3rd INTERNATIONAL WORKSHOP ON INTERIM-PET IN LYMPHOMA

Abstract Discussion in NHL – technical

Menton (France), Palais de l'Europe,
September 26-27th, 2011

Are we one step closer to our mission of
Right Therapy, Right Dose, Right Patient?

pressing PET issues in NHL

tumor related
- FPs (inflammation)
- FNs (residual microscopic tumor)
- dependence on timing of imaging
- dependence of therapy regimens

PET evaluation method
- Qualitative
- Quantitative
    - SUVmax/reference ratio
    - ΔSUVmax
    - ΔMTV
    - ΔTLG

issues addressed

- Evaluation of midtherapy PET using quantitative and qualitative PET parameters
  - Deauville criteria
  - Absolute SUVmax
  - ΔSUVmax
  - ΔMTV
  - ΔTLG

- Evaluation of mid therapy PET using combination of above parameters

- Inter and intra subject variability of reference organ uptake values (liver and MBP) among various PET scans

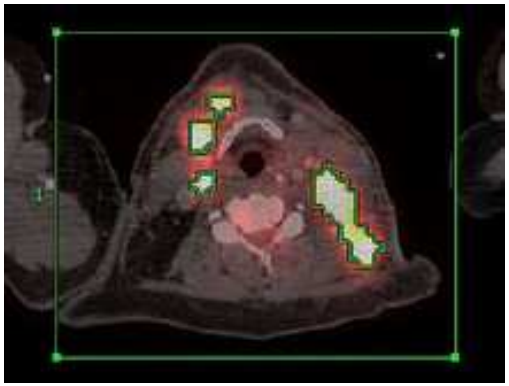
- Whole body MRI feasibility in lymphoma (C category)

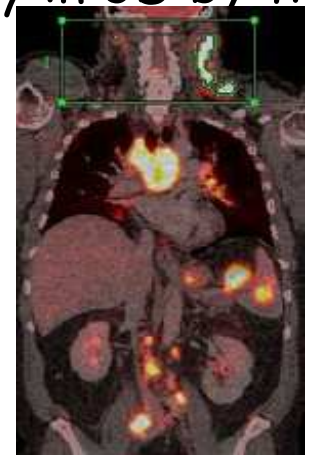
Metabolic tumor volume (MTV): the volume of tm tissue demonstrating increased FDG uptake, is a novel measure to test as an independent adverse prognostic factor

Graves EE et al, *Technol Cancer Res Treat 2007; 6:111*
Lee P et al, Clin Lung Cancer, 2011
Huang W, et al. Eur J Nucl Med Mol Imaging, 2011: 38:1628

MTV measurement method

Each tm is segmented automatically in 3D by the software





-the voxel of max intensity along the selected projection line is used as the starting point

-the algorithm finds the voxel of local max intensity within a specified radius (default value of 1 cm) of the starting voxel

- Once all of the hypermetabolic tm foci are segmented, the software calculates the MTV, defined as the total volume in mL

ΔTLG

Total lesion glycolysis integrates noninvasively measured tm volume and glycolytic activity (unit measurement = gms)

TLG obtained by multiplying the MTV by SUV_{mean}

The global TLG of each patient is defined as the sum of TLGs of all focal lesions selected

Summary of abstracts

B 106 ***CHANGES IN LIVER AND MEDIASTINUM DURING CHEMOTHERAPY IN DLBCL: IMPACT ON THE EVALUATION OF INTERIM PET-CT*** . L Ceriani, S Suriano,T Ruberto, E Zucca, L Giovanella – Onc. Inst. S Switzerland (IOSI) – Bellinzona, CH

To assess inter- and intra-subject variability of MBP and liver (L) SUVs

N=50, retrospective, PET/CT: baseline, mid cycle (2x rCHOP; 6x rMACOP-B or rVACOP-B)

27 pts R-CHOP and 23 R-MACOP-B/R-VACOP-B treatment.

