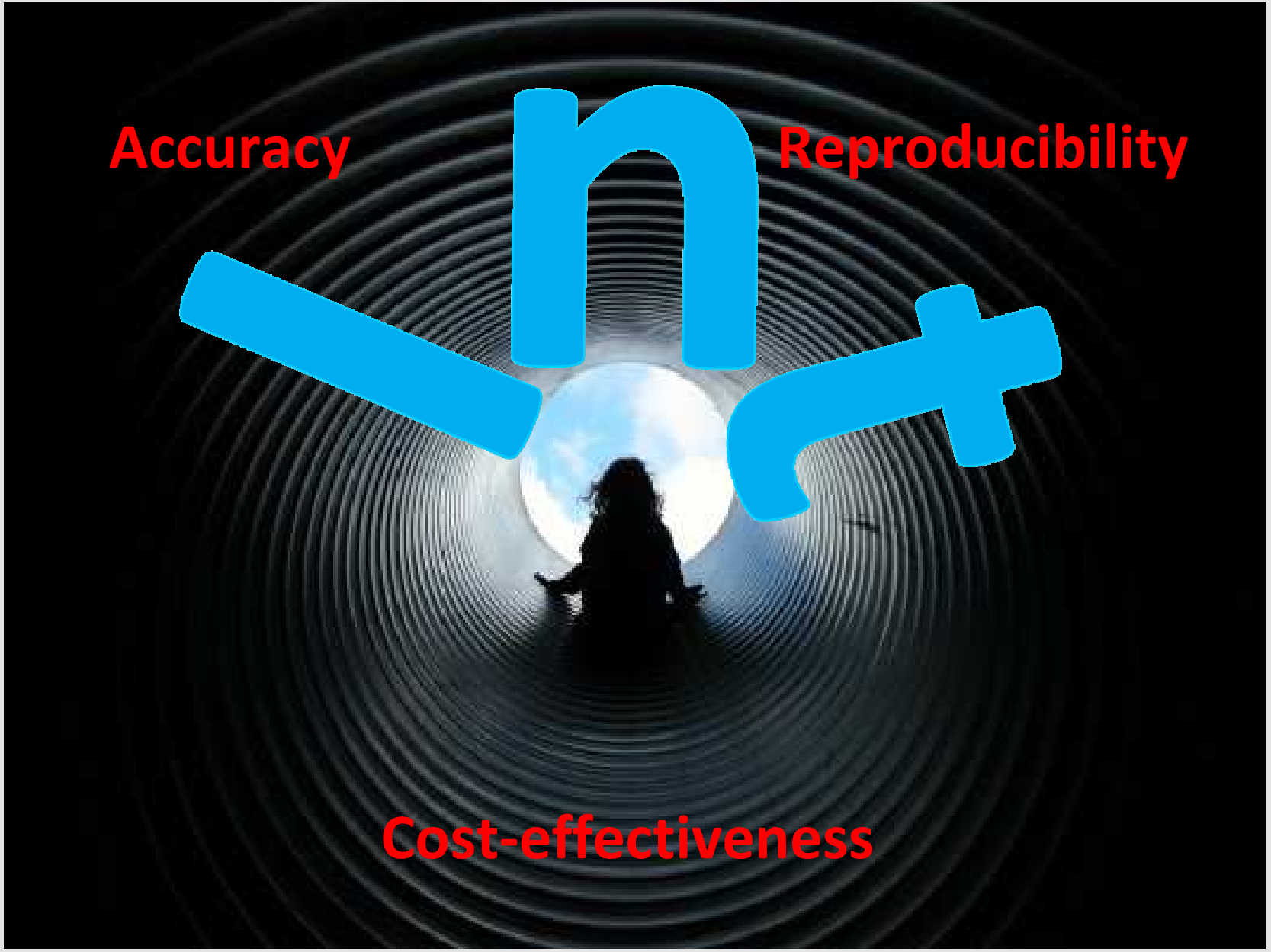
4th INTERNATIONAL WORKSHOP ON PET IN LYMPHOMA

