Second International workshop

on Interim-PET in Lymphoma

April 8th-9th Menton (France)

Is Time for a European PET-response adapted protocol for DLBCL?

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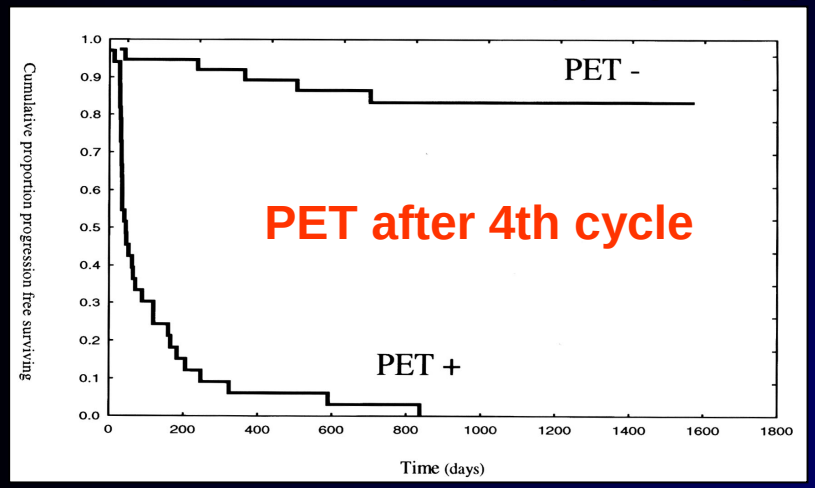
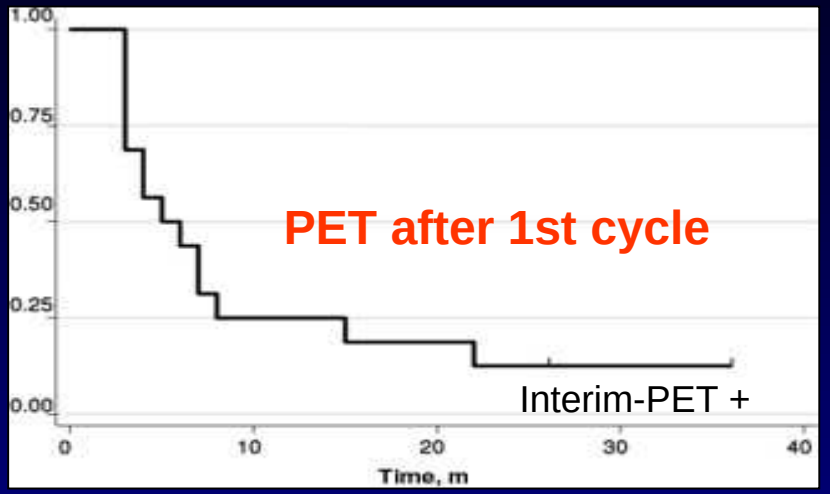
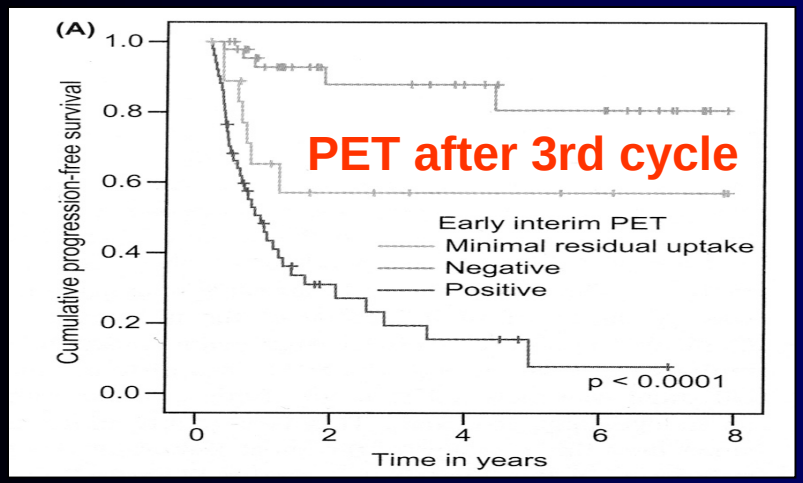
Early clinical trials of interim PET in lymphoma in patients treated mainly without Rituximab



