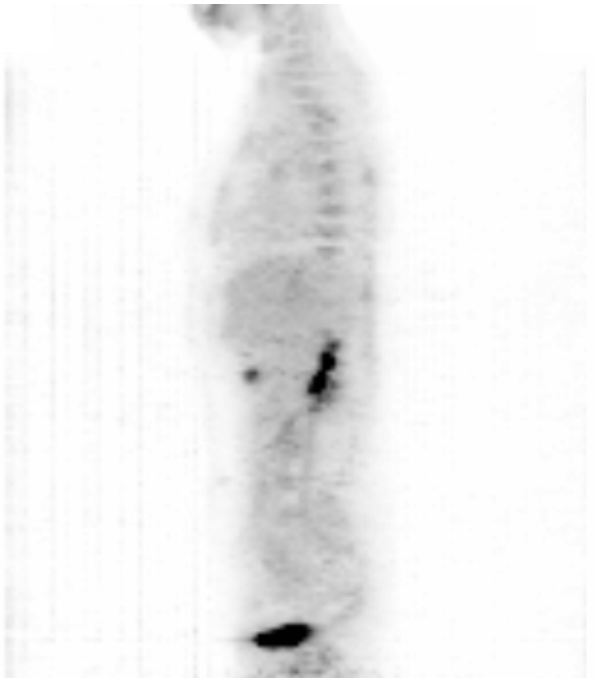
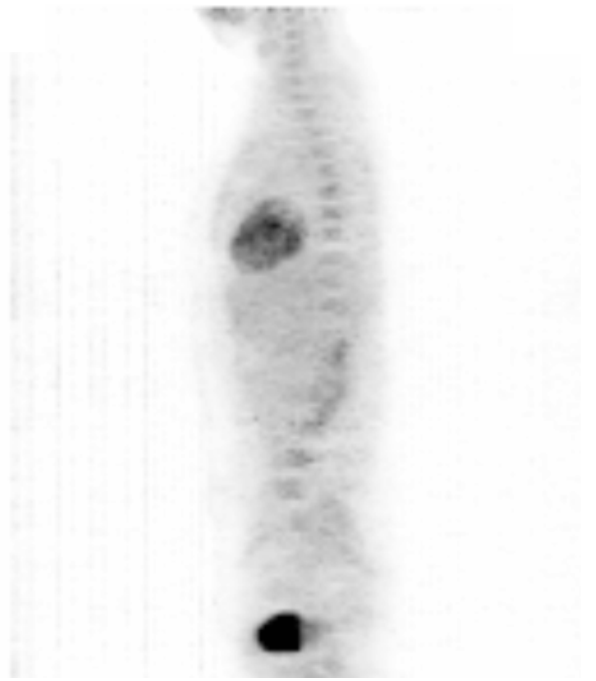
Inflammatory cells



