Potential applications of PET/CT in MALT and PMLBC lymphoma

Luca Ceriani, Gaetano Paone and Emanuele Zucca

Nuclear Medicine PET-CT Centre and Research Division
Oncology Institute of Southern Switzerland
Ospedale San Giovanni Bellinzona

PET-CT in MALT lymphoma

Annals of Oncology 21 (Supplement 5): v175–v176, 2010
doi:10.1093/annonc/mdq182

clinical practice guidelines

Gastric marginal zone lymphoma of MALT type: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

E. Zucca[1] & M. Dreyling[2]
On behalf of the ESMO Guidelines Working Group*

staging and risk assessment

The value of positron emission tomography (PET) scan is controversial and has little clinical utility [IV, D]*.

*IV Retrospective cohort studies or case-control studies
D Moderate evidence against efficacy or for adverse outcome, generally not recommended

PET-CT in MALT lymphoma

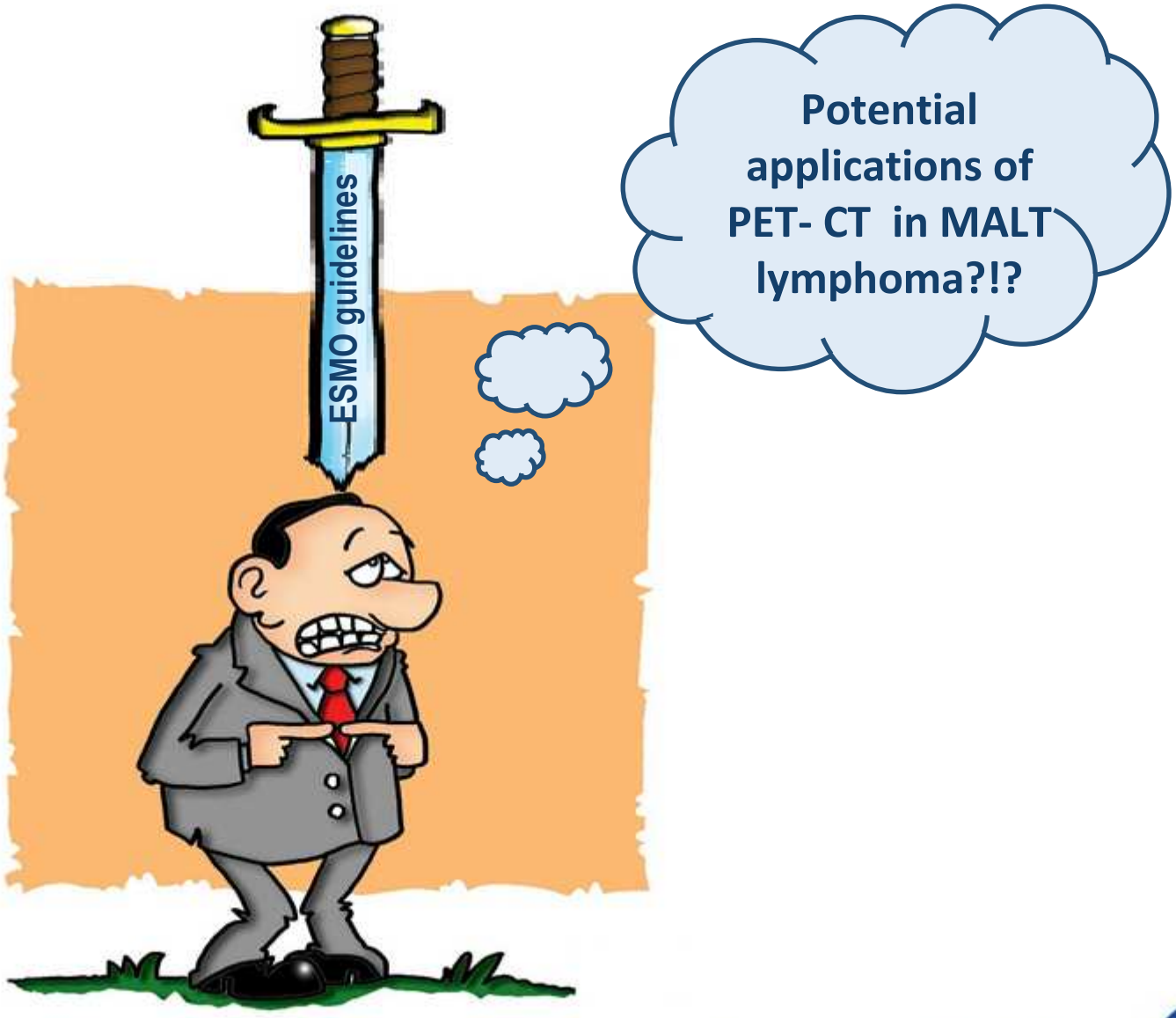
ESMO GUIDELINES consensus conference on malignant lymphoma. Part 2. Marginal zone lymphoma, mantle cell lymphoma, peripheral T-cell lymphoma.

M. Dreyling, et al. Ann Oncol 2012, *in press*

- **Staging and risk assessment of marginal zone lymphoma:**

"…The value of positron emission tomography (PET) scan is controversial, has uncertain clinical utility and is not recommended…"

A sword of Damocles



PET-CT in MALT lymphoma

Table 1. Recommended Timing of PET (PET/CT) Scans in Lymphoma Clinical Trial

Histology	Pretreatment	Mid-Treatment	Response Assessment	Post-Treatment Surveillance
Routinely FDG avid				
DLBCL	Yes*	Clinical trial	Yes	No
HL	Yes*	Clinical trial	Yes	No
Follicular NHL	No†	Clinical trial	No†	No
MCL	No†	Clinical trial	No†	No
Variably FDG avid				
Other aggressive NHLs	No†	Clinical trial	No†‡	No
Other indolent NHLs	No†	Clinical trial	No†‡	No

†Recommended only if ORR/CR is a primary study end point.
‡Recommended only if PET is positive pretreatment.