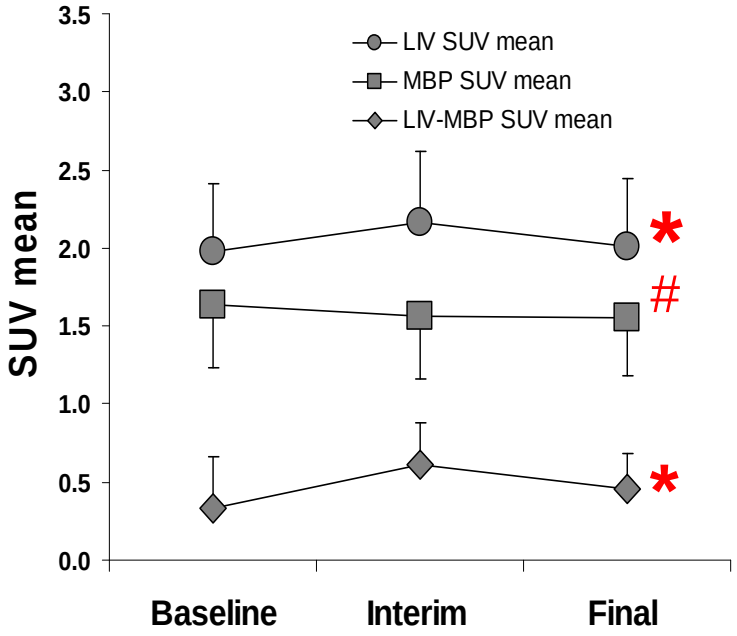
Results:
inter-subjects variability (SD/mean x100) MBP and L SUVs high, ranged from 20 to 26%

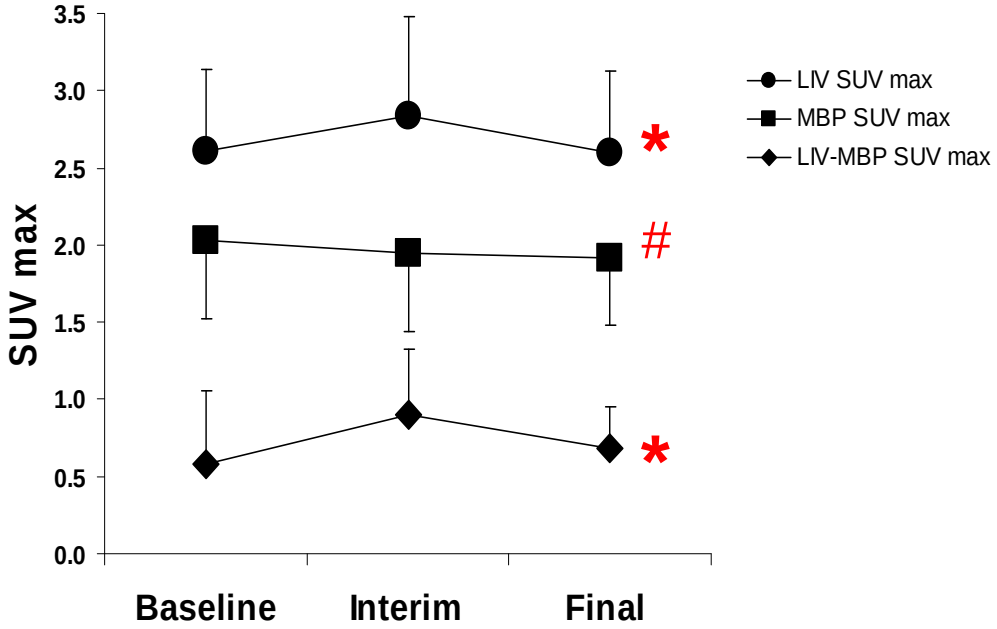
intra-subject variability
-L SUVs increased at interim and decreased at end of therapy
-MBP SUVs stable throughout therapy

L Ceriani, S Suriano,T Ruberto, E Zucca and L Giovanella -

Nuclear Medicine Dpt. and (*) Oncology - Oncology Institute of Southern Switzerland (IOSI) - Bellinzona (Switzerland)

18FDG UPTAKE CHANGES IN LIVER AND MEDIASTINUM DURING CHEMOTHERAPY IN DLBCL: IMPACT ON THE EVALUATION OF INTERIM PET-CT





Legends - * p < 0.001 ; # p= ns

Conclusions

- L and MBP SUVs may not be reliable references for the evaluation of early response to R-based regimens
- caution for L intra-subject variability during chemorx in risk-adapted therapeutic strategies

B 101 -*INİTİAL TLG AND SUVTOTAL CAN PREDİCT THE OUTCOME OF DLBCL.* LS Park, SJ Kim, JY Choi, SH Moon, WS Kim, Dept of Med. & Nuc Med, Samsung Med. Ctr, Sungkyunkwan Univ Sch. Med

to investigate the most appropriate PET parameter for prediction of disease progression in pts with all IPI scores vs IPI 1-3.

