II international workshop on interim-PET in lymphoma

Menton (France), Palais de l'Europe, April 8-9th, 2010

Under the auspices of GELA, IIL, EORTC, SFMN

H10 trial (#20051)

Annibale Versari

on behalf of

EORTC/GELA/IIL

EORTC European Organization for Research and Treatment of Cancer

Gela GROUPE D'ÉTUDE DES LYMPHOMES DE L'ADULTE

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H10 trial (#20051)

EORTC/GELA/IIL RANDOMIZED INTERGROUP TRIAL ON EARLY FDG-PET SCAN GUIDED TREATMENT ADAPTATION VERSUS STANDARD COMBINED MODALITY TREATMENT IN PATIENTS WITH STAGES I/II HODGKIN'S LYMPHOMA

H10 (#20051): coordination

Study coordinators

J. Raemaekers, R. van der Maazen, E. Lugtenburg, T. Girinsky	**EORTC**
M. Andre, O. Reman	**GELA**
M. Federico, E. Brusamolino	**IIL**

Central PET review

S. Stroobants, M. Hutchings	**EORTC/IIL**
M. Meignan	**GELA**

Central statistician

C. Fortpied	**EORTC**

Central data management

T. Raveloarivahy	**EORTC**
A. Zarour	**GELA**
M. Bellei, A. Dondi	**IIL**

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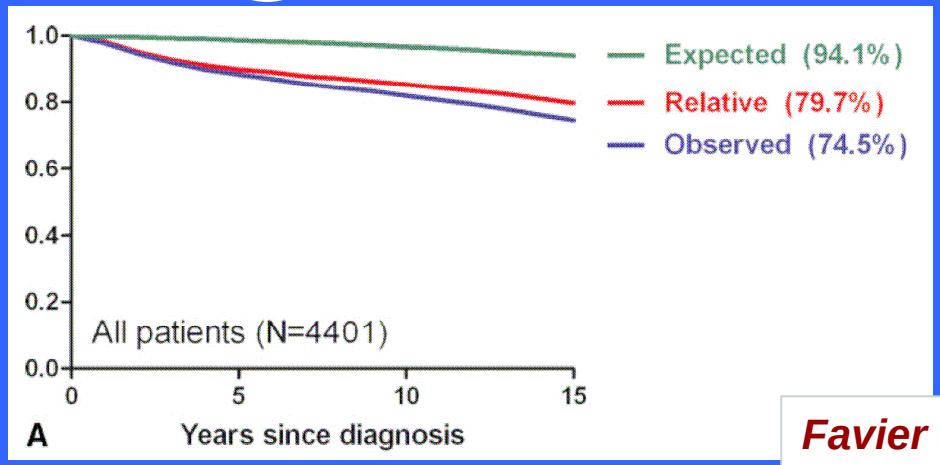
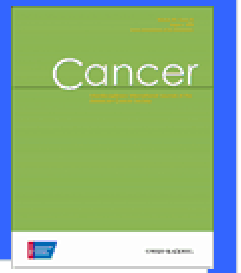
Background

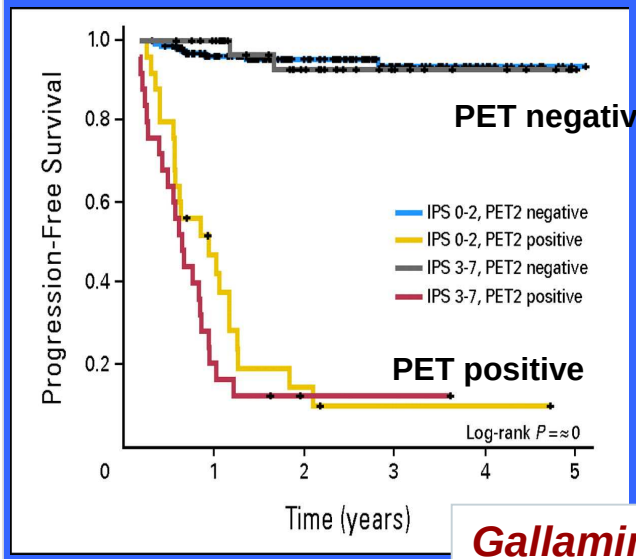




Favier et al, 2009

Survival of HL

Advanced HL



Gallamini et al, 2007

Causes of death

51% HL
10% treatment
18% second cancer
5% cardiovascular
2% infections
14% other cause