Poster Discussion Session: Interim PET in Lymphoma

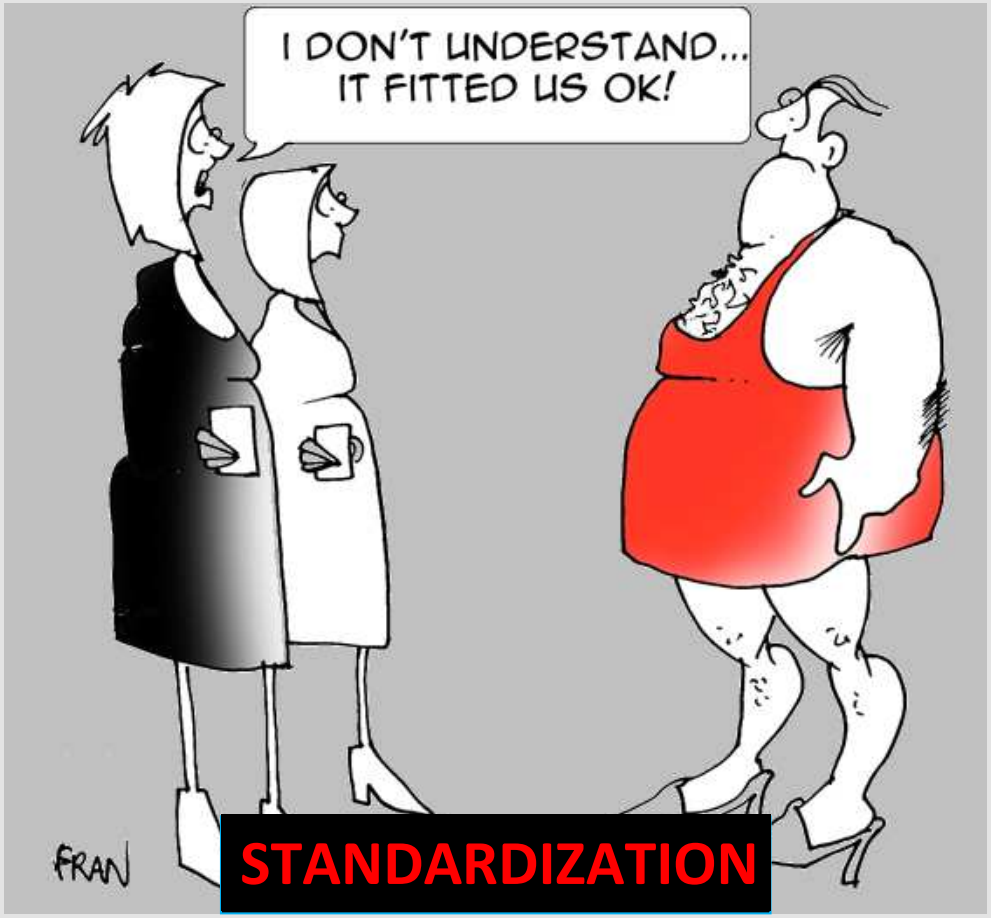
B. Cheson – T. Vander Borght

Interim PET in Lymphoma


Accuracy
Reproducibility
Cost-effectiveness

Key messages on FDG uptake

- Highly sensitive for measuring tumor load, but limited specificity
- Dynamic process
- Difficult to quantify
  - ⇒ Standardization for
    - Preparation
    - Acquisition
    - Reading



Common reading system

- Visual scale: 5-PS or “Deauville criteria”*
  1. No uptake
  2. Uptake ≤ mediastinum
  3. Uptake > mediastinum but ≤ liver
  4. Uptake moderately > liver uptake, at any site
  5. ++ increased uptake at any site and new sites

- Web-based centralized reading systems

*Meignan et al. *Leuk Lymphoma* 2009;50:1257-60.

A3. FDG-PET AS A BIOMARKER IN RESPONSE ASSESSMENT IN ABVD TREATED HODGKIN LYMPHOMA PATIENTS

S. Chauvie (1), A. Biggi (2), E. Lanzi (1), F. Bergesio (1), A. Gallamini (3)
(1) Medical Physics, (2) Nuclear Medicine and (3) Hematology Unit, S. Croce e Carle Hospital, Cuneo

- 260 advanced-stage HL/520 PET from 17 centers
- iPET : Deauville 5-point scale (1-3 negative/4-5 positive)
- Adherence to EANM guidelines for uptake time (60±10min) in 38% (n=100)

iPET	82±35min (45-128min)	60±10min	
Specificity	0.94	0.99	
PPV	0.73	0.91	p<0.01
3y FFS for - iPET	95%	95%	
3y FFS for + iPET	28%	14%	p<0.01

➢ The adherence to international guidelines for PET scanning = ESSENTIAL

Use of Dual-Point Fluorodeoxyglucose Imaging to Enhance Sensitivity and Specificity

Orazio Schillaci, MD, PhD*,†

..... A lesion is likely to be malignant if the standard uptake value increases over time, whereas it is likely to be benign if the standard uptake value is stable or decreases. It is worth noting that in many of these studies, dual-time-point PET improved not only the specificity but also the sensitivity in assessing breast, pulmonary, liver, and other tumors because of increased lesion-to-background ratio, as a consequence of FDG washout from the surrounding normal tissues and increasing neoplastic uptake.
Semin Nucl Med 42:267-280

B1 DUAL-POINT FDG-PET: A NEW SCANNING TECHNIQUE TO DISTINGUISH UNSPECIFIC AND NEOPLASTIC FDG UPTAKE IN HODGKIN LYMPHOMA

[1]Bianchi A, [2]Borra A, [3]Zaucha JM, [4]Malkowski B, [5]Thyss A, [6]Mounier N, [7]Razzouk M, [8]Darcourt J, [7]Zwarthoed C, [9]Chauvie S, [10]Miglino M, [11]Battistini R, [1]Biggi A, [2]Gallamini A.

SUV uncertainties

$$SUV = \frac{\text{Regional Tracer Activity (Bq/ml)}}{\text{Administered Tracer Dose (Bq) / Pt Weight (g)}}$$

- Biologic factors
  - Uptake period (15%)
  - Patient motion and breathing (30%)
  - Blood glucose levels (15%)
- Technical factors
  - Relative calibration between PET sca ner (10%)
  - Residual activity in syringe (5%)
  - Incorrect synchronizati n lo ks (1 %
  - Injection vs calibr tio m (0 %)
  - O ity f i s a o (5%)
- Physi l fac ors
  - Scan c isi n parameters (15%)
  - Im reconstruction parameters (30%)
  - Use of contrast agents (15%)
  - ROI (50%)

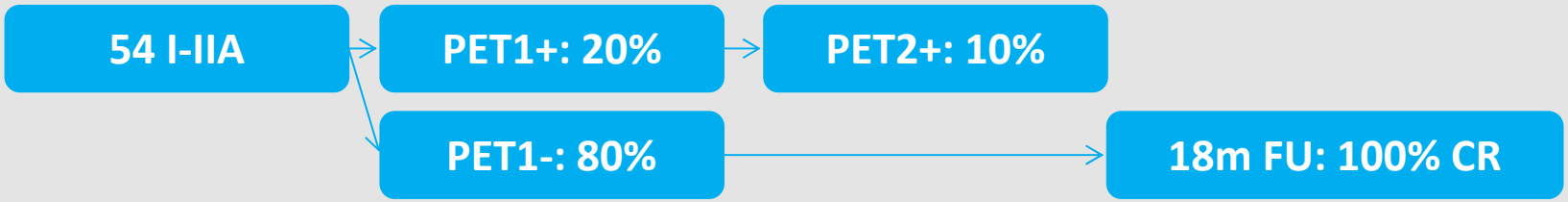
Standardization

Boellaard *J Nucl Med* 2009;50 Suppl 1:11S-20S.