Spaepen et al, Eur J Nucl Med Mol Imaging 30: 682, 2003

Interim PET

Interval between chemotherapy and PET

Pretreatment PET	Interim PET day 13	Interim PET day 20
		
Reduction SUV_{max}:	**56%**	**83%**

Hüttmann et al, J Clin Oncol 28: e488, 2010

Interim PET

Requirements in multicenter clinical trials

Standardization of the procedure

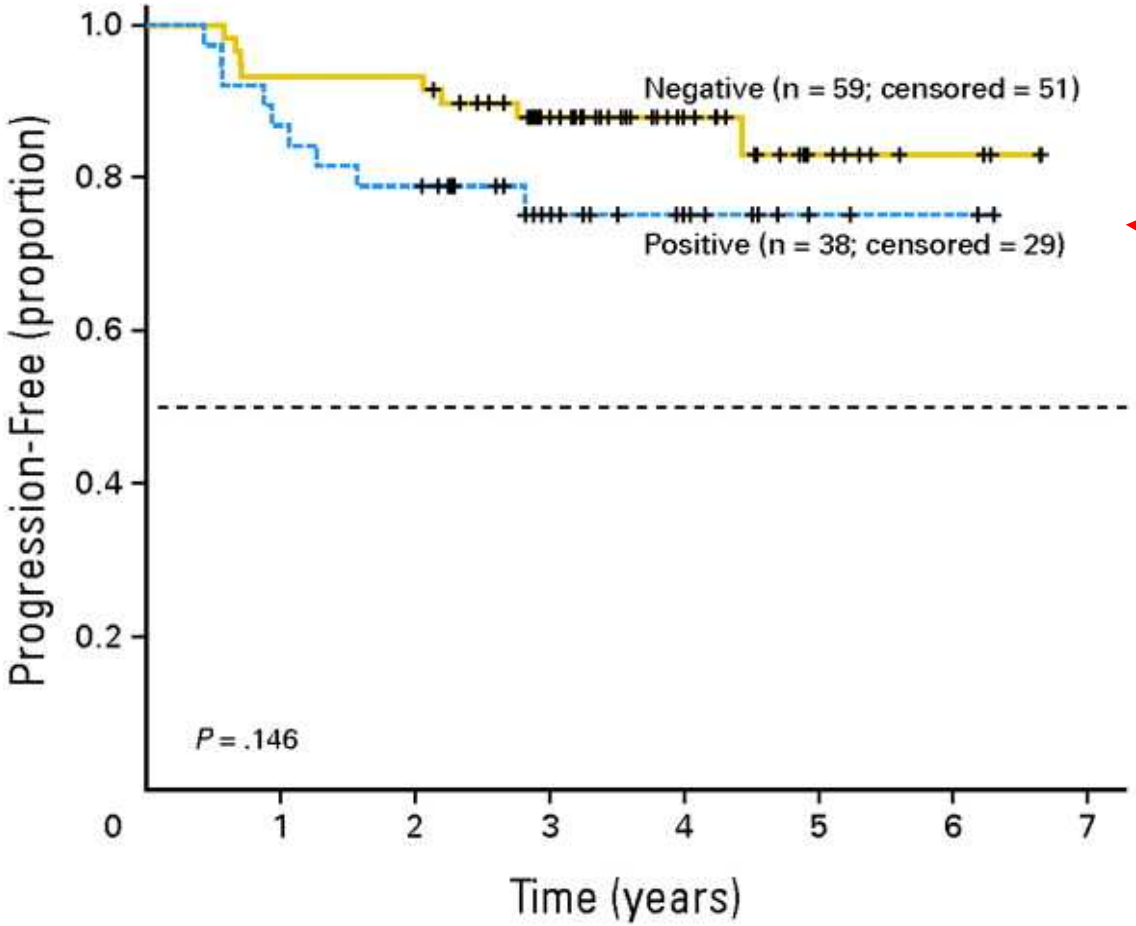
- interval from last chemotherapy: as long as possible
- control of comedication: no G-CSF
- preparation of the patient: fasting conditions, glucose level
- scanning conditions: type of scanner, interval injection-scanning