Cheson B. et al. JCO 2007

PET-CT in MALT lymphoma

Table 1. Recommended Timing of PET (PET/CT) Scans in Lymphoma Clinical Trial

Histology	Pretreatment	Mid-Treatment	Response Assessment	Post-Treatment Surveillance
Routinely FDG avid				
DLBCL	Yes*	Clinical trial	Yes	No
HL		trial	Yes	No
Follicular NHL	Not	Clinical trial	Not	No
MCL	Not	Clinical trial	Not	No
Variably FDG avid				
Other aggressive NHLs	Not	Clinical trial	Not‡	No
Other indolent NHLs	Not	Clinical trial	Not‡	No

Marginal Zone Lymphoma

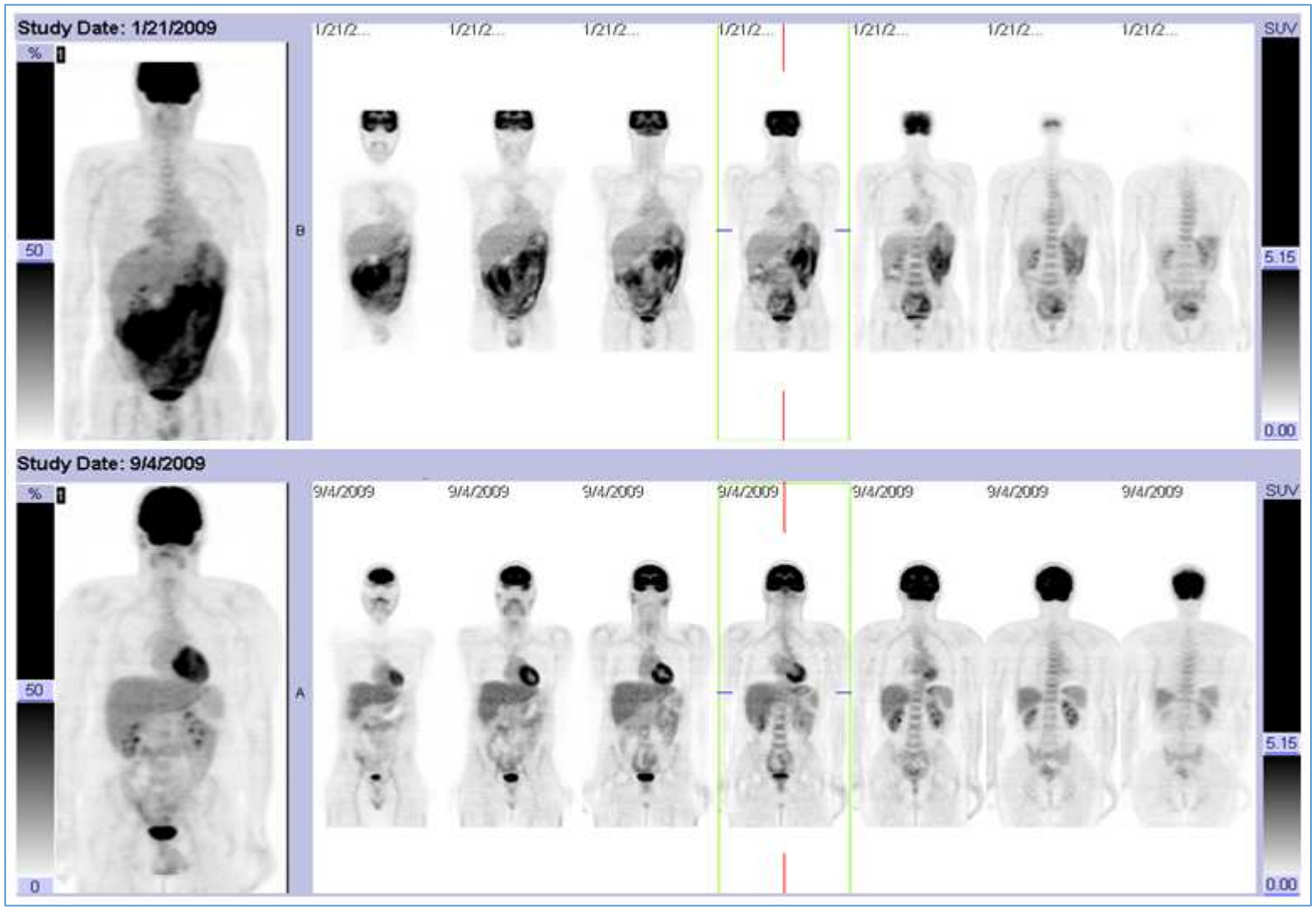
†Recommended only if ORR/CR is a primary study end point.
‡Recommended only if PET is positive pretreatment.

Cheson B. et al. JCO 2007

PET-CT sensitivity in MALT lymphoma

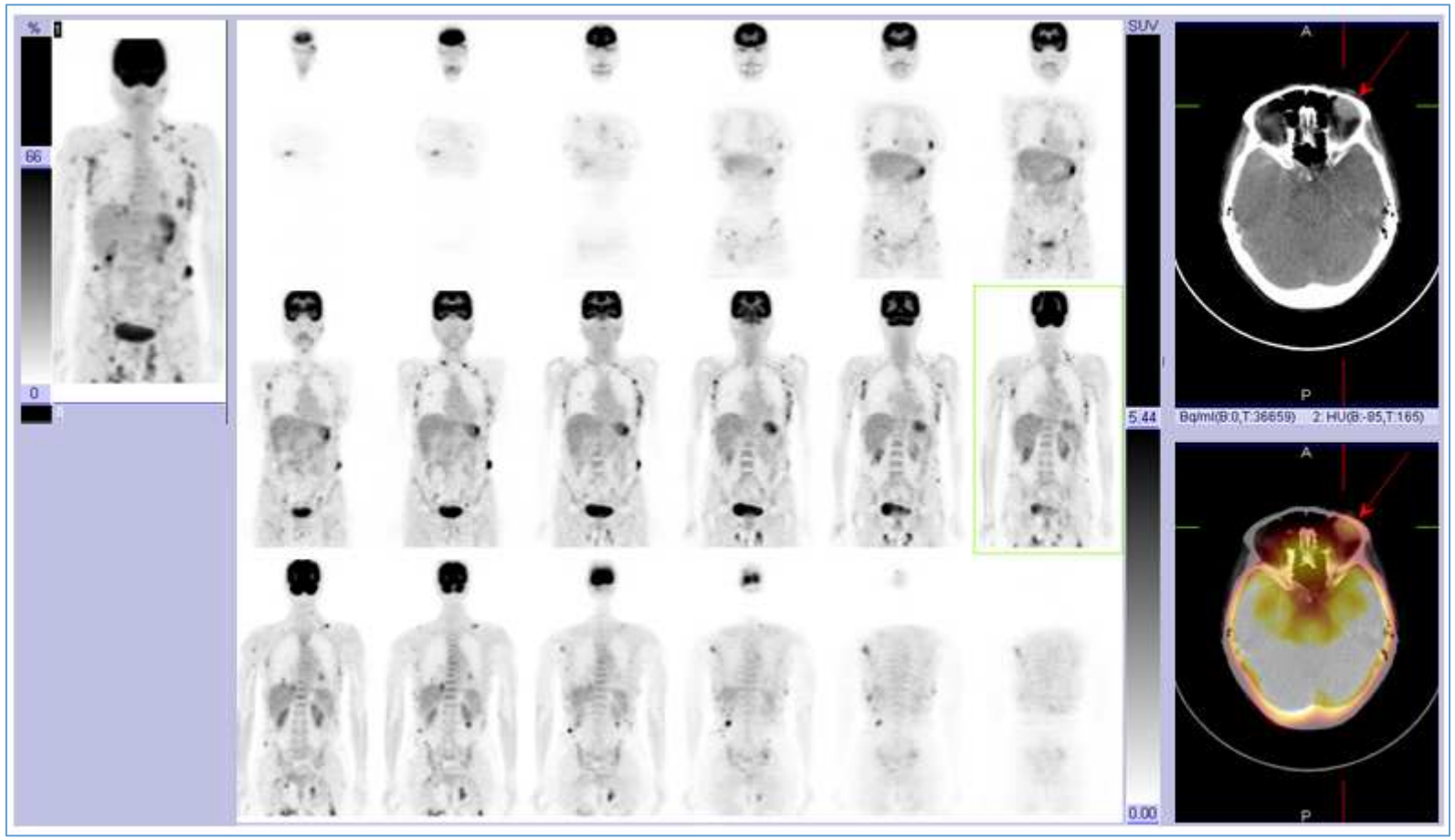
Author	Year	Primary site	No of cases	Sensitivity (95% C.I.)
Beal	***2005***	gastric	10	60% (26-88%)
		extragastric	32	88% (71-96%)
		all sites	**42**	**81%** (66-91%)
Alinari	***2006***	gastric	7	100% (59-100%, one-sided)
		extragastric	19	73% (49-91%)
		all sites	**26**	**81%** (61-93%)
Hoffman	***2006***	gastric	9	44% (14-79%)%
		extragastric	26	58% (37-77%)
		all sites	**35**	**54%** (37-71%)
Ambrosini	***2006***	**gastric**	**9**	**100%** (66-100%, one-sided)
Karam	***2006***	**all sites**	**12**	**75%** (43-94%)
Radan	***2008***	**gastric**	**24**	**71%**(49.87%)
Perry	***2007***	gastric	18	39% (17-64%)%
		extragastric	15	73% (45-92%)
		all sites	**33**	**54%** (36-72%)
Tsukamoto	***2007***	**all sites**	**52**	**82%** (73-88%)
Economoto	***2008***	gastric	5	0% (0-52%, one-sided)
		extragastric	8	100% (66-100%, one-sided)
		all sites	**13**	**62%** (32-86%)
Weiler-Seige	***2010***	**all sites**	**50**	**54%** (39-68%)
Total			**296**	**70% (64-75%)**

