

PET-based decisions in non Hodgkin's lymphoma

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Disclosure slide

- In the context of this presentation, I have nothing to declare.

PET-based decisions in NHL

- Staging
- Restaging
- Interim-assessment

Two new publications in JCO Aug 2014

Role of Imaging in the Staging and Response Assessment of Lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group

Sally F. Barrington, N. George Mikhaeel, Lale Kostakoglu, Michel Meignan, Martin Hutchings, Stefan P. Müller, Lawrence H. Schwartz, Emanuele Zucca, Richard I. Fisher, Judith Trotman, Otto S. Hoekstra, Rodney J. Hicks, Michael J. O'Doherty, Roland Hustinx, Alberto Biggi, and Bruce D. Cheson

Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification

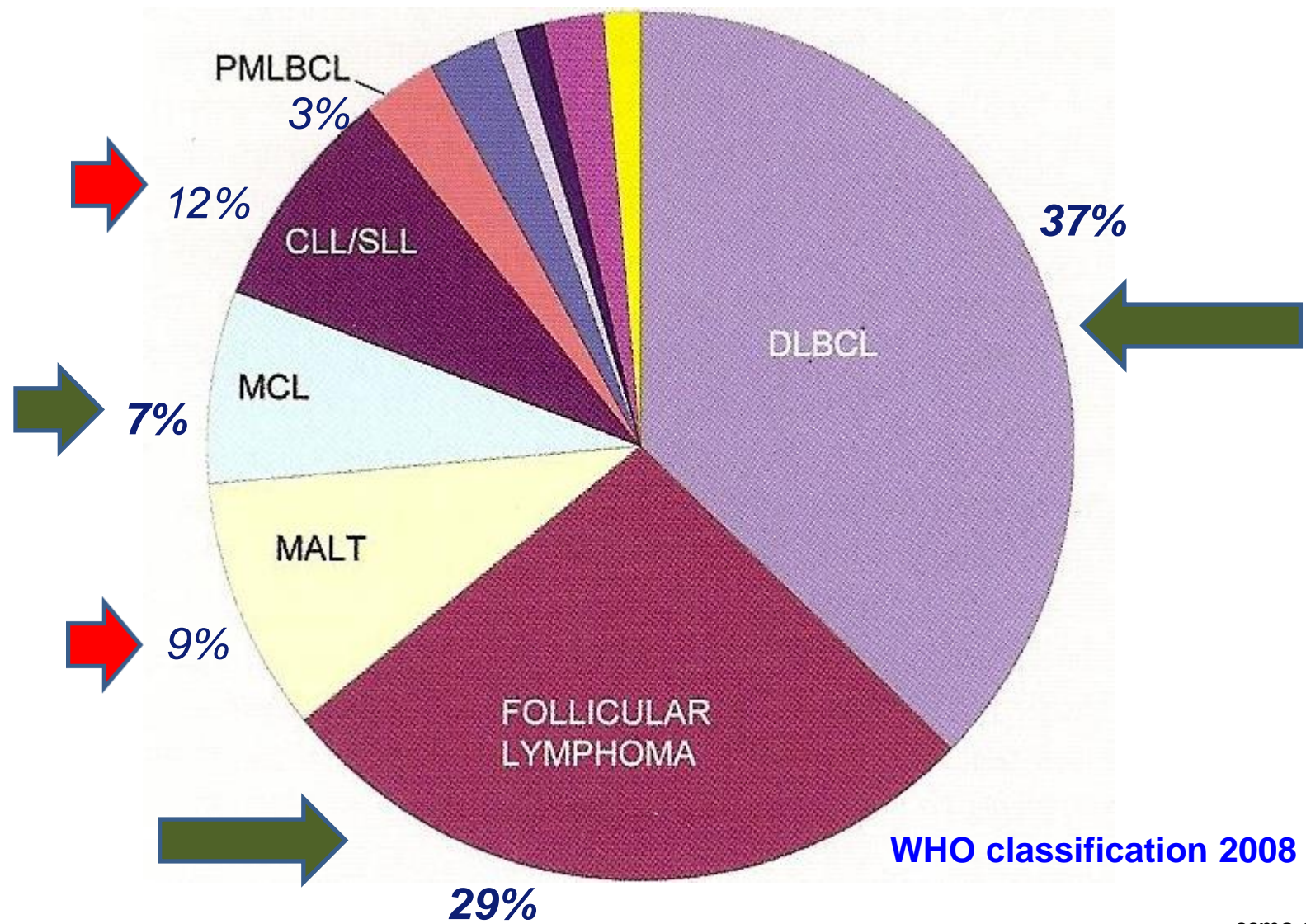
Bruce D. Cheson, Richard I. Fisher, Sally F. Barrington, Franco Cavalli, Lawrence H. Schwartz, Emanuele Zucca, and T. Andrew Lister