N=120, retrospective, PET/CT: baseline, mid cycle (2-3; med, 3 cycles)

SUVtotal, SUVmax, and TLG for initial and ΔSUVtotal, ΔSUVmax, and ΔTLG as interim PET parameters

Results:
- IPI predicted PFS in all pts with DLBCL ($p<0.01$)
- Initial SUVtotal and TLG predicted PFS in all ($p<0.01$ and $p=0.03$) and in pts with an IPI scores of 1-3
- No significant diff. in PFS btw pts with high and low initial SUVmax
- ΔSUVtotal ($p=0.9$), ΔSUVmax (89%;$p=0.24$), and ΔTLG (98%;$p=0.8$) no difference in PFS in IPI 0-5
- ΔSUVtotal ($p=0.05$), ΔSUVmax (89%;$p=0.06$), and ΔTLG (98%;$p=0.02$) in pts with PFS in IPI 1-3

Conclusions: initial PET/CT parameters, ΔSUVtotal and ΔTLG in pts with IPI 1-3, seem to better predict PFS

B 103 ***THE ROLE OF SUVMAX REDUCTION IN THE PROGNOSIS OF DLBCL BASED ON INTERIM 18FDG PET/CT.*** S. Barna,F. Magyari,ZS. Miltényi, L. Váróczy, L. Gergely ,ZS Simon,J. Varga, Á. Illés , I Garai, Scanomed Ltd, Int. Med. Dept, Univ. Debrecen, Hungary

to assess the value of ΔSUVmax in prediction of PFS, EFS, OS

N=50, retrospective, PET/CT baseline, 2-4-cycle, rCHOP, mean fu 581 dys

baseline SUVmax, ΔSUVmax,

Results:

- the relative change of SUVmax (p=0.022) only single significant factor identified as a predictor of outcome variable defined as RFS

- K-M analysis showed a significantly different RFS in subgroups of pts with relative SUVmax Δ in each quartile (p=0.033)

-The most relevant difference was found btwn the subgroups with ΔSUVmax below and over **80%**

-Since 27/50 pts did not reach any of the states considered as non-successful outcome this value should be refined based on a longer fu

B 109 ***QUANTITATIVE AND QUALITATIVE ANALYSIS OF METABOLIC RESPONSE AT INTERIM PET-SCAN IS HIGLY PREDICTIVE OF OUTCOME IN DLBCL*** N Nols, N Mounier, S Bouazza, R Lhommel, T Vanderborght, A Sonet, M André, A Bosly, E Van Den Neste. UCL, Belgique; Nice, France

to assess whether interim metabolic response using qualitative and quantitative criteria had prognostic value in DLBCL.

N=74, retrospective, IPI: 50% L-L-I, PET/CT 3-4 cycle rCHOP, 2-year survival

ΔSUVmax (quantitative) and Deauville's criteria (DS)

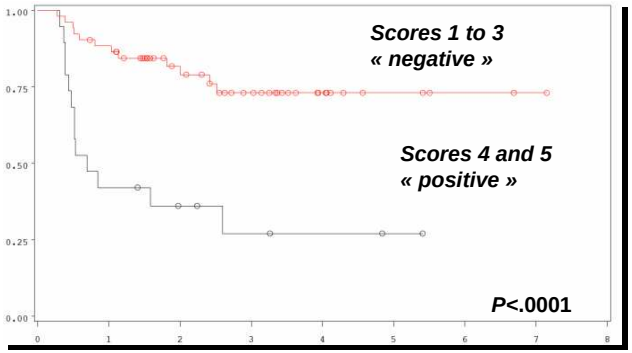
Results

- DS at int PET and ΔSUVmax independently predicted
  - EFS (HR 4.3, P .001; HR 4.3, P.003, respectively),
  - PFS (HR 3.2, P.01; HR 3.5, P .02), and
  - OS (HR 3.6, P.01; HR 4.2, P.01, respectively)

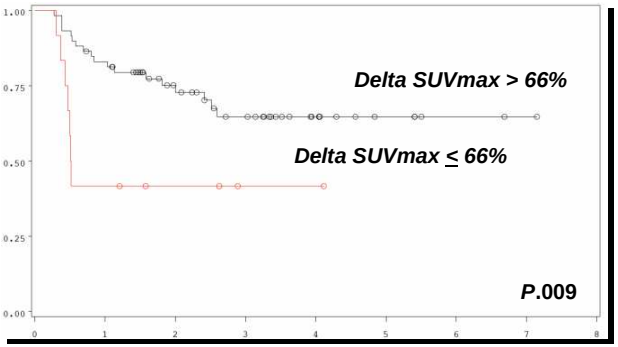
- poor outcome: +ve int PET (DS4-5) & a ΔSUVmax < 66% (OS: 20%)
- good outcome: aaIPI 0-1, & -ve int PET (DS1-3) or ΔSUVmax criteria, (EFS: 85%, PFS: 88%, OS: 94%)