PET-CT in MALT lymphoma



PET-CT in MALT lymphoma

MALT originating from the left lacrimal gland



Factors affecting PET-CT sensitivity in MALT: thickness of the lesion

ANNALS OF NUCLEAR MEDICINE
Volume 22, Number 4 (2008), 261-267, DOI: 10.1007/s12149-007-0125-9

ORIGINAL ARTICLE

Mucosa-associated lymphoid tissue lymphoma studied with FDG-PET: a comparison with CT and endoscopic findings

Keisuke Enomoto, Kenichiro Hamada, Hidenori Inohara, Ichiro Higuchi, Yasuhiko Tomita, Takeshi Kubo and Jun Hatazawa

- 13 untreated MALT lymphoma
  - 5 gastric
  - 8 nongastric
- 8 of 8 non-gastric lymphoma were FDG-PET positive
- no abnormal FDG accumulation was observed in all gastric cases
- Non-gastric lymphoma lesions could be confirmed on CT
- Mucosal lesions of gastric lymphoma detected only by EGD

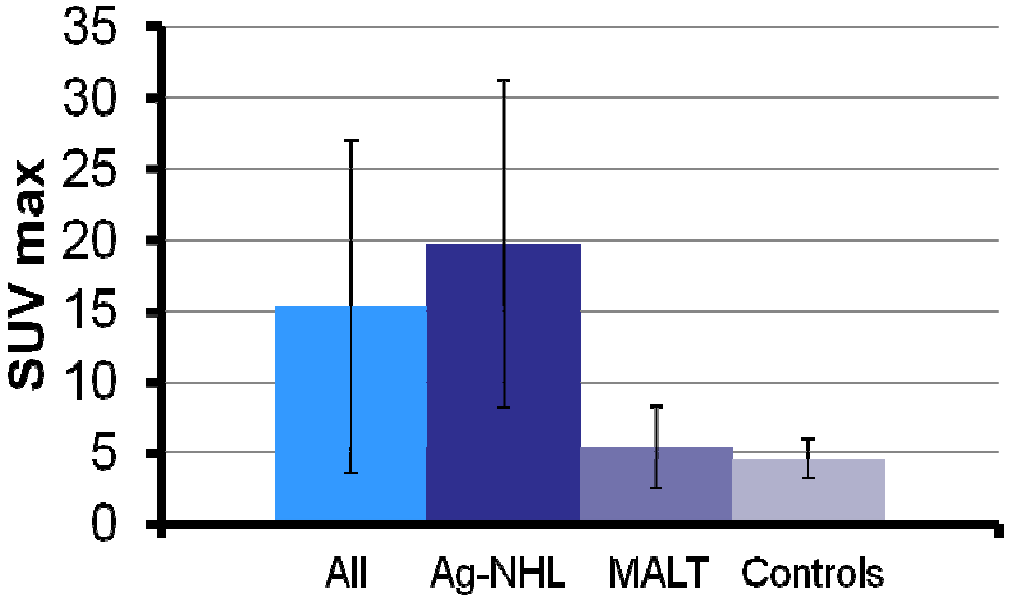
FDG-PET detects MALT lymphoma when it forms gross lesions, whereas it is difficult to detect gastrointestinal mucosa infiltrates

Factors affecting PET-CT sensitivity in MALT: FDG avidity of the lesion

FDG avidity and PET/CT patterns in primary gastric lymphoma
Radan et al. EJNMMI 2008

- In primary gastric lymphoma, FDG uptake can be differentiated from physiologic tracer activity by intensity but not by pattern...

- Defining FDG avidity and PET/CT patterns in Ag-NHL and a subgroup of MALT before treatment may be important for response monitoring.