PET-based decisions in NHL

- Staging in NHL

PET-CT staging is gold standard

- PET-CT: higher accuracy of staging compared to CT for nodal and extranodal sites
- Sub-types of NHL (WHO classification 2008)
- Different FDG-avidity



WHO classification 2008

PET-CT staging

Table 1. Criteria for Involvement of Site

Tissue Site	Clinical	FDG Avidity	Test	Positive Finding
Lymph nodes	Palpable	FDG-avid histologies	PET-CT	Increased FDG uptake
		Nonavid disease	CT	Unexplained node enlargement
Spleen	Palpable	FDG-avid histologies	PET-CT	Diffuse uptake, solitary mass, miliary lesions, nodules
		Nonavid disease	CT	> 13 cm in vertical length, mass, nodules
Liver	Palpable	FDG-avid histologies	PET-CT	Diffuse uptake, mass
		Nonavid disease	CT	Nodules
CNS	Signs, symptoms		CT	Mass lesion(s)
			MRI	Leptomeningeal infiltration, mass lesions
			CSF assessment	Cytology, flow cytometry
			PET-CT*, biopsy	Lymphoma involvement
Other (eg, skin, lung, GI tract, bone, bone marrow)	Site dependent			

Abbreviations: CSF, cerebrospinal fluid; CT, computed tomography; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography.

*PET-CT is adequate for determination of bone marrow involvement and can be considered highly suggestive for involvement of other extralymphatic sites. Biopsy confirmation of those sites can be considered if necessary.

Cheson et al JCO 2014

PET-CT for staging NHL

Baseline PET-CT should be used

- for staging in routinely FDG-avid lymphomas
- to direct biopsy

(especially in case of suspected transformation)

- for optimal response assessment

Contrast enhanced CT (ceCT)

Reserved for

- measurement of nodal size for trials
- radiation therapy planning
- distinguishing bowel from nodes or assessing compression/thrombosis of central/mediastinal vessels
- if required at staging

Bone marrow assessment

- Focal FDG uptake in aggressive NHL sensitive for BM involvement
- Bone marrow biopsy no longer indicated *for HL*
- PET may also obviate the need for biopsy in DLBCL
unless discordant histology is important for management
- Bone marrow biopsy required for other lymphomas
(IHC & flow cytometry)

PET-based decisions in NHL

- Restaging after therapy
 - (chemo-immunotherapy/ radiotherapy)

What do we need for a reliable diagnostic test?

- High PPV
- High NPV

PET-CT evaluation after treatment

For “aggressive” NHL

- Negative predictive value 80-100%
- Positive predictive value 50-100%
 - Further therapy considered: biopsy or follow up scan

Mikhaeel et al Ann Oncol 2000
Zijlstra et al Haematologica 2006

PET-CT restaging

For FDG-avid lymphomas;

- PET-CT for response assessment using 5-Point Scale (5-PS)
- PET-CT standard of care for remission assessment

5 Point Scale (Deauville criteria)

1. no uptake
2. uptake \leq mediastinal bloodpool
3. uptake $>$ mediastinal bloodpool but \leq liver
4. moderately increased uptake compared to liver
5. **markedly** increased uptake compared to liver and/or new lesions

**** markedly** increased uptake: $> 2-3 \times$ SUV max normal liver

Response according to 5-PS

with standard treatment

**scores 1-3 is Complete Metabolic Response
(CMR)**

Note: in response-adapted trials exploring de-escalation, score 3 may be deemed inadequate response to avoid under-treatment

Interpretation of score 3 depends on timing of assessment, clinical context & treatment.

