5th International Workshop on PET in Lymphoma

Palais de l'Europe. Menton, France
September 19 -20, 2014

POSTER SESSION

A 1 - Zsófia Miltényi1, Sándor Barna2, Ildikó Garai2, Zsófia Simon1, Ádám Jóna1, Ferenc Magyari1, Árpád Illés1
Department of Hematology, University of Debrecen 1, Scanomed Ltd., Debrecen2

Prognostical value of interim and restaging PET/CT in Hodgkin-lymphoma. Hungarian results

Prognostical value of interim 18FDG-PET/CT is obvious nowdays. Very few investigation were done for determine prognostical value and long term evaluation of interim and restaging PET/CT with using standard therapy - based on the current treatment guidelines - among patients who treated outside clinical trials.

Methods: January 1st 2007 and December 31st 2011 staging, interim and restaging PET/CT scans were performed in Hodgkin-lymphoma patients. Deauville criteria was used for evaluation of interim PET/CT scans.

Results: One hundred and thirteen patients with Hodgkin-lymphoma (57 male and 56 female) had staging, interim and restaging PET/CT scans. There was no modification on therapy based on the results of interim PET/CT scan. Average follow up time was 48.5 months (ranging from 7-70 months). There were 62 early stage patients, 51 advanced stage patients, and 59 patients had B symptom. Interim PET/CT was negative in 83 cases (73.45 %), and positive in 30 cases (26.55 %). NPV was 92.7% and PPV was 56.6%. Five-year OS rate was 93.4 % in negative interim PET group, in contrast with positive interim PET group, where this value was 58% (p<0.001). Five-year relapse-free survival rate for negative and positive groups were 92.7% and 40.8% (p<0.001) respectively. In early and advanced stage disease NPV was 100% and 82.35%, whereas, PPV were 53.8% and 58.8% respectively in these two groups. In positive interim PET group patients with age over 40 have significantly higher probability to have relapse (p=0.057).

Conclusion: Our data showed high NPV of the interim PET/CT. Clinical routine use of interim PET/CT is highly suggested based on our investigation.

A 2 - Zwarthoed C (1), Ouvier M (1), Borra A (2), Bergesio F (2), Chauvie S (2), Biggi A (2), Hutchings M (3), El-Galaly T (4), Gallamini A (1,2)
1. A. Lacassagne, Nice; 2. Cuneo; 3. Copenhagen; 4. Aalborg

Patterns of PET/CT-assessed bone-marrow involvement and prognosis in newly diagnosed Hodgkin lymphoma; a detailed review of 122 ABVD treated patients

Background: Bone (B) and Bone marrow (BM) lesions in Hodgkin lymphoma is polymorphous and interpretation can be challenging.
Aims:1) to give a detailed description of FDG-uptake in the B/BM, 2) to assess the inter-observer agreement of PET/CT-ascertained B/BM disease, 3) to examine the prognostic impact of FDG-uptake in the B/BM.
Patients and methods: PET/CT studies from 122 ABVD-treated advanced-stage HL patients originally included in the IVS cohort were reviewed blinded by two nuclear medicine specialists.
Results: Focally increased B/BM FDG-uptake were present in 17 (14%) patients with corresponding CT lesions in 9 of them. Diffuse uptake > liver was recorded in 40 patients (33%) and these patients were characterized by higher leukocyte count (p=0.002), lower hemoglobin levels (p=0.0008), and higher prevalence of B-symptoms (p=0.049). Diffuse uptake in the spleen > liver was correlated to diffuse uptake in the BM >liver (p=0.002). There was high concordance between the two reviewers on the reporting of B/BM lesions with k-coefficient of 0.87 (excellent).HL was found in the BM biopsy of 8 patients of whom 5 had focal FDG-avid lesions in the BM (sensitivity 63%). BM biopsy led to upstaging in 3 patients (III->IV). The 3 year PFS was 60% for patients with focal lesions vs. 79% for patients without focal BM lesions (P=0.09, log-rank).
Conclusions: Focal B/BM lesions justifies a stage IV upgrading in newly diagnosed HL, whereas diffuse uptake is more likely to reflect reactive BM changes. BM biopsy did not lead to relevant upstaging in any patients and reviewer concordance was excellent for PET-assessed BM disease.

A 3 - J. Zaucha, B. Małkowski, S.Chauvie, A.Warszewska, M.Dziuk, M. Kobylecka, E. Subocz, J.Tajer, W. Kulikowski, J. Rybka, R. Kroll, E. Woszczyk, A. Romanowicz, F.Fallanca, J. Walewski, A.Gallamini

POLISH LYMPHOMA RESEARCH GROUP OBSERVATIONAL STUDY OF THE PROGNOSTIC ROLE OF INTERIM PET AFTER FIRST 1 ABVD CYCLE IN HL PATIENTS

PLRG in 2009 launched the observational study in HL pts aimed at assessing the role of iPET1. We hypothesized that NPV of iPET1 will be very high identifying highly chemosensitive patients. PET was performed after 1ABVD and interpreted according to the Deauville scale. Score 1 to 3 were considered negative(-), 4 to 5 positive(+). If iPET1 was (+), iPET2 after 2ABVD should be performed. Subsequently all PET scans were scored afresh by the Italian-Polish Reviewer Panel (RP). 327 patients from 9 centers were registered. 48 patients were excluded from the current analysis resulting in 71 assessable patients with early and 167 with advanced HL. At a median follow-up of 32.2 months 88% of pts achieved CR, 18%(43) patients (3 "early"pts and 40 "advanced") experienced a PFS event. At the time of abstract submission 174 (73%) patients have been reviewed by the RP. Based on combined local and RP assessment in "early" group iPET1 was(+) in 11(15%) pts. In 2 of them iPET2 remained (+) after 2ABVD. In "advanced" group PET1 was(+) in 52(31%) and remained(+) in 22 (13%) after 2ABVD. All "early" patients with iPET1(-) remain in CR whereas 12(7%) advanced pts with iPET1(-) progressed. All these pts except 1 had score 3. NPVs were 100% and 88% in pts with early and advanced stages, respectively. 32 pts (8 "early") with PET1(+) became PET2(-), only 4 such pts relapsed so far. In contrast 20/24 (83%) patients with PET1(+)/PET2(+) experienced PFS event. PFS at 2 years for iPET1(-) and (+) were 100% and 80% in early stages and 91% and 47% for advanced. Conclusion: NPV of iPET1 is high in early pts whereas in advanced progressions in few PET1(-) pts suggest some limitations of 5-point scale.

A 4 - Zsófia Simon, Zsófia Miltényi, Ferenc Magyari, 1SándorBarna, Anna Kenyeres, Ádám Jóna, Árpád Illés
University of Debrecen, Clinical Center Department of Internal Medicine, 1Scanomed Ltd.

Prognostic role of peripheral lymphocyte/monocyte ratio and interim PET/CT in Hodgkin lymphoma patients

Introduction: Elevated tumor-associated macrophage ratio and correlating decreased peripheral absolute lymphocyte / monocyte ratio (LMR) was reported to be an unfavorable prognostic marker in Hodgkin lymphoma (HL). We aimed to investigate, whether combining LMR and interim PET / CT scan (PET2) holds stronger prognostic value than PET2 alone.
Patients and methods: 72 HL patients were investigated, who were diagnosed between 2007 and 2012 and had available PET2 results. Absolute lymphocyte and monocyte values measured at the time of diagnosis were considered as LMR. Cut-off value was determined by the ROC curve, which was 2.2 in the case of our patients (LMR> 2.2: affordable, LMR <2.2: negative). Results: There were 43 early and 29 advanced stage patients; median follow up time was 51 months. PFS was significantly worse both in the lower LMR (<2,2) (p=0,003) and PET2 positive group (p=0,000). Investigating the combined role of the two variables, we found that results in the double positive (LMR <2.2 and PET2 positive) group were significantly worse, compared with patients who had only one positive variable (LMR> 2.2 but positive or LMR PET2 <2.2 but PET2 negative), or who had both negative variables (LMR> 2.2 PET2 and negative) (p = 0.000). Both LMR and PET2 proved to be independent prognostic factors by multivariate analysis, which strengthened each other. No significant difference was found regarding overall survival neither in the LMR <2.2 / LMR> 2.2 nor in the PET2 negative / positive patient groups.Discussion: LMR measured at the time of diagnosis could be an easily available, cheap prognostic factor in the daily routine, which may increase PPV and NPV of PET2.

A 5 - Jean François Grellier, Laetitia Vercellino, Thierry Leblanc, Pascal Merlet, Catherine Thieblemont, Pierre Weinmann, Marie-Elisabeth Toubert, Nathalie Berenger, Josette Brière and Pauline Brice

PERFORMANCE OF FDG-PET/CT AT INITIAL DIAGNOSIS IN A RARE LYMPHOMA : THE NODULAR LYMPHOCYTES PREDOMINENT HODGKIN LYMPHOMA

Introduction: Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) is a rare Hodgkin lymphoma distinguished from classical Hodgkin lymphoma (cHL) by the nature of the neoplastic cell which expresses B-cell markers.

Objectives: We wanted to determine the diagnostic performance of FDG-PET/CT in initial assessment and its therapeutic impact on staging.

Materials and Methods: We retrospectively studied a population of 35 patients with NLPHL (8 previously treated for NLHPL, 27 untreated). All patients underwent an initial staging by pre-therapeutic FDG-PET/CT. Impact on initial stage or relapse stage was assessed by an independent physician.

Results: By per-patient analysis, the sensitivity of the pre-therapeutic FDG-PET/CT was 100%. Per-site analysis shows sensitivity, specificity, PPV, NPV and accuracy of pre-therapeutic FDG-PET/CT respectively of 100%, 99%, 97%, 100% and 99%. The pre-therapeutic FDG-PET/CT modified the initial stage/ relapse stage in 12/35 patients (34%). Contrasting with previous literature data established without FDG-PET/CT, 20% of patient had osteomedullar lesions.

Conclusion: pre-therapeutic FDG-PET/CT has excellent performance for initial staging or relapse staging of NLPHL.

A 6 - Dann EJ, Bar-Shalom R, Kagana O, Bairey O, Izak M, Korenberg A, Akria L, Attias D, Filanovsky K, Abadi U, Ruchlemer R, Abdah-Bortnyak R, Goldschmidt N, Epelbaum R, Lavie D, Paltiel O

INTERIM PET/CT DYNAMIC VISUAL VERSUS DEAUVILLE SCORE FOR TAILORING THERAPY IN HODGKIN LYMPHOMA PATIENTS, TREATED IN ISRAELI H2 STUDY

This multicenter study, initiated in 2006, prospectively evaluated outcomes of HL pts whose therapy was chosen according to baseline prognostic factors and was tailored based on PET/CT results performed after 2 cycles of chemotherapy. Pts with classic HL stages I-IV, aged 18-60 yrs, were eligible. After 2XABVD, early favorable (EFD) pts with negative PET/CT undergo involved nodal radiation (INRT) and early unfavorable (EUD) pts receive 2 more ABVD cycles (a total of 4) followed by INRT. If interim PET is negative, RT is substituted with 2XABVD.Pts with positive interim PET are given 2 more ABVD cycles (total 4-6) followed by RT. Advanced HL pts with IPS 0-2 initially receive 2XABVD and those with IPS ≥ 3 receive 2X escalated BEACOPP (EB). If interim PET is negative or shows minimal residual uptake in a single site, further therapy with 4XABVD is given without RT to bulky mediastinal masses. If interim PET is positive with no evidence of HL progression, therapy is escalated to EB with RT given to bulky mediastinal masses. Dynamic visual score (DS) comparing interim to baseline PET was used to evaluate PET positivity; Deauville score (DVL) was used for retrospective analysis of interim PET. To date, 308 pt results have been analyzed. 85% of pts were negative according to both scoring systems, with concordance in 92% of cases. At a median follow-up of 24 months (4-74), the current study has shown PFS of 86% for the whole group. PPV, NPV and accuracy of the DVL score were 37%, 95% and 85%, respectively; these parameters of DS were 30%, 90% and 79%, respectively. Thus, the DVL score seems to be superior. However, 63% of relapsing patients were negative by both scores.

