



Fourth international workshop on PET in lymphoma

Under the auspices of ELI, LYSA, FIL, SFMN, EANM, EHA, EORTC



Menton October 5th 2012

Interim PET in lymphoma: 2012 consensus

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Are we ready to introduce the routine clinical use of interim PET and Deauville 5-PS rules for HL?

Review process in the IVS

- Baseline and interim PET were available for the review process
- Interim PET were reviewed independently by 6 reviewers from 5 different country
- All scans were reviewed using the same software (Positroscope ®, Keosys)
- Reviewers were completely blinded to patient history, follow up and clinical data.

**according to
the 5-PS**

and

**using a set of detailed
additional instructions**

Deauville score - 5PS

Score 1: no uptake

Score 2: uptake \leq mediastinum

Score 3: uptake $>$ mediastinum but \leq liver

Score 4: moderately \uparrow uptake $>$ liver

Score 5: $\uparrow\uparrow$ uptake $>$ liver and/or new sites of disease

5-PS score was applied either to nodal and extranodal disease.

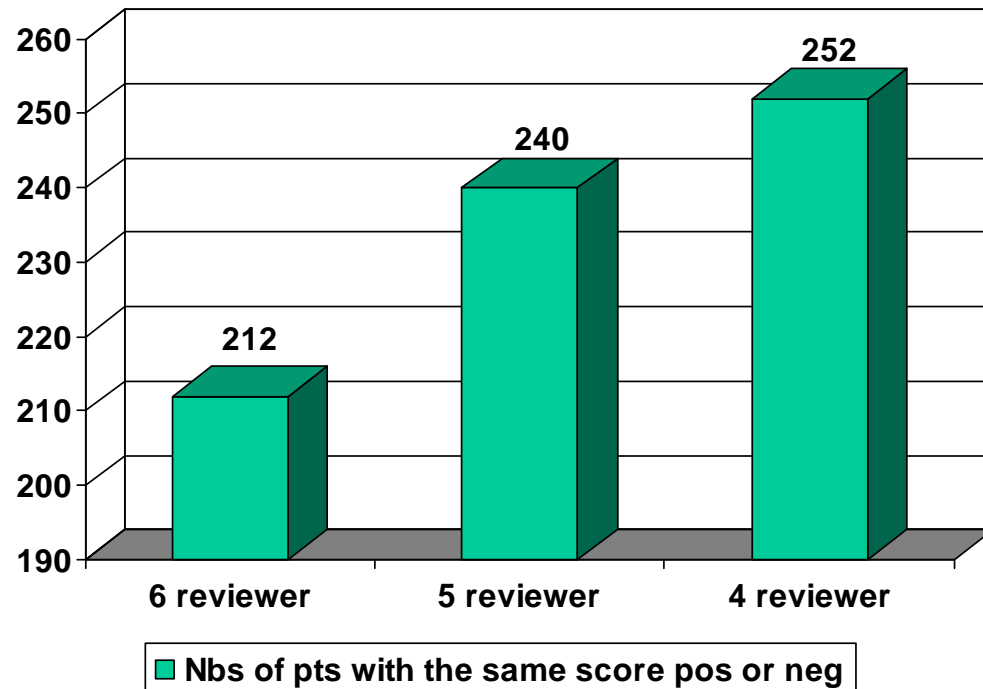
Reviewers agreed that

- score 4-5 are positive and score 1-2-3 are negative
- the score for each patient was defined by an agreement of at least 4/6 reviewers

Additional instructions

- *Positive lesion*: a FDG uptake in a lesion present at baseline
- *New lesion at a different site in patient otherwise in CR*: probably NOT lymphoma
- *New lesion in patient not in CR*: new site of lymphoma.
- *Diffuse uptake in bone marrow and/or spleen*: no disease (Chemo effect)
- *Focal cold lesion in bone marrow in a site previously involved, with/out surrounding bone marrow increased uptake*: successful treatment with/out “mirror effect”.
- *Symmetrical tonsillar uptake*: usually not disease.

At the end of the review process the blind agreement among reviewers was reached in 252/260 patients (97%).