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H10 (#20051): **objectives**

- ***Primary***
  - Is chemotherapy alone as effective -but less toxic- as combined modality treatment in patients with stage I/II HL who are FDG-PET scan negative after two cycles of ABVD?
- ***Secondary***
  - Does early change from ABVD to escalated BEACOPP improve the outcome of patients with stage I/II HL who are FDG-PET scan positive after two cycles of ABVD?

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H10 (#20051): **endpoints**

- ***Main endpoint:***
  - The primary end-point for all objectives is **progression free survival**. Progression is defined as progressive disease during protocol treatment, or relapse of HL after previous complete remission/complete remission unconfirmed (CRu), partial remission (PR) or disease stabilization (no change, NC) at the end of protocol treatment.
- ***Secondary endpoints:***
  - Event-free survival
  - Overall survival
  - Long-term toxicity in terms of: secondary malignancies, cardiovascular events, pulmonary events

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H10 (#20051): **eligibility**

- Histologically confirmed Hodgkin's lymphoma, except for nodular lymphocyte predominant (NLPHL) subtype
- Supradiaphragmatic disease (infradiaphragmatic is excluded)
- Previously untreated
- Clinical stages I/II
- Age 15-70 years
- WHO performance 0-3
- **FDG-PET scan prospectively planned after two cycles of ABVD in all patients**
- Informed consent

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Favorable & Unfavorable (EORTC criteria)

Unfavorable

- CS II ≥4 nodal areas involved ***or***
- Age ≥50 years ***or***
- ESR ≥50 (no B symptoms) ***or***
- ESR ≥30 (B symptoms present) ***or***
- MT ratio ≥0.35