A 7 - Safia khan, Shazia Riaz, Mehboob Ahmed, Humayun Bashir, Syed Ather Kazmi
Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, Pakistan.

IMPACT OF FDG-PET/CT IN DECISION OF RADIOTHERAPY IN PEDIATRIC HODGKIN LYMPHOMA

PURPOSE: To review role of FDG-PET/CT in decision of radiotherapy among Hodgkin Lymphoma patients

MATERIALS & METHODS: 114 hodgkin lymphoma patients up to 18 yrears of age evaluated with FDG-PET/CT for treatment response during 2010-2012 in SKMCH & RC, LHR were retrospectively reviewed for this research. 93 out of 114 patients included in this study were evaluated in mid treatment with FDG-PET/CT by giving F18 FDG dose 0.14 mCi/Kg intravenously in resting condition followed by imaging over 25-30 min; contrast enhanced CT was acquired as part of PET/CT protocol. Remaining 21 patients were evaluated for treatment response with isolated contrast enhanced CT.

RESULTS: SPSS version 15 was used for data analysis. The demographic information shows that majority of the patients (48%) fall under the age group of 5 to 10 years. 74% of selected patients were male. From Chi square analysis it is revealed that there is substantial association between staging with FDG-PET/CT and conventinal contast enhanced CT. However, from cross tabulation it is observed that FDG-PET/CT downstaged one patient and up staged eight patients. On the base of interim CT XRT was given to 7 patients of which 5 were relapsed and on base of FDG-PET/CT 17 patients received XRT. From these 17 patients only 8 were relapsed.

CONCLUSION:Based on data analysis it is concluded that FDG-PET/CT is more senstive than convential CT in decision making for XRT.

A 8 - Vassilakopoulos TP,Rondogianni Ph,Pangalis G,Prassopoulos V, Chatziioannou S, Sotiropoulos V, Moschogiannis M,Matsouka H, Symeonidis A,Panayiotidis P, Datseris I, Konstantopoulos K, Angelopoulou M.

COMPARATIVE ASSESSMENT OF BONE MARROW INVOLVEMENT (BMI) BY BM BIOPSY (BMB) OR PET/CT IN PATIENTS (PTS) WITH HODGKIN LYMPHOMA (HL)

Background: ~6% of HL pts have BMI, which can be predicted by our published clinical prediction rule (CPR) (Blood. 2005;105: 1875-80). PET/CT may overcome the need of BMB. We aimed to correlate BMB and pt characteristics with BM-PET/CT findings in 172 HL pts, assess the impact of our CPR on the frequency of BMI detected by either method, and assess the ability to omit BMB in selected or even all pts.Patients/Methods: Data regarding BMB and clinical characteristics of 172 pts were retrieved and electronic PET/CT data were reviewed regarding osseous/BM findings and visually graded as:(1)no increased BM uptake;(2)increased BM uptake≤liver;(3)increased BM uptake >liver;(4)solitary osseous/BM focus without CT correlate; (5)multiple osseous/BM foci. Pts were also classified according to our CPR in low,standard and high-risk groups. Results: PET/CT was negative for BMI in 142 pts (82%; scores 1,2,3) and positive in 30 (18%; single focus 3, multiple 27). Only 13 pts had BMI by BMB(7.6%). 0/145 pts with BM-PET/CT scores 1-4 had pos BMB vs 13/27 (48%) graded as "5". The CPR was well validated: The frequency of BMI by BMB and PET/CT was 0% in low, 1.7% and 6.9% in standard and 20.8% and 37.7% in high-risk pts. Pts with BMI by PET/CT and neg or pos BMB had similarly poor 3-yr FFS (44% vs 57%, p=0.54). Pts with diffuse BM uptake >liver had higher leukocyte, platelet, ESR and CRP levels. Conclusions:PET/CT detects >2x cases of BMI than BMB, which carry a similarly poor prognosis. Increased diffuse BM uptake is associated with cytokine-related activity but not BMI. BMB can be safely omitted in PET/CT-staged HL, with no identifiable high-risk group, which could obtain a benefit from BMB.

A 9 - Carsten Kobe (1), Georg Kuhnert (1), Deniz Kahraman (1), Heinz Haverkamp (2), Hans-Theodor Eich (2, 3), Mareike Franke (4), Thorsten Persigehl (4), Susanne Klutmann (5), Holger Amthauer (6), Andreas Bockisch (7), Regine Kluge (8), Hans-Heinrich Wolf (9), David Maintz (4), Michael Fuchs (2, 10), Peter Borchmann (2,10), Volker Diehl (2), Alexander Drzezga (1), Andreas Engert (2, 10), Markus Dietlein (1)
Author's institutional affiliation:
(1) Department of Nuclear Medicine, University Hospital of Cologne, Germany, (2) German Hodgkin Study Group, University Hospital of Cologne, Germany, (3) Department of Radiation Oncology, University Hospital of Münster, Germany, (4) Department of Radiology, University Hospital of Cologne, Germany, (5) Department of Nuclear Medicine, University Medical Center Hamburg-Eppendorf, Germany, (6) Klinik für Strahlenheilkunde, Charité-Universitätsmedizin Berlin, Campus Virchow-Klinikum, Germany, (7) Department of Nuclear Medicine, University of Duisburg-Essen, Germany, (8) Department of Nuclear Medicine, University of Leipzig, Germany, (9) Department of Internal Medicine IV, Martin-Luther-University Halle-Wittenberg, Germany, (10) Department of Internal Medicine I, University Hospital of Cologne, Germany

PURPOSE Positron emission tomography (PET) after chemotherapy can guide consolidating radiotherapy in advanced stage Hodgkin lymphoma (HL). This analysis aims to improve outcome prediction by integrating additional criteria derived by computed tomography (CT) and to evaluate consistency in PET interpretation

METHOD AND MATERIALS The analysis set consisted of 739 patients with residues ≥ 2.5 cm after chemotherapy from a total of 2,126 patients treated in the HD15 trial performed by the German Hodgkin Study Group (GHSG). After local PET interpretation, a central panel performed image analysis and interpretation of CT scans before and after chemotherapy as well as PET scans after chemotherapy. Prognosis was evaluated using progression free survival (PFS); groups were compared with the log rank test. Potential prognostic factors were investigated using ROC analysis and logistic regression.

RESULTS 548 of 739 patients (74%) had PET negative residues after chemotherapy; these patients did not receive additional radiotherapy and showed a 4-year PFS of 91.5%. The 191 PET positive patients (26%) receiving additional radiotherapy had a 4-year PFS of 86.1% (p=0.022). CT alone did not allow further separation of patients in partial remission by risk of recurrence (p=0.9). In the subgroup of the 54 PET-positive patients with a relative reduction of less than 40%, the risk of progression or relapse within the first year was 23.1% as compared to 5.3% for patients with a larger reduction (difference 17.9% (95% CI 5.8% to 30%). Concordance between local and central PET-review was 90%.

CONCLUSION HL patients with PET positive residual disease after chemotherapy and poor tumor shrinkage are at high risk of progression or relapse. A population of high-risk patients has been identified for whom alternative treatment options could be evaluated.

A 10 - Georgi T, Epstude M, Kurch L, Elsner A, Mauz-Körholz C, Körholz D, Hasenclever D, Holzendorf V, Wallace WH, Balwierz W, Cepelova M, Karlen J, Landman-Parker J, Fossa A, Sabri O, Kluge R

Semiautomatic detection of skeletal lesions in PET/CT in pediatric patients with Hodgkin´s lymphoma (PHL)

Aim: PHL patients, treated in the EuroNet-PHL-C1 study, underwent a PET/CT examination for initial staging. Skeletal involvement leads to an upstaging into the highest treatment group. Our aim was the development of a semiautomatic algorithm to facilitate and standardize the detection of skeleton lesions in PHL patients.

Methods: In cooperation with the Hermes Medical Solutions AB a semiautomatic algorithm, called tumorfinder-s was developed. The first step represents the creation of a skeletal mask in the CT images based on the Hounsfield units. This skeletal mask is transferred to the PET images. A reference VOI is placed in a non-involved lumbar vertebral body and a search algorithm detects all skeletal sites larger than 0.25 ml with a SUV > SUVmean(reference region) + 2.5 SD. 192 EuroNet-PHL-C1 patients were tested by the tumorfinder-s, among them 142 patients with visual detectable skeletal lesions as well as 50 patients without skeletal involvement.

Results: In 130/142 (91.5%) PHL patients with skeletal involvement the tumorfinder-s detected skeletal lesions. Overall 774/1015 (76.3%) visual described skeletal lesions were found (6.0 lesions per patient on average). In the group without visual skeletal involvement 49 possibly false positive skeletal lesions were detected in 25/50 (50%) patients, 34 (69%) of these lesions were smaller than 0.5 ml.

Conclusion: The tumorfinder-s is suitable for the detection of skeletal involvement in PHL patients. It provides a sensitive, objective and reproducible preselection of skeletal lesions, which can either be accepted or rejected and supports the visual assessment. It also enables a quantification of the skeletal tumor burden.

A 11 - Kluge R, Kurch L,Hasenclever D, Mauz-Körholz C, Elsner A, Georgi T,, Wallace H, Landman-Parker J, Moryl-Bujakowska A, Cepelová M, Karlén J, Alvarez Fernández-Teijeiro A, Hoffmann M,Sabri O, Körholz D

qPET - a quantitative extension of the Deauville scale to assess response in interim FDG-PET scans in lymphoma

BACKGROUND: Interim FDG-PET (iPET) is used for treatment tailoring in lymphoma. Deauville response criteria consist of five ordinal categories (D1 - D5) based on visual comparison of residual tumor uptake to physiological reference uptakes. However, PET-response is a continuum and visual assessments can be distorted by optical illusions. OBJECTIVES: With a semi-automatic quantification tool we eliminate optical illusions and extend the Deauville score to a continuous scale.

METHODS: SUVpeak of residual tumors is determined by a semi-automatic region-growing algorithm and normalised to a standardized VOI in the liver. Deauville scores and qPET-values were determined and compared in 898 pediatric Hodgkin's lymphoma patients after two OEPA chemotherapy cycles.

RESULTS: In 150 patients no qPET value could be calculated due to missing or very low residual tumor uptake. The remaining 748 iPET were classified according to Deauville scoring. qPET-values in the D2-, D3-, D4- and D5-group were determined as 0.84+-0.22; 1.10+-0.26; 1.62+-0.52 and 3.72+-1.83, mean ± sd, respectively. The best thresholds D2/D3, D3/D4 and D4/D5 were determined at qPET-values of 0.95, 1.3 and 2.0, respectively.

DISCUSSION: qPET methodology provides semi-automatic quantification for interim FDG-PET response in lymphoma extending ordinal Deauville scoring to a continuous scale. Deauville categories correspond to certain qPET cut values, thus enabling translation of results achieved with both methods.