RESULTS

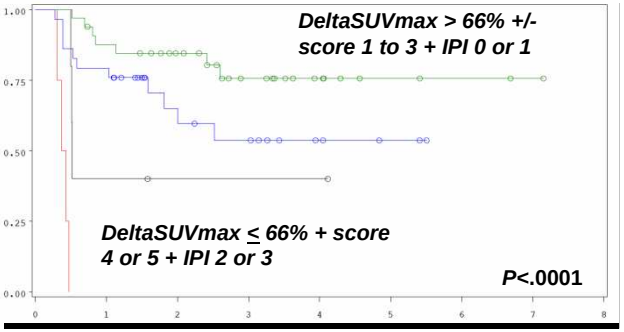
Qualitative analysis	Quantitative analysis	Association of the two analysis



EFS



EFS



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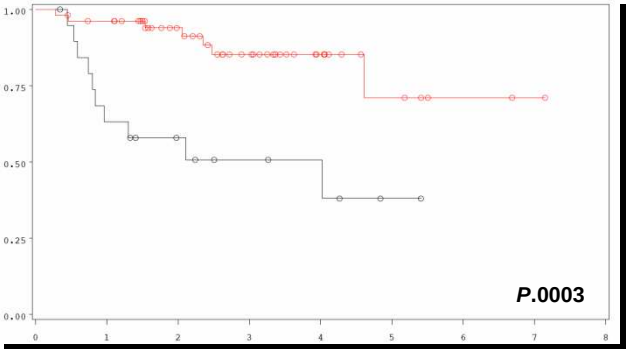

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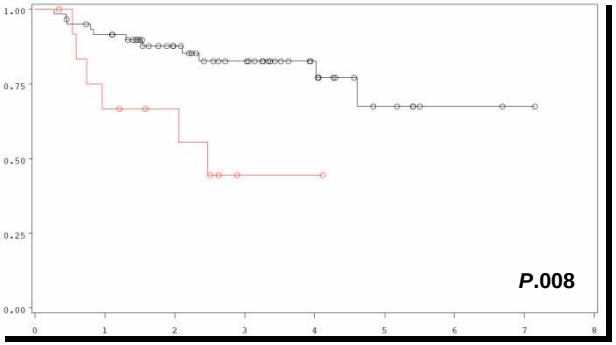
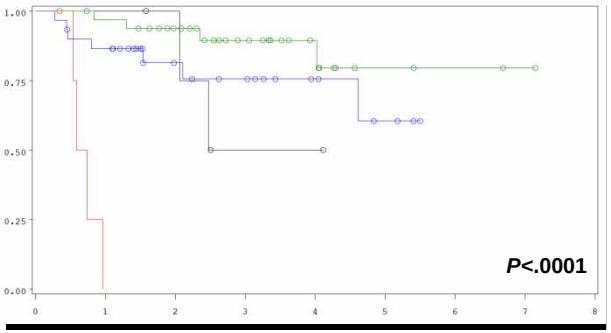


OS



OS

Conclusions: In this retrospective study, quantitative or qualitative analysis of metabolic response at mid-treatment was highly and independently predictive of any outcome (EFS, PFS, OS).

B 110 *CLINICAL USEFULNESS AND PROGNOSTIC SIGNIFICANCE OF INTERIM 18F-FDG PET/CT FOR THE TREATMENT OF PERIPHERAL T CELL LYMPHOMAS (PTCL)*

D-H Yang, BB Hyun, J-J Min, J-S Ahn, Y-K Kim, H-S Bom, I-J Chung, H-J Kim, WS Kim, J-J Lee

to determine whether interim PET/CT provides additional prognostic information for the treatment of PTCL

N=59, prospective, PET/CT baseline, interim, rCHOP, 59% adv stage 24% BM inv., med fu 12.9 mo

Combined ΔSUVmax, ΔMTV2.5 (quantitative) and Deauville scoring

Results:. 52 pts assessed based on DS
-int PET+, a significant prognostic factor, HR: 3.2
-2-yr PFS different btwn PET+ (28%) and PET- (57%) pts (P=0.004)
- ΔSUVmax predicted outcome
- ΔMTV2.5 failed to differentiate the pts for predicting the progression
Conclusions: Response assessment using DS, ΔSUV and ΔMTV may have a differential potential for predicting the prognosis in PTCL.

B 113 ***COMPARISON OF QUANTITAIVE & QUALITATIVE RESPONSE CRITERIA IN THE UK-NCRI PET STUDY IN DLBCL- AN INTERIM ANALYSIS.*** NG Mikhaeel, MJ. O'Doherty, S Barrington: Clin Onc, PET Imaging Ctr, Guy's &St Thomas' Hosp, London, UK

to compare 3 sets of criteria in a cohort of pts who underwent FDG-PET after 2 cycles of RCHOP as part of an ongoing UK-NCRI study.