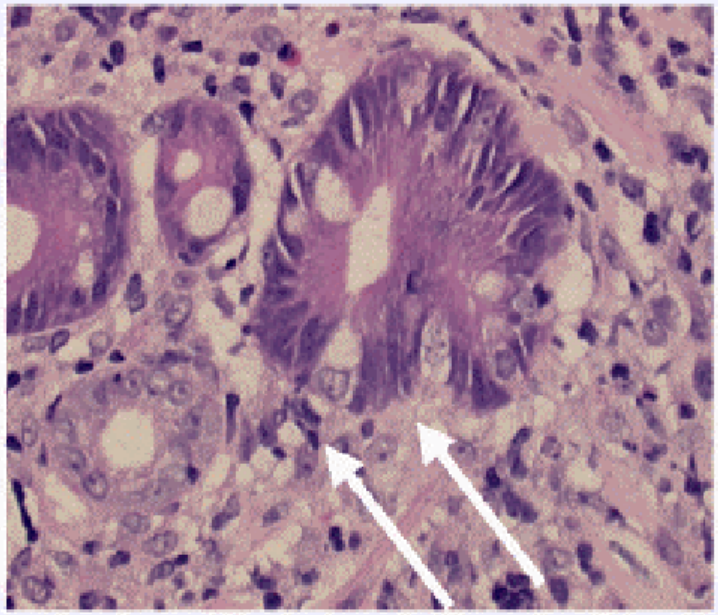


MALT lymphoma

(Extranodal Marginal Zone B-Cell Lymphoma of MALT)

HISTOLOGICAL FEATURES

- **centrocyte-like cells** (usually)
- lympho**epithelial** lesions
- **plasma cell differentiation**
- scattered transformed **blasts**
- admixed non-neoplastic **T-cell**
- follicular colonisation



http://www.ncl.ac.uk/pathology/teaching/

Factors affecting PET-CT sensitivity in MALT: histology of the lesion

original article

Annals of Oncology 17: 1761–1765, 2006
doi:10.1093/annonc/mdl295
Published online 15 September 2006

18F-Fluoro-deoxy-glucose positron emission tomography in lymphoma of mucosa-associated lymphoid tissue: histology makes the difference

M. Hoffmann[1]*, S. Wöhrer[3], A. Becherer[1], A. Chott[2], B. Streubel[2], K. Kletter[1] & M. Raderer[3]

Departments of [1]Nuclear Medicine, [2]Pathology and [3]Internal Medicine I, Medical University Vienna, Vienna, Austria

	FDG–PET scan findings			
	True positive	False positive	True negative	False negative
Total patients (35)	19	0	0	16
pMALT (19)	16	0	0	3
MALT (16)	3	0	0	13

MALT, mucosa-associated lymphoid tissue; pMALT, MALT lymphoma with plasmacytic differentiation.

Factors affecting PET-CT sensitivity in MALT: histology of the lesion

original article

Annals of Oncology 17: 1761–1765, 2006
doi:10.1093/annonc/mdl295
Published online 15 September 2006

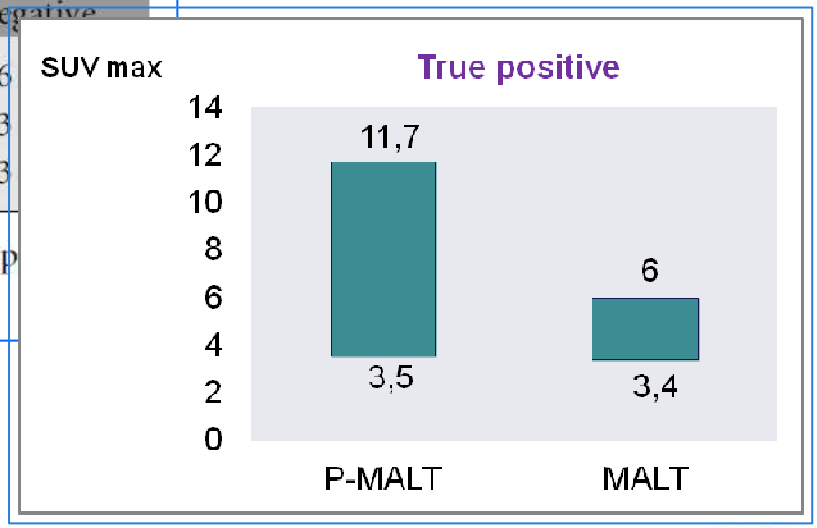
18F-Fluoro-deoxy-glucose positron emission tomography in lymphoma of mucosa-associated lymphoid tissue: histology makes the difference

M. Hoffmann[1]*, S. Wöhrer[3], A. Becherer[1], A. Chott[2], B. Streubel[2], K. Kletter[1] & M. Raderer[3]

Departments of [1]Nuclear Medicine, [2]Pathology and [3]Internal Medicine I, Medical University Vienna, Vienna, Austria

	FDG–PET scan findings			
	True positive	False positive	True negative	False negative
Total patients (35)	19	0	0	16
pMALT (19)	16	0	0	3
MALT (16)	3	0	0	13

MALT, mucosa-associated lymphoid tissue; pMALT, MALT lymp
with plasmacytic differentiation.



PET-CT in MALT lymphoma – any predictive value ?

Role of ^{18}F-FDG PET Scans in Patients with *Helicobacter pylori*-Infected Gastric Low-Grade MALT Lymphoma

Kyung Ho Song*, Mijin Yun†, Jie-Hyun Kim‡, Woo Ick Yang§, Dae Ryong Kang ||, Jae Bock Chung¶, and Yong Chan Lee¶

Gut and Liver, Vol. 5, No. 3, September 2011, pp. 308-314

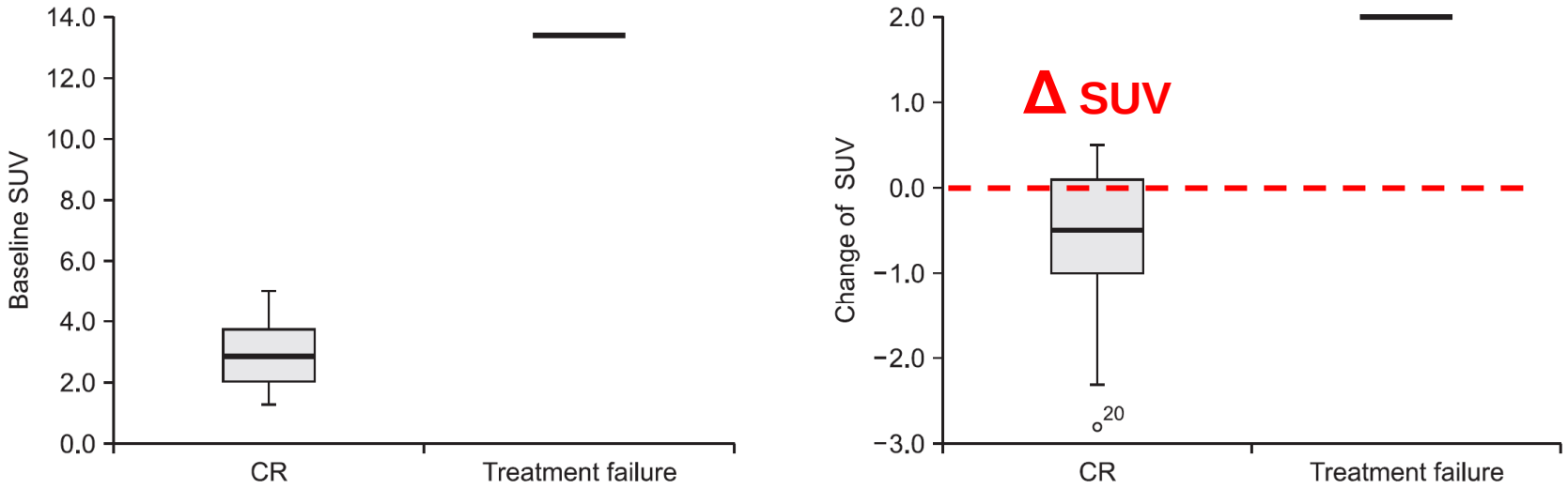


Fig. 2. Baseline standardized uptake values (SUVs) and changes in the SUV according to clinical outcome. The boxes represent the 25th and 75th percentile, the thick horizontal bars represent the median, and the upper and lower horizontal bars represent the maximum and minimum data. CR, complete remission.

