Workshop key imaging questions

Relevance of current imaging staging systems

Influence of tumour burden

Need for bone marrow biopsy

Use of interim PET-CT in clinical practice

Integration of PET-CT and dedicated CT in interim and post treatment response criteria

Potential prognostic value of volumetric assessment of tumour in trials and feasibility in routine practice

Use of imaging during surveillance after 1st line treatment

Workstream leads: R Fisher, E Zucca, B Cheson, A Lister.

‘Imaging Task Force’

SF Barrington, NG Mikhaeel, L Kostakoglu, M Hutchings,
S Müller, LH Schwarz, M Meignan

Staging and response

Literature review

Gather knowledge about research in progress

1. The state of current knowledge (category 1)
2. Identify emerging applications (category 2)
3. Highlight key areas for research (category 3)

PET and CT – advances since IHP 2007

- PET almost completely replaced by PET-CT
- More evidence for use of interim PET
- Emerging evidence for use in FL

In context of response adapted trials :

- Increased efforts to standardise PET methods and reporting
- More interest in using quantitative measures

School of Medicine

at Guy's, King's College & St Thomas

Hospitals, Division of Imaging

KING'S College LONDON

University of London

WORKSHOP : **9-10 May 2012 at St Thomas' Hospital London SE1 7EH**

Interim PET DLBL + ? update on NCRI DLBL substudy — George

The use of iPET outside trials, recommendations when to use iPET during the course of treatment for HL and DLBL — George

WORKSHOP : 9-10 May 2012 at St Thomas' Hospital London SE1 7EH

Aim:

Reach consensus and devise draft recommendations for staging & response assessment in FDG avid lymphomas for clinical and research use

- to be presented for discussion in Menton, October 2012
- & integrated with other workstreams for final presentation at Lugano June 2013 prior to publication

Quantitative measures for CT and MRI in response assessment — Larry

11.00 – 12.00

Relevance of initial bulk disease and other prognostic factors: HL vs NHL — George

Day 1 pm

Focus on visual response assessment methods for HL/DLBL

12.00 - 13.00

Interim PET in HL (vs end PET vs CT) including iPET after 1 cycle data — Martin

14.00 – 15.00

Summary of state of current trials — Lale

Day 2 pm

14.00 – 16.00

Summarise WIP; Preparation of draft presentation and document for Menton — ALL

M André
A Avigdor
S Bardet
A Biggi
F Bodere
R Boellaard
E Brusamolino
D Caballero
O Casasnovas
A Cashen
J Cerci
L Ceriani
S Chauvie
B Coiffier
O Couturier
E Dann
E de-Kerviler

U Duehrsen
A Engert
M Federico
C Fortpied
A Gallamini
C Gisselbrecht
M Gregianin
C Haouin
R Hicks
O Hoekstra
A Huettmann
R Hustinx
O Israel
E Itti
A Julian
C Kobe
S le Gouill
S Luminari

U Molinetter
N Mounier
MJ O'Doherty
G Paone
A Polliak
M Pfreundschuh
J Radford
A Riedinger
H Schoder
A Thyss
H Tilly
J Trotman
C Tychyj-Pinel
T Vander Borght
A Versari
J Zaucha
PL Zinzani
J Zijlstra

sally.barrington@kcl.ac.uk

Summary of recommendations

STAGING

1. PET-CT should be used for staging in routine clinical practice and in clinical trials *(category 1)*.
2. FDG scans can be used to image most subtypes of lymphoma and to target biopsy but is not routinely recommended in lymphomas with low FDG avidity e.g. CLL/SLL, extranodal MZL and some cutaneous lymphomas *(category 1)*.
3. In HL staged by PET-CT there is no role for routine BMB. BMB is indicated only for confirmation if there is unexpected marrow involvement on PET in early good prognosis disease (*category 1*).
4. In DLBCL, if PET suggests BM involvement, this could obviate the need for BMB as PET-CT has a high positive predictive value. In the absence of abnormal marrow uptake on PET, BMB may be indicated to detect a small proportion of patients with low volume marrow involvement where it would influence prognosis and/or treatment. (*category 1*).
5. PET-CT with ceCT is desirable for staging patients likely to undergo radiotherapy ideally within a single scanning session, but a two stage approach using unenhanced PET-CT followed by regional ceCT for equivocal lesions may be preferred taking into account patient age, disease type and clinical stage (*category 2*)
6. Bulk remains an important prognostic factor in lymphoma. Volumetric analysis of tumour bulk and total tumour burden as well as methods combining metabolic activity and anatomical size or volumes should be explored as potential prognosticators *(category 3)*.
7. Optimal reproducible methods for volumetric analysis are yet to be defined and will require prospective testing in multicentre studies or carefully selected retrospective datasets *(category 3)*.