A 12 - Kluge R, Hasenclever D, Kurch L, Elsner A, Georgi T, Mauz-Körholz C,Wallace H, Landman-Parker J, Moryl-Bujakowska A, Cepelová M, Karlén J, Alvarez Fernández-Teijeiro A, Hoffmann M, Sabri O, Körholz D

Border between normal and abnormal metabolic response in interim PET during Hodgkin lymphoma treatment derived from qPET density curves

BACKGROUND: The optimum cut-off for interpretation of interim PET during lymphoma treatment as negative or positive is widely discussed. Most treatment-reduction studies currently restrict negative PET results to Deauville (D) scores 1 and 2. Thresholds between the D scores 2/3, 3/4 and 4/5 correspond to qPET-values of 0.95, 1.3 and 2.0, respectively (see previous poster). The qPET method enables mathematical analysis of the distribution of the residual uptake intensity in a cohort of patients.

METHOD: qPET-values were determined in 898 pediatric Hodgkin's lymphoma patients after two OEPA chemotherapy cycles and displayed in a density curve. Mixture models describing the deviation of the curve from symmetry on a linear scale (model I) and on a log scale (Model II) were fitted. Models enable splitting the curve in parts with normal and abnormal metabolic response.

RESULTS:In 150 patients no residual tumor uptake was present or it was too low for determination of qPET. The density curve of the remaining 748 qPET values formed a dominant peak with a mode at a qPET-value of 0.95 and with outliers to the right. The best cut-off between normal and abnormal parts was determined at a qPET-value of 1.3 (model I, sensitive approach) or 2.0 (model II, specific approach).

DISCUSSION: The threshold D2/3 at a qPET-value of 0.95 corresponds to the center of the normal part of the density curve in our study setting. This is obviously too causious for definition of PET-positivity. Putting the cut-off to a qPET-value of 1.3 corresponding to D3/4 (liver uptake) should be a sufficently sensitive approach for use in treatment reduction protocols.

A 13 - Kurch L, Hasenclever D, Tchavdarova L, Georgi T, Pelz T, Stoevesandt D, Wallace H, Landman-Parker J, Fossa A, Balwierz W, Cepelova M, Karlen J, Sabri O, Mauz-Körholz C, Körholz D, Kluge R

Relevance of Non-FDG-avid areas inside a tumour mass in Paediatric Hodgkin Lymphoma (PHL) patients

AIM: Necrotic areas within solid tumours are known to be a source of impaired progression free survival (PFS) and overall survival (OS) since anaerobic conditions may lead to hypoxia resistant cells. FDG-uptake is missing in such necrotic areas. Our aim was to further characterize this phenomenon within a population of PHL patients.

METHOD: PET/CT images of 1422 EuroNet-PHL-C1-trial patients were retrospectively reviewed for the occurrence of non-uptake areas (NUA). If so, NUA volumes were measured. Patient and disease specific data were compared between PHL patients with and without NUA.

RESULTS: 102 of 1422 PHL patients (7,2%) displayed NUA, mostly within a mediastinal tumour bulk (93%). In 81% the NUA had disappeared or had markedly reduced and in 19% volume reduction was inadequate following 2 courses of OEPA chemotherapy. The average NUA volume decreased from 48ml (range 0,24-525ml) to 19,5ml (range 0-361ml). Patients with NUA had in comparision to the control group 1) a larger mediastinal tumour volume (467ml vs 122ml), 2) more B-symptoms (59% vs 39%, p=0,000) and 3) more indication for radiotherapy (81% vs 53%, p=0,000). 36 months PFS between the control group and NUA group differed significantly (p=0,001). The area of PET-positivity (>mediastinal bloodpool) after 2 OEPA courses was in 66% located on the egde of the former NUA and was therefore the reason for radiotherapy recommendation.

CONCLUSION: Tumour areas with locally missing tracer uptake at initial staging are a risk factor of PET-positivity after 2 courses of OEPA. Patients with NUA had a reduced PFS compared to patients without NUA after standard treatment.

B 1 - Vassilakopoulos TP, Pangalis GA, Angelopoulou MK, Prassopoulos V, Chatziioannou S, Papageorgiou S, Sotiropoulos V, Panayiotidis P, Roussou P, Konstantopoulos K, Rondogianni Ph.

PROGNOSTIC SIGNIFICANCE OF POST-RITUXIMAB-CHOP (R-CHOP) PET/CT IN PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA (PMLBCL)

Background: The use of PET in PMLBCL is based on the projection of data derived from Hodgkin and aggressive B-cell lymphomas. Patients/Methods: Among 120 consecutive pts with PMLBCL responding to R-CHOP, 100 underwent PET/CT, which was assessed according to IHP and Deauville criteria. Results: The median follow-up was 38 months; 61 pts were PET-neg and 39 PET-pos (Deauville 2,3,4,5 in 1,11,14 and 13 pts). Only 30/61 PET-neg pts (49%) received RT (median 3560 cGy). Three (3/31) non-irradiated pts relapsed (mediastinum and 2 isolated CNS relapses) vs. 0/30 irradiated pts. Among 39 PET-pos pts, 35 (90%) were irradiated (median 4000 cGy): 10/39 pts relapsed (all irradiated). The 2-year PFS was superior for PET-neg vs. PET-pos pts (95% vs. 72%, p=0.003). Among PET-neg pts, 2-year PFS was 96% vs. 100% for 31 non-irradiated and 30 irradiated pts (p=0.33; isolated CNS relapses censored). According to Deauville criteria, the 2-year PFS was 96%,92% and 100% for scores 1,2,3 and 62%,55% for scores 4 and 5 (p=0.0002). Among 39 PET-pos pts, 2-year PFS was 94% vs. 52% (p=0.007) for pts with SUVmax<5 (1/19 relapsed) and SUVmax≥5 (9/20 relapsed). Several PET-pos pts remained PET-pos after RT but did not progress in the long-term. Conclusions: PET/CT positivity is observed in ~40% of R-CHOP responders in PMLBCL and is associated with ~25% inferior PFS, despite additional RT. However, Deauville score 4 may be a more reasonable cutoff to define positivity.Similarly, higher SUVmax predicted a much higher relapse risk. Our data further suggest that R-CHOP responders should not be forwarded to ASCT simply based on a positive PET/CT and that RT can be spared in the majority of PET-neg pts.

B 2 - L. Ceriani1,S. Barrington2,A. Biggi3,B. Malkowski4,U. Metser5, A. Versari6, E. Zucca1, S.Chauvie3. 1-Bellinzona (CH); 2-London (UK); 3-Cuneo (I), 4-Bydgoszcz (PL);5-Toronto(CAN); 6-Reggio Emilia (I)

IMPACT OF SPECIFIC TRAINING IN THE PERFORMANCE OF THE CENTRAL REVIEW PANEL IN THE ONGOING IELSG37 STUDY OF PRIMARY MEDIASTINAL LYMPHOMA.

Aim: To measure agreement between reviewers reporting PET-CT scans for the IELSG37 study and to determine the effect of training upon concordance rates. Methods:The review panel comprises 6 nuclear physicians experienced in reading PET-CT. Scans were read using Deauville criteria with score 1-2 regarded as 'negative'. The web based system (WIDEN) was used by the review panellists for image exchange. Agreement rates for all reviewers were measured at three time-points:1) after initial reading of a 'training set' of 22 paired PET-CT scans from patients with PMBCL enrolled in the previous IELSG26 study 2) after the first 10 clinical cases 3) following a further 50 cases. After the feedback from the training set and the first 10 cases, a meeting was held to discuss controversial points in image interpretation and a detailed set of instructions for the review procedure was agreed and acted upon. Results: By April 2014, 60 pts had been centrally reviewed and 24 classified as negative, 36 as positive. The binary concordance between pairs of reviewers (Cohen's κ) ranged from 0.5 to 0.83. Overall concordance between the 6 reviewers (Krippendorf's α) was 0.56. Harmonization among reviewers improved from phase 1 to 3, (Krippendorf's α from 0.42 to 0.59; Cohen's κ from 0.23-0.72 to 0.54-0.91).

Conclusions:Our experience to date indicates that the agreement among expert nuclear physicians in reporting PMBCL, even using standardized criteria, was only moderate when the study began. However, improved agreement in PET reporting was rapidly obtained using a training process which involved revision and discussion of practical rules in the application of commonly adopted interpretation.

B 3 - Vassilakopoulos TP, Kanellopoulos A, Papageorgiou S, Pangalis GA, Anastasopoulou A, Moschogiannis M, Petevi K, Boutsikas G, Papageorgiou L, Viniou N, Pappa V, Angelopoulou MK, Konstantopoulos K

CLINICAL IMPLICATIONS AND PROGNOSTIC SIGNIFICANCE OF PET/CT IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) AFTER IMMUNOCHEMOTHERAPY

BACKGROUND: ~30-40% of patients (pts) with DLBCL are primary refractory or relapse after first line R-CHOP. PET/CT is increasingly used for the identification of pts with active disease at the end of treatment (Tx), but relevant data are scarce in the literature. AIM: The retrospective analysis of PET/CT findings in DLBCL pts after conventional response to R-CHOP and the assessment of their impact on outcome in relation to other prognostic factors. PATIENTS/METHODS: 151 DLBCL pts (2004-2013), who achieved CR,CRu or PR by conventional imaging, underwent post-Tx PET/CT. All pts had been treated with R-CHOPx4-8. PET/CT scans were interpreted according to the International Harmonization Project crieria. RESULTS: Baseline pts' characteristics were: median age 61 (18-89), 65% male, 55% stage III/IV, 17% ECOG PS ≥2, 23% ≥2 E-sites, 53% abnormal LDH, IPI-L 42%,IPI-LI 21%,IPI-HI 24%, IPI-H 14%. Among 151 pts, 117 (77%) became PET(-) and 34 (23%) remained PET(+) with 4-yr PFS of 86% vs 40% ($p<0.0001$). Among PET(-) pts, 10/117 relapsed: 4-yr PFS was 89% vs 69% for pts with PS 0-1 vs 2-4 ($p=0.02$); male gender, multiple extranodal and bone marrow involvement were of marginal significance. Among 34 PET(+) pts, 16 progressed (4-yr PFS 40%). Biopsy-proven false positive results and use of consolidative irradiation (RT) (although limited) may have contributed to this promising figure (details to be presented at the meeting). CONCLUSION: 15% of PET(-) DLBCL pts relapsed. This risk increased with worsening PS. 40% of PET(+) DLBCL pts remained disease free despite the limited use of consolidative RT. Our findings could facilitate the design of follow-up and guide consolidative treatment.

B 4 - Karen Mylam, Lale Kostakoglu, Martin Hutchings, Morton Coleman, Myron S Czuczma, Anne L. Nielsen, Paw Jense, Annika Loft, Helle W. Hendel, Sirpa Leppä, Harald Holte, Peter Brown & Lars M. Pedersen

FDG-PET/CT after one cycle of chemotherapy in patients with diffuse large B-cell lymphoma: Results of a Nordic/US intergroup study.

Aim: The aim of this study was to evaluate the predictive value of I-PET after one course of chemoimmunotherapy in patients with newly diagnosed DLBCL.

