11th INTERNATIONAL CONFERENCE ON MALIGNANT LYMPHOMA
Lugano, Switzerland, June 15-18, 2011
11-ICML

Summary of talks, discussions from the afternoon workshop about PET…

Response assessment:

Use of interim PET

How to combine PET and CT

Surveillance

Co chairs Barrington, Cheson

Use of interim PET with FDG

Basic points:

The methods used for response assessment should be the methods which have the strongest prognostic performance

For FDG-avid lymphomas:

Interim PET/CT is better than CT alone

- to predict the final treatment response
- to predict long-term disease-free survival

Post-treatment PET/CT is better than CT alone

- to predict long-term disease-free survival

M Hutchings, Copenhagen , DK

PET response assessment

- Interim PET widely used in clinical practice to monitor tx (but not necessarily to change standard tx)

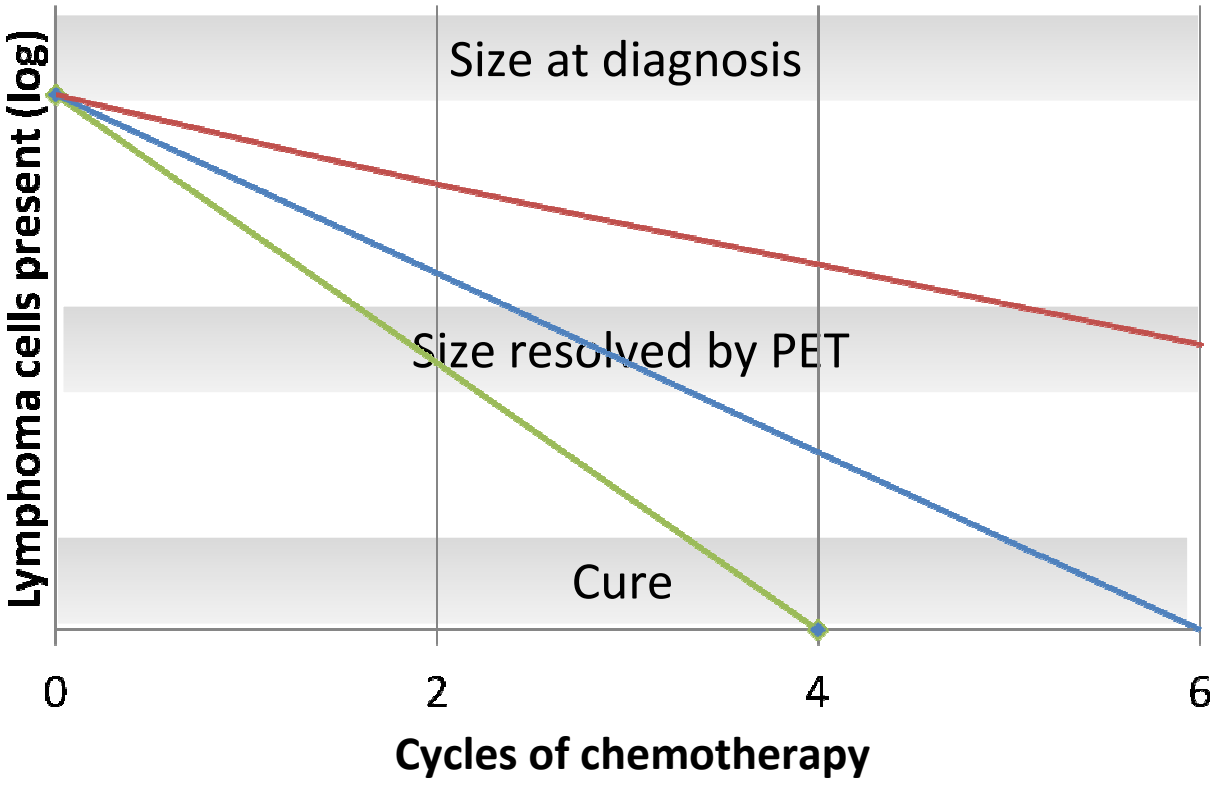
- Role of interim PET in response adapted tx under investigation in trials ….