Residual masses

Biopsy of residual metabolically active tissue recommended

- if salvage treatment is considered

Residual size mass and location should be recorded in PET-CT reports where possible

as significance of the size of masses is unclear but may be complementary to metabolic information and data should be collected prospectively in clinical trials

PET-based decisions in NHL

- Interim PET-CT assessment

Why?

- To detect bad responders -> timely switch to more effective therapy
- To detect very good responders and tailor therapy -> less cycles? Less toxicity..

Interim PET-CT Response Assessment

To assess early response..

NPV ..?

PPV .. ?

— Varies in each different trials.

- Response adapted trials

- Treatment de-escalation for good-responders

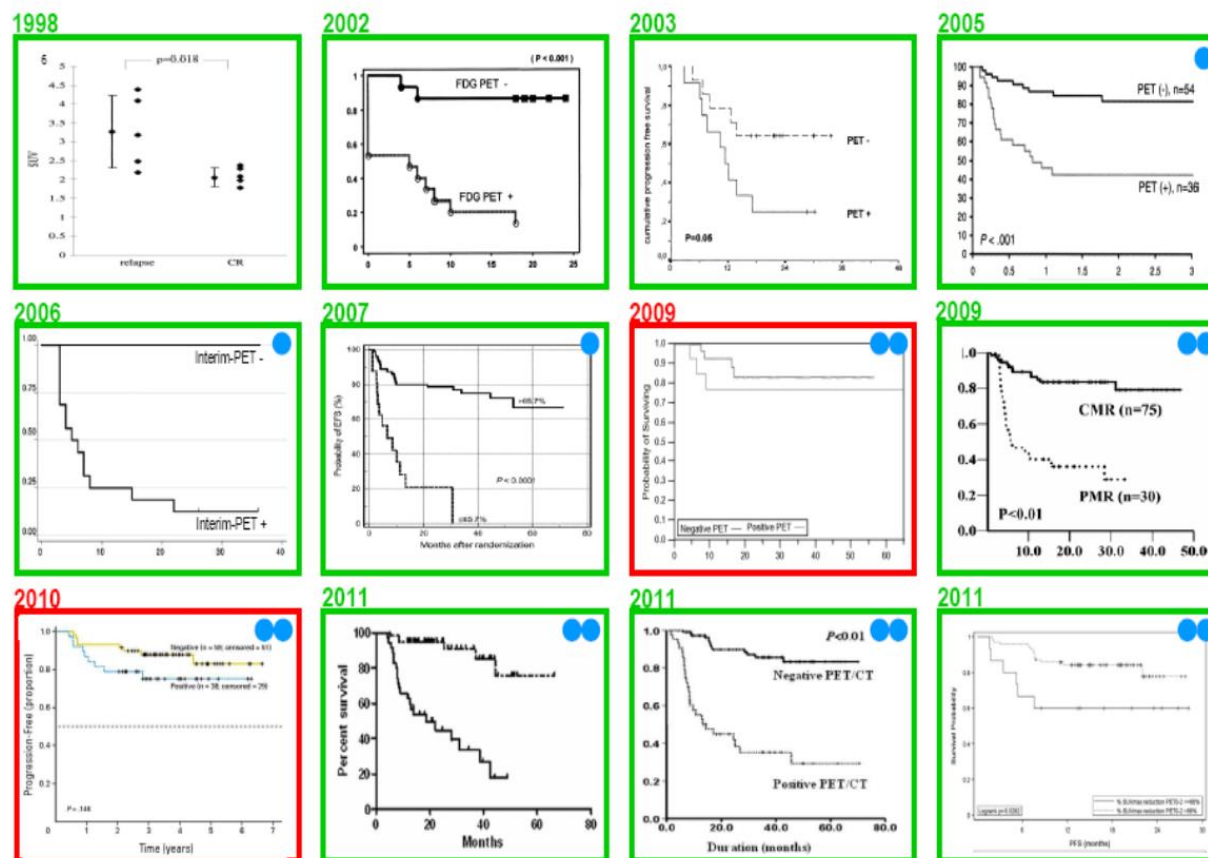
- Treatment escalation for bad-reponders:

- improved outcome??**

Interim PET

● +/- Rituximab
●● + Rituximab

Predictive value in aggressive non-Hodgkin's lymphomas



^{18}F -FDG PET/CT for Early Response Assessment in Diffuse Large B-Cell Lymphoma: Poor Predictive Value of International Harmonization Project Interpretation