Patients and methods: 112 DLBCL patients were enrolled. All patients had PET/CT scans performed prior to therapy (PET-0) and after one course of chemotherapy (PET-1). I-PET scans were centrally reviewed. I-PET scans were grouped in positive and negative categories according to International harmonization criteria (IHP) and retrospectively according to the recently recommended Deauville 5 point scale (D 5PS) with scores 1-3 considered negative (D 5PS>3) III) and D 5PS with scores 1-4 considered negative (D 5PS = 5). In order to explore the distinction between groups D 5PS score of 4 and 5, ratios of tumor SUVmax to liver SUVmax were retrospectively analyzed .

Results: We found no difference in progression-free survivals (PFS) between PET-negative and PET-positive patients according to IHP (p=0.513) and D 5PS>3 (p=0.309). In contrast, the 2-year estimate for PFS using D 5PS = 5 was 50.9% (95%CI 23.6-72.9%) in the PET-positive group compared with 84.8% (75.6-90.1%) in the PET-negative group (p=0.002). A tumor/liver SUVmax cut-off of 3.1 to distinguish a D 5PS scores of 4 and 5 provided the best prognostic value (2-year PFS 89.7% and 57.1%, respectively).

Conclusion: Our data demonstrated that PET after one course of chemotherapy was not able to safely discriminate PET positive and PET negative patients in different prognostic groups for the use in PET-adapted therapy. Semi-quantitative analysis might be a promising method for the discrimination between D 5PS scores of >3 and >4.

B 5 - Andreas Hüttmann, Stefan Müller, Ulrich Dührsen; on behalf of the PETAL study group
Dept. of Haematology and Dept. of Nuclear Medicine, University Duisburg-Essen, Hufelandstr. 55, 45122 Essen, Germany

Outcome of Aggressive Non-Hodgkin's Lymphoma Patients with a Negative Pretreatment Positron Emission Tomography Scan

Background: The multicenter Positron Emission Tomography Guided Therapy of Aggressive Non-Hodgkin's Lymphomas (PETAL) trial was initiated in 2008 to resolve the question whether a change in treatment may improve the outcome of patients with a positive midtreatment 18FDG-PET scan (EudraCT-Nr.: 2006-001641-33; NCT00554164). This explorative additional analysis of pretreatment 18FDG-PET negative patients explores the outcome of this presumably favourable subgroup.

Results: 1075 patients were registered in the PETAL-trial, 80 of whom had a negative pretreatment 18FDG-PET scan (7,4 %). More males than females were pretreatment 18FDG-PET negative (55 vs. 23; numbers not adding up to 80: data incomplete) and 68 had a favourable International Prognostic Index. As of May 2014, median follow-up time for staging-PET negative and staging-PET positive patients is 618 and 757 days, respectively (p = n.s. (Wilcoxon)). However, with a short median follow-up no overall survival difference between pretreatment PET negative and pretreatment PET positive patients is observed. Data collection for the PETAL trial is still ongoing and progression-free survival cannot be reported at the current stage. In two out of four fatalities in the staging-PET negative group the cause of death was unrelated to lymphoma. The two lymphoma-related deaths in this group were due to central nervous system / meningeal disease.

Conclusion: It is likely that lymphoma relapse is a rare event in staging-PET negative patients. Brain or meningeal involvement may escape routine PET assessment in the setting of aggressive lymphoma staging. The male preponderance in pretreatment PET negative patients is unexplained.

B 6 - M Hutchings,1 L Kostakoglu,2 G Fingerle-Rowson,3 A de Crespigny,4 C Vignal,3 M Mobasher,4 AD Zelenetz 5;
1 Department of Hematology, Rigshospitalet, Copenhagen, Denmark, 2The Mount Sinai Hospital, NYC

PROSPECTIVE EVALUATION OF INTERIM AND END OF TREATMENT PET IN PATIENTS WITH DE NOVO DLBCL TREATED WITH GA101+CHOP IN PHASEII GATHER STUDY

In DLBCL, PET is valuable in end of treatment (EOT) response assessment but the role of interim PET (iPET) has been controversial. GATHER study included prospective analysis of iPET by independent reviewers that is the subject of this abstract.

The first 40 pts in study were to have an iPET after Cycle 1 (PET-1), and the subsequent 40 were to have iPET after Cycle 2 (PET-2). Responses were assessed 6–8 wks after treatment according to the Cheson 2007 criteria (PET by IHP). The Deauville criteria (5PS) was used as the primary assessment and maximum standard uptake value (SUVmax) was secondary in iPETs.

Seventy pts had a tumor response at EOT, 37 had PET-1 and 33 had PET-2. The enrolled pts who did not have a response assessment at EOT were excluded from analysis. PET-1 was negative in 18 pts (49%) and positive in 19 (51%) pts. PET-2 was negative in 21 (64%) and positive in 12 (36%) pts. Using the 5PS, there was no association between EOT response and the PET-1 (OR=1.03, 95%CI [0.25, 7.00]) or PET-2 (OR= 0.5, 95% CI [0.08, 2.99]).

The %ΔSUV of the hottest lesion at PET-0 with the corresponding lesion on iPET showed a weak association with EOT response for PET-0 to PET-1 (OR=1.029, 95%CI [1.007,1.135]); however, the opposite result was seen for PET-0 to PET-2 (OR=0.97, 95% CI [0.908, 1.036]).

In this prospective study, iPET did not predict EOT response established by IHP criteria when 5PS criteria was used as the primary criteria for iPET. Analysis of %ΔSUV was limited by the small sample size and relatively low number of non-responding pts. Further analysis will be presented at the meeting. Future analyses need to evaluate the correlation with PFS.

NCT01414855

B 7 - E.Scherman, C Copie-Bergman, E Itti, J Moroch, V Safar, M Baia, C Fruchart, P Vera, S Bardet, M Meignan, C Haioun Hematology, Nuclear Medicine, Pathology, CHU Créteil, CHU Rouen, CHU Caen

MOLECULAR FEATURES COMBINED WITH EARLY FDG-PET/CT RESPONSE IN DIFFUSE LARGE B-CELL LYMPHOMA

Introduction: Diffuse large B cell lymphoma (DLBCL) constitutes the most frequent type of adult's non Hodgkin lymphomas and a group of heterogeneous diseases, with variable clinical, morphological, immunophenotypical and molecular features. Immunohistochemistry (IHC) for BCL2 et MYC protein expression and fluorescence in situ hybridization (FISH) for BCL2, BCL6 and MYC gene alterations are helpful diagnostic tools to stratify DLBCL into different prognostic subgroups. In addition, early interim response by 18fluorodeoxyglucose positron emission tomography (PET/CT) is considered on the basis of both visual or semi-quantitative criteria (delta SUV), as a powerfull prognostic factor to predict outcome in patients treated with rituximab-based chemotherapy.

Methods: this retrospective and muticentric study included 91 patients with de novo DLBCL, characterized by IHC and FISH (BCL2, BCL6 and MYC), and evaluated with PET/CT at diagnosis and after two cycles of immunochemotherapy.

Results: Results significantly highlight, in a multivariate analysis, that combination of BCL2 protein overexpression and/or BCL2 gene alteration with slow metabolic response, are independently associated with a poorer prognosis.

Conclusion: Combined evaluation of BCL2 expression with rapidity of metabolic response by PET/CT identifies patients with good outcome (BCL2 neg/rapid metabolic response) and poor outcome (BCL2 pos/slow metabolic response). Such results should be validated in larger studies of patients homogeneously treated with immunochemotherapy

B 8 – Malik Juweid1, Ranjana Advani2, Julie Vose3, Luis Fayad4, Felix Mottaghy1, Ryogo Minamimoto2, Andrew Quon2. 1.RWTH Aachen University, 2.Stanford University, 3.University of Nebraska, 4.MD Anderson Cancer Center

MULTICENTER STUDY FOR COMPARISON OF 18F-FLT AND 18F-FDG PET/CT FOR EARLY THERAPEUTIC MONITORING OF DIFFUSE LARGE B-CELL LYMPHOMA

The aim of this multicenter prospective study is to investigate whether 18F-fluorothymidine positron emission tomography with integrated computed tomography (FLT PET/CT) has significantly higher positive predictive value (PPV) and comparable negative predictive value (NPV) as 18F-fluorodeoxyglucose (FDG) PET/CT for early therapeutic monitoring of diffuse large B-cell lymphoma (DLBCL). Patients with newly diagnosed DLBCL underwent both FLT and FDG PET/CT 18-24 days after cycle 2 R-CHOP. For FDG PET/CT interpretation, International Harmonization Project (IHP), Deauville criteria, European Organization for Research and Treatment of Cancer (EORTC), and PET Response Criteria in Solid Tumors (PERCIST) criteria were utilized. FLT PET/CT was interpreted using visual assessment. Patient outcomes were based on clinical evaluation (including imaging) and classified as complete response (CR) or residual disease (RD). Of 24 patients, 21 had CR and 3 had RD. FLT PET/CT had a significantly higher PPV (75%) to predict residual disease than FDG PET/CT using IHP (18.8%, p=0.03) or EORTC (18.8%, p=0.03) criteria (FLT was also better than FDG with Deauville (30.0%) and PERCIST (23.1%) but without statistical significance (p=0.12 and p=0.06, respectively)). FLT and FDG PET/CT had an equally high NPV (100%) regardless of interpretation criteria. Overall, FLT PET/CT showed a superior PPV and comparable NPV compared to FDG PET/CT for early therapeutic monitoring of DLBCL.

B 9 - Y.W.S.Jauw (1), M.C.Huisman (2), G.A.M.S. van Dongen (2), O.S. Hoekstra (2), J.M. Zijlstra (1). Dept. of Hematology (1) and Radiology & Nucleair Medicine (2), VUMC, Amsterdam, the Netherlands.

Biodistribution and uptake of 89Zr-rituximab and 89Zr-ofatumumab in patients with relapsed diffuse large B cell lymphoma

Introduction:The efficacy of second line chemo-immunotherapy for diffuse large B cell lymphoma (DLBCL) has decreased, due to more effective first line treatment with rituximab (R). The 2nd generation anti-CD20 antibody ofatumumab (O) has a different binding site than R, and therefore might have a better tumor targeting efficiency. The aim of this proof-of-concept study is to determine biodistribution and uptake of 89-Zirconium(Zr)-R and Zr-O.

Methods:6 patients with relapsed DLBCL were injected with a bolus of 75.0 +/- 3.1 MBq Zr-R (n=5) or Zr-O (n=1) within 1 hour after a therapeutic dose of cold antibody. PET/CT scans and venous blood samples were obtained at 1, 72 and 144 hours post injection. Visual assessment of tumor targeting was performed by 2 nuclear medicine physicians. Venous whole blood (WB) activity concentrations (ACs) were derived using a well counter and organ ACs were derived from the PET scans, allowing for an estimate of the effective radiation dose.

Results: In all CD20-positive DLBCL patients (n=4/5) tumor uptake was visible on Zr-R, while tumor uptake of Zr-O was observed in a CD20-negative patient (n=1/1). Biodistribution in normal tissue was similar for Zr-R and Zr-O. The image derived bloodpool AC and the venous WB ACs were tightly correlated (R2=0.997, slope=0.85). The effective radiation dose for Zr-R was 0.53 +/- 0.01 mSv/MBq (n=4 males) and 0.52 mSv/MBq for Zr-O (n=1 male).

Conclusion: 89Zr-immuno-PET can be used for assessment of tumor targeting efficiency with R and O. Further investigation with administration of Zr-R and Zr-O within the same patient is needed to evaluate differences in tumor uptake. WB AC can be directly image-derived.