Favorable

- None of the above

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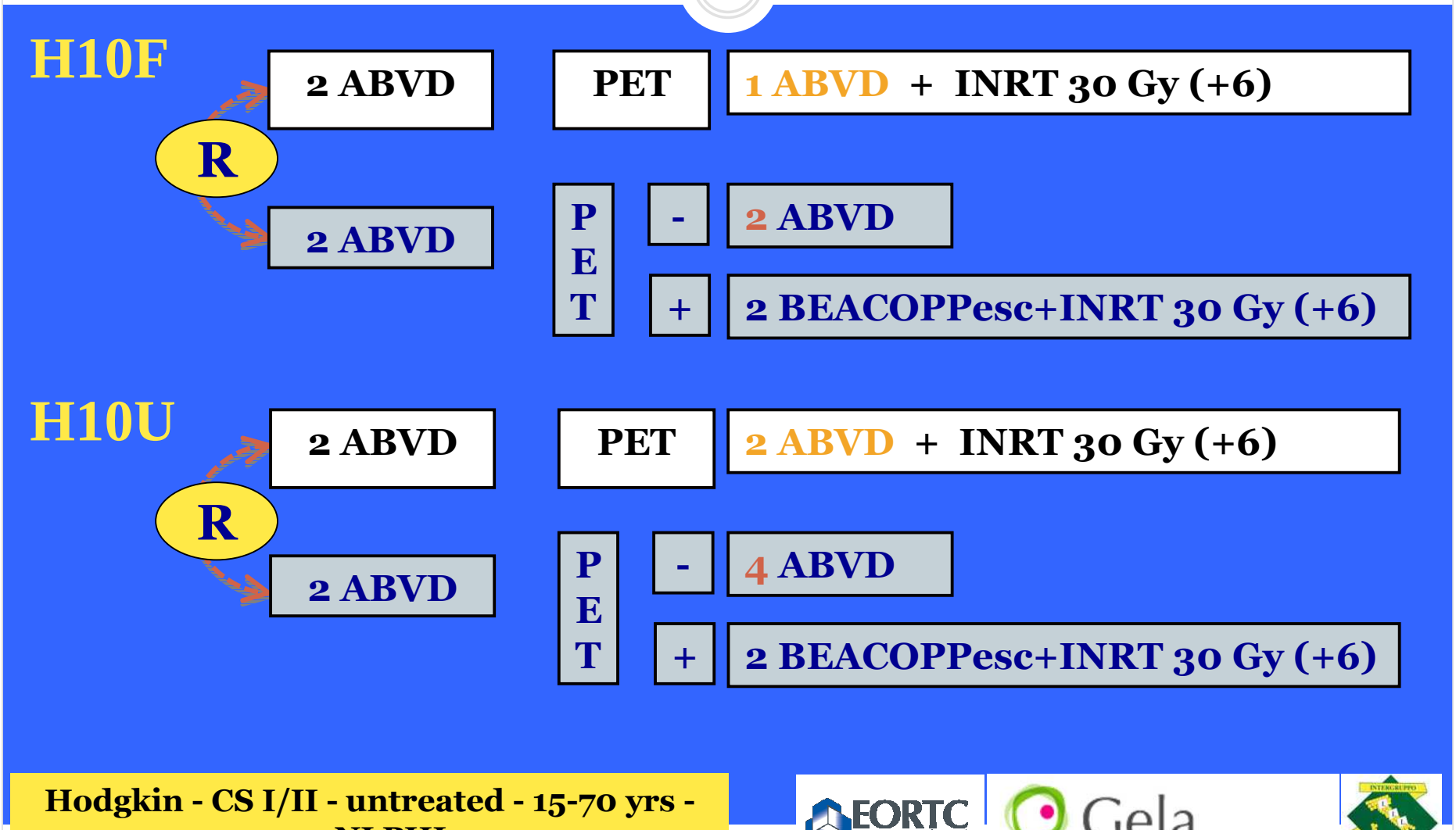
H10 (#20051): **study design**



Hodgkin - CS I/II - untreated - 15-70 yrs - no NLPHL

H10 (#20051): **sample size definition**

Group	Favorable	Unfavorable
Standard 5-yrs PFS	95%	90%
Experimental 5-yrs PFS	>85%	>80%
Hazard ratio	3.2	2.1
Log rank	One-sided	One-sided
Alpha	0.025	0.025
Beta	0.2	0.2
# events required	26	63
Potential recruitment	135	160
# pts required (PET2 neg)	**608**	**720**
Interim analysis	1 *(12 events)*	1 *(22 events)*