A8. INTERIM PET AFTER FRST AND SECOND ABVD CYCLE IN PATIENTS WITH HODGKIN LYMPHOMA (HL)-POLISH OBSERVATIONAL STUDY

J. Zaucha, B. Małkowski, A. Warszewska, M. Kobylecka, M. Dziuk, S. Chauvie, J. Tajer, E. Subocz, W. Kulikowski, J. Dzietczenia, D. Woszczyk, R. Kroll, A. Romanowicz, J. Walewski-Polish Lymphoma Research Group, PL

- PET after 1 ABVD cycle
  if + (scores 4-5) or equivocal (score 3) then PET after 2 ABVD cycle
- N=199 HL



NPV 100%, PPV 44%

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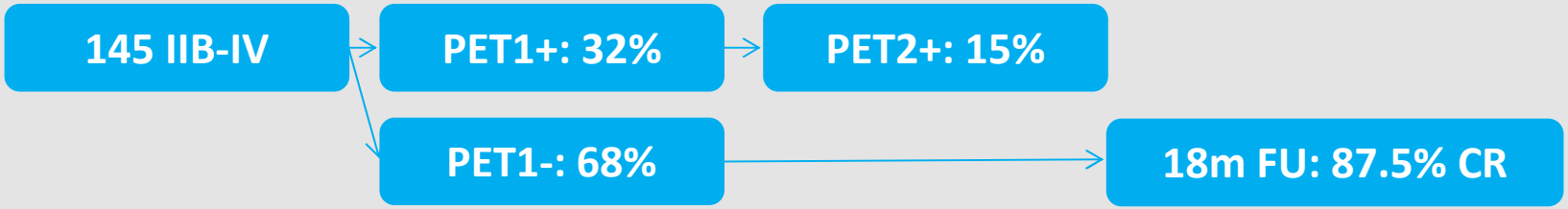


NPV 88%, PPV 48%

➢ High NPV of PET1

A13. NEGATIVE INTERIM PET PREDICTS FOR BETTER OUTCOME OF DLBCL IN AN IAEA-SPONSORED, 9 COUNTRY INTERNATIONAL STUDY

Carr R (1), Paez D (2), Fanti S (3), Cerci j (4), Morris T (1), on behalf of the International Atomic Energy Agency NHL Investigator Group. 1 London UK, 2 IAEA, 3 Bologna It., 4 São Paulo Br.

- Is value of iPET (2-3 R-CHOP) outside Western Europe and USA worse?
- Brazil, Chile, Hungary, India, Italy, Philippines, Thailand, Turkey, Korea
- Visual reading: if MRU or PR → central review
- N=395

2-years EFS		
iPET negative	iPET positive	HR
90%	59%	4.6
95%CI 85–94%	95%CI 49–68%	95%CI 2.8–8.6

➢ **i-PET = independent predictor of outcome in DLBCL generalisable to non-western populations**

Deauville

The Myth of Prometheus – The Thief of Fire

^{18}F-FDG Uptake Changes in Liver and Mediastinum During Chemotherapy in Patients With Diffuse Large B-cell Lymphoma

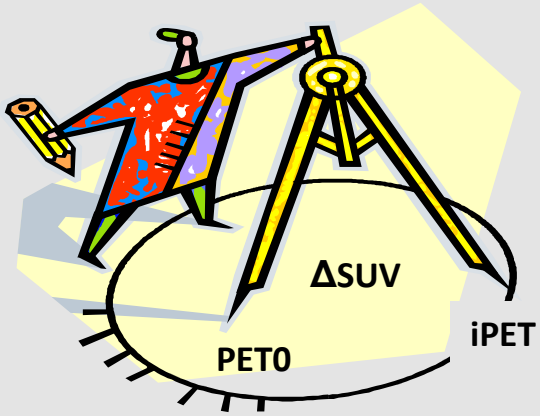
Luca Ceriani, MD, Sergio Suriano, MD,* Teresa Ruberto, MD,* Emanuele Zucca, MD,† and Luca Giovanella, MD**

Results: Liver uptake significantly increased in the interim in comparison with baseline and final PET, respectively, whereas MBP activity remained stable during chemotherapy. The intersubject variability of ^{18}F-FDG uptake in LIV and MBP ranged from 20.2% to 25.4%.

Conclusions: The variability of the LIV uptake during chemotherapy should be taken into account when this parameter is used to score the interim PET scan and to make decisions in defining response-adapted therapeutic strategies. Vice versa, the stability of MBP activity during therapy provides a more reliable benchmark for the response assessment.

Finally, the intersubjects variability of both parameters should be considered when the visual evaluation of the interim PET is performed by point score models.

(*Clin Nucl Med* 2012;37: 949–952)



?

- Lesion target ?
- Type of SUV ?
- Cut-off value ?