N=125, prospective, PET/CT baseline, 2 cycle. rCHOP,

original study criteria (SS), Deauville criteria (DS) & ΔSUV compared; also compared 2 definitions of DS 5; 2x&3x liver activity

Results

-54 excellent response who had SS 1 (no uptake), 2a (MRU) & corresponding DS 1, 2 were classified as responders with ΔSUV >66%
- Only 3 pts had SS 2c (stable) who were classified as DS 4 and DS 5.
- No patients had SS 2d (progression).
-69 patients had SS 2b (partial response) and were distributed in DS 2-5, with the majority being DS 3 (25) and 4 (32).

4/5 cut-off

Deauville Score (DS)		
Score	No of Patients (Score 5= 3x liver)	Score 5= 2x liver
1	28	
2	25	
3	28	
4	36	29
5	8	15
TOTAL	125	

Does 4 include some good prognosis patients?

Deauville Score		SUV reduction	
Score	No of Patients	>66%	≤ 66%
1	28	28	0
2	25	25	0
3	28	25	3 **
4	36	32	4
5	8	1	7
	125	111	14

Conclusions:

- Good concordance between the 3 criteria in pts with excellent response (DS 1+2) & poor response (DS 5).

-Pts with PR are classified differently by different criteria & most of DS 3+4 classify as responders by ΔSUV

-DS 5 defined as 2x changes 7 pts from DS 4 to 5.

-Outcome data is awaited to define the best criteria.

C 102 *WHOLE-BODY MR DIFFUSION IN PATIENTS WITH LARGE B-CELL LYMPHOMA: A PRELIMINARY ADC MAPPING STUDY AT 3T.* A Rahmouni, S Toledano, C Lin, E Itti, C Haioun, A Luciani. Dept. Med Imaging, Nuc Med & Hematology, CHU, Henri Mondor, France

to evaluate the feasibility of whole-body MR diffusion imaging in patients with DLBCL before and after 4 cycles of chemotherapy

Methods: Axial single-shot echo-planar images were acquired at b= 50, 400, 800 s/mm2 with chemical fat suppression and respiratory gating. MRI technique surface phased-array coils , 24 5mm-thickness images per station. ADC mapping. Image quality, total acquisition time, ADC values of nodal lesions measured before and after 4 cycles of chemo.

Results:

-Image quality 3.4 (1 to 4 scale)

-Mean total time of acquisition 19 min.

-Mean ADC was $0.79 \times 10^{-3} mm^2/s$ (SD: 0.24) before treatment and - increased to $1.30 \times 10^{-3} mm^2/s$ (SD: 0.79) after treatment.

7 pts had no FDG post therapy uptake with increased ADC value

1 had a persistent FDG uptake with a restricted ADC (0.6×10^{-3} mm^2/s

Whole-body MR diffusion imaging is feasible at 3T with a decreased time of acquisition

B 108 ***FDG-PET IN AGGRESSIVE NON-HODGKIN LYMPHOMA (NHL): ΔSUV VS. LYMPHOMA-TO-REFERENCE TISSUE RATIOS IN THE GERMAN MULTICENTRIC PETAL STUDY.*** SP. Müller, HV. Ngo, U Dührsen, A Bockisch, A Hüttmann. Nuc Med, Hematology, Universitätsklinikum, Essen, Germany

to evaluate whether interim PET alone may provide similar classification of non-responders using ratios of SUV in lymphoma to reference tissues employed for comparison in visual scales

N=145, prospective, PET/CT baseline, 2 cycles. rCHOP,

ΔSUVmax vs. ratios of interim SUVmax in lymphoma to max and mean SUVs in spherical reference ROIs with 2 cm Ø in MBP, liver, and spleen

Results: The classification based on lymphoma/reference organ ratios yielded areas under the ROC curves of 0.82 - 0.84 (no signif. difference). At 10% false-positives the sensitivities, i.e. the agreement with the PETAL classification, was between 48 and 59%.

Conclusions: Only every other pt in the randomized intensified treatment arms of the PETAL study population would be identified if the treatment stratification were based on lymphoma/reference tissue ratios instead of ΔSUV. Therefore the criteria for classifying NHL patients by interim FDG-PET may not be exchange-able because of the prognostic implications inherent in the different populations.