PET-CT in MALT lymphoma – any predictive value ?

Role of ^{18}F-FDG PET Scans in Patients with *Helicobacter pylori*-Infected Gastric Low-Grade MALT Lymphoma

Kyung Ho Song*, Mijin Yun†, Jie-Hyun Kim‡, Woo Ick Yang§, Dae Ryong Kang ||, Jae Bock Chung¶, and Yong Chan Lee¶

Gut and Liver, Vol. 5, No. 3, September 2011, pp. 308-314

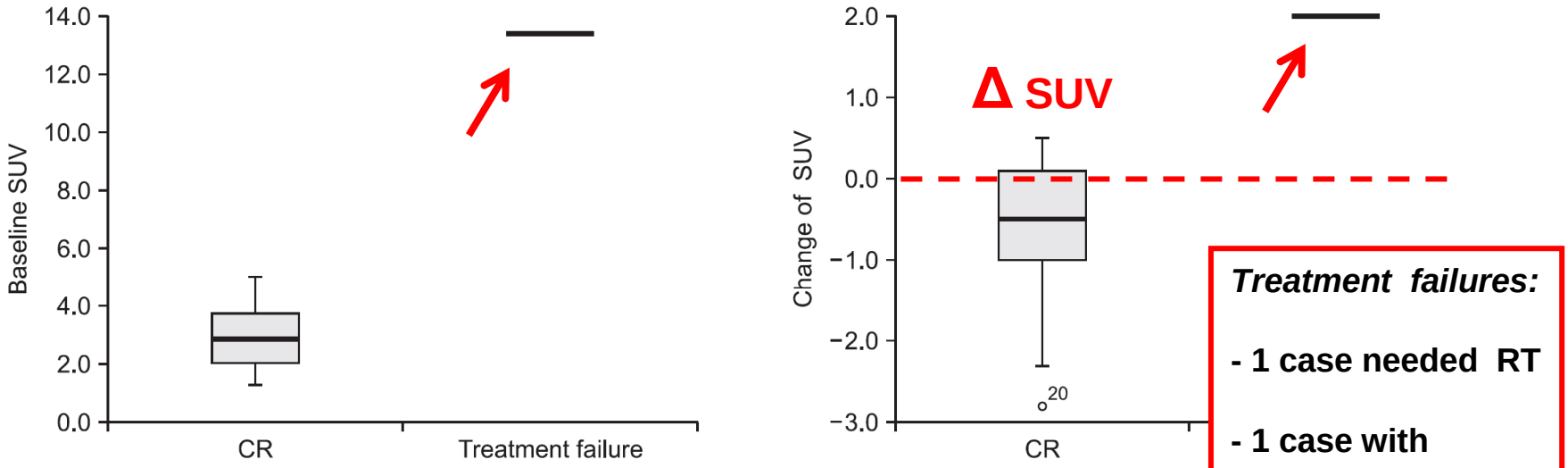


Fig. 2. Baseline standardized uptake values (SUVs) and changes in the SUV according to clinical outcome. The boxes r
percentile, the thick horizontal bars represent the median, and the upper and lower horizontal bars represent the maxim
CR, complete remission.

Treatment failures:

- 1 case needed RT

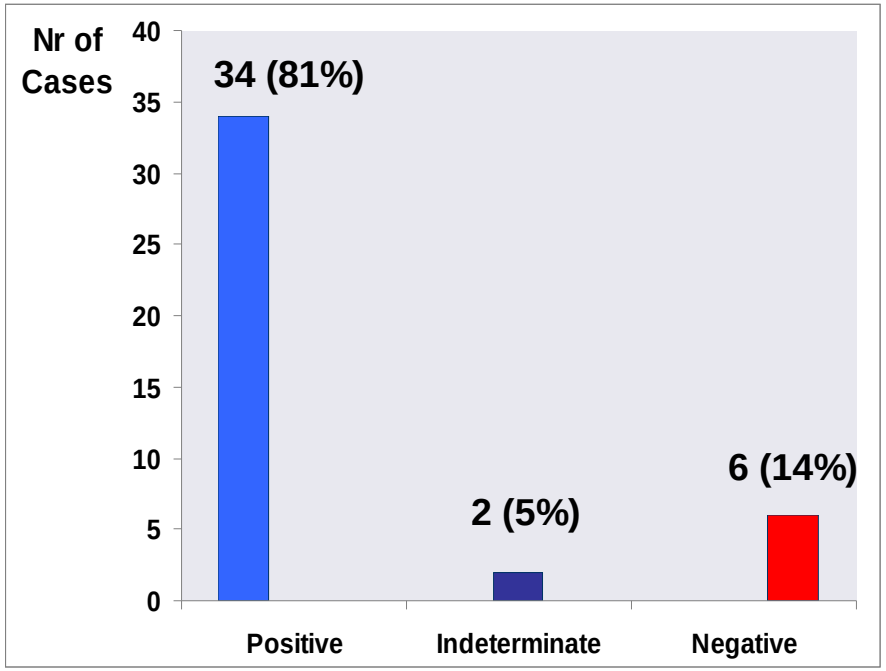
- 1 case with Transformation to DLBCL

PET-CT in MALT lymphoma – any clinical value ?

K. P. Beal , H. W. Yeung & J. Yahalom

FDG-PET scanning for detection and staging of extranodal marginal zone lymphomas of the MALT type: a report of 42 cases

Annals of Oncology 16: 473–480, 2005



- 4 of 42 (10%) patients upstaged due to FDG-PET findings
- 8 pts with post-treatment PET:

  5/8 CR
  3/8 indeterminate or mixed response
- The 6 patients with negative initial FDG-PET scans were NED at a median follow-up of 12.5 months.

Clinical relevance of 18F-FDG uptake in staging and follow-up of primary gastric lymphoma

Yi JH, et al. Hematol Oncol. 2010;28:57-61

42 primary gastric lymphoma:
32 DLBCL
10 extranodal MZL (MALT lymphomas)

9 (7 DLBCL, 2 MALT) up-staged based on the PET/CT results compared to CT
6 down-staged after PET/CT

high SUVmax significantly associated with advanced Lugano stage ($p < 0.001$).