B 10 - S.Luminari, M.Bellei, A.Dondi, S.Galimberti, A.Versari, E. Ciabatti, A.Franceschetto, S.Chauvie, L.Guerra and M.Federico on behalf of the Fondazione Italiana Linfomi (FIL)

PET RESPONSE AND MINIMAL RESIDUAL DISEASE IMPACT ON PROGRESSION-FREE SURVIVAL IN PATIENTS WITH FOLLICULAR LYMPHOMA.

FL is an indolent FDG avid B-cell lymphoma whose lymphocytes are characterized by the Bcl2/IgH rearrangement (RA). Not only PET response is highly prognostic but also the use of Polimerase Chain Reaction (PCR) for Bcl2/IgH RA has been proposed as a tool to improve response definition. So far no study has combined PET and PCR. We analyzed a sample of 41 patients with FL from the FIL-FOLL05 trial for whom final PET was centrally reviewed applying the Deauville scale (PET+ if score 4-5). All patients were positive for Bcl2/IgH RA by PCR before treatment and were reassessed for minimal residual disease (MRD) on a bone marrow sample collected at the end of therapy. PCR tests were centrally perfomed. The distribution of cases according to PET response and molecular status was the following: PET-/MRD-, 28 (68%); PET-/MRD+, 8 (20%); PET+/MRD-, 2 (5%); PET+/MRD+, 3 (7%). PET/MRD concordance was 76%, with a Kappa=0.249, suggesting that PET and MRD information are not interchangeable. At univariate analysis PET+ was associated to a poorer progression-free survival (PFS) (HR 3.61, 95%CI 1.15-11.4, P=.028), while MRD+ had a trend towards a shorter PFS (HR 2.54, 95%CI 0.96-6.72, P=.060). PFS evaluated taking into account both PET and MRD data and by splitting patients in two groups (PET-/MRD- vs PET+ and/or MRD+) showed that achievement of both PET and MDR negativity was associated to a better outcome (HR 3.42, 95%CI 1.31-8.95, P=.012). Based on this preliminary study there is a rationale to combine PET and MRD analysis to improve accuracy of response assessment in FL. These results are currently being validated by the FIL-FOLL12 trial.

B 11 - A.Versari1, S.Chauvie2 , A.Franceschetto3, L.Guerra4, G.Storto5, S.Peano2, A.Dondi3, S.Luminari3, M.Federico3
1Reggio Emilia, 2Cuneo, 3Modena, 4Monza, 5Rionero in Vulture - ITALY

INITIAL EXPERIENCE ON THE APPLICATION OF DEAUVILLE CRITERIA TO THE END THERAPY PET IN FOLL 12 STUDY

FOLL12 is a multicenter, phase III, randomized study to evaluate the efficacy of a response-adapted strategy to define maintenance after standard chemoimmunotherapy in patients with advanced-stage Follicular Lymphoma Methods:PET scan is|performed at baseline, after 4 courses of R-CHOP-21 (not mandatory) and at the end of treatment (End-PET). Therapy is modulated on Minimal Residual Disease (MRD) and on End-PET results.

The blinded independent central review process is managed with WIDEN ®. Five expert nuclear medicine reviewers evaluate the scans according to the Deauville criteria. End-PET scans with score 4–5 are considered positive.

Binary and overall concordance among reviewers will be calculated automatically by WIDEN. Results: thirty-three centres participate to the study. All the PET scanner used in the study underwent a procedure for Clinical Trial Qualification in the Cuneo Core Lab. 108 patients were enrolled, 77 performed baseline PET and 51 already performed the End-PET that were uploaded with a median time of 39 seconds. 6/51 cases were positive (12%).Overall levels of agreement for independent reporting were fair. The coefficients were in the range 0.44-0.89 (kappa) and 0.66 (alpha) respectively. Concordance was reached at 100% in 43 cases, at 80% in 3, at 75% in 3 and at 60% in 2. After the first 20 cases of training, agreement among the reviewers increased.Conclusions: There is a good concordance between central reviewers using the Deauville criteria confirming that it is a reliable tool for End-PET reporting in Follicular Lymphoma. However a period of training is essential.

B 12 - L Kostakoglu1, A Goy, G Martinelli, D Caballero, M Crump, G Gaidano, T Baetz, R Buckstein, G Fine, G Fingerle-Rowson, C Berge, D Sahin, O Press , and L Sehn
1Mount Sinai Hospital, New York, NY, USA

POST-INDUCTION THERAPY FDG-PET IS PROGNOSTIC FOR PFS IN RELAPSED FOLLICULAR LYMPHOMA: A PRELIMINARY ANALYSIS OF THE GAUSS STUDY

Use of FDG-PET as a prognostic tool after post-induction therapy (post-IT) in follicular lymphoma (FL) has not been fully investigated, particularly following immunotherapy alone. We examined whether post-IT FDG-PET response assessment using IHP, D5-PS and EORTC criteria is a suitable prognostic endpoint for progression-free survival (PFS) in pts with relapsed FL randomised to obinutuzumab (GA101) or rituximab monotherapy in the phase II GAUSS trial (BO21003; NCT00576758). FDG-PET was performed at baseline and 4–6 weeks post-IT and was interpreted using IHP as the primary reading criteria, with D5-PS and EORTC-c as secondary reading criteria. Of 147 evaluable pts, 132 (median age=62 years) were analysed at baseline and 118 at post-IT, using IHP as the primary reading criteria. After a median follow up of 32.1 months, 44.6% of pts in the obinutuzumab arm and 56.1% in the rituximab arm had died or progressed. The post-IT PET results significantly correlated with response by all criteria (IHP, $p=0.0002$; D5-PS, $p=0.0003$; EORTC, $p=0.0012$). Using IHP criteria, the median PFS was 517 days for PET+ pts versus 'not reached' for PET- pts (95% confidence interval [CI], 309–772). The risk of disease progression was reduced in PET- compared with PET+ pts using IHP (hazard ratio [HR], 0.25; 95% CI, 0.117–0.522; $p<0.0001$), D5-PS (HR 0.31; 95% CI, 0.155–0.603; $p=0.0003$) and EORTC criteria (HR 0.39; 95% CI, 0.191–0.807; $p=0.0083$). Post-IT PET results ($p=0.0041$) and conventional response (overall $p=0.0442$) were significant prognostic factors for PFS. Overall, post-IT PET status was a strong predictor of PFS regardless of the PET assessment criteria used in this pre-treated FL cohort.

B 13 - J Trotman, S Luminari, S Boussetta, A Versari, J Dupuis, C Tychyj-Pinel, L Marcheselli, A Berriolo-Riedinger, A Franceschetto, A Julian, F Ricard, L Guerra, C Haioun, I Biasoli, H Tilly, M Federico, G

Prognostic value of PET-CT after frontline therapy in follicular lymphoma: applying the 5PS in three multicenter studies

The value of 18F-FDG PET-CT (PET) in response assessment after induction rituximab-chemotherapy for advanced stage symptomatic follicular lymphoma (FL) has been documented. To provide more precise survival estimates from a larger patient cohort with longer follow-up we conducted a pooled analysis of centrally reviewed scans in three studies.

PET was assessed independently by three reviewers applying the 5PS in all patients with a PET performed at the end of induction chemotherapy in the prospective multicenter GELA (PRIMA & PET Folliculaire), and FIL (FOLL05) studies.

246 scans were analyzed, 68 (27.6%) were positive with a cut-off ≥3 and 41 (16.7%) with a cut-off ≥4. Concordance across the three studies was better using a cut-off ≥4 (Cohen's Kappa 0.6-0.71 vs. 0.30-0.57). With a median follow-up of 55 months, both PET cut-offs were highly predictive of PFS and OS but cut-off ≥4 had best separation of the survival curves. The HR for PFS and OS of PET+ vs. PET- patients was 3.9 (95% CI 2.5-5.9, P<.0001), and 6.7 (95% CI 2.4-18.5, P=0.0002) respectively. For PET+ patients 4-y PFS was 23.2% (95% CI 11.1-37.9%) vs. 63.4% (95% CI 55.9-70.0%) in those who became PET- (P<.0001). 4-y OS was 87.2% (95% CI 71.9-94.5%) vs. 97.1% (95% CI 93.2-98.8%), (P<.0001). Conventional CT-based response (CR/CRu vs.PR) was predictive of PFS (HR 1.7, p=0.02) but not OS. This analysis confirms PET status applying the 5PS with a cut off ≥4 is most predictive of survival in FL after first-line therapy. PET-CT rather than contrast enhanced CT scanning should be considered the new gold standard for response assessment in clinical practice and a platform for study of response adapted therapy.

B 14 - G.Treglia(1), E.Zucca(1), R.Sadeghi(2), F.Cavalli(1), L.Giovanella(1), L.Ceriani(1)
1) Oncology Institute of Southern Switzerland, Bellinzona (CH) 2) Nuclear Medicine Research Center, Mashhad (IR)

DETECTION RATE OF F18-FDG PET IN PATIENTS WITH MARGINAL ZONE LYMPHOMA OF THE MALT TYPE: A META-ANALYSIS

Objective: To meta-analyze published data about the detection rate (DR) of fluorine-18-fluorodeoxyglucose (F18-FDG) positron emission tomography (PET) and PET/computed tomography (PET/CT) in the evaluation of patients with marginal zone lymphoma of the mucosa-associated lymphoid tissue (MALT).

Methods: A comprehensive literature search of studies published through February 2014 on this topic was performed. All retrieved studies were reviewed and qualitatively analyzed. Pooled DR of F18-FDG PET or PET/CT including 95% confidence intervals (95%CI) was calculated on a per patient-based analysis. Subgroup analyses considering the device used (PET or PET/CT) and the primary site of the MALT lymphoma were carried out.

Results: Twenty studies including 376 patients with MALT lymphoma were selected. The pooled DR of F18-FDG PET or PET/CT was 71% (95%CI: 61-80%). A significant difference between the DR of PET/CT (69%; 95%CI: 61-80%) compared to that of PET alone (73%; 95%CI: 60-84%) was not demonstrated. A better DR of F18-FDG PET or PET/CT in bronchial (94%; 95%CI: 85-99%) and head & neck (90%; 95%CI: 78-98%) MALT lymphomas compared to gastric (62%; 95%CI: 46-77%) and ocular (49%; 95%CI: 36-63%) MALT lymphomas was found.

Conclusions: This meta-analysis demonstrates that MALT lymphoma is a F18-FDG-avid tumor in most of the cases, suggesting a potential clinical role of F18-FDG PET or PET/CT in the initial evaluation of these patients. In particular, the DR of F18-FDG PET or PET/CT is related to the primary site of the MALT lymphoma, being superior in bronchial and head & neck lymphomas compared to the other sites.

B 15 - Viau P, Schiazza A, Razzouk-Cadet M, Michiels JF, Durant J, Karsenti JM, Vinti H, Mannone L, Cassuto JP, Rosenthal E, Darcourt J, Mounier N.

Interim FDG-PET/CT in AIDS-related lymphoma: evaluation of qualitative and quantitative criteria for prognostic value.

Introduction: Interim FDG-PET/CT for HIV negative lymphoma is one of the most important survival prognostic tools after 2-3 cycles of chemotherapy. However, equivalent studies in AIDS related lymphoma (ARL) need to be further studied in order to propose de-escalation treatment strategies.