B 105 ***INTERIM FDG PET SUVMAX REDUCTION IS SUPERIOR TO VISUAL ANALYSIS BASED ON DEAUVILLE CRITERIA TO PREDICT EARLY PATIENT'S OUTCOME IN DLBCL.*** RO Casasnovas, M Meignan, A Berriolo-Riedinger,S Bardet, A Julian, C Thieblemont, P Vera, S Bologna, JP Jais, C Haioun, B Coiffier, F Morschhauser on behalf of the GELA, *CHU Dijon, France.

to evaluate the impact of interim PET interpretation according to 5PS and Δ SUVmax on pt outcome in LNH2007-3B GELA trial

N=84, prospective, PET/CT baseline, 2 cycles, 4 cycles R-ACVBP or R-CHOP14

Δ SUVmaxPET0-2) or PET4 (Δ SUVmaxPET0-4).
PET result considered positive if >liver uptake.

Pts with Δ UVmaxPET0-2>66% and Δ SUVmaxPET0-4>70% considered as good responders after 2 and 4 cycles respectively

Using 5PS criteria, respectively 46% and 65% of pts achieved a negative PET2 and PET4. 36 of 48 PET2+ pts had a Δ SUVmaxPET0-2>66% and 22 of 30 PET4+ pts reached a Δ SUVmaxPET0-4>70%

PET2 and PET4 results assessed by the 5PS criteria had no influence on

B 100 ***INTERIM PET/CT-BASED PROGNOSTIC MODEL FOR THE TREATMENT OF DIFFUSE LARGE B CELL LYMPHOMA IN POST-RITUXIMAB ERA*** D-H Yang, BB Hyun, J-J Min, J-S Ahn, Y-K Kim, H-S Bom, I-J Chung, H-J Kim, WS Kim and J-J Lee

to evaluate the prognostic accuracy of interim PET/CT using 3 different methods for response assessment during R-CHOP chemotherapy in DLBCL patients

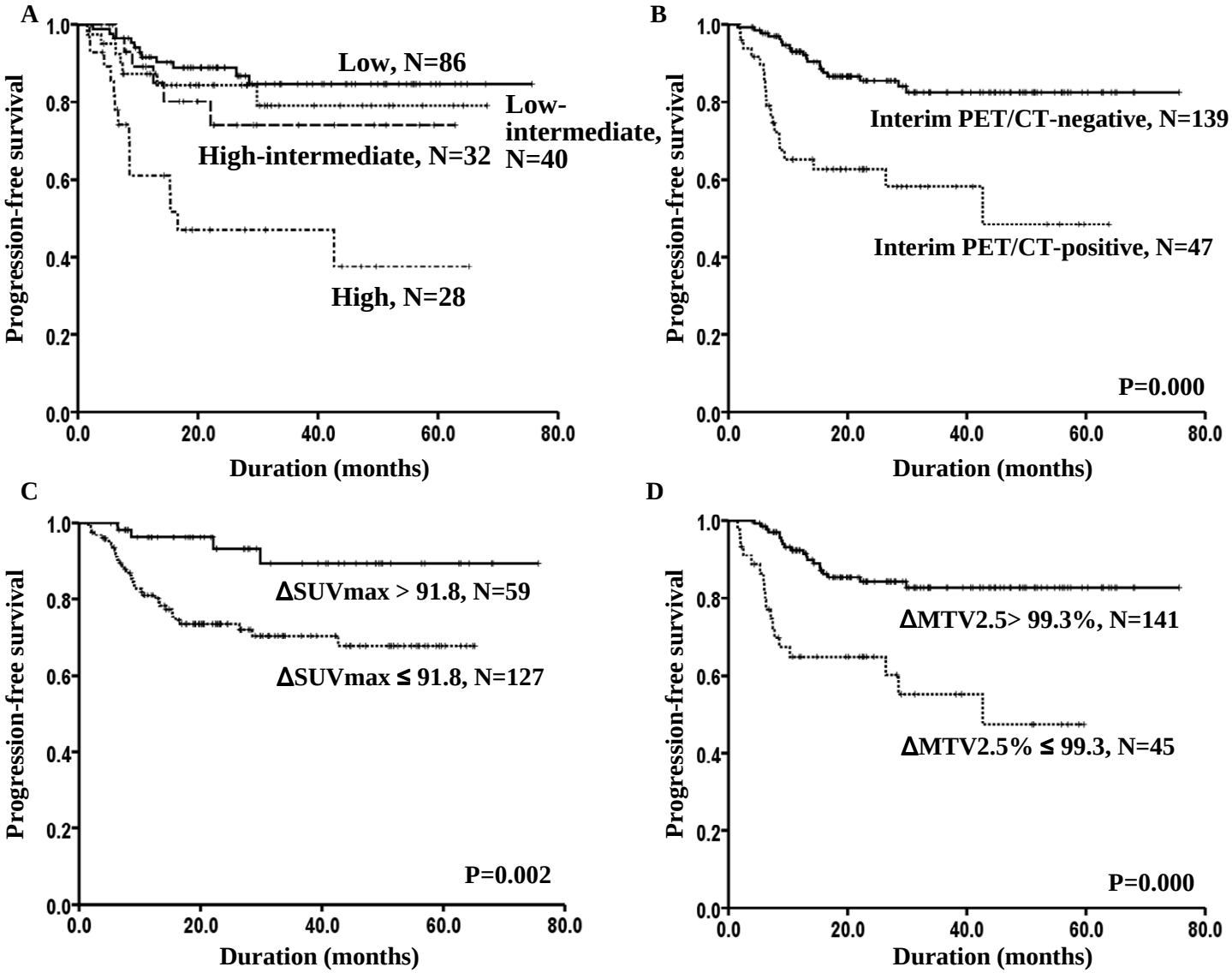
N=186, retrospective, PET/CT baseline, 3-4 cycles and at end of rCHOP, med fu 22.8 mo