NEG	210/252
POS	42/252

consensus

NEG	5/8
POS	3/8

final

NEG	215/260
POS	45/260

After the joint review session in London, the agreement among reviewers was 100%

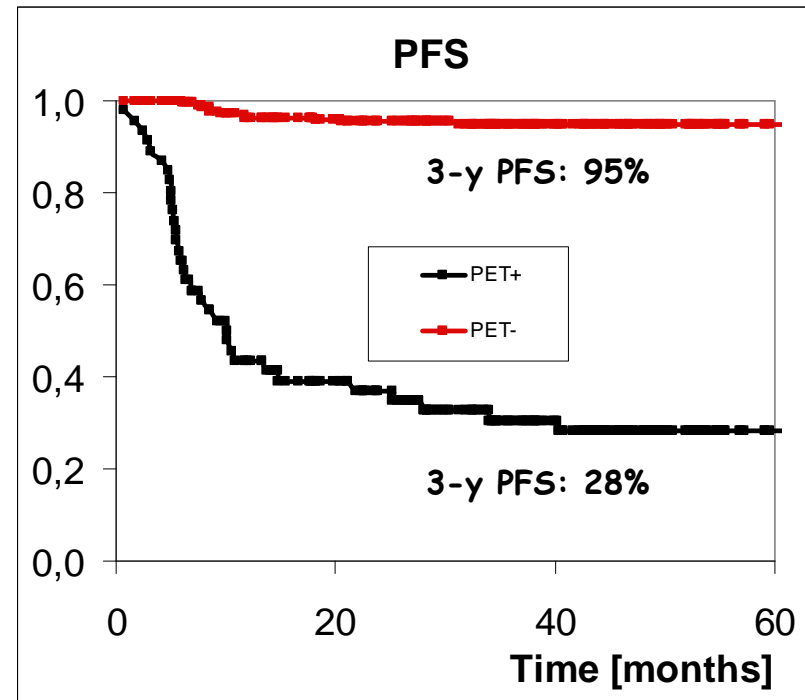
Accuracy and PFS

Prediction of outcome

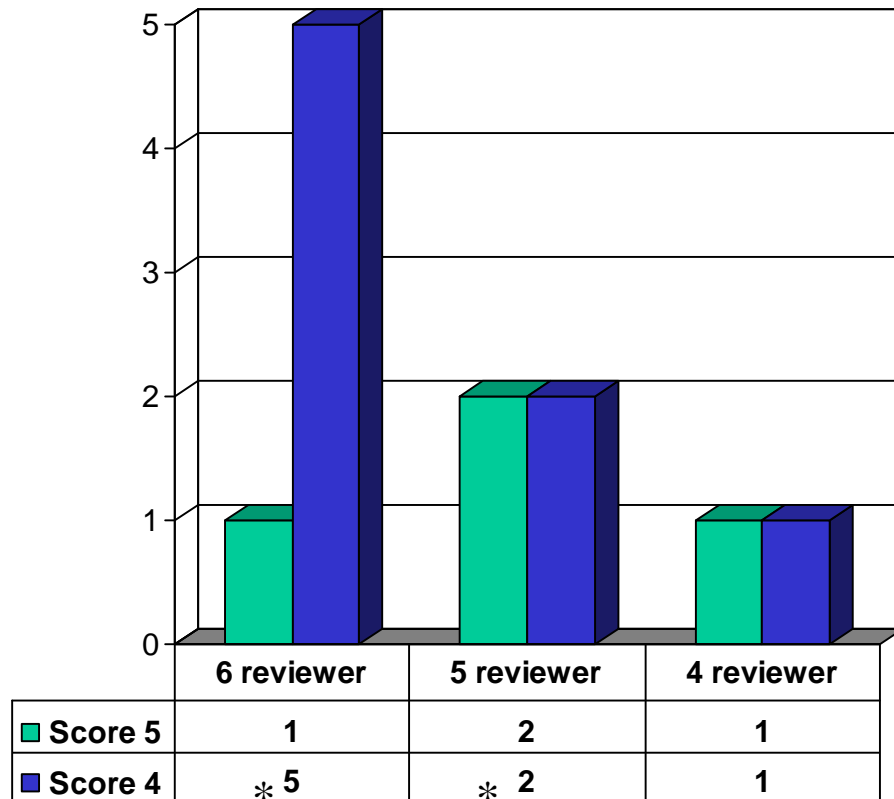
		Interim PET	
		neg	pos
Treatment failure	no	203	12
	yes	12	33

SE 0.73
SP 0.94
ACC 0.91

PPV 0.73
NPV 0.94



False positive results



12 pts

- 5 mediastinum
- 2 laterocerv.
- 1 right pulmonary hilum
- 1 axilla
- 1 lung
- 1 bone
- 1 different site

