PET

215 QUANTITATIVE INTERIM PET IS MORE ACCURATE THAN QUALITATIVE ASSESSMENT IN PREDICTING OUTCOME IN DLBCL

R. L. Elstrom[1], P. Martin[1], L. Solnes[2], R. R. Furman[1], J. Ruan[1], F. Novruzov[2], M. Coleman[1], J. P. Leonard[1], J. Osborne[2]
[1]*Medicine, Weill Cornell Medical College, New York, United States,* [2]*Radiology, Weill Cornell Medical College, New York, United States*

Background: Approximately half of patients with diffuse large B cell lymphoma (DLBCL) are cured with standard initial therapy. Although the International Prognostic Index (IPI) defines prognostic groups, it does not predict outcome for an individual patient. In Hodgkin lymphoma, functional imaging with FDG-PET is highly predictive of outcome when performed early in treatment. In DLBCL, however, positive vs. negative interim FDG-PET has been less useful.

We explored the utility of evaluating quantitative change in FDG uptake, rather than achievement of metabolic complete response, at early interim PET as a predictor of outcome in DLBCL.

Materials and Methods: Patients with newly diagnosed DLBCL who were to receive standard R-CHOP chemotherapy were prospectively enrolled and provided informed consent. FDG-PET scans were performed prior to treatment (PET-1) and after 2 cycles (PET-2) of R-CHOP. Interim scans were scored as positive or negative according to ECOG criteria. For quantitative analysis, percent change in SUV was calculated after correcting for background.

Results: Thirty-five patients have been enrolled to date, of which 6 are not yet evaluable. Median follow up of evaluable patients is 24 months (range 0.5-47 months). All patients achieved complete remission (CR) by PET criteria at end of treatment. Three patients experienced disease recurrence at median of 5.5 (range 2-7) months, while 26 were in continued CR at last follow up. Of 22 patients with negative PET-2, 21 (95%) remained in remission, while 5 of 7 (71%) patients with positive PET-2 remained in remission. Although there was a trend to better outcome with negative PET, the difference was not significant ($p=0.07$). When analyzed quantitatively, 27 patients showed ≥80% reduction in SUVmax, of whom one relapsed. Two patients showed less than 80% reduction, and both relapsed. The difference in outcome between patients with ≥80% and <80% reduction was significant ($p<0.01$). In this small sample, the positive predictive value of residual FDG uptake using the 80% cutoff was high (100%). Evaluation of IPI or individual factors composing the IPI did not provide additional prognostic information.

Conclusion: These data suggest that quantitative change in SUV on interim PET may be more predictive of outcome than qualitative assessment (positive or negative) and that this approach should be prospectively tested in comparison to other risk-defining strategies.

216 DISCRIMINATORY POWER OF THE 111-INDIUM SCAN (111-IN) IN THE PREDICTION OF ALTERED BIODISTRIBUTION OF RADIO-IMMUNOCONJUGATE IN THE 90-YTTRIUM IBRITUMOMAB TIUXETAN THERAPEUTIC REGIMEN: DATA FROM 5 TRIALS AND 9 YEARS OF CLINICAL EXPERIENCE IN 45 COUNTRIES

J. W. Kylstra[1], M. Huang[1], C. Emmanouilides[2], A. Hagenbeek[3], G. Wiseman[4], C. Von Schilling[5]
[1]*Clinical Development, Spectrum Pharmaceuticals, Irvine, United States,* [2]*Hematology, InterBalkan Hospital, Thessaloniki, Greece,* [3]*Hematology, Academic Medica Centre (AMC), Amsterdam, Netherlands,* [4]*Nuclear Medicine, Mayo Clinic, Rochester, MN, United States,* [5]*Innere Medizin III, Klinikum Freising, Freising, Germany*

Background: At the time of regulatory approval of ibritumomab tiuxetan (Zevalin™-Z) in 2002 (USA) and subsequently elsewhere, 3 countries (USA, Switzerland, Japan) required labeling specifying that a 111-In imaging scan be performed 7-9 days before the therapeutic 90-Y Z dose, to guard against that the hypothetical risk that altered biodistribution (AB) of the radio-immunoconjugate could cause unintended end organ damage; 42 other countries (incl. EU, Canada) approved Z without requiring a 111-In scan.