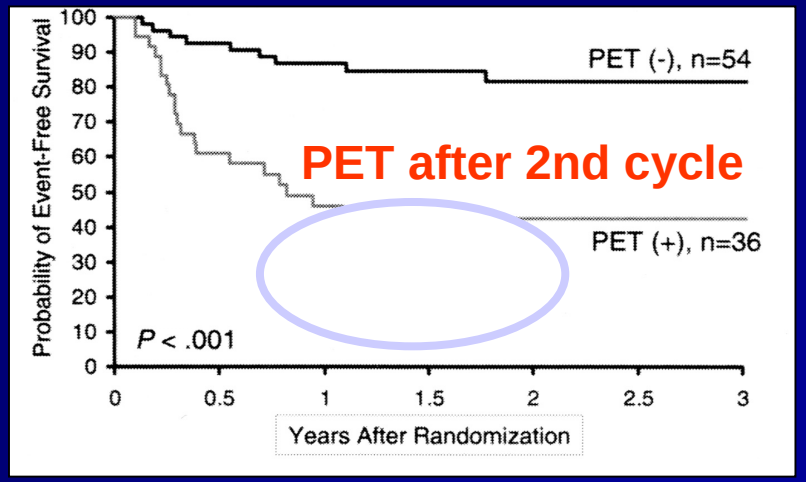
Spaepen et al, Ann Oncol 13: 1356, 2002



Kostakoglu et al, Cancer 107: 2678, 2006



Mikhaeel et al, Ann Oncol 16: 1514, 2005



Haioun et al, Blood 106: 1376, 2005

Issues for Interim PET in DLBCL

- ✓A "new" prognostic tool should be reassessed into the Rituximab era. Many prognostic factors have lost predictive value with the addition of Rituximab (TMA, bcl2 etc)
- ✓Is early response identified by PET always associated with different PFS in DLBCL?
- ✓Are interim PET results able to separate patients with a large difference in the outcome that can justify a change of the treatment?
- ✓Is early change in the first-line treatment in PET+ patients associated with a better outcome compared to salvage therapy?
- ✓PET negative patients may benefit from a reduction of the treatment?

INTERIM 18-FDG-POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY (PET) FAILED TO PREDICT DIFFERENT OUTCOME IN DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) PATIENTS TREATED WITH R-CHOP

April 2004 - December 2008: 82 newly diagnosed DLBCL or FL IIIb

All patients were treated according to the planned treatment without modification by Interim PET results:

- ✓ **6-8 R-CHOP14 in young poor prognosis patients according to IPI score: intermediate-high (IH) or high risk (H)**
- ✓ **6-8 R-CHOP21 in all elderly or young good prognosis patients according to IPI score: low (L) or low-intermediate risk (LI)**
- ✓ **IF-RT consolidation to bulky lesions or bone lesions**

Pregno P, ASH 2009

CLINICAL CHARACTERISTICS (82 patients)

Median age 56 years (range 22-81)

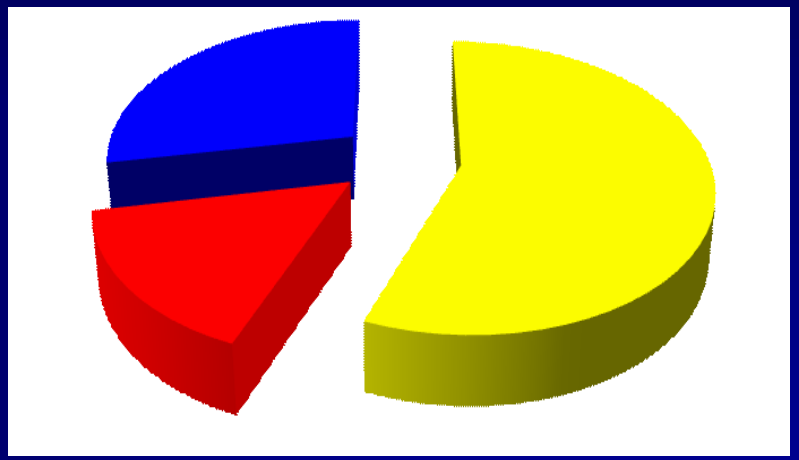
Gender		Stage	
Males	42	I-II	29
Females	40	III-IV	53
LDH		**IPI score**	
normal	45	L-LI risk	47
> normal	37	IH-H risk	35
PS		**No Extranodal sites**	
0-1	58	0-1	55
>1	24	>1	27
Bulky		**Bone Marrow**	
Yes	13	Yes	22
No	69	No	60