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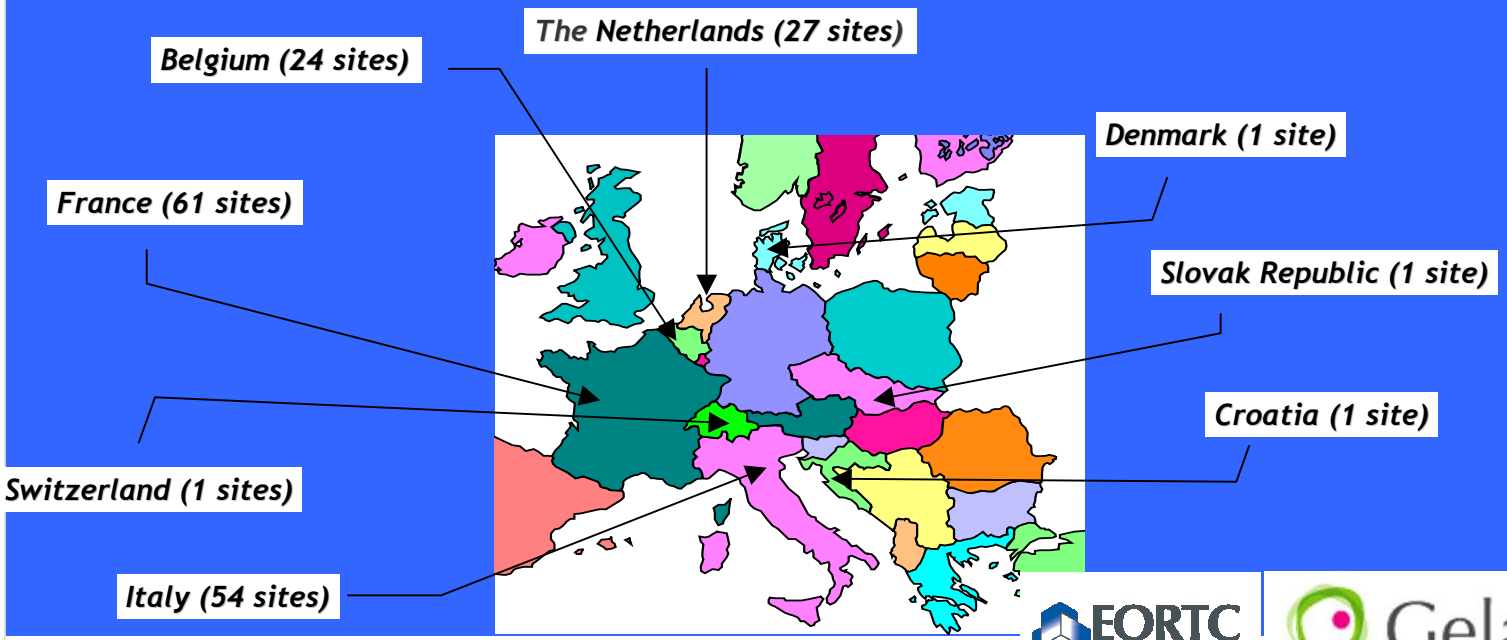
Active sites : March 2010

- EORTC 36 Recruiting: 35
- GELA 80 Recruiting: 75
- IIL 54 Recruiting: 44



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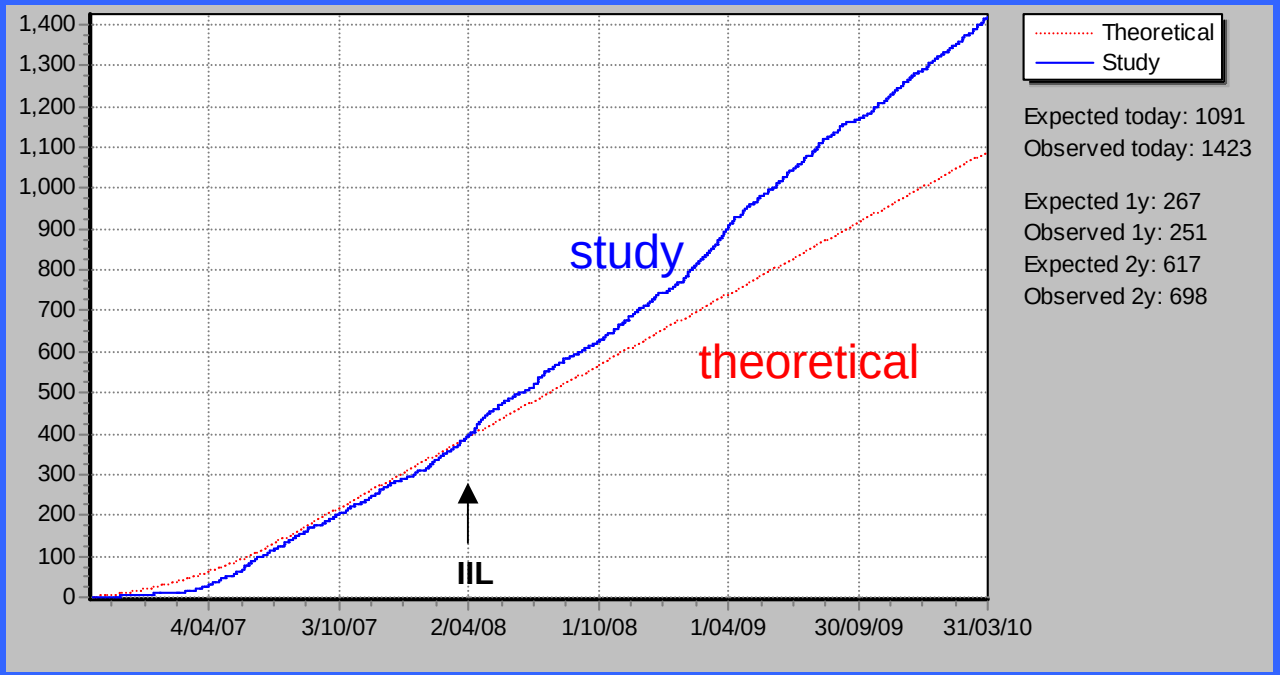
Accrual (31/03/2010)