Methods:

1. Establishment of the false positive and true positive rate (positive predictive value) of the 111-In scan in predicting AB with data from 5 clinical trials that supported approval of Z for follicular lymphoma. Trials had subjected 111-In scans to both local- and secondary (expert) review.
2. Comparison of safety surveillance data from pts treated in countries that do- versus do not require the 111-In scan as part of the Z therapeutic regimen, with focus on anaphylactoid reactions and Grade III/IV bone marrow suppression states.

Results: In 5 clinical trials, 11 of 253 scans (4.3%) showed AB based on local review. In only 3 of these pts, the local finding of AB was confirmed in central review. Of pts with 111-In scans reviewed by a trained reader in central review, 3/233 (1.3%) were found to have true AB and 7/233 (3%) were found to have had a false positive local judgement of AB. Three pts with true AB on central review who had proceeded with 90-Y Z treatment based on a scan result locally judged normal, showed safety and efficacy outcomes within the range of those shown by other pts on study. Comparison of post-marketing safety databases between countries with (USA, CH, JP) and without (Rest of World) 111-In requirement showed no differences in the general pattern of safety signals reported, with resp 3% and 4% of pts reporting grade III/IV bone marrow suppressive states, and anaphylactoid responses reported at 0.3% in both geographic clusters.

Conclusion: The 111-In scan shows poor discriminatory power in identifying cases of AB. Analysis of safety results of pts treated with 90-Y Z despite true AB does not indicate that removal of the 111-In requirement from the Z labeling in countries currently requiring it would constitute a safety risk.

217 18FDG UPTAKE CHANGES IN LIVER AND MEDIASTINUM DURING CHEMOTHERAPY IN DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): IMPACT ON THE EVALUATION OF INTERIM PET-CT

L. Ceriani[1], S. Suriano[1], T. Ruberto[1], A. Moccia[2], E. Zucca[2], L. Giovanella[1]
[1]*Department of Nuclear Medicine, PET/CT Centre, Bellinzona, Switzerland,* [2]*Lymphoma Unit, Oncology Institute of Southern Switzerland (IOSI), Bellinzona, Switzerland*

Background: 18F-FDG PET scan performed early during the therapy of DLBCL has emerged as a prognostic tool with a great potential in predicting treatment outcome. However, the standardization of interpretation rules for the interimPET-CT scan still remains an unsettled issue. The mediastinum blood pool (MBP)18F-FDG activity and the liver (LIV) 18F-FDG uptake have been proposed as references for the visual analysis of interim-PET scans in lymphoma patients during chemotherapy but consensus about their integration into standardized criteria has not yet reached. Nevertheless, it has been recently suggested that the use of LIV background should replace the MBP (which is the current international reference for end-of therapy evaluation) in the analysis of interim PET (Itti et al. JNM 2010). This study aimed at assessing the inter- and intra-subjects variability of MBP and LIV uptakes in patients with DLBCL treated with the R-CHOP regimen.

Materials and Methods: Twenty-five DLBCL patients with 18F-FDG PET-CT performed at baseline, after 2 cycles (interim-PET) and after the end of therapy (final-PET) were analysed retrospectively. SUVmean values (SUVm) for LIV and MBP, their difference (LIV-SUVm – MBP-SUVm) and their changes were calculated, respectively.

Results: The inter-subjects variability (SD/mean x 100) of MBP-SUVm and LIV-SUVm ranged from 13%-18.5% and 12%-14%, respectively. The LIV-SUVm significantly increased in the interim as compared with baseline-PET and slightly decreased at the final-PET. Viceversa, the MBP-SUVm showed no significant changes during chemotherapy. The difference between LIV-SUVm and MBP-SUVm ranged -0.17 to1.21, 0.3 to1.36 and 0.08 to 0.76 in basal, interim and final-PET examinations, respectively. The inter-subjects variability was 88%, 41% and 42%, in basal, interim and final PET respectively. In two cases the MBP-SUVm was higher than LIV-SUVm and in 7 the difference was ≤ 0.25. An increase in this difference was found in final and, particularly, in the interim-PET examination ($p<0.05$).

Conclusions: Our data suggest that both liver and mediastinum 18F-FDG uptake may be inadequate as references for the evaluation of different degrees of early response to R-CHOP. Particularly, the intra-subject variability of the liver uptake during immunochemotherapy recommends great caution in employing it as gatekeeper in risk-adapted therapeutic strategies.