Patients and methods:
Nineteen consecutive ARL patients (pts) had interim PET in our center for Hodgkin (8), DLBC (6) or Burkitt (5) lymphoma.There were 13 males, median age 48 yo [28 to 65], median CD4 count 350/mm3, undetectable HIV load in 12 pts, stage III-IV disease in 12 pts. Blinded to treatment outcome, we retrospectively measured quantitative parameters as DSUVmax, DSULmax and DMTV (cut-off 66%). Deauville criteria (1-3 vs 4-5) and the ratio SULmax/HepaticSULmean were also studied.

Results: With a 3 years median follow-up, OS was 70% (60% for NHL and 83% for HL). Quantitative parameters were found statistically significant : 3-year OS at 87% for DSUVmax> 66% versus 33% for DSUVmax<66% (p<0,0001). Sames results were observed with DSULmax (p<0,0001) but not for DMTV (p=0,55). Qualitative Deauville criteria was non significant (3yr OS 81% vs 44%, p=0,11). However, the ratio SULmax/HepaticSULmean less than 5 was promising (3yr OS 84% vs 33%, p<0,0001).

Conclusion: In ARL, DSUVmax and DSULmax reduction showed higher predictive value than Deauville's criteria after interim PET suvival analysis. If not feasable, the ratio SULmax/hepaticSULmean may be a promising tool. Theses findings have to be confirmed according to ARL subtypes in larger population before leading to de-escalation .

B 16 - Edeline V *, Champion L *, Elias-Shamieh R **, Alberini JL *,
Soussain C **
* Service de Médecine Nuléaire ** Service d'Hématologie
 Institut Curie, Hôpital René Huguenin, Saint-Cloud, France

Post-treatment FDG-PET poorly predicts patient's outcome in primary central nervous system lymphoma (PCNSL)

Purpose : FDG-PET is now mandatory for post-treatment assessment for systemic DLBCL. However, its role for PCNSL assessment has not been extensively studied. Our purpose was to determine the usefulness of FDG-PET in the prediction of PCNSL outcome after first line therapy.

Methods : Brain imaging at our institution is performed on a GE Discovery 690 , using a single bed position. A 8 min emission scan was acquired 45 min after FDG injection.

Results: From 04-2011 to 07-2013, 10 immunocompetent patients (pts) with newly diagnosed PCNSL had pre- and post-treatment PET/CT. Median age was 54.5 years (range 45-63), 8/10 pts had at least 1 FDG avid lesion (one pt was totally resected before PET and the other had received high-dose steroids before PET). Median SUV max was 19.9 (range 10-27.5). All the lesions identified by MRI were FDG avid. 10/10 pts had a negative post-treatment PET, but out of 9 patients followed in our center, 6 relapsed (1 followed in another center). Sites of relapse were brain in 4 pts, isolated menigeal in one pt and intraocular in one pt. 5 out of 6 relapses occurred <3 months after the post-treatment PET.

Post-treatment MRI was considered normal in 5 pts including 2 pts with isolated meningeal and intraocular relapses respectively, the other 3 pts are in maintained remission. The other 4 pts with residual lesions on MRI relapsed. None of the pts with a normal brain MRI relapsed within the brain.

Conclusion : In spite of the limited number of pts included in our study, the preliminary results strongly suggest that FDG-PET imaging have a poor negative predictive value for post-treatment PCNSL assessment and did not add information to MRI.

B 17 - C. Algrin, A. Van Der Gucht, S. Amorim, J. Ohnona, L. Vercellino, M-E Toubert, N. Berenger, P. Brice, N. Mounier, J. Brière, P. Merlet, C.Thieblemont. Hôpital Saint-Louis, Paris, CHU l'archet Nice, Fr

IMPACT OF INTERIM-POSITRON EMISSION TOMOGRAPHY WITH [18F]FLUORODEOXYGLUCOSE (PET) EVALUATION IN MEDIASTINAL LYMPHOMA

Introduction. No specific criteria for interpretation of interim-PET have yet been defined in mediastinal lymphoma. This study investigates the prognostic value of different evaluations of interim-PET after 2 or 4 courses of chemotherapy (PET2 or PET4) in mediastinal lymphoma. Methods. We retrospectively included 112 patients with either primary mediastinal lymphoma (PMBL) (n=44) or mediastinal Hodgkin's lymphoma (HL) (n=68), previously untreated, aged under 60 and who underwent at least one interim-PET. Qualitative evaluation included global visual evaluation, Deauville 5-point scale, Cheson's criteria, Gallamini's score and Dann's dynamic score. Semi-quantitative evaluation consisted in maximum standardized uptake value (SUVmax) and SUV reduction (ΔSUV) between the baseline PET (PET0) and PET2 or PET4. Results. Tumoral mass was more than 7.5 cm in 79% of the patients. Fourty seven percent of the patients were classified stage IV (pulmonary or pericardial localisation). Median SUVmax at PET0 (n=66), PET2 (n=79) and PET4 (n=69) were respectively 12.8 (IQR, 9.9-16.2), 2.5 (IQR, 1.8-3.4) and 2.2 (IQR, 1.8-3.1). With a median follow-up at 4.2 years, five-year progression-free survival (PFS) was 78%, with significant difference between HL and PMBL with 5-y PFS of 68% and 93% respectively (p=0.004). Interim-PET has a prognostic value in mediastinal lymphoma. Indeed, Deauville 5-point scale was predictive for PFS both at PET2 and PET4 (p<10-4). ΔSUV>66% at PET4 had an impact on PFS, but not PET2. Conclusion. Interim-PET evaluation has a prognosis impact in mediastinal lymphoma.

C 1 - Touati M.1, Boulesteix M.2, Abraham J.1, Olivrie O.1, Verbeke S.2, Delage-Corre M.3, Bordessoule D.1 and Monteil J.2
1 Hématologie Clinique; 2 Médecine Nucléaire, 3 Pathologie, CHU Limoges, France.

Initial FDG Metabolic Tumor Volume: a new EFS predictor factor in Hodgkin lymphoma

Introduction: The main objective of this study was to determine the prognostic value of metabolic tumor volume (MTV) measured by FDG-PET and potential correlation with CD68 expression, in Hodgkin lymphoma (HL).

Patients and method: The study focused on 46 histologically proven LH pts with available CD68 immunostaining and quantitative initial and post-C2 SUV (Standardized Uptake Value) FDG-PET data. MTV was computed with 3D technical delineation and thresholding method.The threshold (T) corresponds to the average liver SUV (+3 SD) calculated in 50 cm3 of normal liver. All voxels (3D pixels) equal or greater than T belong to MTV. ROC curves were plotted for MTV and SUVmax. CD68 staining was evaluated with a positive threshold of 25% for relative cell expression. EFS, univariate and multivariate analysis were performed using Cox regression model.

Results: n = 46 patients (pts). Median age was 34,5 years (16-77) and sex ratio 0.84. Pts were classified following Ann Arbor stages, I: 4 pts, II: 19 pts, III: 10 pts, IV: 13 pts. Median follow-up was 40 months (12-88). ROC and univariate analysis showed that a high MTV was a significant predictor of an inferior 2 years EFS. MTV cut-off value was 310 cm3 for 2 years EFS (p <0.0001). For pts with MTV > 310 cm3 (n = 19), 2 years EFS was 28% versus 89% when MTV ≤ 310 cm3 (n = 27) (p = 0.0002). MTV was not correlated with CD68 expression. Multivariate analysis showed that MTV is an independent factor to predict outcomes (p <0.001).

Conclusion: In this monocentric HL cohort, a high initial MTV (> 310 cm3) appears to be a predictive marker of adverse outcomes in terms of EFS at 2 years.

C 2 - Salim Kanoun, Ilan Tal, Alina Berriolo-Reidinger, Cedric Rossi, Jean-Marc Reidinger, Jean-Marc Vrigneaux, Louis legrand, Olivier Casasnovas, Francois Brunotte and Alexandre Cochet

Assessment of different thresholds for calculating the total metabolic volume (TMTV) in FDG PET to predict survival in Hodgkin lymphoma

Objective:To investigate the prognostic values of several TMTV calculation methods on baseline PET for Hodgkin lymphoma.Methods:59patients with a first diagnosis of HL were retrospectively included. All patients received 4 to 8 cycles of chemotherapy including ABVD in 50 cases and BEACOPP in 9 cases. Radiotherapy was performed in 14 responding patients with localized disease. PET was performed before any treatment. TMTV was calculated with Beth Israel free software. We used four TMTV calculations methods: fixed absolute cut-off (SUV>2.5), relative threshold (>41% of SUVmax) and per-patient adapted SUV cut-off (>125% and >140% of SUVmax of the liver background). ROI definition was done once by including each foci uptake in a separate ROI and were used for all MTV calculations. ROC curves were used to determine the optimal threshold of TMTV to predict DFS.Results: Median follow-up was 39 months. The mean TMTV value for SUV>41% SUVmax, SUV>2.5, SUV>125% and 140% of liver background were respectively 243 (used as reference), 335 ([28;154] p=0.005), 299 ([-4;114] p=0.06) and 247ml ([-58;64] p=0.9). The respective optimal threshold and AUC were respectively: 313 and 0.70, 432 and 0.65, 450 and 0.65, 330 and 0.63. There was no significant difference between ROC curves. High TMTV value was predictive of worst DFS in all methodologies: OR=4.1 [1.1;15.2] p=0.0053 for 41%, OR=3.8 [1.1;13.8] p=0.0088 for SUV>2.5, OR=5.1[1.4;18.1] p=0.0013 for 125% of liver and OR=5.5 [1.5;20.4] p=0,0006 for 140% of liver.Conclusion: All methodologies had similar prognosis value but with different cut-off. These results need to be validated with reproducibility data before reaching a clinical practice

C 3 - Chirag Patel, Eleanor Jones, Patricia Arce-Calisaya, Cathy Burton. Departments of Nuclear Medicine and Haematology, St James's University Hospital, Leeds, UK; University of Leeds, Leeds, UK

CAN BASELINE VARIABLES ON STAGING FDG PET/CT PREDICT OUTCOME IN ADVANCED HODGKIN LYMPHOMA?

Aim: To investigate whether baseline variables on staging PET/CT can be used to predict progression-free survival in patients with advanced stage II and III Hodgkin lymphoma.

Methods: Retrospective analysis of 77 patients with histologically confirmed Hodgkin lymphoma undergoing staging 18F-FDG PET/CT with advanced stage II or III disease was performed. All patients had a negative bone marrow biopsy. The PET factors assessed were continuous variables SUVmax, metabolic tumour volume (MTV) and total lesion glycolysis (TLG) as well as binary bone marrow uptake pattern as 'normal' or 'reactive marrow hyperplasia'. MTV and TLG were measured at 30% and 40% of maximum SUV. Statistical analysis was performed using Cox-regression analysis and Kaplan Meier survival analysis.

Results: 15 of the 77 patients relapsed during follow-up (mean follow-up time 32 months, range 4-53 months). No significant association was found between SUVmax, MTV or TLG. However, there was a significant association between the 'reactive' bone marrow uptake pattern and progression-free survival (HR 2.78; $p < 0.039$).

Conclusions: Baseline PET variables of SUVmax, MTV and TLG are not prognostic markers of survival in Hodgkin lymphoma, but reactive bone marrow uptake on PET is a significant predictor of poorer progression-free survival.

