Third international workshop on interim-PET in lymphoma
Menton (France), Palais de l'Europe,
September 26-27th, 2011

International Validation Study of the Prognostic Role of Interim-PET Scan in ABVD-treated, Advanced Stage Hodgkin Lymphoma.

Gallamini A, Barrington S, Biggi A, Gregianin M, Hutchings M, Kostakoglu L, Meignan M, Chauvie S

Is the evidence of the prognostic role of interim PET in HL robust enough ?

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- Kostakoglu L et al. Cancer 107:2678–2687, 2006
- Sher DJ et al. Ann Oncol 20:1848-1853, 2009
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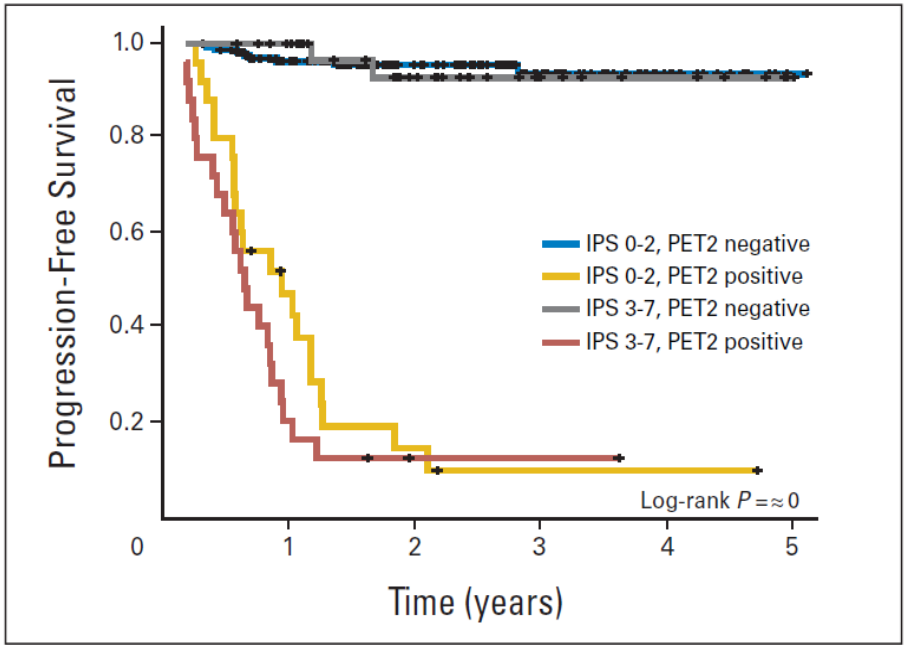
- Furth C et al. J Clin Oncol 27:4385-4391, 2009
- Markova J et al Ann Oncol 20:1270-1274, 2009
- Avigdor A et al Ann Oncol 21:126-312, 2010
- Cerci JC et al. J. Nucl. Med 51: 1337-43, 2010
- Le Roux et al. Eur. J. Nucl. Med Mol Imaging e-pub 10 feb.2011
- Zinzani et al.: Eur J Nucl Med Mol Imaging. 2011 Sep 6. [Epub]

Why do we need IVS ?

…interim-PET scan has been proven the most powerful tool to predict treatment outcome in ABVD-treated HL patients. We feel now the responsibility with the international scientific community for the consequences of this assumption. We propose simple, reproducible rules for interim PET interpretation, in order to share our results with other teams worldwide.

Joseph Connors, PET conference, Lugano 2008

What should be validated ?



Gallamini A et al. J Clin Oncol 2007; 25:3746-52.

DEAUVILLE RULES

- Score 1 no uptake
- Score 2 uptake ≤ mediastinum
- Score 3 uptake > mediastinum but ≤ liver
- Score 4: moderately ↑uptake > liver
- Score 5 markedly ↑uptake > liver and/or new sites of disease

IVS endpoints

Primary endpoint

Overall accuracy and Predictive Value of interim-PET scan in terms of 2-year failure-free survival

Secondary endpoints

- Propose easy reproducible international rules for early PET interpretation during ABVD chemotherapy for Hodgkin lymphoma.
- Concordance rate of reviewers among he members of Central review panel.