218 FIRST RESULTS OF A PROSPECTIVE EVALUATION OF INTERIM PET IN PATIENTS WITH DLBCL TREATED WITH R-CHOP-14 (SAKK 38/07)

C. Mamot[1], D. Klingbiel[2], M. Bargetzi[1], C. Renner[3], F. Hitz[4], T. Pabst[5], U. Mey[6], R. Herrmann[7], M. Pless[8], M. Schaedler[2], T. Hany[3], E. Zucca[9], G. Martinelli[10]
[1]*Onc, KSA, Aarau, Switzerland,* [2]*TC, SAKK, Bern, Switzerland,* [3]*Onc, USZ, Zürich, Switzerland,* [4]*Onc, KSSG, St. Gallen, Switzerland,* [5]*Onc, Inselspital, Bern, Switzerland,* [6]*Onc, KSGR, Chur, Switzerland,* [7]*Onc, UHBS, Basel, Switzerland,* [8]*Onc, KSW, Winterthur, Switzerland,* [9]*Onc, EOC, Bellinzona, Switzerland,* [10]*Onc, IEO, Milano, Italy*

FDG-PET provides functional tissue characterisation and has been used in patients with various lymphomas. Early assessment of therapeutic response by a robust imaging tool is potentially useful in order to stratify patients for risk-adapted therapy strategies. Our main objective was to determine the prognostic value of FDG-PET after 2 cycles of R-CHOP-14, prospectively and under standardized conditions.

Patients with all stages of DLBCL were treated with 6 cycles of R-CHOP-14, followed by 2 cycles of rituximab. FDG-PET exams were performed at baseline, after 2 cycles, after 4 cycles (if positive PET after 2 cycles) and at the end of treatment. PET positivity was defined as a measurable and evaluable lesion(s) with a SUVmax (lesion) > SUVmax (blood pool). A modified definition subtracted 15% of the lesion SUVmax and added 15% to the blood pool value. PET exams are evaluated locally and by central review. The primary endpoint was Event Free Survival (EFS) at 2 years.

Between 01/2008 and 05/2010 156 patients with newly diagnosed DLBCL were prospectively enrolled. By Dec 2010, data from 114 patients were available. Median age was 60 years with a WHO performance status (PS) of 0 in 55%, PS1 in 37% and PS2 in 8% of cases. According to IPI, low risk was found in 54 patients (49%), low-intermediate risk in 22 (20%), high-intermediate risk in 18 (17%), and high risk in 15 (14%) with missing information of 5 patients. PET exams of all patients before and after 2 cycles of R-CHOP-14 are available for this analysis, while 51 patients had an additional PET exam after 4 cycles. 61% (for modified definition = 43%) of PET exams were defined as positive after 2 cycles by local institution. 71% (59%) of these exams remained positive after 4 cycles of therapy while 29% (41%) changed to negative. 100% (90%) of patients with a negative PET after 2 cycles reached a complete response (CR) at the end of treatment. For PET positive patients a CR was achieved in 52% (45%), respectively. Updated results on response will be presented at the conference. Data on EFS at 2 years are not mature at the time of this analysis.

We conclude from this preliminary analysis, that a negative PET after 2 cycles of R-CHOP-14 predicts a very high probability of CR. However, a positive PET cannot exclude complete remissions subsequently. PET has to confirm its usefulness in standardized studies like this one before it can be used in risk-adapted therapies.

219 POSITIVE INTERIM ^{18}F[FDG] POSITRON EMISSION TOMOGRAPHY SEEMS NOT TO PREDICT RELAPSE IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

F. Gigli[1], A. Gardellini[1], P. Bertazzoni[1], L. Travaini[2], M. Negri[1], L. Nassi[1], L. Preda[3], G. Martinelli[1]

[1]Haematoncology, European Institute of Oncology, Milan, Italy, [2]Nuclear Medicine, European Institute of Oncology, Milan, Italy, [3]Radiology, European Institute of Oncology, Milan, Italy

Diffuse Large B-Cell Lymphoma (DLBCL) is the most frequent aggressive non-Hodgkin's Lymphoma in adults. Prognostic stratification relies on clinical characteristics and International Prognostic Index (IPI) is the most useful tool to identify high-risk patients (pts). Positron Emission Tomography (PET) with fluorodeoxyglucose (^{18}F[FDG]) has been used to assess chemosensitivity in Hodgkin's lymphoma: we investigated the role of ^{18}F[FDG]-PET as prognostic tool in DLBCL treated with a R-CHOP-like treatment.