C 4 - A.S.Cottereau, S.Becker, P.Vera, E.Itti, M.Meignan, C.Haioun, H.Tilly
Nuclear Medicine, Hematology, Rouen, France
Nuclear Medicine, Hematology, Créteil, France

PRONOSTIC VALUE OF METABOLIC TUMOR VOLUME MEASURED ON 18F-FDG PET/CT IN PATIENTS WITH NODAL PRESENTATION T CELL LYMPHOMA

Purpose: The aim of this study was to determine whether total metabolic tumor volume (TMTV) measured on pretreatment 18F-FDG PET/CT can predict prognosis in T cell lymphoma patients with nodal presentation.
Methods: From June 2006 to August 2013, 39 patients with newly diagnosed nodal presentation T cell lymphoma were retrospectively included: 15 angioimmunoblastic T-cell lymphoma, 14 anaplastic large cell lymphoma, 10 peripheral T-cell lymphoma not otherwise specified. All had a baseline PET/CT and were treated with anthracyclines. 95% were stage 3 or 4. TMTV was computed by summing the metabolic volumes of all nodal lymphomatous lesions, measured with constant 41%SUVmax thresholding. Optimal TMTV cut-off to predict PFS and OS was determined by ROC curves, and Kaplan Meier curves were obtained. A multivariate analysis   was   performed   using   a   Cox   model.
Results: Median follow up was 19 months. Median pre therapy TMTV was 220cm3 (21-1950cm3) and SUVmax 13 (6.5-37). The TMTV, with a cut off of 249cm3 was predictive of OS (p=0,0032 HR= 5,7) and PFS (p=0,0007 HR=4,6). The 2-year estimates of PFS was 72% in the low TMTV group vs 15% in the high TMTV group, and 85% versus 35% for OS. Combining TMTV and LDH allowed to identify a group of 14 patients with a bad pronostic : they all relapsed at 2 years (p=0,0004 HR=4,6) and had 2-year OS of 30% versus 86% for the patients with no or only one factor (p=0.0006 HR=7.1). Cox regression showed independency of TMTV for OS and PFS prediction compared with PIT (p=0.02, p=0.01).
Conclusions: For patients with advanced nodal T cell lymphoma, pre-therapy total metabolic nodal tumor volume is highly predictive of PFS and OS.

C 5 – Salim Kanoun, Ilan Tal, Alina Berriolo-Reidinger, Cedric Rossi, Jean-Marc Reidinger, Jean-Marc Vrigneaux, Louis Legrand, Olivier Casasnovas, Francois Brunotte and Anlexandre Cochet

Beth Israel plugin : A new free software tool for metabolic tumor volume calculation on PET/CT

Objective : The project was to build a new free software tool to simplify the calculation of whole-body MTV calculation. Methods : ImageJ is a public domain image processing program developed at the NIH and available for Windows, Mac OS and Linux. The software developed at Beth Israel Hospital is an image J plugin which offers MPR (Multiplanar reconstruction) and MIP (Maximum Intensity Projection) display of PET/CT images. For MTV calculation, the software handles absolute SUV and relative SUVmax threshold. The software allows drawing of irregular and overlapped ROIs. The SUVmax position and the selected voxels for MTV can be displayed for visual control. The accuracy of the MTV results was controlled using phantom images and in a dataset of 59 patients with a baseline PET/CT for Hodgkin lymphoma. We compared the MTV values, area under ROC curves and prognosis value of our software with Keosys software (using 41 % SUV max threshold). Results : With BI plugin, the MTV calculation on the phantom images shows the same value of MTV, SUVmax and SUVmean as the Keosys software (0% difference).In the patients database : the mean MTV value was significantly higher with BI than Keosys (243 vs 207 ml [16.4-54.9] p <0.001). Pearson correlation coefficient was difference between the two packages (AUC=0.711 for Keosys and 0.692 for BI, p=0,64). The optimal MTV cut-off to predict patient outcomes was 225ml for Keosys and 313ml for Beth Israel. Both MTV value using Keosys or BI were predictive of DFS (HR=4.98 [1.4-17.7] p=0.0015 and HR=4.11[1.1-15.2] p<0.005 respectively). Conclusion : Beth Israel software provides the first free and validated software for MTV calculation. This software is open for further developments.

C6 - Dr Sneha Shah, Ashish Jha, Dr Nilendu Purandare, Dr Archi Agrawal, Dr Abhijit Singh, Dr Brijesh Arora, Dr Venkatesh Rangrajan.
Tata Memorial Hospital, Parel, Mumbai, India

TOTAL LESION GLYCOLYSIS (TLG) ESTIMATION IN BURKITT'S LYMPHOMA & UTILITY OF INTERIM RESPONSE ASSESSMENT.

Introduction: The tumor burden in Burkitt's lymphoma often involves a large area making tumor volume estimation difficult. We tried to evaluate a reproducible method to calculate the tumor burden using TLG as a metabolic parameter.

Materials and method : Patients of Burkitts lymphoma patients who underwent a FDG PET/CT study for initial staging and interim response assessment (post 2/3 cycle chemotherapy) from June 2010 to December 2011 were included in the retrospective analysis. FDG PET/CT study was performed on a TOF PET/CT scanner (Astonish TOF, Philips, Cleveland OH) and the analysis was done using an automated software on the EBW NM workstation. The TLG, product of metabolic tumor volume and mean SUV was obtained by drawing region of interest (ROI) using a SUV threshold off 25%. The maximum standard uptake value (SUV max) of the same region was also obtained. Based on the interim scan (PET/CT 1) patients were grouped into responders – Group A and patients with residual metabolism - Group B. Delta (δ) SUV max and TLG were obtained using the formula: 100 (baseline TLG/SUV – PET 1 TLG/SUV/ baseline TLG/SUV in the group B patients. Conventional clinical parameters for response assessment of Burkitts lymphoma like LDH levels, CBC and symptoms of well being were used as a reference. Metabolic response was assessed using SUV and TLG parameters and used to differentiate responders from non responders.

Results: 21 patients: 14 children (median age 6 yrs) and 7 adults (median age 60 yrs), 19 male & 2 female) were included in the analyses.

The disease distribution seen was bowel involvement (n-8) ,nodal disease (n-9) with or without extranodal involvement. One patient each of solitary brain lesion, nasoporoharyngeal mass, only extranodal organ involvement and only marrow disease. 13 patients which showed complete metabolic response as seen by 100% fall of SUV and TLG were grouped into Group A. All these patients (except one who was lost to follow up after 4 month of treatment) had a DFS at the follow up period of minimum 2.5 yrs. One patient lost to follow up. 8/22 patients showed increased FDG uptake were included in group B. 3/8 scans were suggestive of very good response visually with δ TLG greater than 95 and δ SUV less than 90. These patients had a good response to treatment and had a DFS of minimum 2 yrs. 5 patients showed metabolism suggestive of significant residual disease. 3/5 patients showed either progression on treatment later or DFS less than a year. 2/5 patients with significant residual disease both on SUV and TLG parameter (δ SUV 50 and 70 and δ TLG 70 and 85 respectively) at interim analysis were however disease free at follow up of 2.5 and 3 yrs respectively.

Conclusion: Interim PET/CT has a high NPV and identifies responders and can be considered as a good prognostic factor. δ TLG appears to be a good parameter in identifying responders with residual disease on interim scan. The small patient population in the study and its retrospective nature did not allow statistical correlation between the parameters and would warrant a large prospective study for evidence.

D 1 – AS. Cottereau, S. Kanoun, E. Itti, C. Haioun, S. Legouil, M. André, O. Reman, J. Chalaye, RO. Casasnovas, M. Meignan.
Nuclear Medicine, Créteil, Dijon, France.
Hematology, Créteil, Dijon, Caen, Nantes, France ; Louvain, Belgique.

VARIABILITY OF 18-FDG LIVER UPTAKE BETWEEN BASELINE AND INTERIM PET/CT IN PATIENTS WITH LYMPHOMA

Introduction: The liver uptake is a main factor for the evaluation of interim PET according to Deauville criteria. The aim of the study was to evaluate the intrapatient variability of 18F-FDG liver uptake for patients with diffuse large B-cell lymphoma (DLBCL) or Hodgkin lymphoma (HL), after two courses of chemotherapy.
Materials and Methods : 775 patients, from randomized phase III studies, underwent PET/CT before treatment (PET0) and after 2 cycles of chemotherapy (PET2): 162 DLBCL from GAINED protocol, 81 treated by R-CHOP and 81 by R-ACVBP, 514 HL from the standard arm of AHL 2011 treated by escalated BEACOPP and 99 early stages HL from H10 treated by ABVD.
Liver SUVmax, calculated from a VOI in the right lobe of the liver were the means of measures obtained independently by 2 nuclear physicians. We compared the liver uptake of PET0 and PET2 for each patient using a paired student t test.
Results: For all patients, either in early or advanced disease, interim liver SUVmax was higher than baseline SUVmax.

	Mean SUVmax 0	Mean SUVmax 2	
CHOP	2.94 (CI=2,78-3,10)	3.16 (CI=3,02-3,31)	$p=0.0002$
ACVBP	3.12 (CI=2,96-3,28)	3.34 (CI=3,20-3,47)	$p=0.0002$
BEACOPP	2.70 (CI=2,64-2,76)	2.93 (CI=2,87-2,99)	$p<0.0001$
ABVD	2.35 (CI=2,24-2,46)	2.53 (CI=2,42-2,64)	$p=0.0001$

Conclusion: Whatever the type of chemotherapy used for the treatment of DLBCL or HL, the liver SUVmax increases after the 2 first cycles of chemotherapy for all patients, including those with early stage. This suggests that it might be a variation of the hepatic metabolism. The impact of the liver SUVmax evolution during treatment on the visual analysis interpretation of interim PET is probably minor, but it encourages to determine more precisely the Deauville score 4 threshold, as it has been done for score 5 (S.Barrington, JCO, 2014).

D 2 - Karen Juul Mylam, Anne Lerberg Nielsen, Poul-Flemming Høilund-Carlsen, Abass Alavi, Oke Gerke, Poul Erik Braad, Anne Birgitte Mehlsen, Morten Damgaard, Lars M Pedersen, Martin Hutchings.

Dual time point 18F-FDG PET/CT in the evaluation of patients with suspected malignant lymphoma

We examined differences in tracer uptake with 1-hour and 3-hour FDG PET/CT imaging in patients with suspected malignant lymphoma to see (a) if late imaging uptake was significantly different, (b) to what degree higher late uptake improved discrimination of malignant from benign disease and (c) if a commercial program (PET VCAR) designed to evaluate lesion metabolic activity over time, showed comparable time-dependent differences. Methods: 35 patients with suspected malignant lymphoma were prospectively enrolled. Seven had benign and 28 malignant lymphadenopathy. FDG-PET/CT was performed 60 and 180 minutes after administration of FDG. Maximum standardized uptake values (SUV) were obtained from liver, spleen, mediastinal blood pool, bone marrow and metabolically active lymph nodes.

Results: Median ΔSUVmax was 4.0 in patients with lymphoma compared to 1.3 in patients without, p=0.005. Median RI was also higher: 0.33 versus 0.10, p=0.02. With time, there was a significant decrease in the uptake in mediastinal blood pool (p=0.02) and significant increase in bone marrow (p<0.001) and spleen (p=0.01), whereas the uptake in the liver and benign lymph node was unchanged (p= 0.67 & p=0.15). Among patients with malignant disease, MTV60 did not differ from MTV180 (p=0.78), whereas TLG180 and SUVmax180 were significantly higher than TLG60 and SUVmax60 (p<0.001 and p<0.001, respectively)Conclusion: Dual time point imaging was useful for discriminating benign from malignant lymphadenopathy because malignant nodes had significantly higher SUVmax and TLG at late imaging. FDG-avidity of the liver appears to be independent of time and a susuitable reference organ.