With Interim PET we are looking at

- **The kinetics of the FDG metabolism in the tumoral sites during the tumoral destruction produced by the first few cycles of chemotherapy**

M Meignan, Creteil , F

PET imaging during 1st line tx



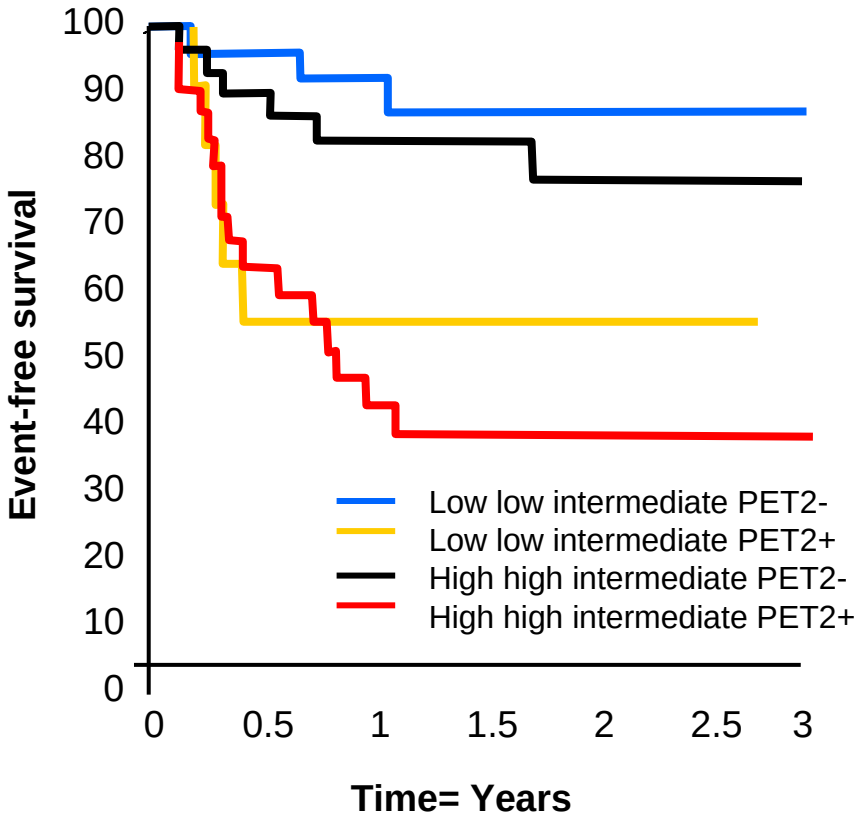
Points:

- Interim PET reflects chemosensitivity
- Significant residual activity may be present even in patients with good prognosis
- Different criteria for interpretation to end PET

Interim PET (2 cycles) in aggressive DLBCL and advanced HL

DLBCL

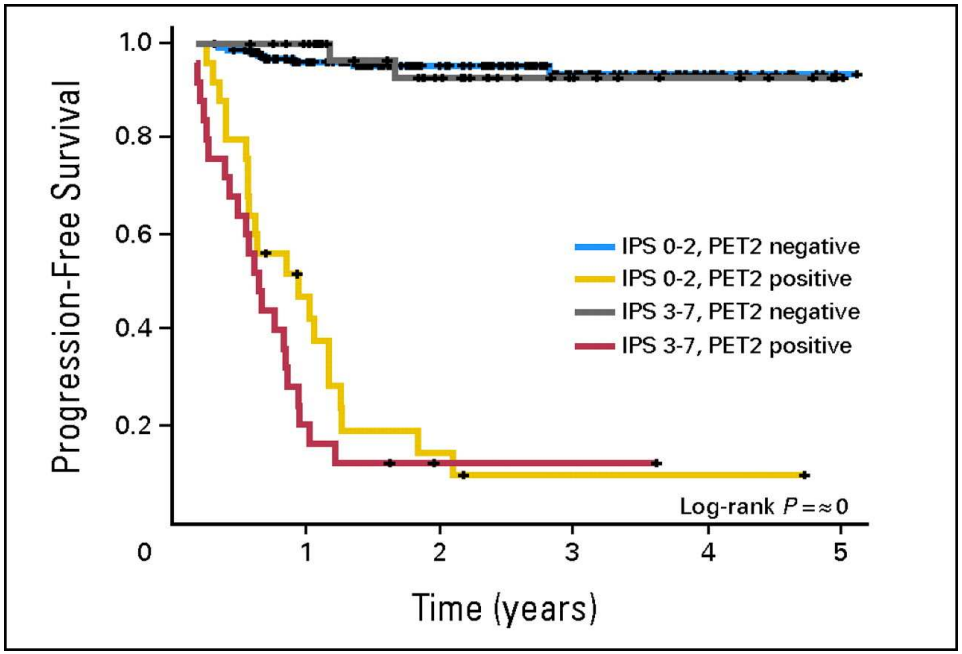
Visual analysis



Haioun C, Blood, 2005

as HL

MRU- SUVmax between 2 and 3.5
Considered negative> Liver SUV



Gallamini A, J Clin Oncol, 2007

M Meignan, Creteil , F

How to define a ‘positive’ scan

Implication of ‘uptake’ may vary according to

- 2 vs 4 vs 6 cycles (cf PERCIST)
- Disease type
- Treatment (ABVD vs BEACOPP, use of rituximab)
- Research question in clinical trial

What do we want from test?