Standardized, reproducible, easy-to-use method of evaluation

- quantitative assessment

Interim PET

False positive PET scans – positive predictive value ↓



False positive PET results

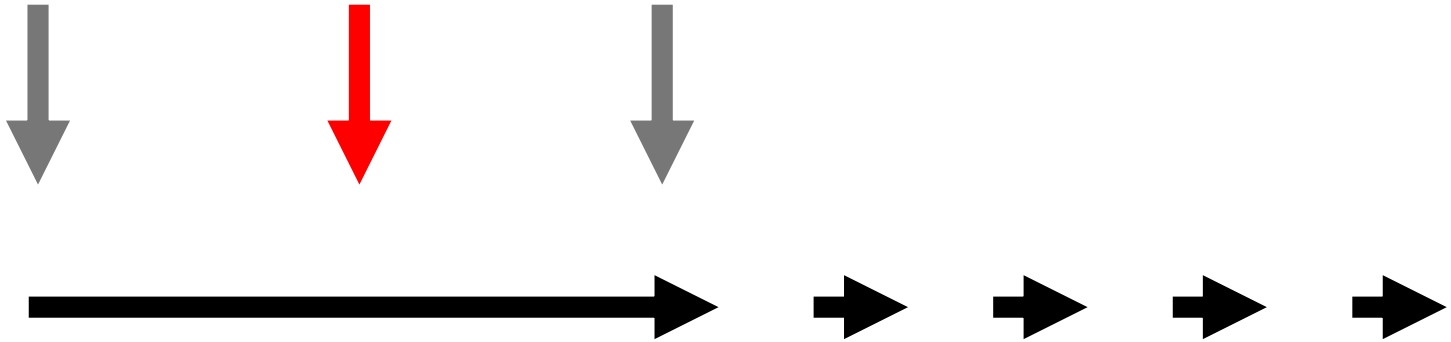
Visual assessment: normal

Interval: 10 – 14 days

G-CSF

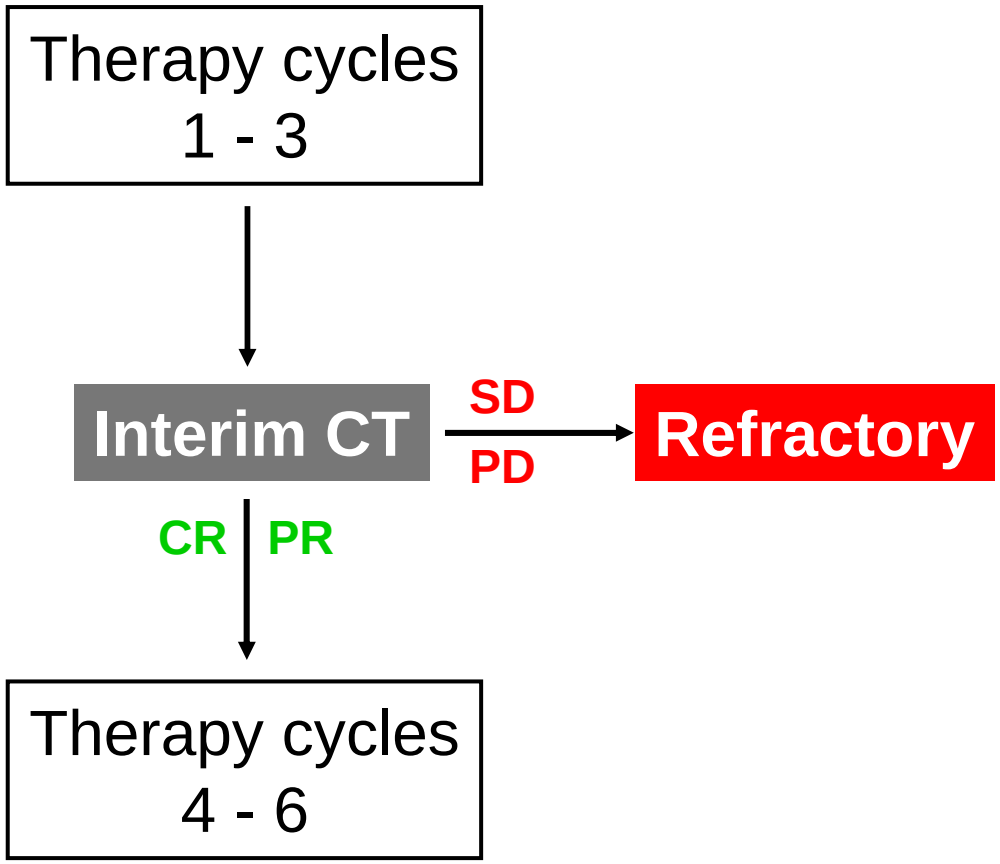
Moskowitz et al, J Clin Oncol 28: 1896, 2010

Can we change treatment on interim PET results ?