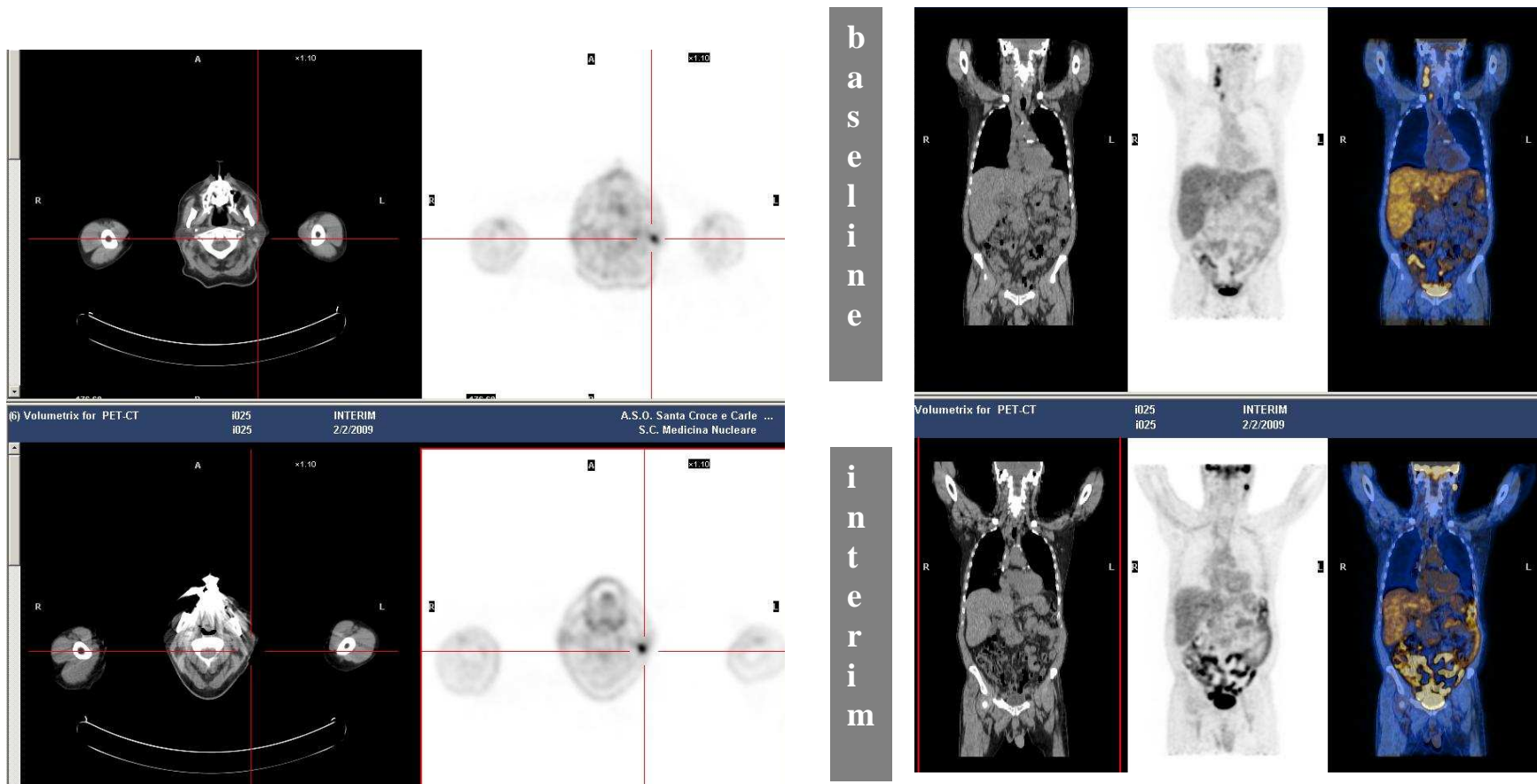
4/12 FP pts in bulky lesion

*One pts after consensus Meeting in London

All 12 patients were alive after a mean follow up of 51 months

False positive results

- Reviewers were completely blinded to the clinical data
- In one case only clinical information were required to confirm left parotid adenoma