	EORTC	GELA	IIL	Total
	354 (25%)	837 (59%)	232 (16%)	1423
2009	104 (19%)	300 (55%)	143 (26%)	547

FDG-PET : **timing and review**

ABVD 2 → D 15

NO STEROIDS

PET2 → D 22-25

PET 2 REVIEW
(5 reviews)

CYCLE 3 → D 29 = D1

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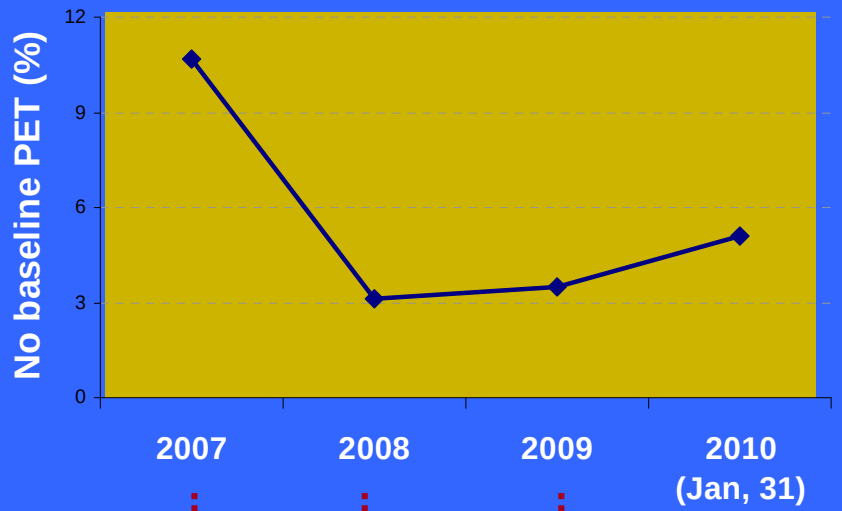
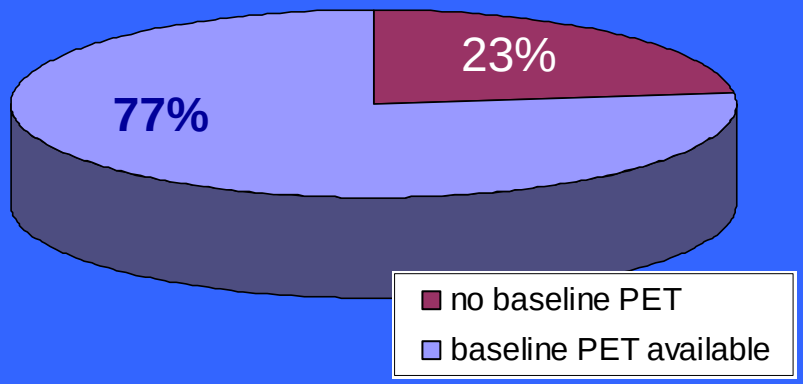
Baseline PET