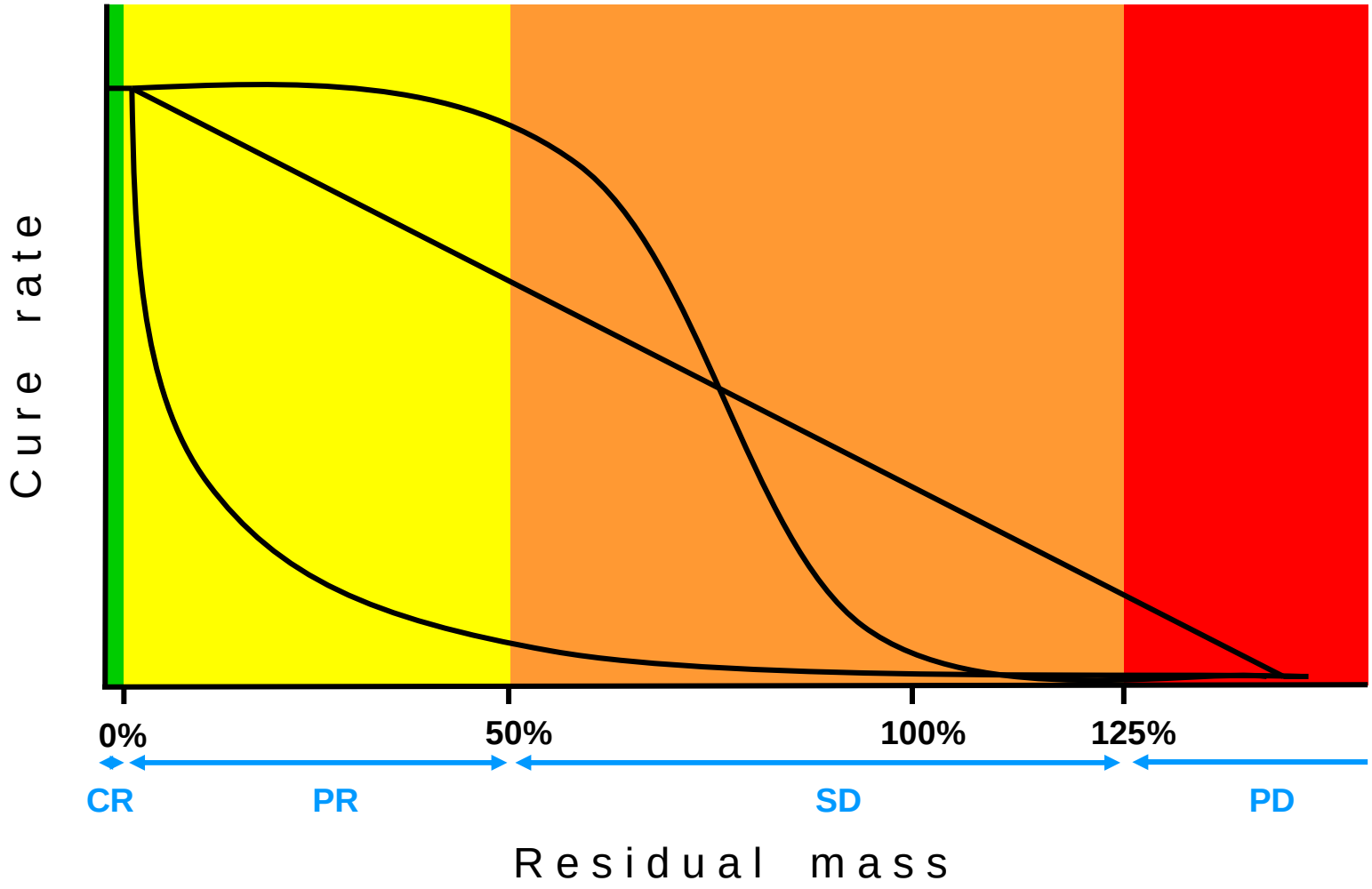
Interim CT

Role in treatment decisions



Interim CT

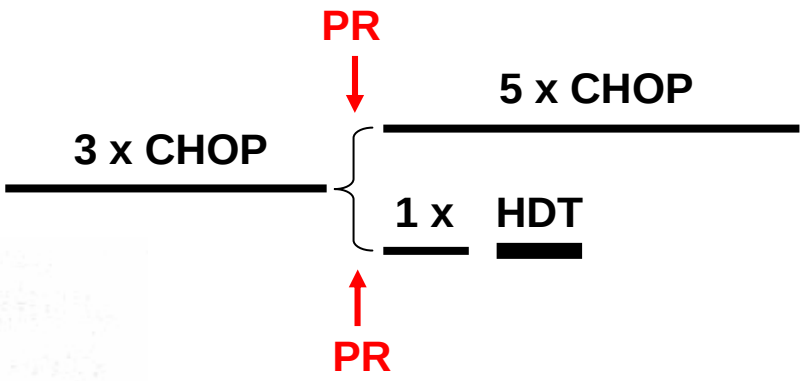
Arbitrary borders between treatment success and failure