A2. INTERIM PET SUV_{MAX} REDUCTION IS SUPERIOR TO VISUAL ANALYSIS USING 5-POINT SCALE CRITERIA TO PREDICT PATIENT'S OUTCOME IN HODGKIN LYMPHOMA

C Rossi, S Kanoun, A Berriolo-Riedinger, O Humbert, I Dygai-Cochet, C Legouge, ML Chrétien, L Berthet, JN Bastie, RO Casasnovas. Hématologie Clinique,CHU Le Bocage; Médecine nucléaire, CGFL; Dijon, France

- 59 HL : PET0, PET2 & PET4
- PET positivity = Deauville score 4-5
- 71% ΔSUVmaxPET0-2 & 75% ΔSUVmaxPET0-4

	3y-PFS			
	-	+	p	HR
Deauville PET2	80%	45%	0.001	
Deauville PET4	74%	33%	0.0002	
71% ΔSUVmaxPET0-2	81%	30%	<0.0001	6.77*
75% ΔSUVmaxPET0-4	77%	25%	<0.0001	6.2

*In multivariate analysis remains the unique independent predictor

A14. PRONOSTIC VALUE OF INTERIM FDG-PET/CT METABOLIC RESPONSE IN DIFFUSE LARGE B CELL LYMPHOMA TREATED WITH R-CHOP

Faes C*, Soubeyran P***, Godbert Y*,Soubeyran I**, Brouste V¤, Hoppe S¤, Cazeau AL* *Médecine nucléaire, **Anatomopathologie, ¤Statistiques, ***Oncologie Institut Bergonie CRLCC Bordeaux France

- Retrospective analysis of 54 DLBCL
- PET0 and PET2-4 after R-CHOP
- 2 local readers: Deauville & $\Delta SUV_{66\%}$
- Genomic expression profil (GCB versus ABC) & IPI

} Correlation with outcome

	2-years EFS		p	K
	1-3	4-5		
Deauville	84.9%	47.6%	<0.001	K=0.85
	>66%	<66%		
ΔSUV	81.1%	18.1%	<0.001	K=0.94
Genomic	GCB	ABC	0.02	
IPI	Low	High	NS	

A15. INTERIM FDG-PET/CT AS A PROGNOSTIC FACTOR IN DIFFUSE LARGE B-CELL LYMPHOMA

S. Fuertes, X. Setoain, A. Lopez-Guillermo, J. Duch, P. Paredes, F. Pons; H.
Clinic i Provincial de Barcelona, Barcelona, SPAIN.

- Prospective study: 50 DLBCL, PET/CT0 & PET/CT2 (R?)
- Reading methods: 3-Point Scoring (PS), Deauville, ΔSUV
- Correlation with PFS and OS

	7-years PFS	OS
3PS	NS	NS
Deauville	79% PET- vs 50% PET+	
Best cut-off ΔSUV	76%	75%

➢ **Optimal cut-off = liver uptake and/or ΔSUV >75%**

A18. BASELINE SUVMAX AND ΔSUVMAX ANALYSIS IN HIGH-TUMOR BURDEN FOLLICULAR LYMPHOMA PATIENTS TREATED WITH IMMUNO-CHEMOTHERAPY : A PROSPECTIVE STUDY

J Dupuis, A. Berriolo-Riedinger, A Julian, E.Itti, P Brice, H Tilly, P Soubeyran, Ph Colombat, A Gallamini, G Paone, O Casanovas,G Salles, C Haioun, M Meignan on behalf of the GELA and the GOELAMS

Thursday October 4th

H14.00-14.30

Follicular lymphoma

The role of PET/CT in the management of Follicular lymphoma: Its predictive and prognostic role:

J Trotmann- M Federico

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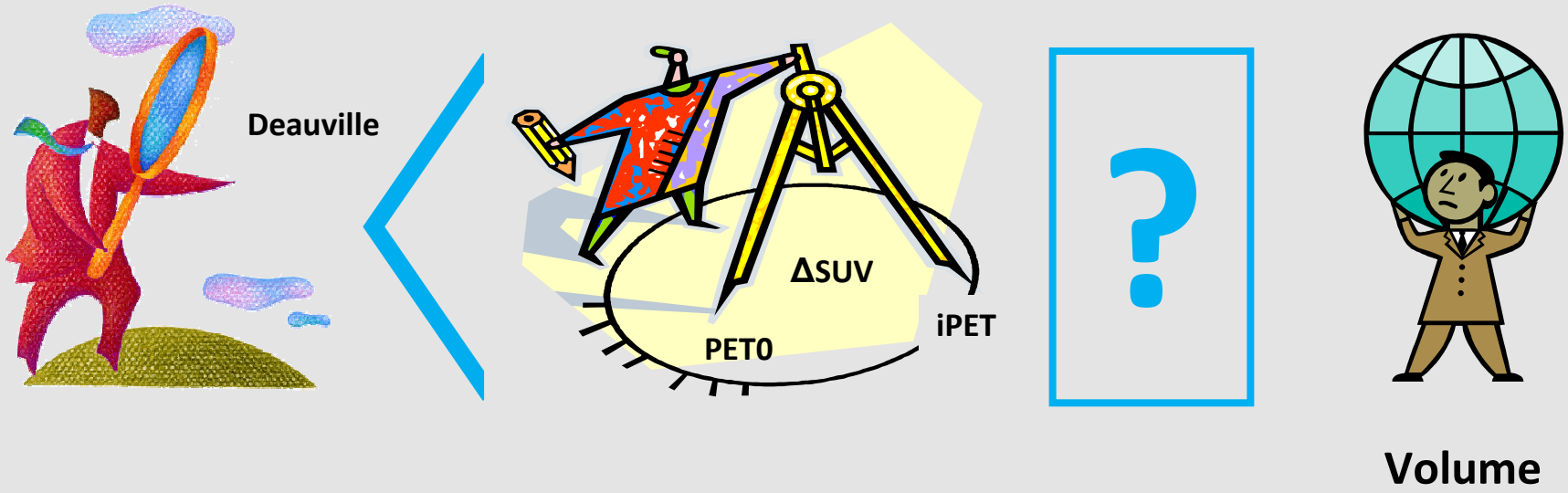
- 121 FL with high tumor burden
- PET0, 4 RCHOP(PET4) and 6 RCHOP+2R (PET8)
- PET reading: Deauville and ΔSUV