- Lower level of FDG uptake used to define ‘negative’ scan where high NPV required to de-escalate tx
- Higher level of uptake used to define ‘positive’ scan where high PPV required to escalate tx

Meignan M, Gallamini A, Haioun C.
Report on the first international workshop on interim-PET scan in lymphoma.
Leuk.Lymphoma 2009;50:1257-1260.

Discussion points

- A ‘one size, fits all’ set of rules to define PET ‘positive’ and PET ‘negative’ scans is not appropriate.
- A scale that gives a measure of the likelihood of relapse more helpful to design trials and in future plan tx in an individual patient ?

Interim PET reporting in lymphoma

'Dichotomized analysis PET+/PET with a fixed background does not describe the biological phenomenon and does not work for iPET'

'We need graded criteria (visual or quantitative) which are robust and have good interobserver agreement'

M Meignan, Creteil , F

Discussion points

- Reproducible results rely on:

Interpretation criteria

Acquisition

QC

- Standardised methods developed for trials are in widespread clinical use

Deauville criteria

1. no uptake
2. uptake ≤ mediastinum
3. uptake > mediastinum but ≤ liver
4. moderately increased uptake compared to liver
5. markedly increased uptake compared to liver and/or new lesions

Meignan, et al. Leuk Lymphoma, 2009
Barrington, et al. Eur J Nucl Med Mol Imaging, 2010
Meignan Eur J Nucl Med Mol Imaging, 2010

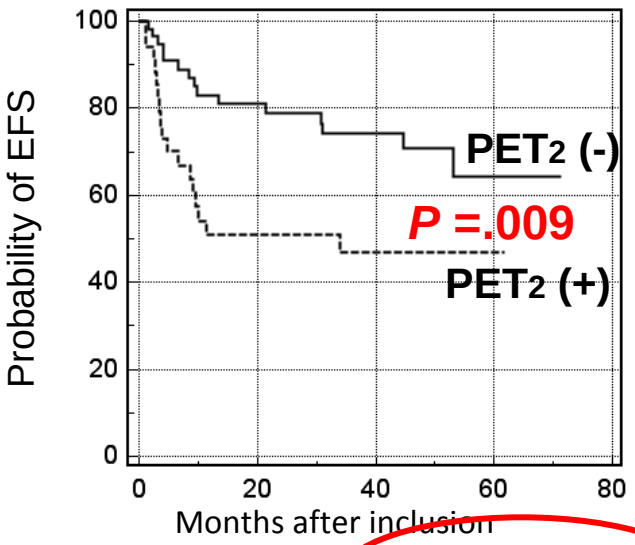
Deauville criteria

- Good accuracy and agreement in HL (Gallamini et al IVS)
- Good agreement in adult HL (Barrington, Gallamini,) paediatric HL (Furth)

Gallamini et al Ann. Oncol. 2011; 22 Suppl. 4, 97. Abstract n° 047.
Barrington, et al. Eur J Nucl Med Mol Imaging, 2010
Furth et al Ann Oncol 2011

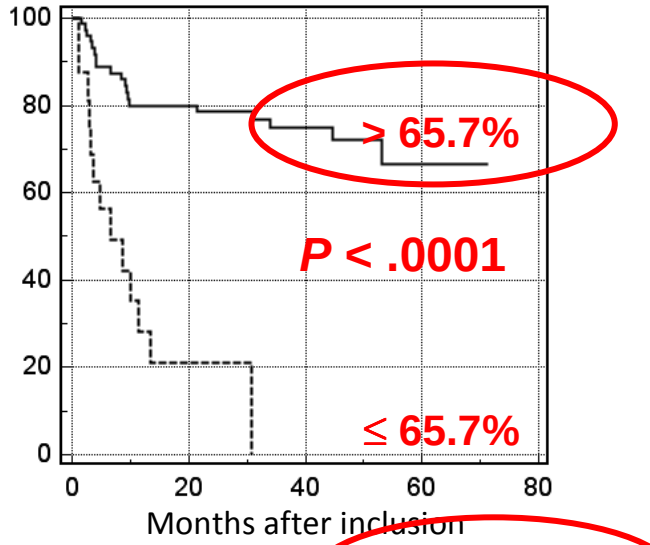
Different threshold at PET2
Visual vs. quantitative analysis
2 cycles, n=92, DLBCL