TREATMENT AND PET TIMING (82 patients)

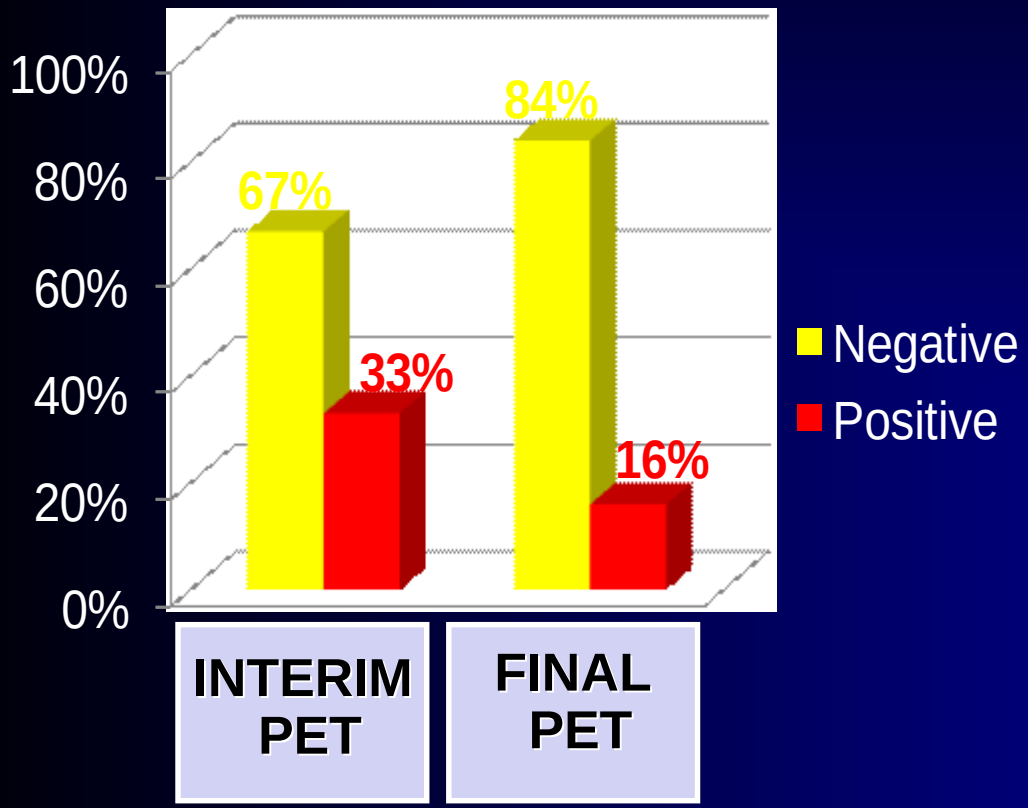
Treatment plan

	patients
R-CHOP14	19
R-CHOP21	63
+ IF-RT	13

Timing of Interim PET



RESULTS (82 patients)