False negative results

Score 1-2 : 167 pts

Score 3 : 48 pts

		Score 1-2	
		neg	
Treatment failure	no	162	
	yes	5	

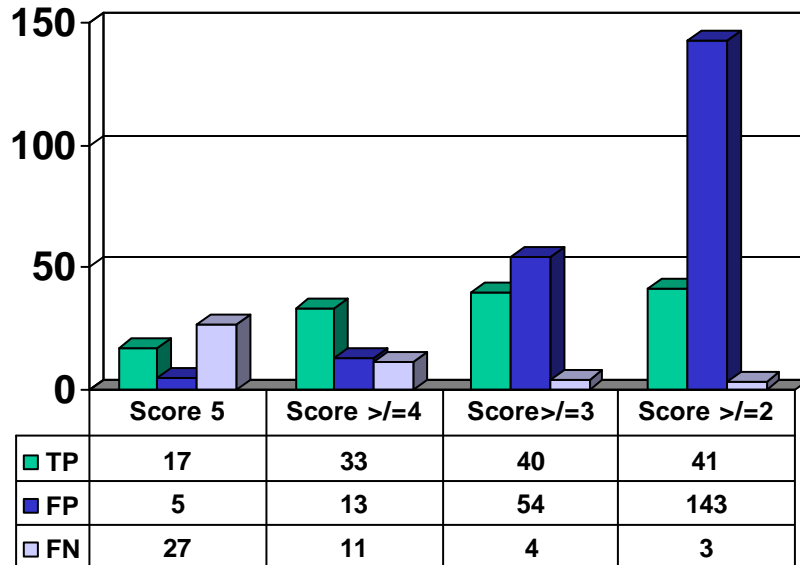
		Score 3	
		neg	
Treatment failure	no	41	
	yes	7	

FN 3%; NPV 97%

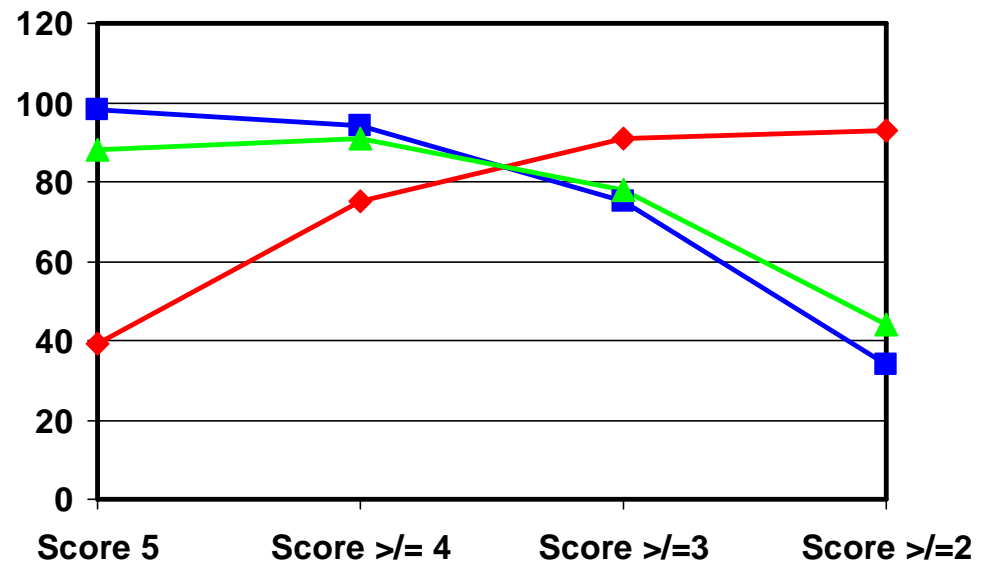
FN: 15%; NPV 85%

All 12 patients relapsed after a mean follow up of 40 months.