Visual analysis
(Créteil, MRU)



NPV=74%, PPV=50%

Quantitative analysis
(% reduction SUVmax)



NPV=73.6%, PPV=84.6%

Lin, Itti et al. J Nucl Med 2007;48:1626-32

M Meignan, Creteil , F

Discussion points:

- ❖ Methods to refine response assessment with PET
  - Use of delta SUV (? max, peak)
  - Assessment of metabolic tumour volume eg TLG
  - Combining with measures of initial tumour bulk
- ❖ Methods need proper validation and must be practical for widespread use with QC and tested in prospective studies

Comment (SB) : Initiatives such as EARL(EANM) QIBA (RSNA) could make semi-quantitative analysis a real option

How to combine FDG PET and CT

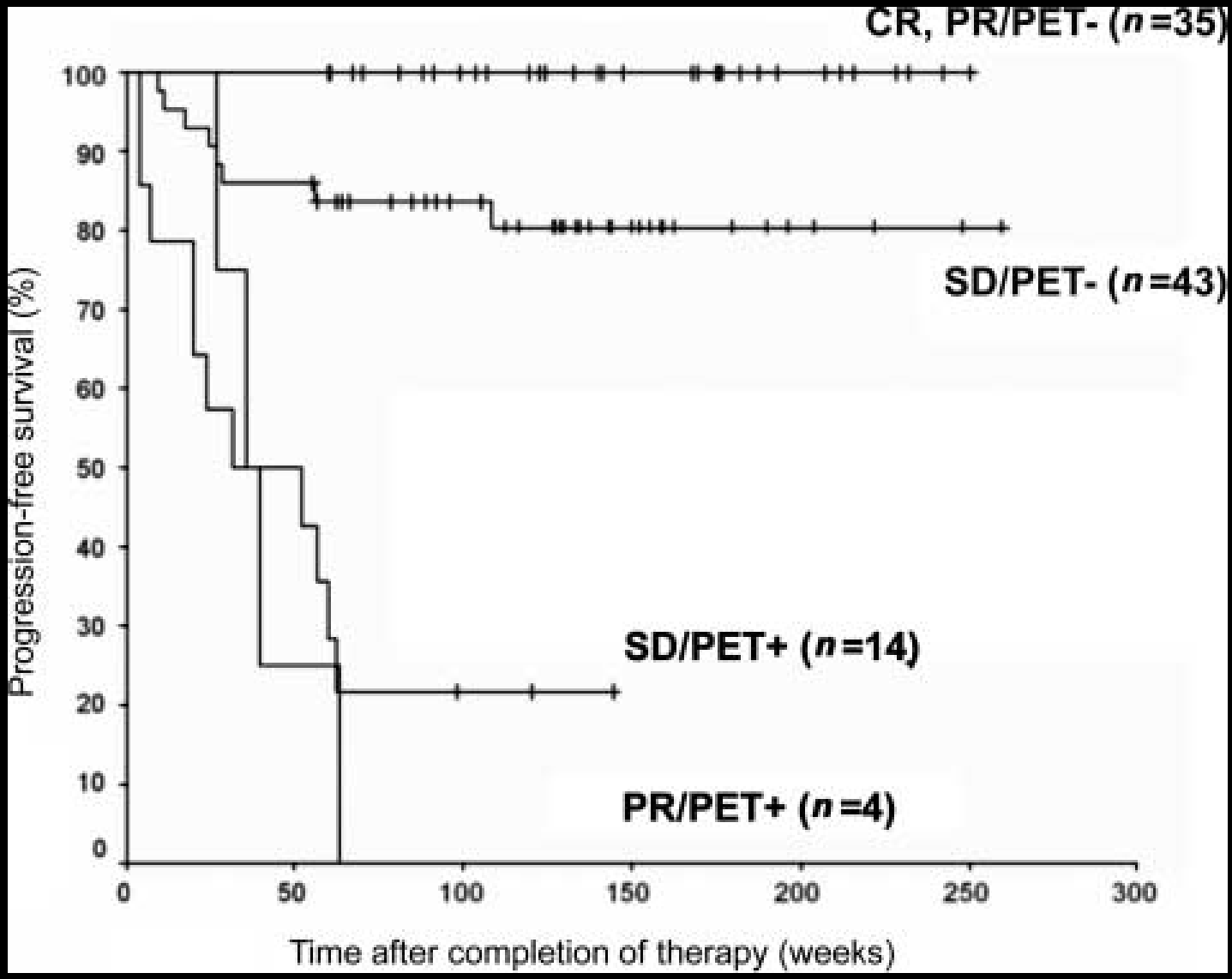
It is not either / or

Response evaluation with PET and CT are two very different surrogates for clinical benefit of the given treatment

How do we combine the metabolic and the structural response in the best way?

M Hutchings, Copenhagen , DK

Reinhardt et al. Ann Oncol 2005;16:1524-29



PFS when CT and PET combined

M Hutchings, Copenhagen , DK

Overall conclusions

If high prognostic accuracy is the aim, PET/CT should be the method of choice for response assessment of aggressive lymphomas, both during and after treatment

The most powerful prognostic stratification is PET-based

CT response may further refine the prognostic stratification:

In PET-negative patients post-treatment (Reinhardt, Hutchings)
In PET-positive DLBCL patients after 4 cycles (Dupuis)
In early stage HL patients after 2 cycles (Kostakoglu)
In PET-negative advanced stage HL patients after 2/4 cycles (Hutchings)

M Hutchings, Copenhagen , DK

Discussion points

- iPET and end PET are better prognostic indicators than CT
- CT can improve prognostication in addition to PET in PET +ve patients (in situations where PET may have lower PPV - DLBL, early HL) and PET -ve patients where PPV of PET is high (adv HL)
- Best way to combine information from CT and PET still undetermined
- More studies needed

Role of surveillance

Accuracy For A Positive Routine Test :

Chances For Relapse = 1/68

Sensitivity CT = 62% *

Specificity CT = 92%*

<u>10%</u>

Calculated using data from Radford et al, UK

*average from 4 large series