RESPONSE ASSESSMENT - VISUAL

1. The Deauville criteria (DC) are recommended for reporting PET scans at interim and end treatment assessment when using visual assessment of response *(category 1)*.
2. If mid chemotherapy assessment is performed, PET-CT is the best imaging modality and is superior to CT alone *(category 1)*.
3. There is currently insufficient evidence to change standard treatment based solely on interim PET-CT outside clinical trials. Imaging findings on interim scans should be related to the anticipated prognosis, clinical findings and other markers of response *(category 1)*.
4. Further investigation of the significance of PET negative residual masses is warranted (*category 3*). Data should be collected prospectively in clinical trials dividing CR into two categories: Complete Metabolic Response (CMR) and Complete Metabolic Response with a residual mass (CMRr) *(category 3)*. Residual mass size should be recorded on end of treatment PET-CT report.
5. Assessment with PET-CT could be used to guide decisions prior to ASCT (*category 3*).
6. Emerging data supports the use of PET-CT in high burden FL for end treatment response using DC. Observational studies are warranted to confirm this finding in patients receiving maintenance therapy *(category 2 and category 3)*.

RESPONSE ASSESSMENT - QUANTITATIVE

1. Standardisation of PET methods is mandatory for the use of quantitative approaches (*category 1*)
2. Data are emerging to suggest that quantitative measures could be used to improve on visual analysis for response assessment in DLBCL but this requires further validation in clinical trials (*category 2*).
3. The ΔSUV_{max} is the only quantitative measure with published data to indicate its possible utility in response assessment but changes in tumour volumes should also be explored (*category 3*).

Proposed Response criteria for lymphoma at interim and end treatment assessment

Interim PET-CT is used to assess early treatment **response**/chemosensitivity and predict efficacy/prognosis and relies on assessment of metabolic change.
End PET-CT is used to establish final **remission** status and relies on assessment of metabolic and anatomical changes.

RESPONSE ASSESSMENT with Interim PET	PET findings	REMISSION ASSESSMENT with End PET	PET-CT findings
Complete metabolic response (CMR)	DS 1,2,3 *	**Complete metabolic response (CMR)**	DS 1,2,3* with or without a residual mass and no evidence of disease in marrow †, spleen or other extranodal sites ** CMR with a residual mass should be denoted as **CMRr** and the size of the mass recorded.
Partial Metabolic response (PMR)	DS 4 or 5 & reduced uptake from baseline	**Residual metabolic disease (RMD)**	DS 4 or 5 & residual mass of any size (but no new lesions)
No Metabolic Response or Progressive Metabolic Disease (NMR/PMD)	DS 5 & no significant change in uptake or new FDG avid foci consistent with lymphoma	**Progressive metabolic disease (PD)**	DS 4 or 5 & new FDG avid foci consistent with lymphoma or increase in uptake in previous disease foci &/or increase ≥50% SPD of masses

* DS 3 probably represents CMR but in response adapted trials involving PET where de-escalation of therapy is intended, it may be preferred to use DS 1,2 to define CMR to increase the NPV of PET and avoid the risk of under- treatment of disease (category 3).
† Bone marrow involvement at diagnosis on BMB requires clearance of marrow infiltration for definition of CMR.
** In Waldeyers ring or in extranodal sites e.g. gut, liver and marrow, FDG uptake may be greater than mediastinum with CMR but should be no higher than surrounding normal physiological uptake. This is seen often with marrow activation following chemotherapy or granulocyte stimulating factor.