Sample size

HYPOTHESIS: “confirmatory study”

END POINT: an hypothetical value of 2-y FFS of 90% and 10% for interim-PET negative and positive patients, respectively.

CALCULATION

We set a C.I: of 90% for both arms and an alpha error of .05 for PET negative and of .10 for PET positive patients.

The reason to allow a wider error margin for PET positive patients depends on the rules proposed for PET interpretation, where the criteria for PET positive scans are more stringent than for PET negative

To confirm the values of a 2-y FFS of 90% for PET negative patients and 10% for PET positive patients, we hypothesize an alpha error of .05 and a potency of 90% for PET-2 negative and an alpha error of .10 and a potency of 90% for PET-2 positive patients, ≥ 310 patients should be enrolled in the validation study.

Inclusion criteria

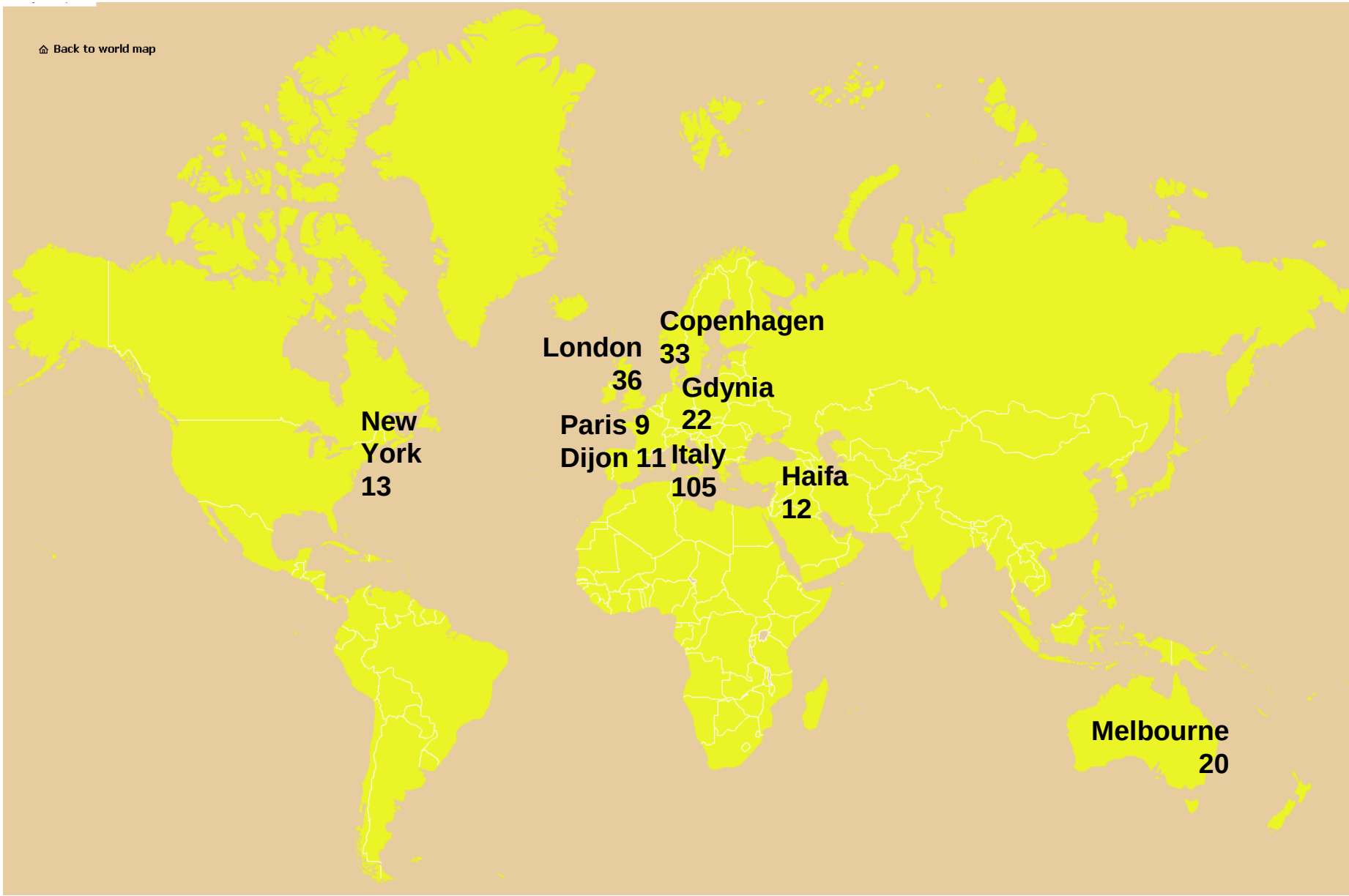
- Advanced-stage (IIB-IVB) or poor-prognosis stage IIA* HL.
- Therapy: ABVD x 6 cycles plus or minus consolidation radiotherapy.
- Staging at baseline and after 2 ABVD with PET-CT(PET-0 and PET-2)
- No treatment change depending on interim-PET results.
- Patients treated with 2-nd line chemotherapy for progressive /resistant lymphoma during ABVD chemotherapy eligible only with **clinical and/or radiological evidence of disease progression.**
- PET-0 and PET-2 performed in the same PET center
- Minimum follow-up of one year after treatment completion