24 with follow-up PET/CT scan and endoscopy:

11 ulcerative or mucosal lesions with residual uptake (all these lesions pathologically benign without evidence of lymphoma)

PET/CT can be used for primary gastric lymphoma staging but…
the residual uptake observed during follow-up should be interpreted cautiously and should be combined with endoscopy and multiple biopsies of the stomach.

PET-CT in MALT lymphoma staging

Relevant issues in staging MALT lymphoma :

- asymptomatic dissemination in patients with apparently localized disease
- high proportion (up to one third) of patients with early dissemination at multiple extranodal sites

Thieblemont et al . Blood 2000
Zucca et al. Blood 2003
Raderer et al. J Clin Oncol 2006
de Boer et al. Haematologica 2008

Hence, extensive staging has been recommended

PET-CT in MALT lymphoma staging

Relevant issues in MALT lymphoma staging:

- asymptomatic dissemination in patients with apparently localized disease
- high proportion (up to one third) of patients with early dissemination at multiple extranodal sites

Thieblemont et al . Blood 2000
Zucca et al. Blood 2003
Raderer et al. J Clin Oncol 2006
de Boer et al. Haematologica 2008

Hence, extensive staging has been recommended

FDG-PET/CT results in upstage in approx. 10-20% of cases

Potential applications of PET-CT in MALT lymphoma

- significant PET-positive rate (< in superficial gastric lesions)

- the degree of FDG uptake may have prognostic/predictive value
- high uptake may identify aggressive subtypes or transformation
- PET-CT may provide more accurate staging than CE-CT (upstaging in 10-20% of FDG-positive cases)
- Potential value for response assessment in non-gastric disease?

Potential applications of PET-CT in MALT lymphoma

- significant PET-positive rate (< in superficial gastric lesions)

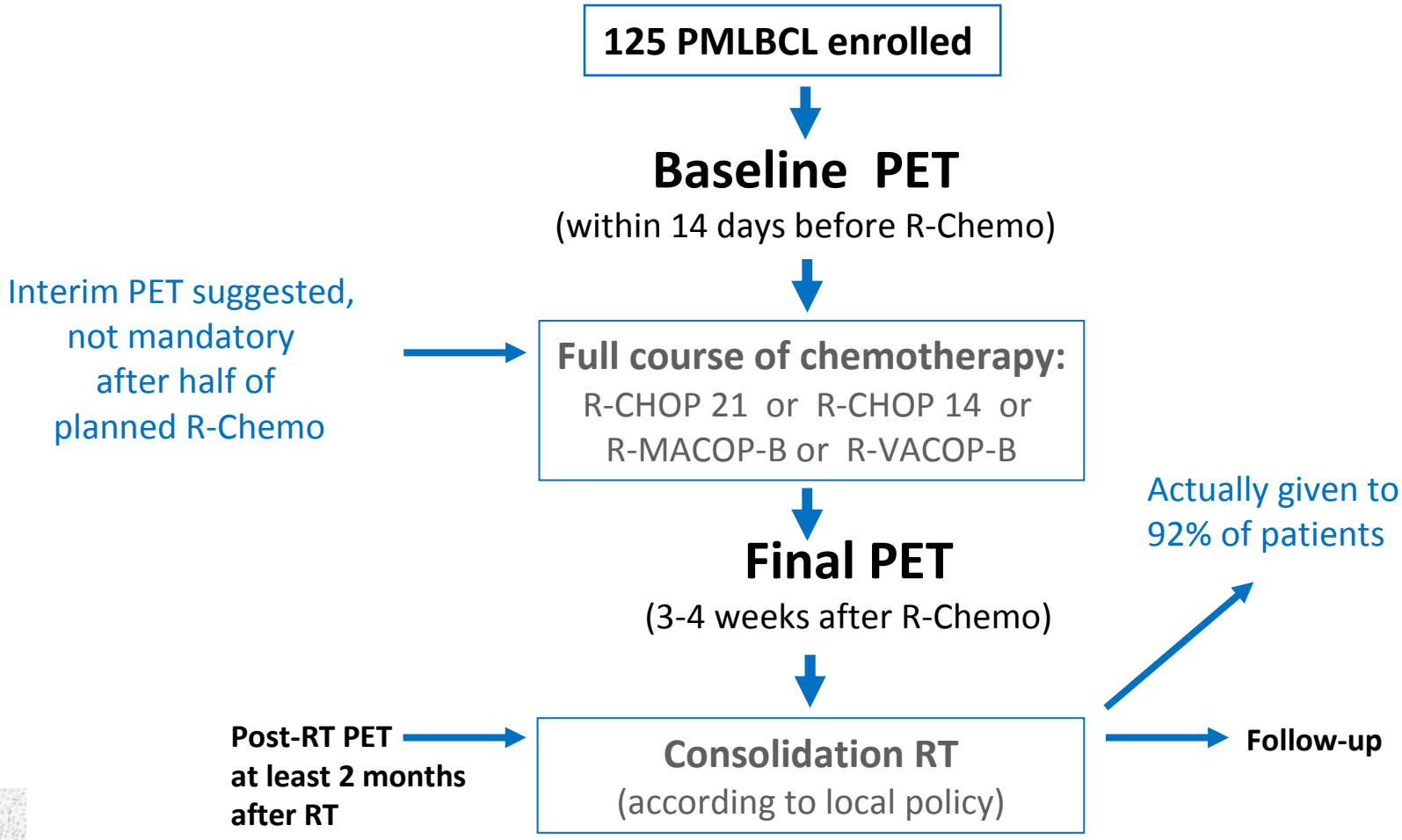
- the degree of FDG uptake may have prognostic/predictive value
- high uptake may identify aggressive subtypes or transformation
- PET-CT may provide more accurate staging than CE-CT (upstaging in 10-20% of FDG-positive cases)
- Potential value for response assessment in non-gastric disease?