	2y-OS				P
PET0	SUV<14.2	100%	SUV>14.2	87%	<0.008
	↓SUV and/or ↓FLIPI	100%	↑SUV and ↑FLIPI	71%	<0.0001
ΔSUV	0-4/43%				NS
	0-8/67%				p<0.005
Deauville					p<0.0001

- **Baseline SUV with FLIPI could identify different risk populations**
- **ΔSUV reduction & Deauville score = good predictor of outcome**

A1. BASELINE METABOLIC TUMOR VOLUME PREDICTS PATIENT'S OUTCOME IN HODGKIN LYMPHOMA

S Kanoun, C Rossi, A Berriolo-Riedinger, O Humbert, I Dygai-Cochet, ML Chrétien, C Legouge, L Berthet, JN Bastie, RO Casasnovas.Hématologie Clinique, CHU Le Bocage; Médecine nucléaire, CGFL; Dijon, France



A10. PROGNOSTIC VALUE OF PRETHERAPY METABOLIC TUMOR VOLUME (MTV) AND EARLY RESPONSE ASSESSMENT (TWO CYCLES) IN DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)

Sasanelli MC, Itti E, Biggi A, Berriolo-Riedinger A, Cashen AF, Tilly H, Djelbani S, Casasnovas RO, Haioun C, Meignan M, Créteil, Dijon, Rouen , FRANCE, Cuneo, ITALY, Saint Louis, USA

A11. BASELINE METABOLIC TUMOR VOLUME IS PREDICTIVE OF OUTCOME IN HIGH RISK PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA

M. Sasanelli, R.O. Casasnovas, A. Berriolo-Riedinger, F.Morschhauser, E. Itti, D. Huglo , A. Versari, M. Meignan on behalf of the GELA Créteil, Dijon,Lille (France), Reggio Emilia (Italy)

Friday October 5th

11.30-13.00:

Metabolic volumes measurement in lymphoma

11.30-13.00:

Chair: A Versari, R Boellaard, M Meignan, L Schwartz.

Metabolic volume measurement (physics and methods)

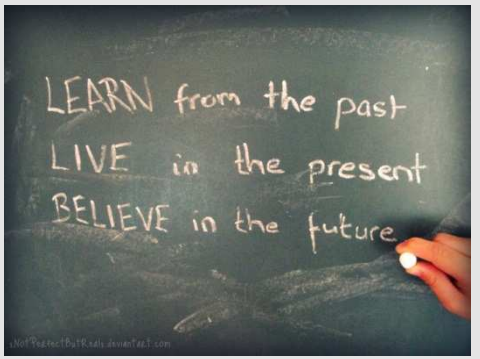
R Boellard

Volume measurement with CT

L Schwartz

Metabolic volume measurement methodology and clinical results (FIL and LYSA)

A Versari, M Sasanelli, E Itti, M Meignan



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- 120 newly-diagnosed DLBCL
- PET0 and PET2 (rituximab-containing regimen)
- MTV: threshold at 41% SUVmax & ΔSUV66%
- No therapy change; mean FU 39.8 months

	N	2y OS (%)
MTV<550mL AND ΔSUV>66%	68	93
MTV>550mL OR ΔSUV<66%	42	83
MTV>550mL AND ΔSUV<66%	10	22

- **MTV (550 ml) is highly predictive of OS before initiation of therapy**
  - **Even better when combined with $\Delta SUV_{66\%}$**

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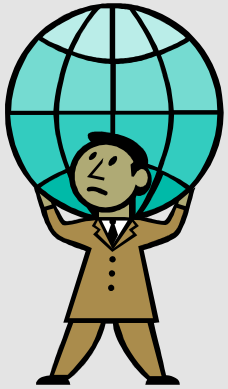
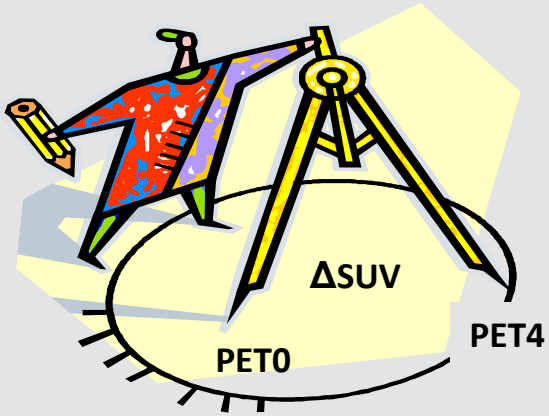
- 121 DLBCL (LNH07-3B: (<60 years,aaIPI2-3)
- PET0 and PET4 (immunochemotherapy)
- MTV: threshold at 41% SUVmax & ΔSUV70%
- Median FU 28 months



MTV



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	2y-PFS (%)	p	2y-OS (%)	p
MTV<625mL	83	0.0032	90	0.002
MTV≥625mL	57		60	
Bulk>10cm		NS		NS
ΔSUV>70%	88	0.0001	94	0.0001
ΔSUV≤70%	40		59	
ΔSUV>70% AND MTV<625mL	90	0.0001	96	0.0001
ΔSUV>70% AND MTV>625mL	77		77	
ΔSUV≤70% AND MTV><625mL		NS		NS

- **Baseline MTV predictive of PFS and OS although tumor bulk was not**
  - **In responders, MTV may improve the NPV of interim PET.**

BASELINE METABOLIC TUMOR VOLUME PREDICTS PATIENT'S OUTCOME IN HODGKIN LYMPHOMA

S Kanoun, C Rossi, A Berriolo-Riedinger, O Humbert, I Dygai-Cochet, ML Chrétien, C Legouge, L Berthet, JN Bastie, RO Casasnovas