J Armitage, Omaha, US

Surveillance PET/CT Scans (Denmark)

- Patients – 53 classical HL, 2 NLPD
- 4 Relapses: 3 detected by PET/CT
- 18 Positive PET/CT's
- Positive Predictive Value = 19%

  Negative Predictive Value = 100%

J Armitage, Omaha, US

PET-CT Surveillance in HL

Patient Characteristics (n=109)

- Median age 31 (18-71)
- 63% stage II; 28% stage III/IV
- 39% bulky disease
- 62% unfavorable ESHL
- IPS: 38% IPS 2-3 ; 12% ≥ 4
- 86% Rx with Stanford V regimen

Results:

- Positive scans: n=25
- False positive scans: n=16 (64%)
  - Median fu after false positive scan: 14 mos
  - 315 scans done to detect 9 relapses
  - Actions prompted:
    - Short-interval repeat scan (n=8)
    - No change of surveillance plan (n=4)
    - Biopsy of suspicious area (n=3)
    - Colonoscopy (n=1)

	Positive	Interminate	Negative	PPV	NPV
Clinician Review of Report	25	26	N/A	36%	100
Nuclear Medicine Review	20	5	26	45%	100

R Advani, Stanford, USA

‘For a routine scan at least 10 patients will have invasive procedures to diagnose one relapse. This may actually under estimate the risk of unnecessary procedures since most relapses will present with symptoms between visits. There is no proven impact on survival’

(Armitage)

Discussion points

- In absence of symptoms, surveillance PET and CT scans not warranted, because low detection of relapse unnecessary tests , patient anxiety, extra radiation
- Discourage excessive use of FU scans (PET and CT) in clinical trials and clinical practice better use of clinically relevant endpoints
- Scans warranted only for clinical suspicion of relapse and possibly for patients at high risk of early relapse? worthy of trial.

Conclusions

1. Interim PET has a place to monitor tx
2. Standardised methods for PET seen as strength
3. Reproducible methods for reporting
4. Lack of consensus how to combine PET and CT to measure response
5. Surveillance PET/CT not currently recommended for patients who achieve CR

Further work

- Assess role of quantitative/volumetric analysis MUST be properly validated and widely applicable across all platforms
- Optimal way to combine PET and CT measures of response
- Whether (any) patients merit FU with CT and or PET after tx