These hypotheses need to be tested in large prospective studies

Open questions in primary mediastinal large B-cell lymphoma (PMLBCL)

- Are third-generation chemotherapy regimens still superior in the era of rituximab?
- **What is the role of PET scanning in determining cure after chemotherapy?**
- Can consolidative radiotherapy be omitted in selected individuals?
- **Can the PET scanning drive this selection?**

IELSG-26 study on the PET/CT response after R-chemotherapy in primary mediastinal (thymic) large B-cell lymphoma (PMLBCL)



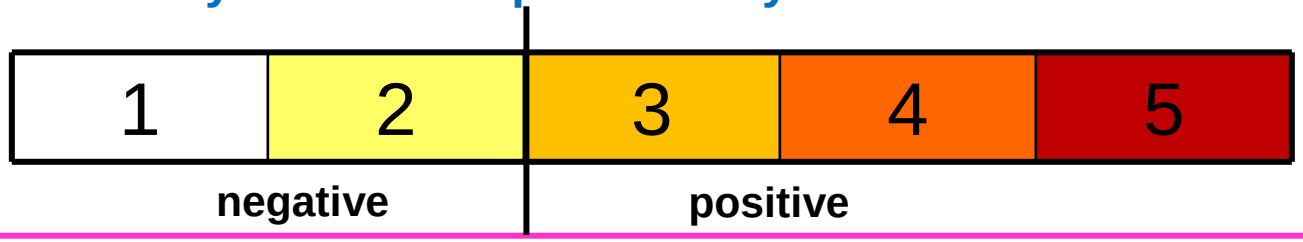
IELSG-26 study: PET/CT response Criteria for final PET (at 3-4 weeks after R-Chemotherapy)

* *IHP criteria (Juweid et al. JCO 2007)*

Negative final PET : no residual uptake or minimal residual uptake ≤ MBP

* *Deauville criteria [5-point visual analysis scale] (Leuk Lymphoma 2009)*

1. **No uptake.**
2. **Uptake ≤ mediastinum.**
3. **Uptake > mediastinum but ≤ liver.**
4. **Uptake moderately more than liver uptake, at any site.**
5. **Markedly increased uptake at any site and new disease sites**

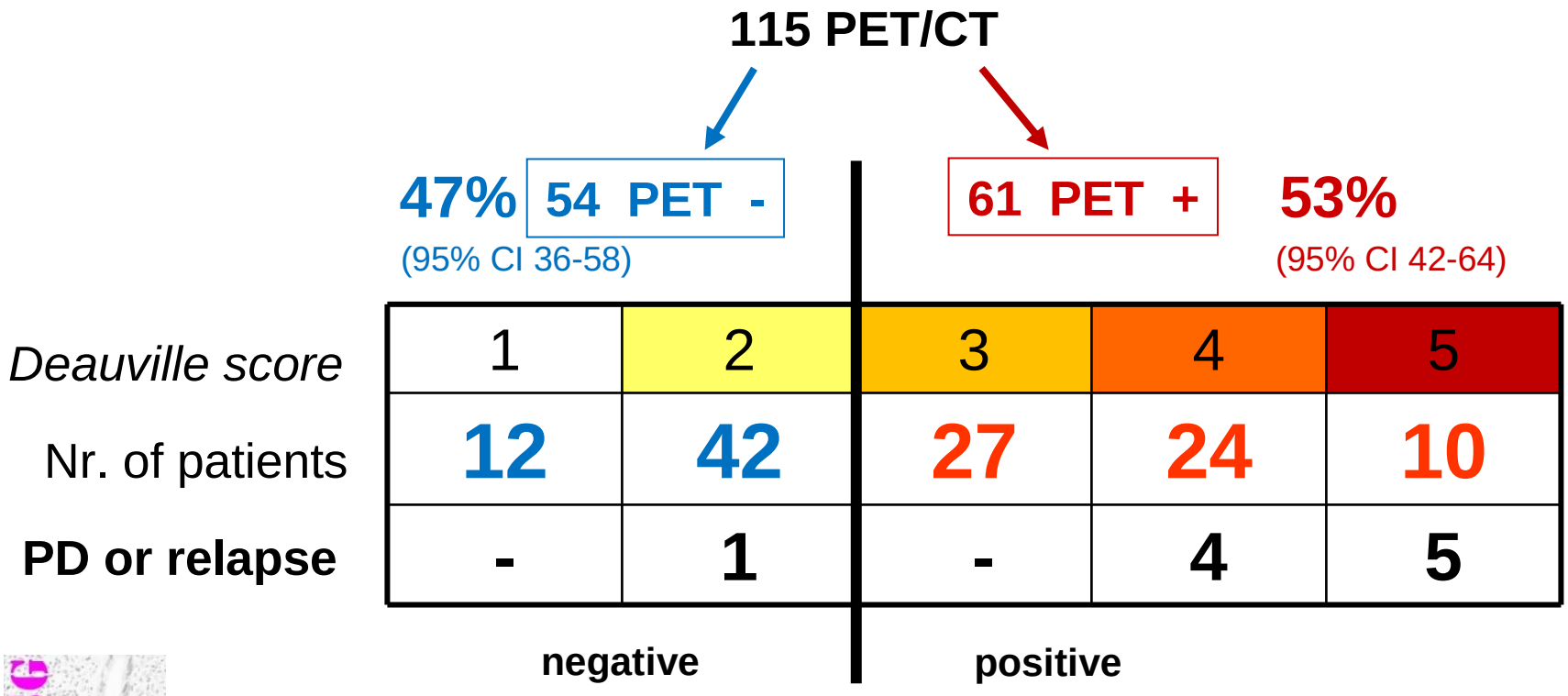


IELSG 26

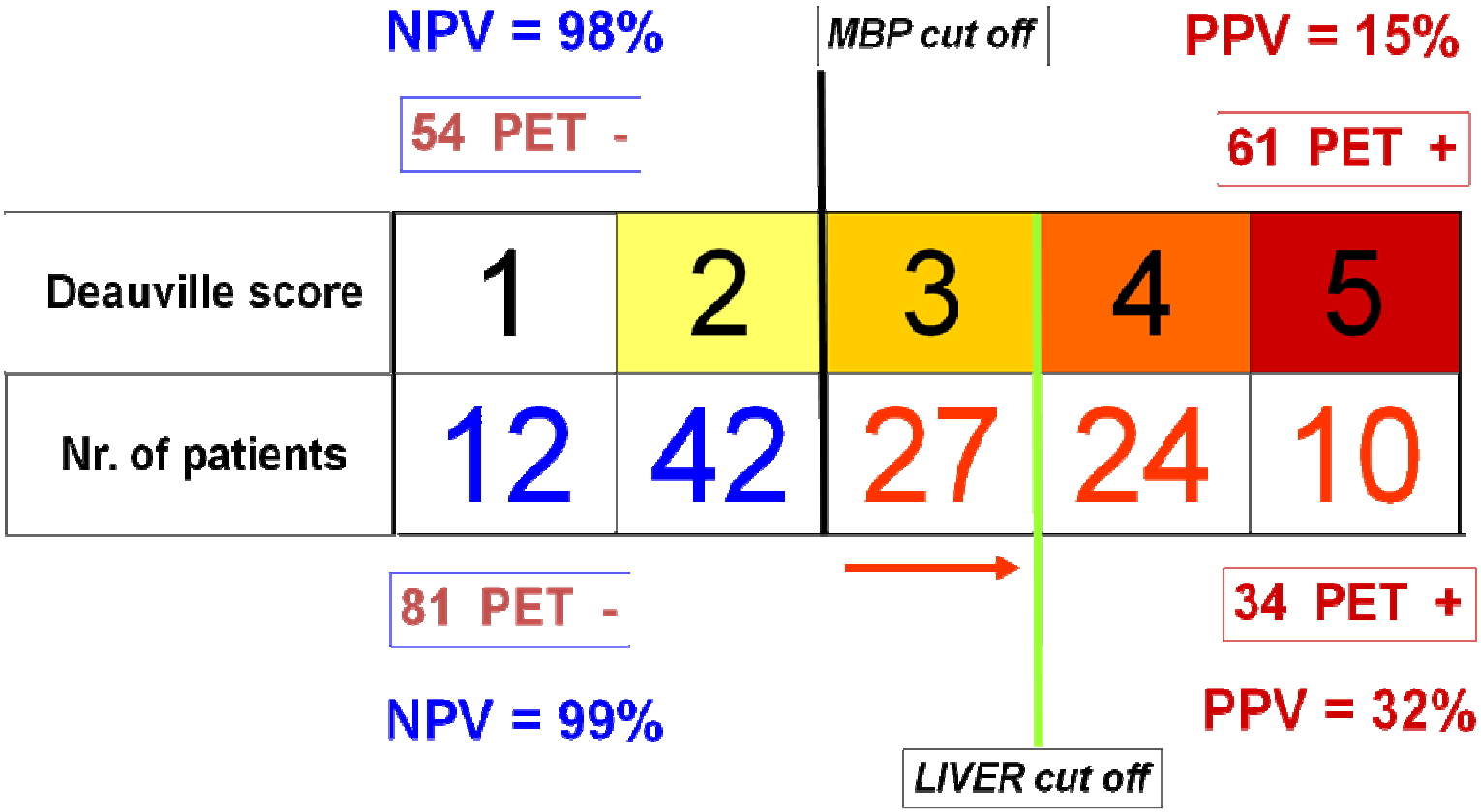
INTERNATIONAL EXTRANODAL LYMPHOMA STUDY GROUP