Hématologie Clinique, CHU Le Bocage
Médecine nucléaire, CGFL
Dijon, France

Study design

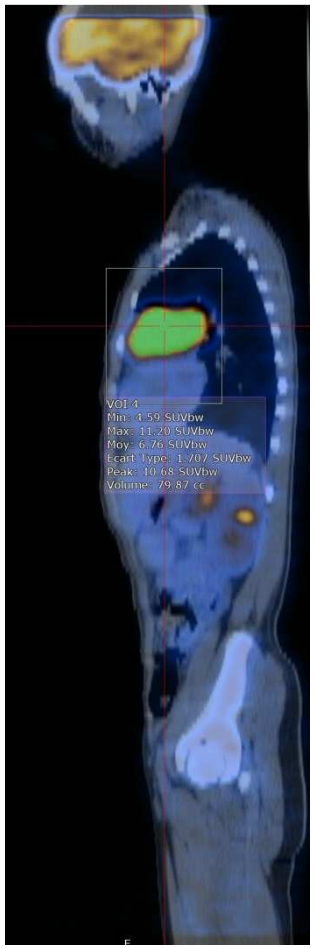
- Retrospective single center study
- **59 consecutive patients** with a first diagnosis of HL between January 2007 and January 2010
- PET performed at baseline (PET0) and after 2 cycles of chemotherapy (PET2)
- **No treatment change on the basis of PET2 results**
- Assessment of:
  - **Metabolic Tumor Volume at baseline (MTV0)**
  - **Tumor bulk (>10 cm) at baseline (CT scan)**
  - **ΔSUVmaxPET 0-2**

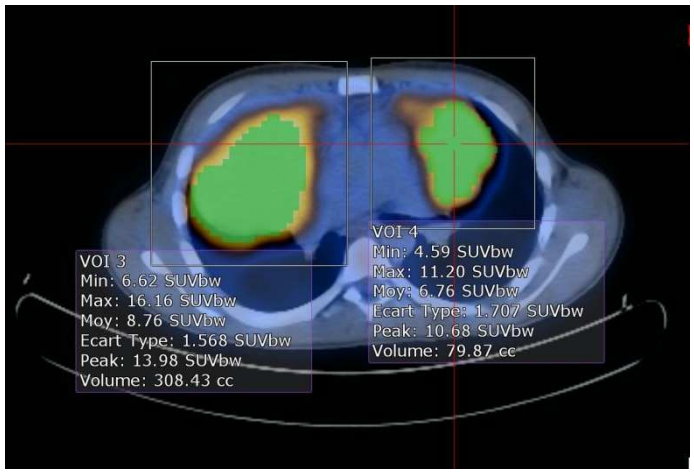
MTV0 Assessment

A region of interest (ROI) was drawn around each foci FDG uptake.

In each ROI, voxels presenting a threshold of 41% SUVmax were incorporated to define tumor volumes.

All tumors volume were added to assess the total metabolic tumor volume at baseline (MTV0)





Results

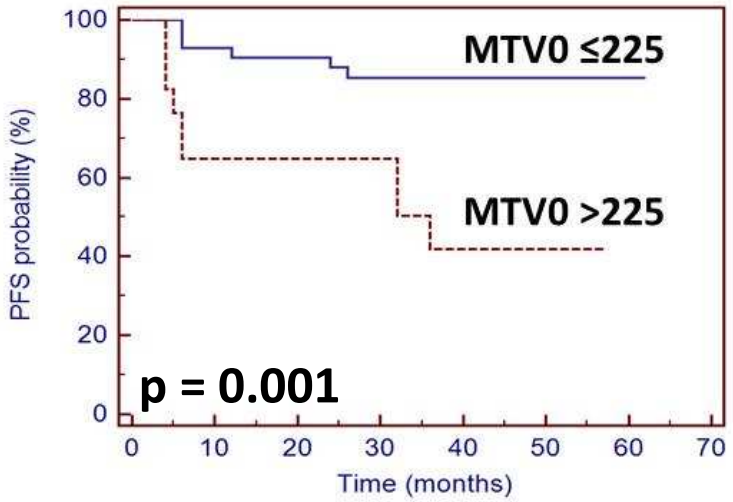
- **Patients**
  - Median age 36 y (16 – 76)
  - Histological type: NS = 76%, MC 12%
  - Stage III/IV = 63%
  - IPS>3 = 61%

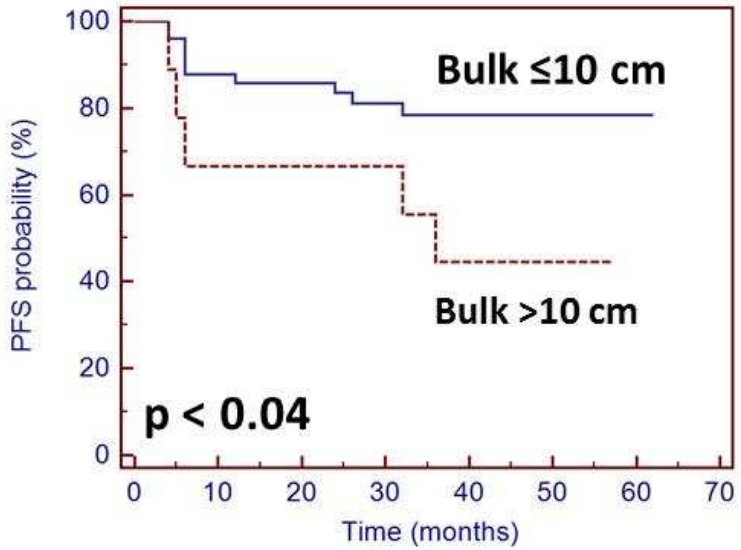
- **Outcome**
- ABVD = 85%
- Median Fu = 39 months : 10 progression/relapse (17%), 5 Death (8%)