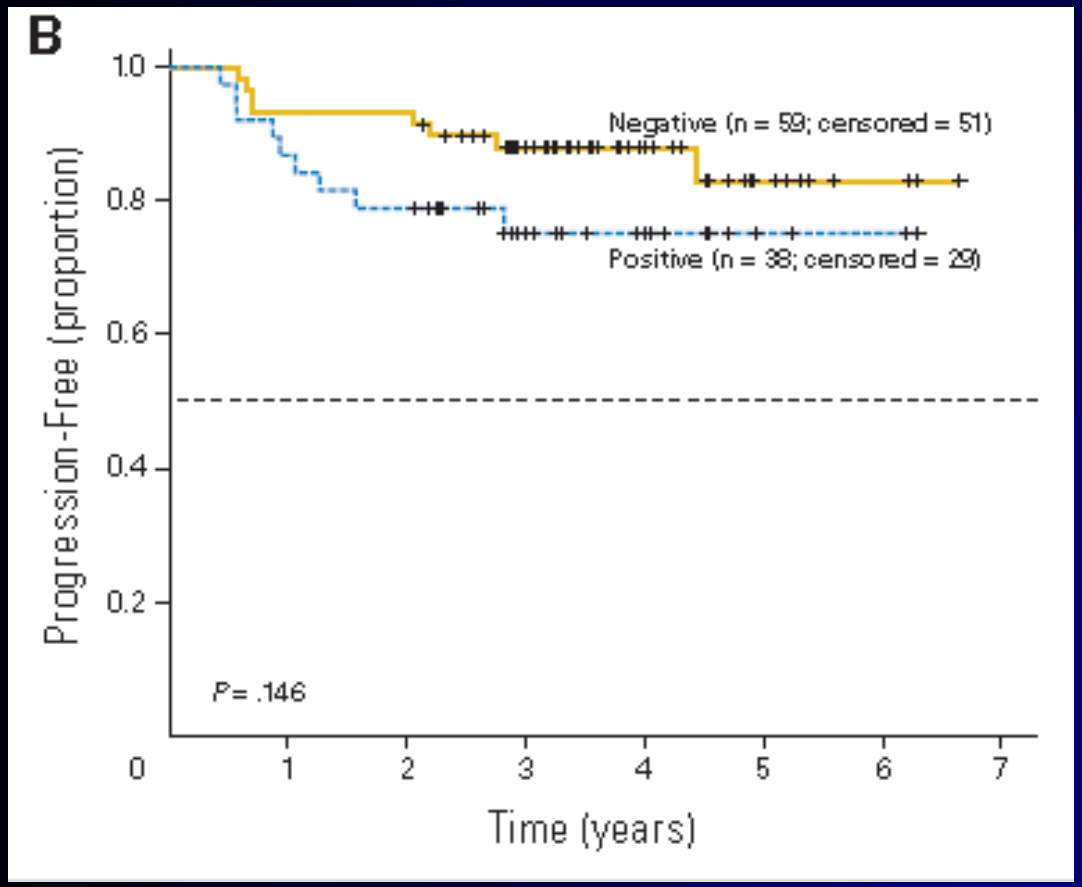


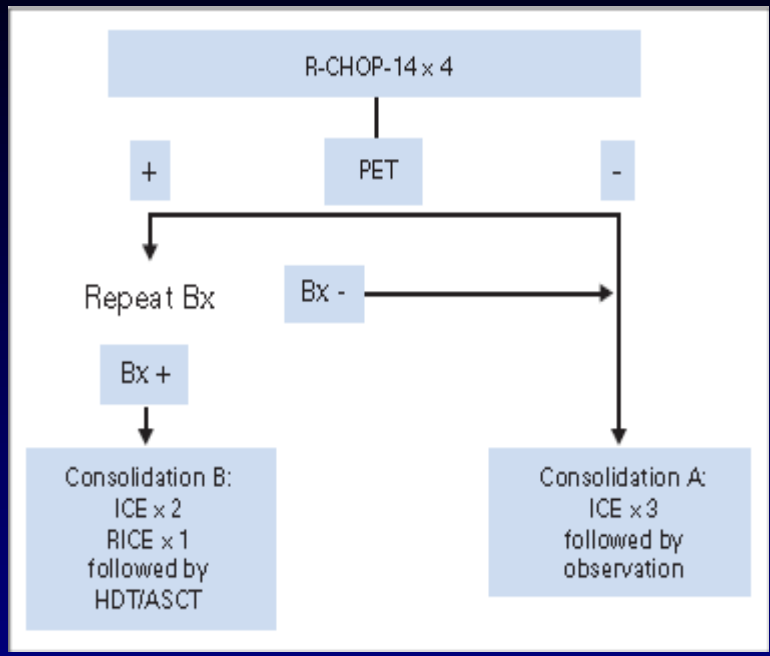
	Interim PET +	Interim PET -	
Final PET+	12	1	13
Final PET -	15	54	69
	27	55	82