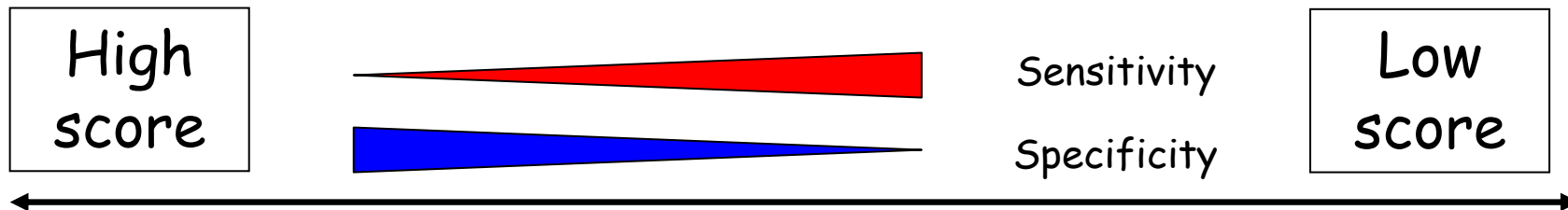
Overall accuracy & score



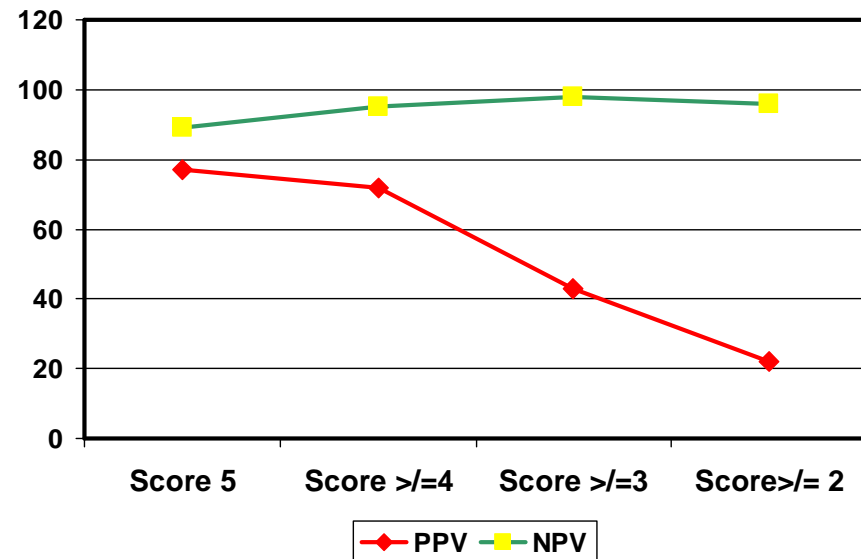
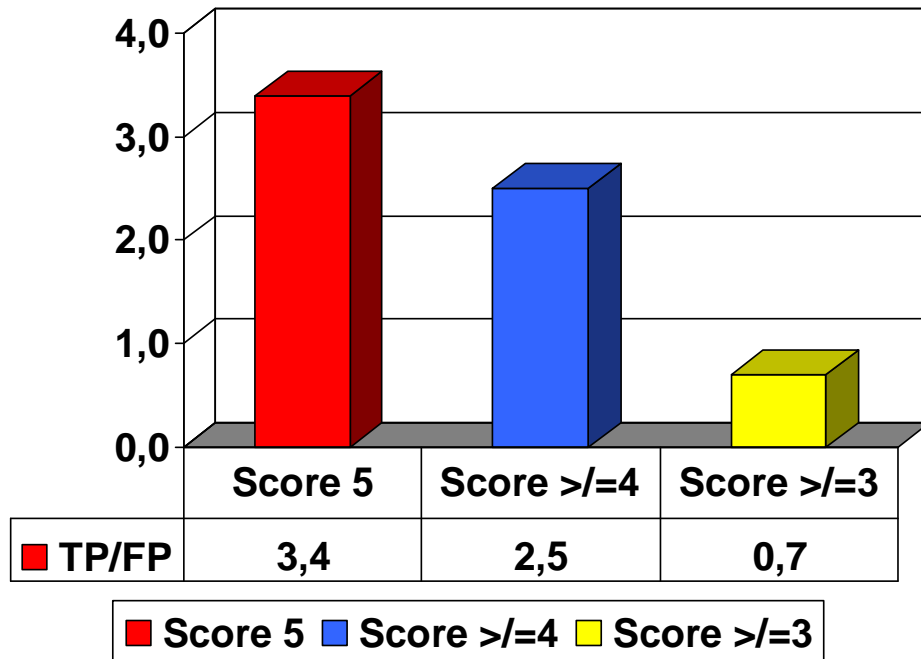
TP FP FN



SENSITIVITY SPECIFICITY ACCURACY



Score ≥ 4 is the optimal treshhold for treatment escalation



	Score 5	Score ≥ 4	Score ≥ 3	Score ≥ 2
Krippendorf α	.0.706	0.758	0.536	0.274

Agreement between reviewers

Binary concordance:

-ve vs. +ve

Cohen's K

0.61–0.80

good

>0.81

very good

Cohen's Kappa:

	Mean						
	0.75	1	0.73	0.77	0.78	0.75	0.73
	0.73	0.73	1	0.75	0.75	0.70	0.71
	0.78	0.77	0.75	1	0.83	0.77	0.77
	0.81	0.78	0.75	0.83	1	0.84	0.84
	0.77	0.75	0.70	0.77	0.84	1	0.78
	0.77	0.73	0.71	0.77	0.84	0.78	1