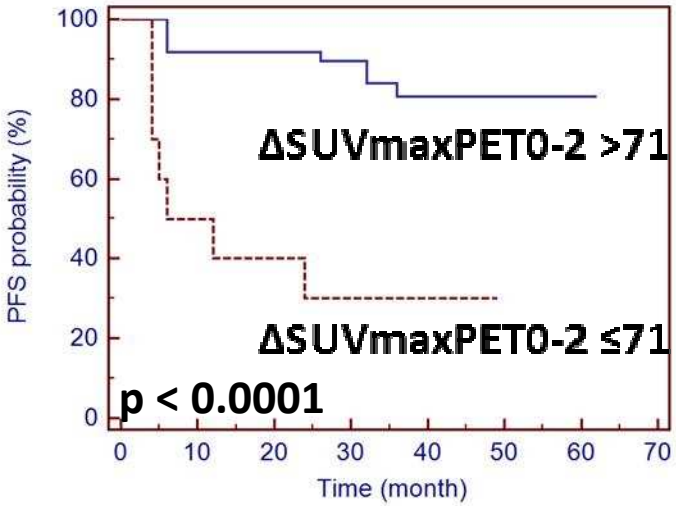
- **In univariate analysis** :
  - **MTV0** (≤225cc vs >225 cc): **3y-PFS = 85% vs 42%;** p = 0.001
  - **Bulky tumor** (>10cm vs ≤10cm): **3y-PFS = 44% vs 78%,** p <0.04
  - **ΔSUVmaxPET0-2** (≤71% vs >71%): **3y-PFS = 81% vs 30%;** p <0.0001

- **In multivariate analysis:**
  only **ΔSUVmaxPET0-2 (p= 0.0005; RR= 6.4) and MTV0 (p< 0.007; RR= 4.2)** remained independent predictors for PFS

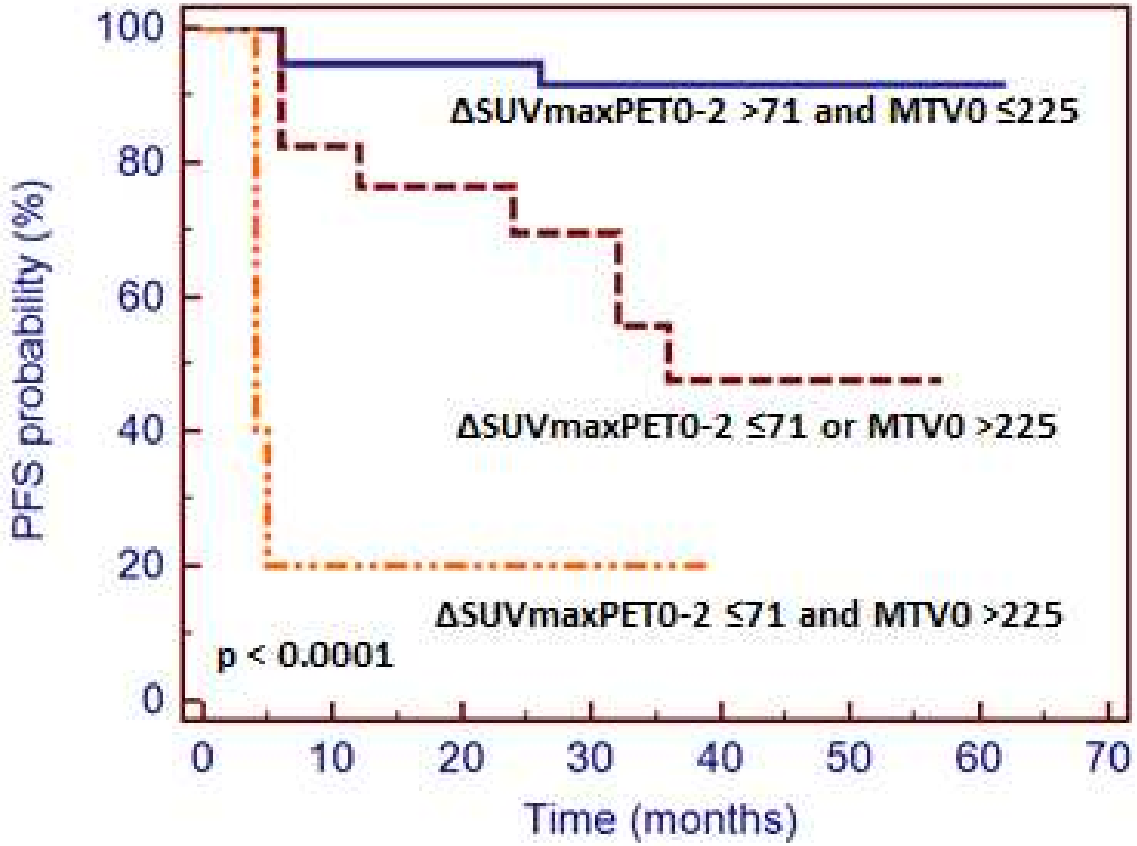
PFS analysis







PFS according to MTV0 and ΔSUVmaxPET-02



N = 37 (63%)

N = 17 (29%)

N = 5 (8%)