Amanda F. Cashen^{1,2}, Farrokh Dehdashti^{1,3}, Jingqin Luo^{1,4}, Andrew Homb³, Barry A. Siegel^{1,3}, and Nancy L. Bartlett^{1,2}

Interim 18-FDG-PET/CT failed to predict the outcome in diffuse large B-cell lymphoma patients treated at the diagnosis with rituximab-CHOP

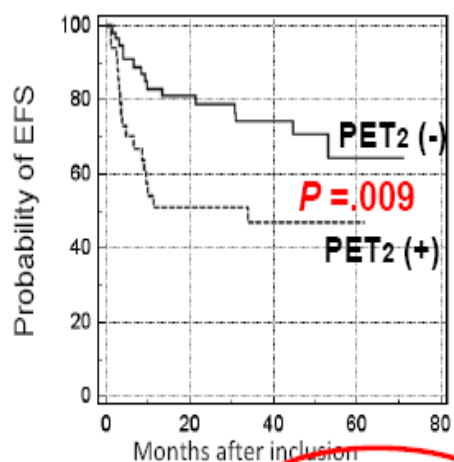
Patrizia Pregno,¹ Annalisa Chiappella,¹ Marilena Bellò,² Barbara Botto,¹ Simone Ferrero,³ Silvia Franceschetti,⁴ Francesca Giunta,² Marco Ladetto,³ Giorgio Limerutti,⁵ Massimo Menga,² Maura Nicolosi,¹ Giorgio Priolo,¹ Benedetta Puccini,⁶ Luigi Rigacci,⁶ Flavia Salvi,⁷ Luca Vaggelli,⁸ Roberto Passera,² Gianni Bisi,² and Umberto Vitolo¹

Different threshold at PET2

Visual vs. quantitative analysis

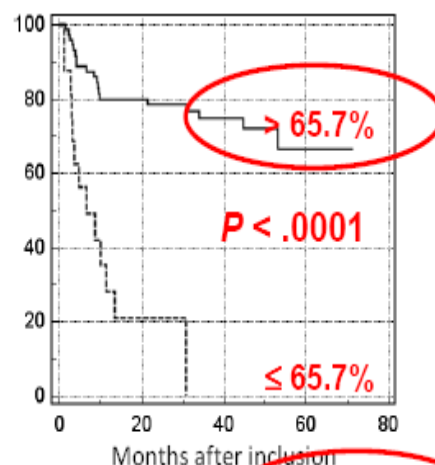
2 cycles, n=92, DLBCL

Visual analysis
(Créteil, MRU)



NPV=74%, PPV=50%

Quantitative analysis
(% reduction SUV_{max})



NPV=73.6%, PPV=84.6%

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

Interim-PET; many questions..

- the optimal timing of interim FDG-PET ?
- which interim FDG-PET response criteria perform best predicting end-of-therapy response rate and PFS
- whether and how chemo-immunotherapy affects the performance of interim FDG-PET
- whether and how type of NHL affects the performance of interim FDG-PET
- cost-effectiveness of interim FDG-PET in DLBCL?



PETRA Consortium

PET-CT ReAnalysis in NHL

Validation of interim PET as a biomarker of response in NHL: individual patient data meta-analysis of interim 18F-FDG PET including re-analysis of PET-CT images

PETRA: a comprehensive and unique shared database of individual patient data (IPD) of studies on interim FDG-PET.



26-30 September 2014, Madrid, Spain

esmo.org

Interim-PET; many questions..

Major clinical problem R-CHOP refractory DLBCL patients

- Early treatment escalation.. (< 65yrs; ASCT)
- But better outcome is not clear..

Interim PET-CT Response Assessment

- If mid therapy imaging is performed, PET-CT superior to CT
- Trials evaluating the role of PET response adapted therapy
 - meantime it is not recommended to change treatment based solely on PET-CT unless clear evidence of progression

Summary of imaging recommendations – NEW since 2007

- PET-CT should be used for routine staging of FDG-avid lymphomas
- Patients with DLBCL can be spared bone marrow biopsy
- The 5-PS is recommended for reporting response
- Standardisation of PET-CT methods is mandatory for quantitative analysis and desirable for best clinical practice