combination of 3 parameters: Deauville criteria, ΔSUVmax, ΔMTV2.5

Results: both the positivity in Deauville 5-PS and the optimal cutoff value of ΔSUVmax could predict the prognostic difference in patients with DLBCL after R-CHOP chemotherapy. The response of interim PET/CT based on 5-PS, ΔSUVmax, and ΔMTV2.5 showed a significant potential as a prognostic value in PFS, respectively. Furthermore, when divided the patients into four groups according to the sum of score for three adverse factors; consisted of grade 4-5 by Deauville 5-PS, ΔSUVmax≤91.8% and ΔMTV2.5≤99.3%,

Conclusion: The combined evaluation with three parameters using

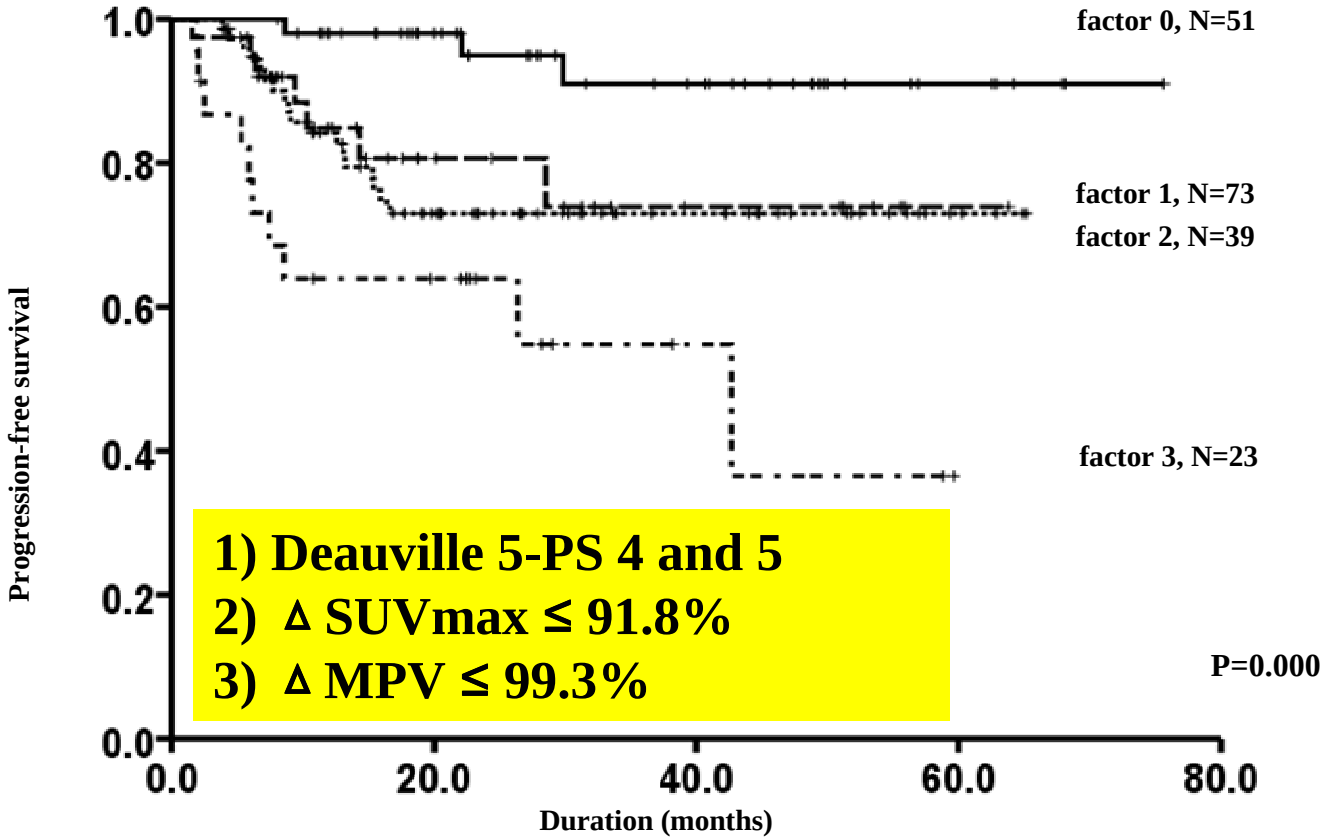
Results (II)