Deauville score (DS)

1. no uptake above background
2. uptake ≤ mediastinum **
3. uptake > mediastinum but ≤ liver
4. uptake moderately higher than liver
5. uptake markedly higher than liver and/or new lesions

X new areas of uptake unlikely to be related to lymphoma

	RECOMMENDATIONS: RESPONSE ASSESSMENT - VISUAL
5.	Assessment with PET-CT could be used to guide decisions prior to ASCT (*category 3*).
6.	Emerging data supports the use of PET-CT in high burden FL for end treatment response using DC. Observational studies are warranted to confirm this finding in patients receiving maintenance therapy *(category 2 and category 3).*

	STAGING RECOMMENDATIONS	
8.40	When to use PET-CT	Lale Kostakoglu
8.50	Imaging of bone marrow	Martin Hutchings
9.05	Assessment of bulk	Lawrence Schwarz
9.15	DISCUSSION	R Fisher B Cheson
	RESPONSE RECOMMENDATIONS	
9.30	Mid treatment assessment	George Mikhaeel
9.40	Use of Deauville criteria	Sally Barrington
9.45	Significance of residual masses	George Mikhaeel
9.55	DISCUSSION	B Cheson, R Fisher,
10.15	COFFEE	
10.30	Quantitation	Stefan Müller, Michel Meignan
10.40	DRAFT CRITERIA	George Mikhaeel, Sally Barrington
10.55	DISCUSSION	R Fisher, B Cheson
11.15	Summing up re staging	R Fisher
11.20	Summing up re response assessment	B Cheson
11.25	Closing statement	Emanuele Zucca

RECOMMENDATION

The Deauville criteria (DC) are recommended for reporting PET scans at interim and end treatment assessment when using visual assessment of response *(category 1).*

IHP criteria

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JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Use of Positron Emission Tomography for Response Assessment of Lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma

Malik E. Juweid, Sigrid Stroobants, Otto S. Hoekstra, Felix M. Mottaghy, Markus Dietlein, Ali Guermazi, Gregory A. Wiseman, Lale Kostakoglu, Klemens Scheidhauer, Andreas Buck, Ralph Naumann, Karoline Spaepen, Rodney J. Hicks, Wolfgang A. Weber, Sven N. Reske, Markus Schwaiger, Lawrence H. Schwartz, Josee M. Zijlstra, Barry A. Siegel, and Bruce D. Cheson

From the Department of Radiology, University of Iowa, Iowa City, IA; Department of Nuclear Medicine, University Hospital Gasthuisberg,

- Mediastinal blood pool activity is recommended as the reference background activity to define PET positivity for a residual mass 2 cm in greatest transverse diameter
- A smaller residual mass or a normal sized lymph node (ie 1 cm in diameter) should be considered positive if its activity is above surrounding background.

Leukemia & Lymphoma, August 2009; 50(8): 1257–1260

informa
healthcare

REVIEW

Report on the First International Workshop on interim-PET scan in lymphoma

MICHEL MEIGNAN[1], ANDREA GALLAMINI[2], & CORINNE HAIOUN[3]

[1]*Nuclear Medicine Department, H. Mondor Hospital, AP-HP/Paris 12 University, Creteil, France,* [2]*Hematology Department and BMT Unit, Az. Ospedaliera S. Croce e Carle, Cuneo, Italy, and* [3]*Hematology Department, H. Mondor Hospital, AP-HP/ Paris 12 University, Creteil, France*

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Gallamini et al Annals of Oncology 22:97-97, 2011
Itti et al Journal of Nuclear Medicine 53, 2012
Barrington et al EJNMMI 37:1824-1833, 2010
Furth et al Annals of Oncology 22:1198-1203, 2011

DC and IHP widely used in interim & end PET

A lot of similarities eg mediastinal threshold in IHP similar to using score 1 or 2 to define response

DC simple and threshold can be adapted

With rapid improvements in scanner technology size based assessments for PET have become less relevant

One method might be preferred

DC could be now be used for PET visual assessment at interim and end treatment ...

Some refinements

‘Activated’ marrow can be > liver uptake

Site of initial BMI ≤ normal marrow

Response in remainder of nodal and extranodal sites

CT changes may be helpful eg development of sclerosis

Liver disease/dysfunction or chemotherapy steatosis:

If liver activity < MBP, uptake in residual lesions should be compared with MBP.

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3.	In HL and DLBCL staged by PET-CT there is no role for routine BMB. BMB is indicated only if it would change staging with a resultant change in therapy *(category 1)*.

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5.	PET-CT with ceCT is desirable for staging patients likely to undergo radiotherapy ideally within a single scanning session, but a two stage approach using unenhanced PET-CT followed by regional ceCT for equivocal lesions may be preferred taking into account patient age, disease type and clinical stage (*category 2*)
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