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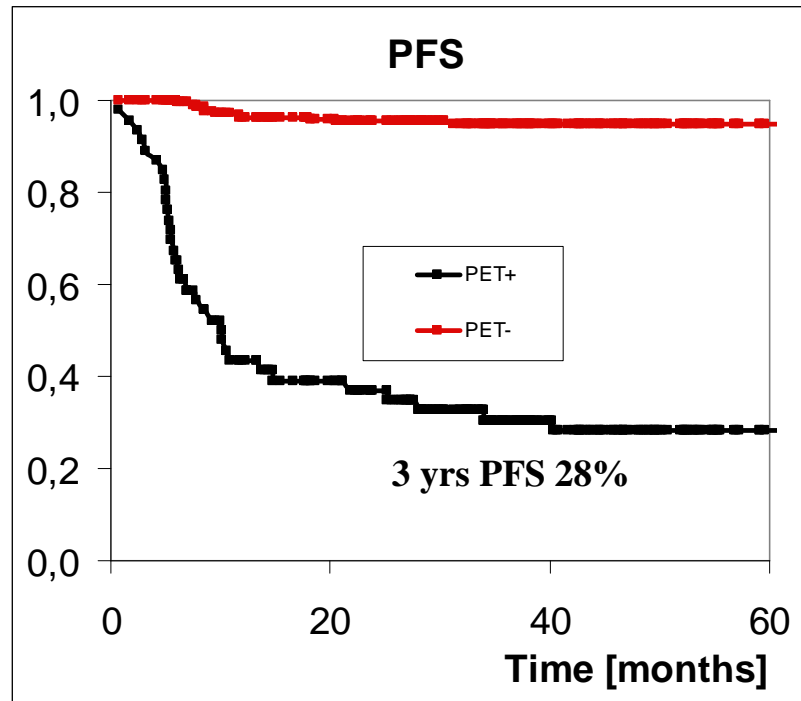
Alpha	D-obs	D-exp	N	R	Reviewers
0.758	118.400	489.908	261	6	Hutchings, Meignan, Barrington, Kostakoglu, Biggi, Gregianin

Experience from FIL HD0607 (prospective studies)

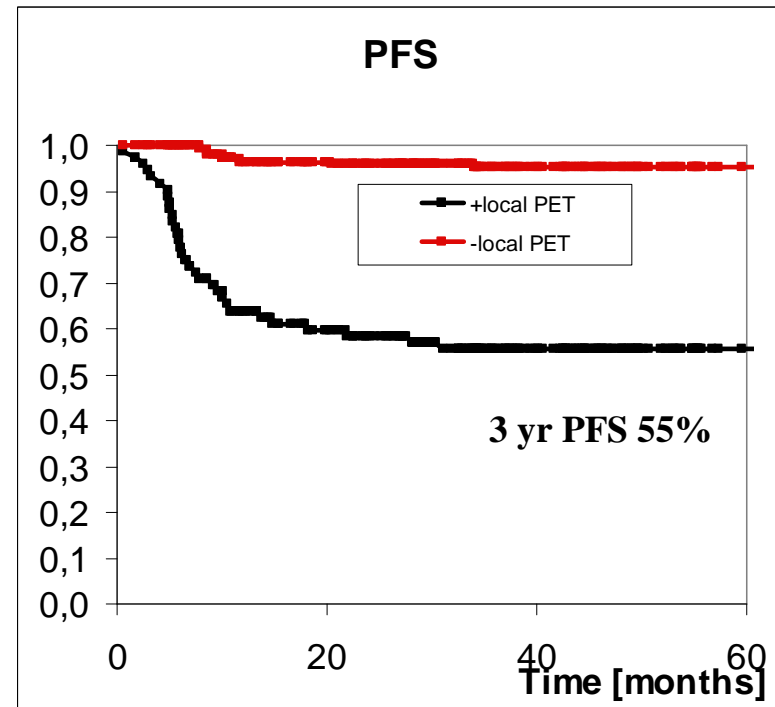
Mean						
0.85	1	0.84	0.86	0.85	0.94	0.76
0.86	0.84	1	0.86	0.96	0.86	0.78
0.87	0.86	0.86	1	0.92	0.92	0.78
0.90	0.85	0.96	0.92	1	0.88	0.88
0.88	0.94	0.86	0.92	0.88	1	0.82
0.80	0.76	0.78	0.78	0.88	0.82	1

Alfa di Krippendorf = 0.84

Review panel vs. local interpretation



Review panel



Local centers

Are we ready to introduce the routine clinical use of interim PET and Deauville 5-PS rules for HL?

YES we are ready!!