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
  - $\text{SUV}_{\text{max}}$/reference ratio
  - $\Delta\text{SUV}_{\text{max}}$
  - $\Delta\text{MTV}$
  - $\Delta\text{TLG}$
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

**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 tumor volume and glycolytic activity (unit measurement = gms)

TLG obtained by multiplying the MTV by SUV$_{\text{mean}}$

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


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

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

Legends - * p < 0.001 ;     p= ns
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
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
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

$\Delta$SUVmax (quantitative) and Deauville’s criteria (DS)

Results
- DS at int PET and $\Delta$SUVmax 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 $\Delta$SUVmax < 66% (OS: 20%)
- good outcome: aaIPI 0-1, & -ve int PET (DS1-3) or $\Delta$SUVmax
criteria, (EFS: 85%, PFS: 88%, OS: 94%)
RESULTS

Qualitative analysis

Scores 1 to 3 « negative »

Scores 4 and 5 « positive »

P < .0001

Quantitative analysis

Delta SUVmax > 66%

Delta SUVmax ≤ 66%

P = .009

Association of the two analysis

DeltaSUVmax > 66% +/- score 1 to 3 + IPI 0 or 1

DeltaSUVmax ≤ 66% + score 4 or 5 + IPI 2 or 3

P < .0001

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)

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.
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) & ∆SUV 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 ∆SUV >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

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<th>Deauville Score (DS)</th>
<th>No of Patients (Score 5= 3x liver)</th>
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<td>Score 5= 2x liver</td>
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<td>Score 3</td>
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<td>Score 4</td>
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<td>Score 5</td>
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Does 4 include some good prognosis patients?

<table>
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<th>Deauville Score</th>
<th>SUV reduction</th>
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<tr>
<td>Score</td>
<td>No of Patients</td>
<td>&gt;66%</td>
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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 ∆SUV
- DS 5 defined as 2x changes 7 pts from DS 4 to 5.
- Outcome data is awaited to define the best criteria.
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 0.79x10⁻³mm²/s (SD: 0.24) before treatment and increased to 1.30x10⁻³mm²/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 (0.6x10⁻³ mm²/s

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

$\Delta$SUVmax 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 $\Delta$SUV. 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.
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
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, $\Delta$SUVmax, $\Delta$MTV2.5

Results: both the positivity in Deauville 5-PS and the optimal cutoff value of $\Delta$SUVmax could predict the prognostic difference in patients with DLBCL after R-CHOP chemotherapy. The response of interim PET/CT based on 5-PS, $\Delta$SUVmax, and $\Delta$MTV2.5 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, $\Delta$SUVmax$\leq$91.8% and $\Delta$MTV2.5$\leq$99.3%,

Conclusion: The combined evaluation with three parameters using
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 $\Delta$SUV$\text{max}$ with the optimal cutoff value of 91.8% and (D) the $\Delta$MTV2.5 with the optimal cutoff value of 99.3% in interim PET/CT.
Results (III)
Prognostic model based on interime PET/CT

1) Deauville 5-PS 4 and 5
2) $\Delta$ SUVmax $\leq 91.8\%$
3) $\Delta$ MPV $\leq 99.3\%$
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 $\Delta S_{\text{UVM}\text{ax}}$ or the optimal cutoff value of $\Delta M_{\text{TV}2.5}$ could each predict disease progression.
- When combining these three parameters from PET/CT, the model can have strong predictive power for prognosis.

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