D 3 - JM Zijlstra, dept Hematology, OS Hoekstra, dept Radiology and Nuclear medicine, HCW de Vet, dept Epidemiology and Biostatistics. VU University Medical Center, Amsterdam, on behalf of PETRA Consortium

Validation of interim PET as a biomarker of response in NHL – a study on PET timing, therapies, response criteria, type of NHL and cost-effectiveness.

In lymphoma, FDG-PET is a promising application for 'early response assessment', meaning that response to treatment is predicted using PET during treatment. Several observational studies have indicated that interim FDG-PET may be effective but inconsistencies prevail, especially in non-Hodgkin's lymphoma. It is unclear to which extent these are due to differences in the timing of PET during therapy, different PET positivity criteria, different therapies and/or different subtypes of lymphoma. There is an urgent need to address these issues but this requires an integral approach using the results of various studies. Therefore, we propose to build a PETRA database for lymphomas. PETRA stands for PET Re-Analysis. The PETRA database is a comprehensive and unique shared database of individual patient data (IPD) of studies on interim FDG-PET to evaluate the potential impact of PET timing, therapies, response criteria and type of lymphoma on the interim FDG-PET test performance. Only after these issues are solved, this promising technique can be implemented in daily clinical practice.

Overall aim is to validate FDG-PET as a biomarker of response in first-line NHL therapy using meta-analysis of IPD and to determine its cost-effectiveness.

Objectives

1.	To build a database consisting of IPD (including PET scan) of clinical studies on interim-PET in NHL

2.	To determine the optimal timing of interim FDG-PET during first-line therapy

3.	To determine which response criteria perform best predicting response and PFS

4.	To assess whether and how therapy affects the performance of interim FDG-PET

5.	To assess whether and how type of NHL affects the performance of interim FDG-PET

D 4 - A.I.J. Arens, B. de Keizer, O.S. Hoekstra, C. Schaefer-Prokop, J. Stoker, J. M. Zijlstra on behalf of the HOVON Imaging Working Group in the Netherlands.

HEMATOLOGISTS' S PERSPECTIVES AND DESIRES ON REPORTING OF PET AND CONTRAST ENHANCED CT IN MALIGNANT LYMPHOMA IN THE NETHERLANDS

Aim. To investigate the variation in reporting PET and contrast enhanced CT (ceCT) in malignant lymphoma in the Netherlands and the perceptions and desires regarding format, content and quality by the referring hematologists.

METHODS. A nationwide web-based survey was distributed among all hematologists, concerning the actual reporting, preferences of the hematologists and need for guidelines on reporting.

RESULTS. 37% of all hematologists responded. 26% is working in a teaching hospital, 30% in a non-teaching hospital without PET/CT and 44% in one with PET/CT. In 46%, the format of the report is divided into body parts, in 21% into disease localisations, and in 17% there are no divisions. Preference for reporting per body part is 47% and per disease localisation 36%. Deauville criteria are used in 49% and desired (whether present or not) in 62%. All hospitals use visual criteria and 29% of respondents request SUV-based assessment. Measurements of lymph nodes are not performed according to any criteria in 41%. Up to 62% prefer the revised Cheson criteria for CT measurements. A combined report of PET and CT is performed in 48% and is desired in 84%. Ann Arbor classification is mentioned in 29% and desired in 42%. In 67%, hematologists report that the multi-disciplinary meeting is of influence on the interpretation. The need for standardisation of reporting is expressed by 69%.

CONCLUSION. A national survey among hematologists reveals considerable variations in methods of reporting of PET/ceCT. Our findings illustrate the need for standardisation of reporting to optimize PET/ceCT in patients with malignant lymphoma.

D 5 - B. de Keizer, A.I.J. Arens, O.S. Hoekstra, C. Schaefer-Prokop, J. Stoker, J. M. Zijlstra on behalf of the HOVON Imaging Working Group in the Netherlands.

VARIATIONS IN PET/(CONTRAST ENHANCED)CT OPERATIONS AND REPORTING: RESULTS OF A NATIONAL SURVEY OF NUCLEAR MEDICINE PHYSICIANS IN THE NETHERLANDS

AIM. To investigate the variation in performing and reporting of PET and contrast enhanced CT (CECT) in malignant lymphoma in the Netherlands.
METHODS.
A nationwide web-based survey was distributed among all nuclear medicine physicians, concerning the acquisition of PET and CECT, the method of reporting PET/CECT and the criteria used for response assesment.
RESULTS. 56 of 166 (33%) nuclear medicine physicians responded. 30% is working in a teaching hospital, 14% in a non-teaching hospital without PET/CT and 55% in one with PET/CT. 59% combine the acquisition of PET and CECT on PET/CT systems when both are indicated. A combined report of PET and CECT is performed by 38%, in 39% reports are not combined and a separate report of the CECT is made by a radiologist. For PET/CECT reporting 23% always use Deauville criteria, 16% use Juweid criteria, 11% use SUV and 34% use different criteria depending on timing of PET in treatment schedule. Measurements of lymph nodes are performed according to revised Cheson criteria in 34%, RECIST criteria in 11% and in 38% of hospitals, this is variable among radiologists. Ann Arbor classification is mentioned in 34%. 61% of nuclear medicine physicians report that the multi-disciplinary tumoboard meeting has impact on their interpretation of the scans. The need for standardisation of reporting is expressed by 61%.
CONCLUSION.
A national survey among nuclear medicine physicians reveals considerable variations in clinical PET/CECT operations and reporting. Our findings underline the need for standardisation to uniform operations and reporting of PET/CECT in patients with malignant lymphoma.

D 6 - Chaitra Ujjani, Elizabeth Hill, Samer Nassif, Hongkun Wang, Metin Ozdemirli, Giuseppe Esposito, Christina Cordova, Yiru Wang, Bruce Cheson, Lombardi Comprehensive Cancer Center, Georgetown University

THE UTILITY OF 18F-FDG PET/CT IN ASSESSING BONE MARROW INVOLVEMENT IN LYMPHOMA

Background: The ability of 18F-FDG PET/CT scan to accurately detect bone marrow involvement (BMI) has been suggested in Hodgkin's and DLBCL, but its accuracy in other histologies is less well established. This retrospective study evaluated the utility of 18F-FDG PET/CT in detecting BMI in subtypes of lymphoma.

Methods: At our center 290 patients underwent coinciding bone marrow biopsies and PET/CT scans from 2005-13.

Results: Of the 149 newly diagnoses, common subtypes included DLBCL (58), follicular (53), and Hodgkin's (25). Most had scans prior to biopsy (69). In DLBCL, sensitivity and specificity of PET/CT were 75% and 92%. PET/CT failed to identify 2 with focal BMI. Both were already advanced stage based on imaging. In the relapsed setting, PET/CT accurately identified 2 with BMI. In follicular, sensitivity and specificity were 43% and 84%. The majority of patients in which PET/CT failed to identify BMI, were already advanced stage by imaging. In Hodgkin's, the sensitivity and specificity were 67% and 73%. PET/CT did not identify 1 with BMI. As the patient was stage III by imaging, this did not impact the treatment decision. PET/CT detected BMI in 4 DLBCL, 5 follicular, and 6 Hodgkin's patients with negative biopsies, presumably due to lack of iliac involvement.
Conclusions: 18F-FDG PET/CT is an accurate test for detecting BMI in DLBCL and Hodgkin's lymphoma. It is able to detect BMI in patients who would have been considered negative by biopsy alone. It was not as accurate in follicular lymphoma, presumably due to the low-grade nature of the disease. Prospective evaluation is necessary and may eliminate the need for biopsies in future patients.

D 7 - Chauvie S1, Biggi A1, Versari A2, Guerra L3, Ceriani L4, Coronado M5, Luminari S6, Federico M6, Zucca E4, Martelli M7, Caballero M8, A Gallamini9

PET SCANNER CLINICAL TRIAL QUALIFICATION FOR WORLDWIDE ONCO-HAEMATOLOGICAL STUDIES

Purpose: to present the results of the procedure for qualifying PET scanners for Clinical Trial (CTQ) adopted by the Italian Foundation on Lymphoma (FIL), International Extra Nodal Lymphoma Research Group (IELSG) and Spanish lymphoma group (GELTAMO).

Methods: Uniform and image quality NEMA/IEC phantoms acquired by local personnel with standard acquisition and reconstruction techniques were uploaded to a central server and analyzed within the CoreLab. Measured activity concentration (AC) was compared to expected values in the uniform phantom. Recovery coefficient (RC) curve was calculated in the NEMA/IEC phantom and compared to EANM guidelines .

Results: At now 76 scanners have been CTQed. The CTQ was carried out with a single iteration in 22% of sites, with 2 in 27%, with 3 in 27% and with ≥ 3 in 24%. The problems during CTQ were: a) incorrect sphere filling (filled with wrong activity in 5 cases, with presence of bubbles in 2 cases and with only 4 sphere hot in 12 cases), b) a measured activity different from that expected (14 cases) and c) missing data for reference activity calculation (10 cases) or CT images (3 cases), d) difference between measured and expected activity (14 cases), e) missing data for activity calculation (6 cases), f) uploaded images were not in DICOM format (1 case) and g) a wrong reconstruction algorithm was applied to the images (5 cases). Two PET sites acquired a NEMA/IEC phantom after CTQ request and one a dose calibrator source. Difference in expected versus measured AC in the uniform phantom were (1.2 ± 7.)% ranging form -9.8% to 9.9%.

Conclusions: Despite the EAMN recommendation not all the PET sites have a quality programi in place .

D 8 - S Chauvie, G Borretto, J Redic, L. Tegelmann, F Bergesio, A Terulla, F Fioroni, M Brambilla, R Caivano, A Biggi, A Versari, G Storto, P.Musto, A Gallamini

68GE-PHANTOM CROSS-CALIBRATION OF PET SCANNERS FOR SUV QUANTITATIVE ANALYSIS

The aim of this work is to verify whether errors due to instrumentation could be reduced using a procedure for PET cross-calibration with a long half-lived phantom.

Material and Methods: a NEMA NU-2 image quality phantom filled with 68Ge/68Ga in an epoxy matrix as seen with 4:1 sphere to background ratio (SBR) and two additional wall-less spheres [Eckert & Ziegler] was then circulated across 7 PET centres in Italy. The phantom was repeatedly imaged as follows: a) 3 acquisitions in the same position on the patient table (repeated studies); b), 10 acquisitions with the phantom removed from the scanner and repositioned again (repositioned studies); c) 10 acquisitions in different days (intra-scanner variability); d) 10 distinct types of scanners from different manufacturers using the acquisition and reconstruction parameter used in clinical practice (inter scanners studies).

Results; average activity concentration (AC) in 2D or 3D regions of interests (ROI or VOI) was the best estimates of the reference AC (<3% diff), while peak was the best estimate for SBR (<3% diff). Recovery Coefficient curves for max AC laid in the upper part of EANM recommendations. Max, peak, hot average (5 hottest voxels) SBR did not change when measuring in ROI or VOI. Averages on VOI of the sphere nominal dimension were lower respect to ROI due to higher spill-out effect, notably being proportional to their volumes.

The reproducibility of the measurements of the different parameters for AC and SBR were always lower than 3% when using a 18F filled phantom in a previous qualification program.

Conclusions 68Ge phantom can be used for absolute scanner calibration within a multicentre consortium.