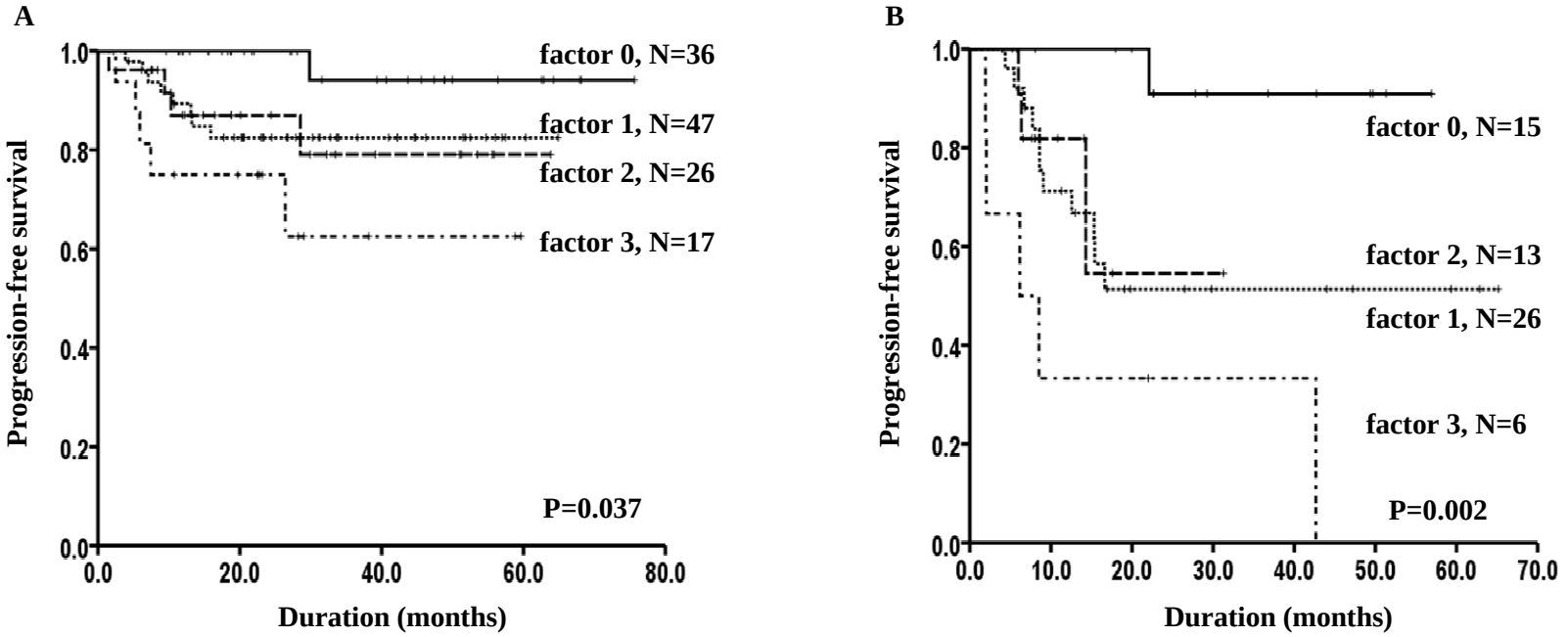
Kaplan-Meier estimates of PFS in (A) all patients with DLBCL according to IPI risk and classified according to (B) positivity by the Deauville five-point scale, (C) the ΔSUVmax with the optimal cutoff value of 91.8% and (D) the ΔMTV2.5 with the optimal cutoff value of 99.3% in interim PET/CT.

Results (III)

Prognostic model based on interime PET/CT



Results (IV)



Kaplan-Meier estimates of PFS by IPI, according to the combined evaluation of visual, SUV-based and MTV-based assessment in the low/low-intermediate IPI risk group (N=126) (A) and in the high/high-intermediate IPI risk group (N=60) (B).

Summary

- **Positivity on the Deauville 5-PS, the optimal cutoff value of ΔSUVmax or the optimal cutoff value of ΔMTV2.5 could each predict disease progression.**
- **When combining these three parameters from PET/CT, the model can have strong predictive power for prognosis.**

Deok-Hwan Yang : drydh1685@hotmail.com