* ≥ 3 nodal sites involved, bulky lesion ESR > 40 mmHg.

Exclusion criteria

- Blood fasting levels before scan > 200 mg/dl.
- Treatment change based **only** on interim-PET results
- Non PET-CT technology
- Therapy intensification after PET-2 for a different reason than disease progression
- PET-0 and PET-2 not performed in the same PET center
- Unavailability/low-quality of dicom images.
- Inadequate follow-up

Participating centers (N=17; pts=261 enrolled from 05.11.2001 to 23.11.2009)



Patient selection

400 patients enrolled

336 patients with PET/CT scans uploaded & quality controlled

261 patients with PET/CT scans approved & sent to review

Reason for PET scan exclusion

- Absence of CT images 22
- Absence of baseline PET 25
- Absence of interim PET 1
- CT slices missing 3
- PET slices missing 10
- Poor quality scans 6
- Miscellaneous 8

- **REVIEWERS**
- Sally Barrington – London – UK
- Alberto Biggi- Cuneo – I
- Michele Gregianin – Padova - I
- Martin Hutchings- Copenhagen – DK
- Lale Kostakoglu – New York – USA
- Michel Meignan – Paris – F

KEOSYS Medical Imaging

Review results acquired and statistical analysed

Demographics

Titolo	Modality	JCO 2007	IVS 2011	p
Age	Years (mean)	35.2	40.4	n.s
Sex	M/F	133/127	140/121	n.s
F-up	Years	2.34	3.12	n.s
Histology	NS vs. non-NS	200 vs. 60	181 vs. 80	n.s
B-symptoms	Y (%)	54.6	57.4	n.s
Extra-nodal disease	Y (%)	28.5	30.6	n.s
Bulky disease	Y (%)	35.3	30.2	n.s
WBC	n/µl	10573	8147.83	n.s
Lymphocytes	n/µl	1612	1372.20	n.s
Hemoglobin	gr/dl	12.6	12.47	n.s
Albumin	gr/dl	3.89	4.20	n.s
Stage	IIA vs. IIB-IVB	67/193	52/209	n.s
IPS	0-2/3-7	195/65	190/71	n.s
PET-2	Pts +/Pts -	50/210	46/215	n.s
Radiotherapy	y/n	104/156	99/162	n.s
1-st line CT outcome	CR vs.Pro + Rel	199/61	220/41	n.s