update on 31/01/2010





	2007	2008	2009	2010 (Jan, 31)
%	10.7	3.1	3.5	5.1
N	30	14	19	2

PET2 evaluated with no BL PET

23

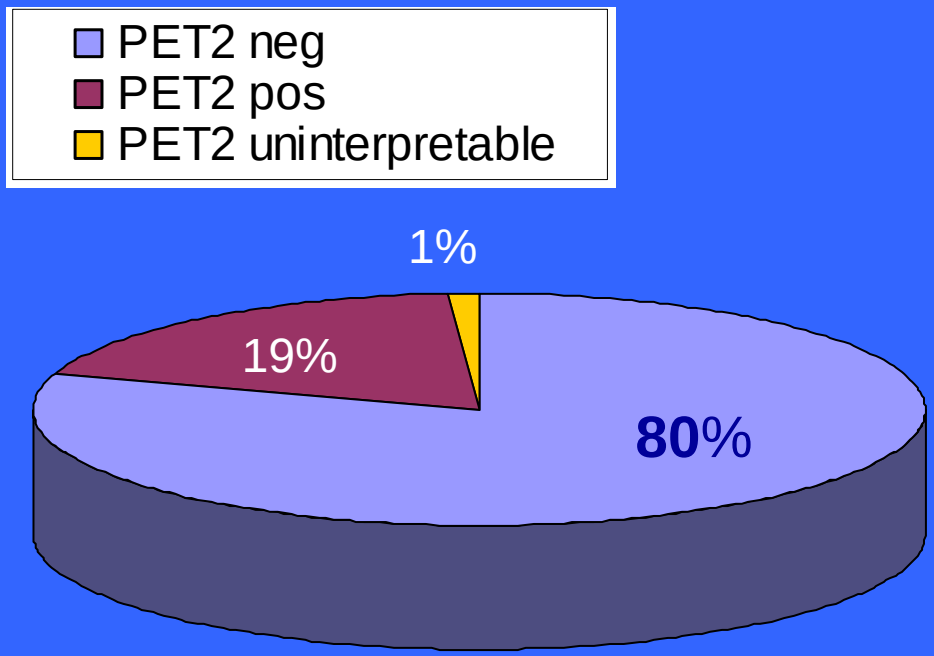
195

= 65 *BL PET missing* **130 *BL PET NOT uploaded***

PET2 results (852 Pts)

interpretation according to

update on 31/01/2010



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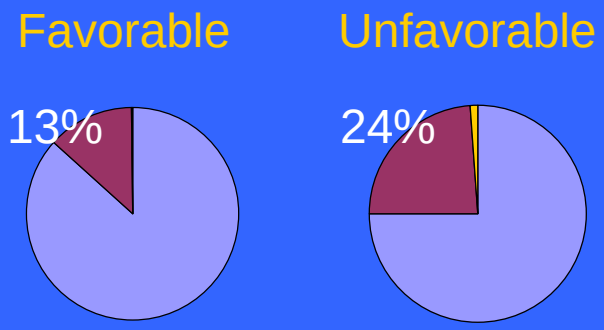
JOURNAL OF CLINICAL ONCOLOGY