IELSG-26 study: Preliminary results

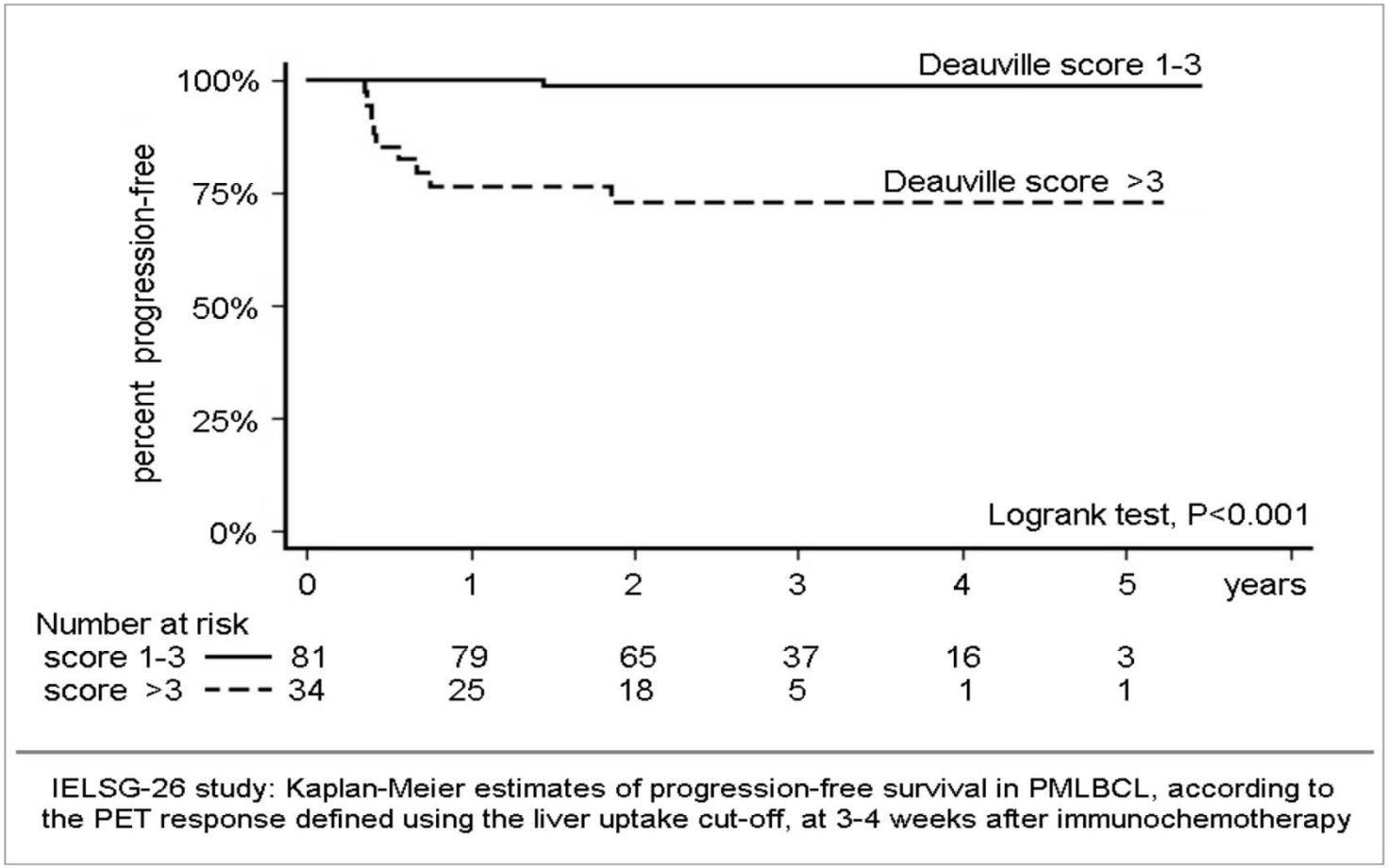
Post R-chemo PET interpretation - blind central review
115 /125 studies reviewed



IELSG-26 study: Preliminary results



IELSG-26 study: Preliminary results



IELSG-26 study: Kaplan-Meier estimates of progression-free survival in PMLBCL, according to the PET response defined using the liver uptake cut-off, at 3-4 weeks after immunochemotherapy

IELSG-26 study: preliminary conclusions

1. with the MBP cut-point, the PET+ rate (Deauville score>2) after R-Chemo in PMLBCL was higher (53%) than in DLBCL or HL
2. >90% of pts are projected to be alive and progression-free at 5 years post treatment and a negative PET/CT after R-Chemo is significantly associated with a longer PFS.
3. pts with Deauville score 3 had a clinical outcome identical to those with score 1-2, suggesting that the liver uptake may represent a more appropriate cut-point for the definition of CR.
4. Pts with score 4 and 5 had a significantly worse PFS and OS
5. a negative PET after R-CHT may select a subgroup of patients who may not need consolidation RT (IELSG 37 study is ongoing)

Thank you for your attention!