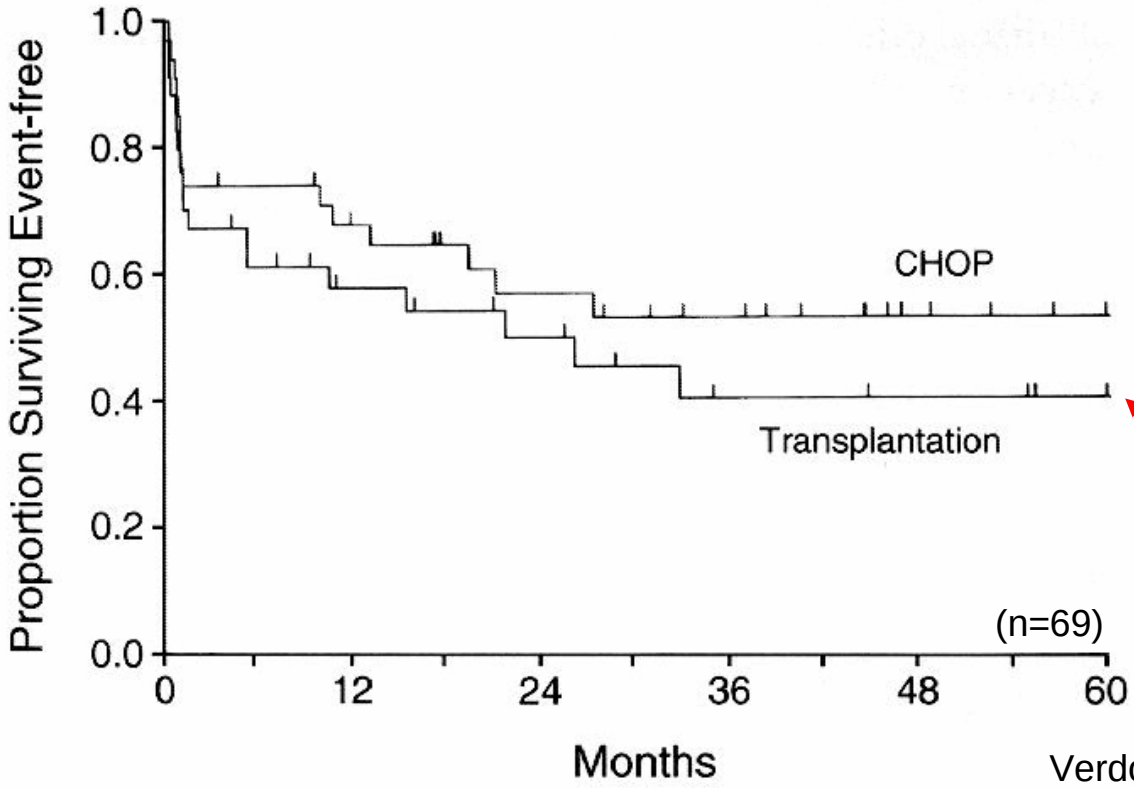


Interim CT

Role in treatment decisions in DLBCL ?

CT-response-adapted therapy :
8 x CHOP versus 4 x CHOP + HDT





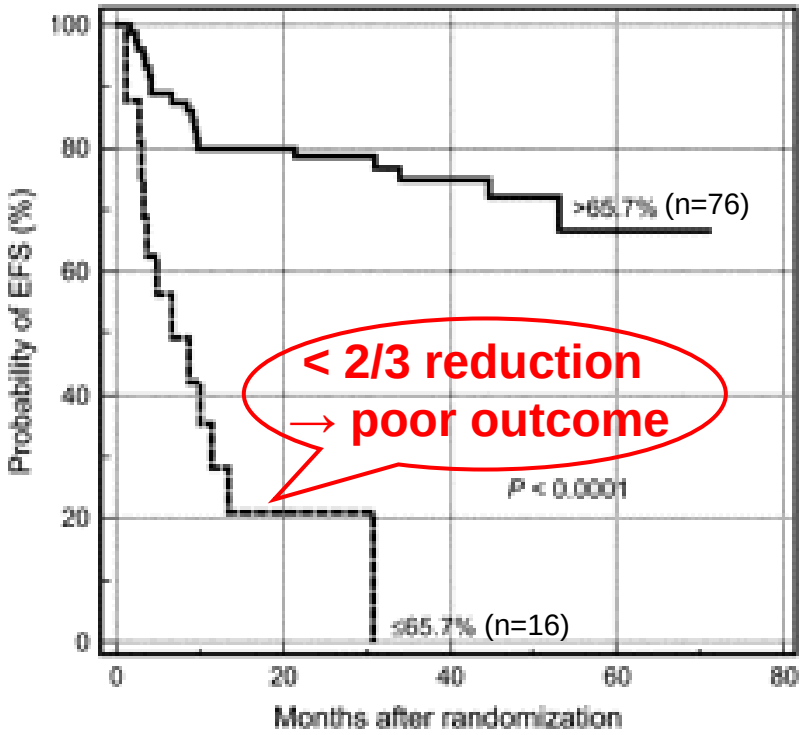
No improvement despite intensification

Verdonck et al, N Engl J Med 332: 1045, 1995

Interim PET

Role in treatment decisions in DLBCL ?