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



Total	Pending	Not done	Done	Reviewed	
1330	66	11	1253	852	67%

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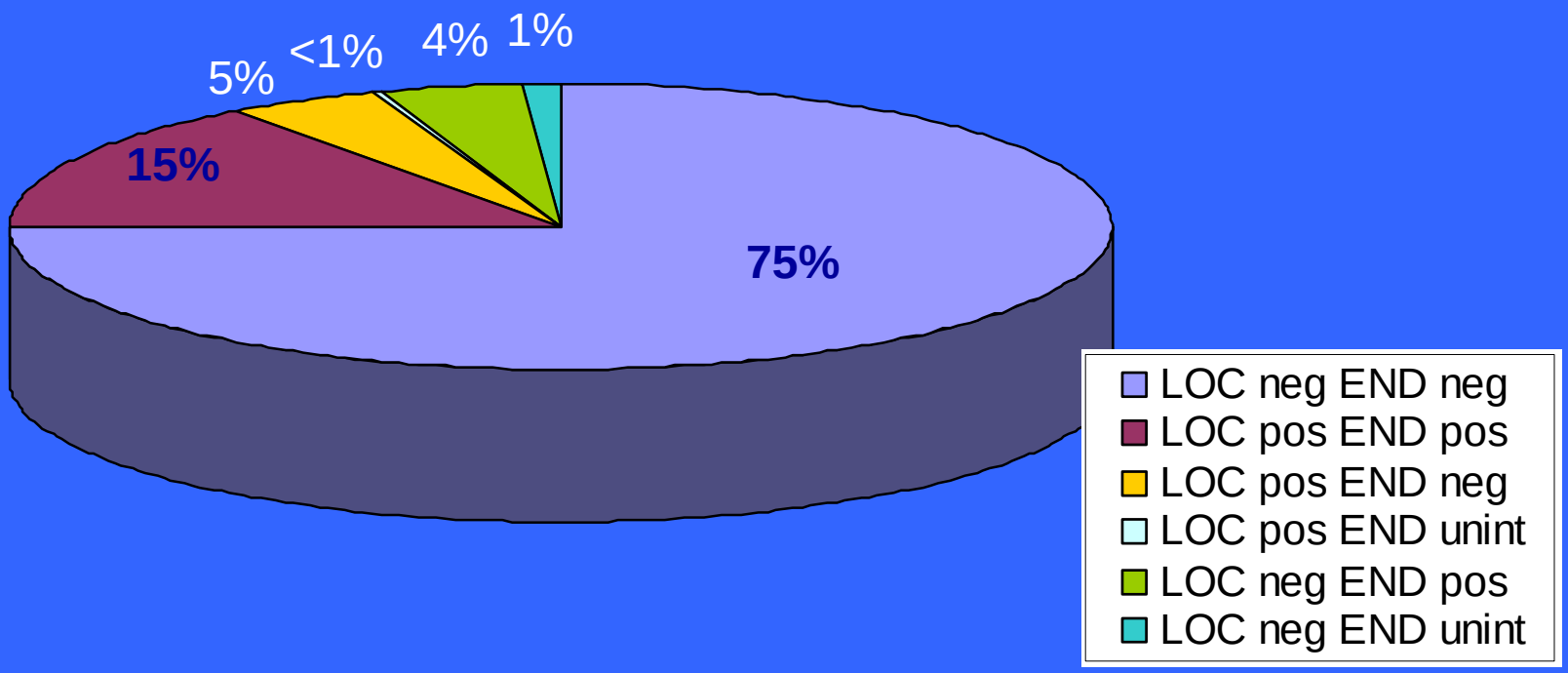
Agreement Local/Central result