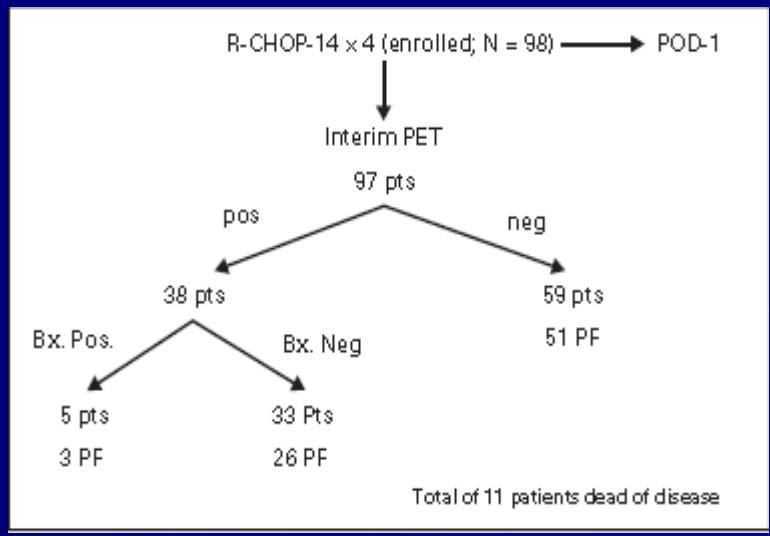
	Interim PET(%)	Final PET (%)
PPV	17	71
NPV	80	83

Early evaluation of 18-FDG-PET in DLBCL

Risk-Adapted Dose-Dense Immunochemotherapy Determined by Interim FDG-PET in Advanced-Stage Diffuse Large B-Cell Lymphoma



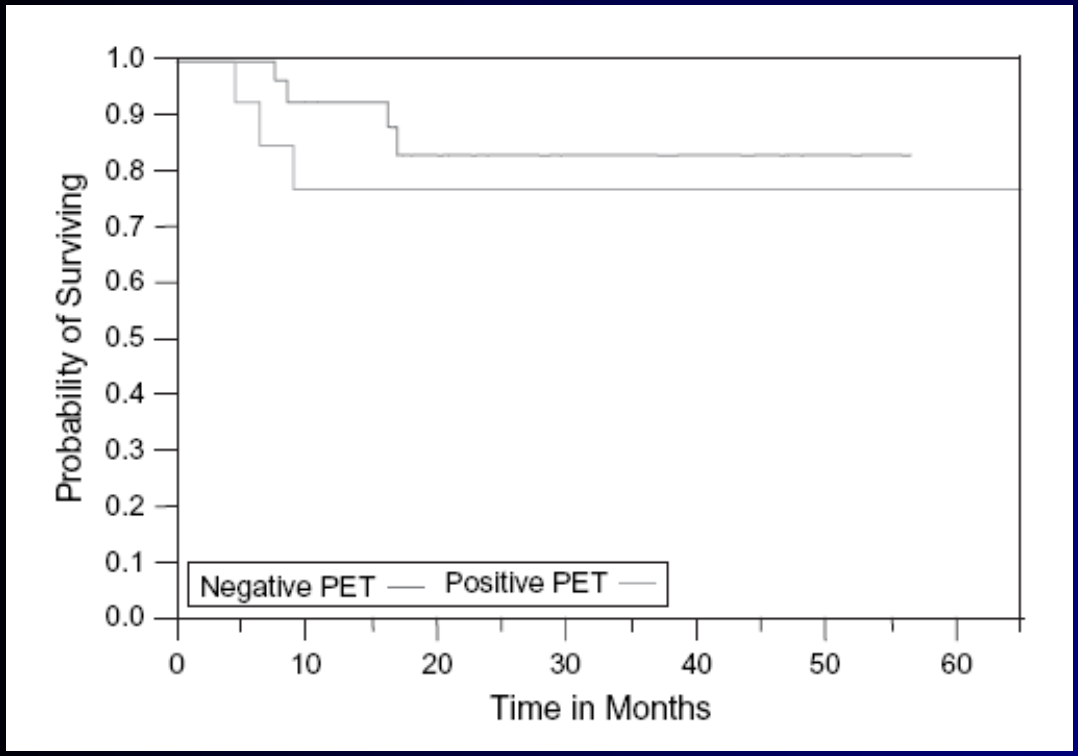




Moskowitz CH, J Clin Oncol 2010

Early evaluation of 18-FDG-PET in DLBCL

High incidence of false-positive PET scans in patients with aggressive non-Hodgkin's lymphoma treated with rituximab-containing regimens