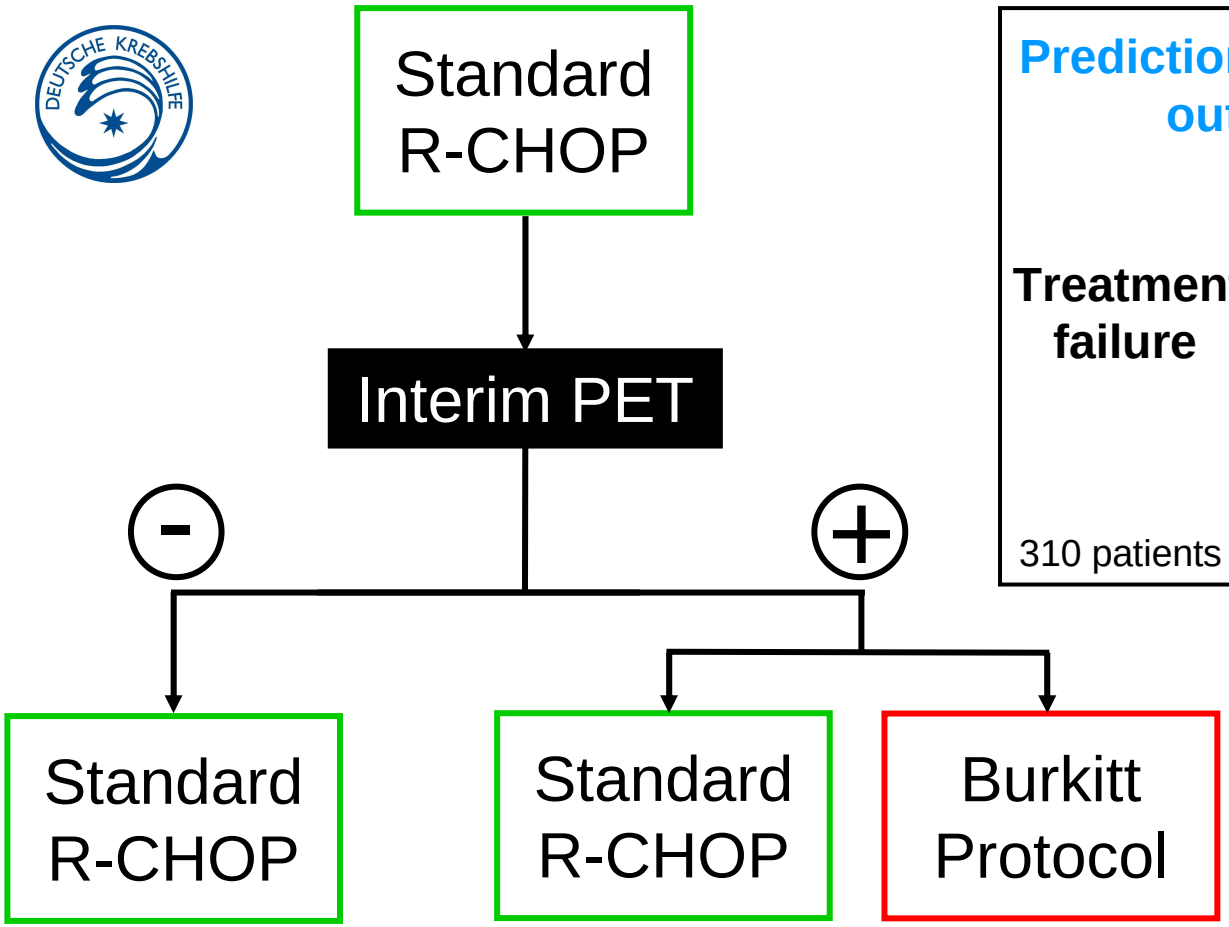
SUV-based assessment



Lin et al, J Nucl Med 48: 1626, 2007

Interim PET

PETAL Trial



Prediction of outcome?	Interim PET: neg.	Interim PET: pos.
Treatment failure: no	242	30
Treatment failure: yes	27	11