update on 31/01/2010

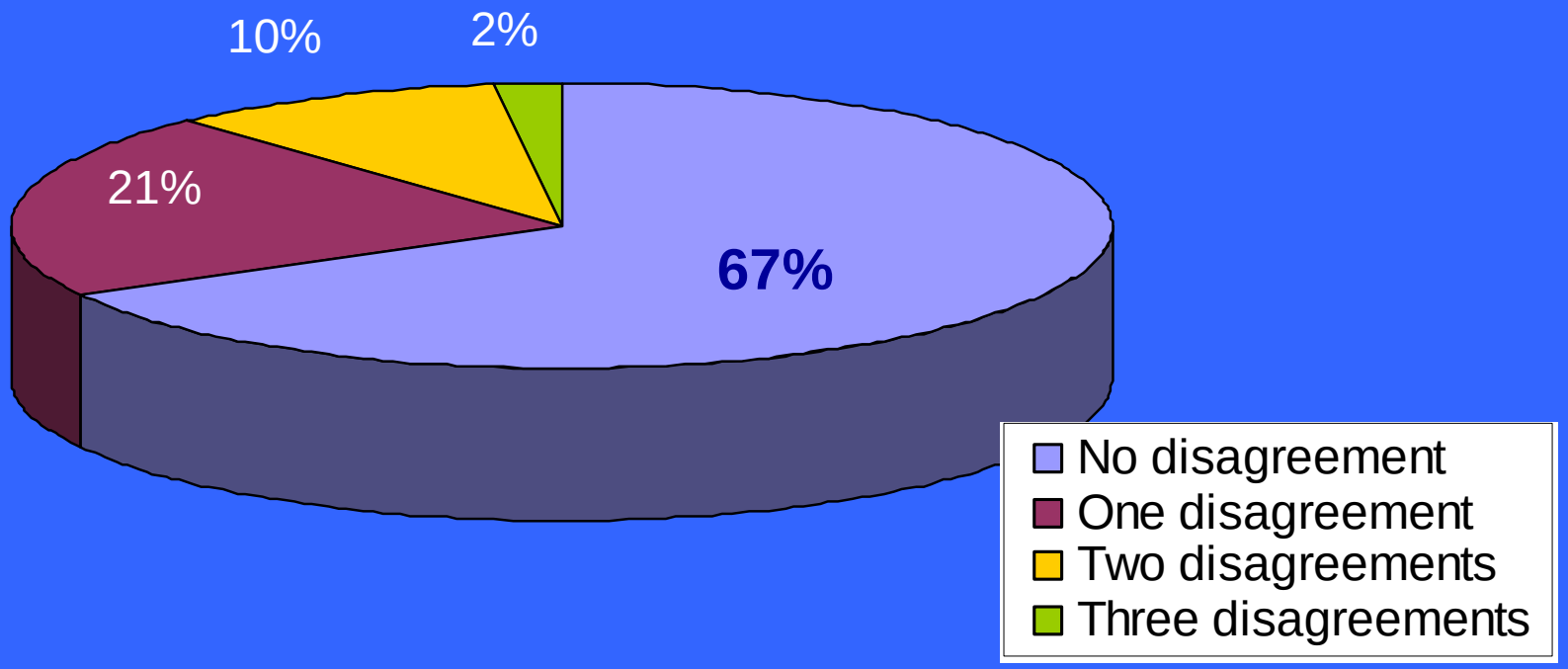
852 Pts



Agreement among the experts

update on 31/01/2010

842 Pts



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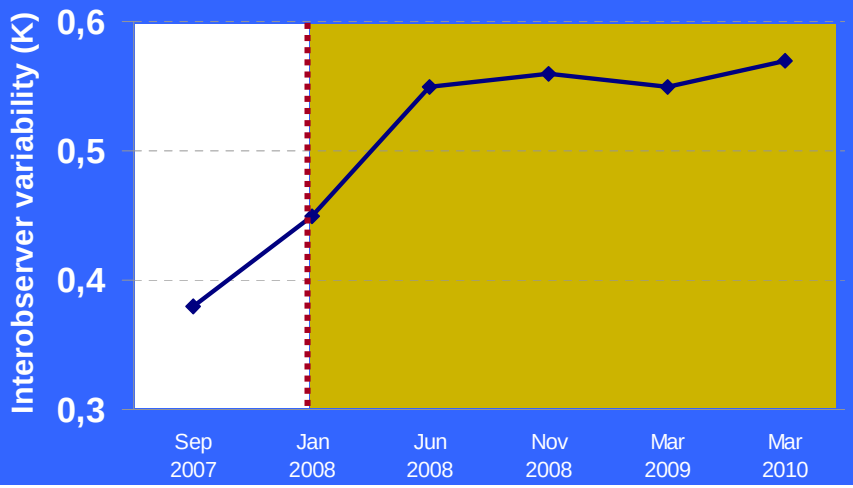
Agreement among the experts: GELA experience (166 Pts)

N	K	K 95% CI	Cumulative agreement
First 46	0.48	0.42-0.54	79% (95% CI 75-81)
Consensus Meeting (January 2008)			
Next 90	0.63	0.58-0.64	85% (95% CI 83-87)



K is better if the baseline PET is available

Meignan et al, 2009

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Conclusions

- FDG-PET is feasible at baseline (95%) and after 2 ABVD (99%) in a large multicentric study
- Good agreement between experts and local nuclear physician
- We have to await the final analysis after completion of the study to answer the question whether early interim FDG-PET can be used to tailor treatment in stage I/II HL.

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H10 (#20051): acknowledgments