42 pts with newly diagnosed DLBCL treated in our Institute from 2006 to 2008 were enrolled in this prospective study. Median age was 59 years (24-80), 17 pts were male. Stage was I-II in 18 and III-IV in 24 pts; IPI was low in 20 pts, intermediate in 17 pts and high in 4. Pts received 6 cycles of R-.CHOP-like therapy every 21 days. An interim ^{18}F[FDG]-PET was performed after 3 cycles (interim PET) and at the end of therapy (PET6). Interim PET result did not modify the treatment; response was assessed with 1997 Cheson's criteria.

36 pts obtained a complete response (CR). Median follow-up was 32 months, 3 pts relapsed and 8 pts died, 2 of them in CR. Overall survival at 52 months was 81% and event-free survival (EFS) at 52 months was 81%. Interim PET was performed after a median interval from the last therapy of 13 days and was negative in 30 pts and positive in 12.

1 positive and 2 negative interim PET pts relapsed: sensitivity was 83%, specificity was 80%, positive and negative predictive values were 42% and 97%, respectively. PET6 was positive in 11 pts and negative in 31 pts; 6 positive and 3 negative PET6 pts relapsed or progressed. The EFS at 52 months in pts with negative interim PET was 93%, in positive interim PET pts was 50% which resulted statistically significant in univariate analysis (p=0.001). Pts with refractory or relapsed disease received a salvage therapy, 4 of them with intensified chemotherapy and autologous stem cells transplantation (ASCT). 3 out of 4 died for progression disease during the ASCT, 1 obtained a CR.

Interim PET was proposed as a prognostic tool in DLBCL. Our data showed that interim PET negative was statistically associated with prolonged EFS, 7 pts with a positive interim PET obtained a CR after 6 cycles of planned therapy and 6 pts did not relapse.

In our experience the low (43%) positive predictive value of interim PET does not justify any change in treatment included ASCT because of the risk of overtreatment a large part of them.

220 RISK-ADAPTED THERAPY USING BIOPSY CONFIRMATION OF ABNORMAL INTERIM FDG-PET FOR PATIENTS WITH ADVANCED STAGE DIFFUSE LARGE B CELL LYMPHOMA (DLBCL), AND EXPLORATORY EVALUATION OF FLT-PET

C. H. Moskowitz[1], H. Schoder[2], P. A. Hamlin[1], J. F. Gerecitano[1], S. M. Horwitz[1], M. J. Matasar[1], A. J. Moskowitz[1], A. Noy[1], M. Palomba[1], C. S. Portlock[1], D. J. Straus[1], T. A. Graustein[1], J. Teruya-Feldstein[3], A. D. Zelenetz[1]

[1]Lymphoma Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, United States, [2]Nuclear Medicine Service, Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, United States, [3]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, United States

Introduction: We previously reported on the use of a sequential treatment (tx) program, R-CHOP-14 x4 followed by ICE x3, with an 80% 5-y PFS (JCO 2010; 28 (23): 3754-3761). Interim (int) FDG-PET scan did not predict outcome. Patients (pts) with a positive (pos) int PET underwent biopsy (bx), of which 85% were negative (neg). PFS was identical for pts with int pos PET and a neg bx, vs. int PET neg. In the current study, the induction tx was altered in an attempt to reduce the rate of false pos int FDG-PET. Based on the prior study we also augmented consolidation for pts with a proliferative index (PI) of ≥80%.

Methods: Eligible pts were <70 with advanced stage DLBCL or primary mediastinal large B cell lymphoma (PMBCL). Pre-treatment evaluation included CT with contrast, FDG-PET and research ^{18}flourothymidine (FLT)-PET scan. Induction consisted of R-R-CHOP-14 x 3 then CHOP-21 x 1 followed 17-20 days later by a repeat FDG-PET, and bx if FDG-PET pos. Consolidation was risk-adapted: int FDG-PET neg or bx neg: ICE x 3 for PI <80% and augmented RICE x2 for PI ≥ 80%. If the bx was pos, augmented RICE x 2 followed by HDT/ASCR. Primary endpoint is 3 year PFS. Use of FLT-PET was exploratory. In the first 30 pts FLT-PET was repeated after cycle 1 and after cycle 2 in the next 30 pts.

Results: To date, 50 pts are evaluable, median age is 52. Pt characteristics: elevated LDH (88%); stage IV (72%); KPS ≤70 (26%); PI≥80 (34%); age-adjusted (aa) IPI: low intermediate (LIR), HIR and HR, 25%, 50% and 25% respectively. At median follow-up of 18 months, the PFS and OS are 86% and 96%, respectively. None of the pretreatment clinical or pathologic risk factors were prognostic including PI>80 (p=0.44), cell of origin (p=0.29), DLBCL vs. PMBCL (p=0.42), and aaIPI HR disease (p=0.38). As in our previous study, pts with int FDG-PET pos scan did not have an inferior PFS compared with those with a neg scan (p=0.27); in addition patients with neg int bx had the same PFS as those with a neg int PET (p=0.91). There was a trend for pts with an int delta SUV of <70% (6 pts) to have an inferior PFS (p=0.08). FDG-PET at end of tx predicted for PFS: 4/6 pts with a true pos scan have progressed (p <0.001).