Fisher's Exact Test: **p = 0.008**

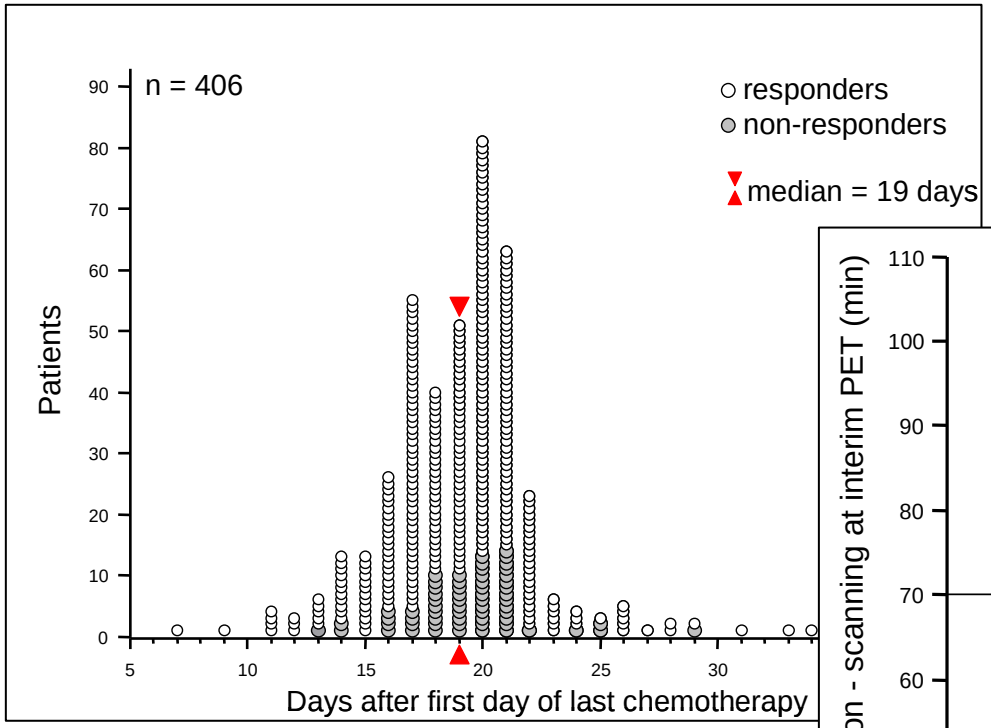
310 patients

Risk ratio: **2.673**

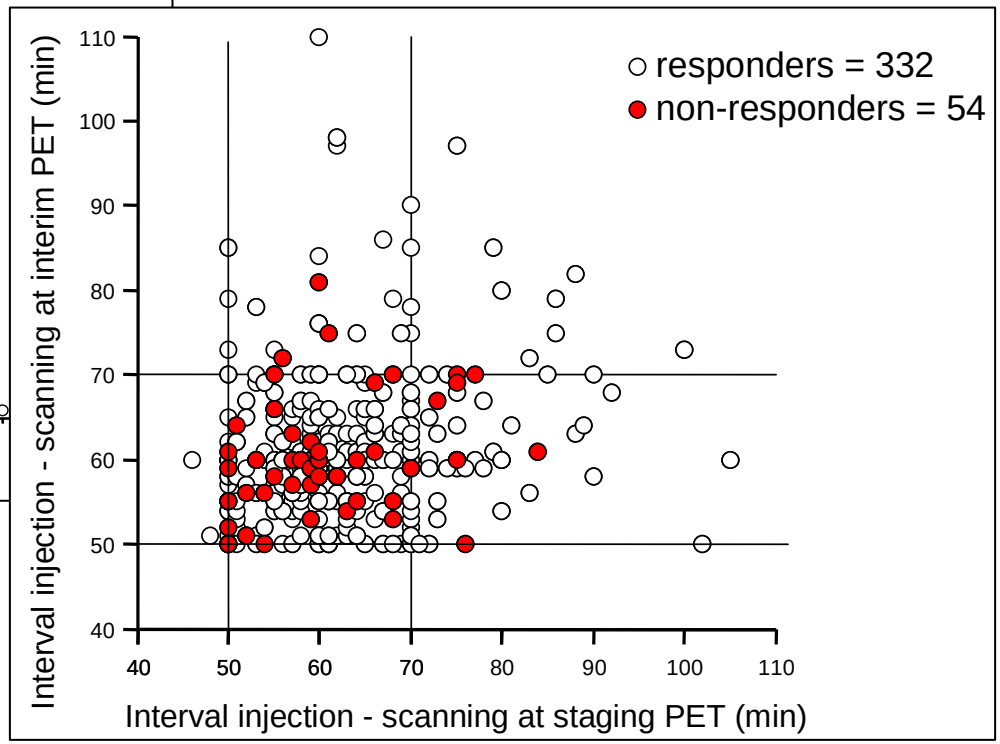
Interim PET

PETAL trial – standardization of scanning conditions

Interval chemotherapy – PET2



Interval injection – scanning

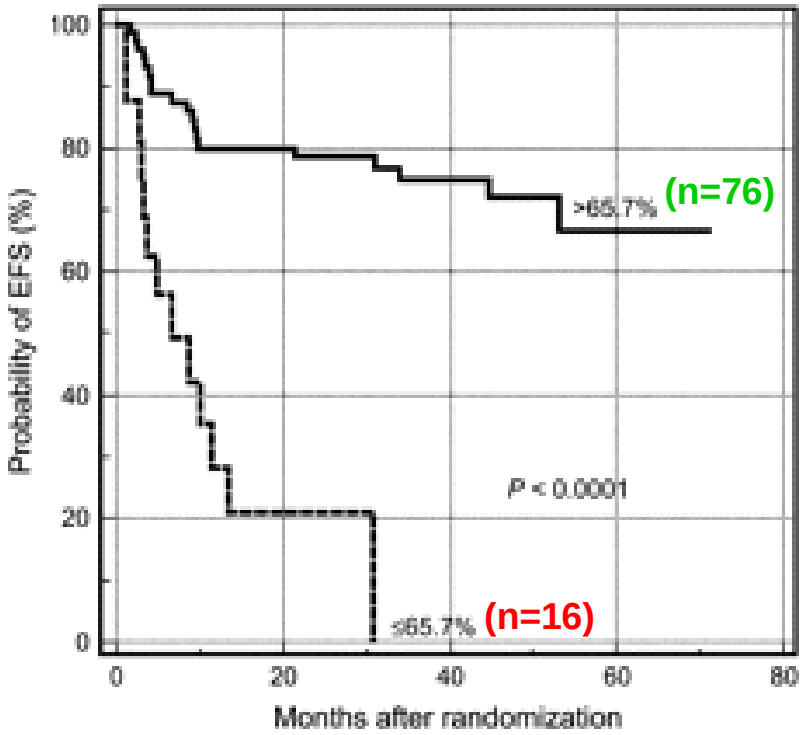


Cons ?

Interim PET

Proportion of treatment failures correctly predicted

SUV-based assessment



Lin et al, J Nucl Med 48: 1626, 2007

Interim PET

Proportion of treatment failures correctly predicted

	No. pts.	Treatment failures	% iPET- TF	% iPET+ TF
Lin 2007	92 (17% iPET+)	34 (37%) at 3 yrs.	53 %	47 %
IVS 2011	120 (22% iPET+)	38 (32%) at 3 yrs.	58 %	42 %
Casasnovas 2011	85 (18% iPET+)	21 (23%) at 2 yrs.	71 %	29 %
PETAL 2010	310 (13% iPET+)	38 (12%) at 10 mo.	71 %	29 %

Only 13 % – 22 % of patients are interim PET positive.

Only 29 % – 47 % of treatment failures occur in the interim PET positive group.

→ **The majority of treatment failures are not predicted by interim PET !**

1. **Is there any evidence that early PET (after 1 or 2 cycles) has a prognostic role in DLBCL ?**

   Yes !

2. **Should we report early PET qualitatively or quantitatively in DLBCL ?**

   Quantitatively !

3. **Is histological confirmation the „gold standard“ reference for patients with mid-treatment positive PET ?**

   No !

4. **Is interim PET feasible in multicenter clinical trials ?**

   Yes !

5. **Can we change treatment on interim PET results ?**

   This needs to be tested in prospective clinical trials !