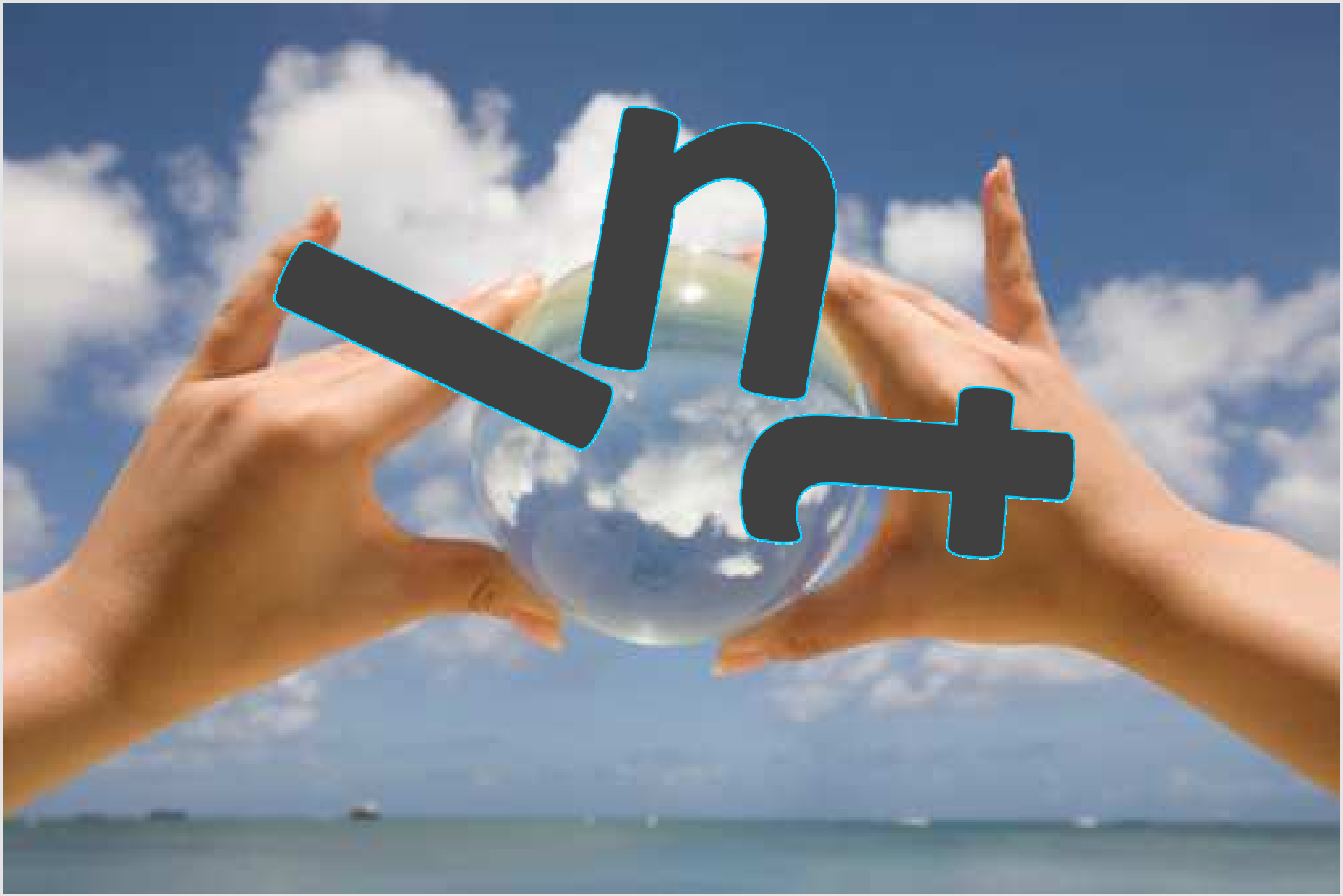
Conclusions

- **MTV0 is more relevant that tumor bulk to predict outcome of patients with HL**, and adds significant prognosis insights to interim PET response assessment

- **The combination of MTV0 with ΔSUVmaxPET0-2 allows identifying 3 subsets of HL patients with significantly different outcomes** that may help clinicians to guide therapeutic strategy

To sum up: iPET in HL and DLBCL

- Owns prognostic information
- Deauville best cut-off = liver uptake
- ΔSUV seems even better
- In HD: PPV ↑ by FDG-PET standardization
- MTV combined with ΔSUV could improve PPV in HD and NPV in DLBCL
- MTV better prognostic index than bulk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- Prospective study: 59 HL, FU 39 months
- Pronostic value of MTV0 (41% thresholding) , ΔSUV0-2, bulky tumor (>10cm) and international pronostic score

	Univariate		Multivariate	
	3y-PFS	3y-FFTF	3y-PFS	3y-FFTF
Bulky tumor (>10cm)	p <0.04	p = 0.09	NS	NS
IPS	/	/	NS	NS
ΔSUV0-2 (71%)	/	/	p< 0.0005	p= 0.0002
MTV0 (225ml)	p = 0.001	p = 0.0015	p= 0.007	p= 0.01

- **MTV0 is more relevant that tumor bulk to predict outcome**
- **The combination MTV0 and ΔSUV0-2 identifies 3 different outcomes that may help clinicians to guide therapeutic strategy.**

Interim [^{18}F]Fluorodeoxyglucose Positron Emission Tomography Scan in Diffuse Large B-Cell Lymphoma Treated With Anthracycline-Based Chemotherapy Plus Rituximab

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Results

Visual analysis showed that 70 patients (62.5%) presented with a negative PET scan after two cycles of treatment. The 3-year PFS and OS rates were 84% and 88%, respectively, in patients with PET-negative results versus 47% and 62%, respectively, in patients with PET-positive results ($P < .0001$ and $P < .003$, respectively). A second analysis was performed on 85 patients by using interim PET in a quantitative approach on the basis of a ΔSUV_{max} evaluation of more than 66%. The 3-year PFS was 77% for patients with PET-negative results and 37.5% for patients with PET-positive results ($P = .002$).

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