51 patients: Interim PET 2-4 courses

38 DLBCL
13 MCL

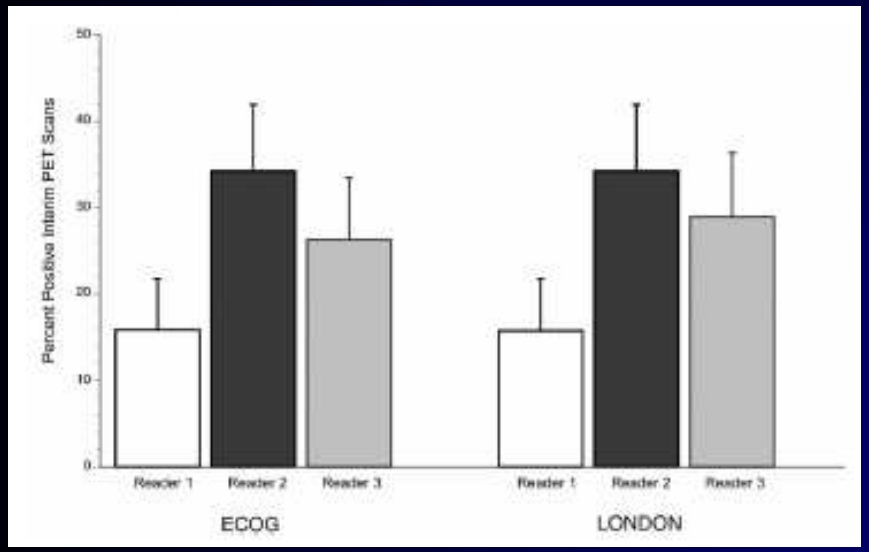
RCHOP21
R-MACLO-IVAM-T

PPV 33%; NPV 68%

Han HS, Ann Oncol 2009

Reproducibility of interim PET interpretation

Interim positron emission tomography scans in diffuse large B-cell lymphoma: an independent expert nuclear medicine evaluation of the Eastern Cooperative Oncology Group E3404 study



38 interim scans

Agreement complete:
- ✓ **68% by ECOG criteria**
- ✓ **71% by London criteria**

Range of PET interim scans:
16% - 34% (p ns) by reviewer.

Moderate reproducibility among nuclear medicine experts

Need to standardize PET interpretation in research and practice.

Horning S, Blood 2010

Interim PET interpretation: possible pitfalls

A negative interim PET is consistently associated with a good outcome

Possible reasons for low PPV of Interim PET

- ✓Interim biopsies show degree of inflammation or necrosis that may cause FDG uptake
- ✓Immunotherapy may increase lesion inflammation (C activation, ADCC) and FDG uptake
- ✓Different induction regimens may have different effect (CHOP vs RCHOP; 14 day vs 21 day interval)
- ✓Different timing of PET imaging relative to chemotherapy (1-2 weeks after chemo in interim PET, 1 month after chemo in final PET)
- ✓Different criteria for PET positive among studies
- ✓Wide differences among observer and reviewers

Interim PET interpretation

PET positive, PET negative, or PET peeve?

….Until criteria for interpretation of PET scans are prospectively validated, and the experts can routinely agree on what is PET positive and what is PET negative, physicians should not change therapy for lymphoma based on an interim PET in practice, and probably should not even routinely perform such scans….

Friedberg JW, Blood 2010

- ✓**PPV ranged from 20-30% to 50% among various studies. A treatment change on this basis means that 50-70% of the patients can be overtreated**
- ✓**Different criteria may be necessary whether the endpoint is descalation (proper identification of negative patients) or intensification (proper identification of positive patients) of the treatment**
- ✓**We need definitive and careful guidelines validated in a homogenous cohort of DLBCL patients treated with R-CHOP before tailoring therapy on interim-PET results**

Ancillary trial 18-FDG-PET in IIL-DLCL04