Conclusions: These results confirm the excellent PFS of sequential R-CHOP-14/ICE program (MSKCC 01-142). Despite altering the chemotherapy schedule and delaying interim restaging by one week, int FDG-PET scans did not predict PFS, although further analysis of delta SUV may be valuable. The study is ongoing and a comparison of FLT and FDG for staging and int evaluation will be presented.

221 PREDICTIVE VALUE OF EARLY PET IN HIGH-RISK AGGRESSIVE LYMPHOMA PATIENTS TREATED WITH VERY INTENSIVE FRONT-LINE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANT

R. Pytlík[1], D. Belada[2], D. Šálek[3], O. Bělohlávek[4], M. Trněný[1]

[1]Department of Clinical Medicine, General University Hospital, Praha 2, Czech Republic, [2]Second Clinics of Internal Medicine, Department of Hematology, University Hospital Hradec Králové, Hradec Králové, Czech Republic, [3]Department of Internal Medicine - Hematooncology, University Hospital Brno, Brno, Czech Republic, [4]Department of Nuclear Medicine, Nemocnice na Homolce, Prague, Czech Republic

Background: In 2008, we presented at Lugano meeting results of a subgroup of patients treated in the R-MegaCHOP-ESHAP-BEAM study (R-MEB), in which early PET after 2-3 cycles of chemotherapy was performed. Early PET negative patients had better lymphoma-free survival (LFS), but not progression-free survival (PFS), or overall survival (OS). Now we are presenting additional data, based on inclusion of patients treated with the same protocol in past three years, who had early PET performed.

Patients and Methods: Patients 18-65 years with diffuse large B-cell lymphoma (DLBCL), follicular lymphoma grade 3 (FL3) or composite DLBCL/FL lymphoma, with aaIPI 2-3 were eligible for the study. Treatment consisted of 3 cycles of high-dose R-CHOP (rituximab, 375 mg/m2, cyclophosphamide, 3g/m2, doxorubicin, 75 mg/m2, vincristin, 2 mg and Prednison 300 mg/m2 + G-CSF) every three weeks, followed by 3 cycles of R-ESHAP and high-dose BEAM with autologous stem cell transplant. PET was performed after 2 or 3 cycles of R-MegaCHOP.

Results: 91 patients were included in this analysis. Median age was 39 years (range, 18-62) and 58% of them were males. 56% of patients had aaIPI 2 and 44% aaIPI 3. Median follow-up was 54.7 months for living patients (range, 8.7-104.2 months). The OS at three years was 82±4%, PFS was 79±4%, and LFS was 82±4%. 36 patients (40%) had their early PET positive and 55 negative (60%). Early PET negative patients had better 3-year LFS (90±4% v. 70±8%, p = 0.03) and PFS (87±5% v. 67±8%, p = 0.05) than PET positive patients, but not OS (88±5% v. 73±8%, p = 0.21). Positive predictive values of positive PET for LFS, PFS and OS were only 28%, 31%, and 22%, while negative predictive values of negative PET were 89%, 85%, and 87%, respectively.

Conclusion: Intensive treatment in early PET positive patients can at least partially overcome the negative prognostic impact of this examination, however, early PET negative patients still fare better in terms of progression-free and lymphoma-free survival.

222 PROGNOSTIC SIGNIFICANCE OF INTERIM ^{18}F-FDG PET/CT AFTER THREE OR FOUR CYCLES OF R-CHOP CHEMOTHERAPY IN THE TREATMENT OF DIFFUSE LARGE B-CELL LYMPHOMA

D. Yang[1], J. Min[2], Y. Jeong[3], S. Bae[1], J. Ahn[1], Y. Kim[1], H. Bom[2], I. Chung[1], H. Kim[1], J. Lee[1]
[1]Hematology-Oncology, Chonnam National University Hwasun Hospital, Jeollanam-do, Korea, Republic of, [2]Nuclear Medicine, Chonnam National University Hwasun Hospital, Jeollanam-do, Korea, Republic of, [3]Radiology, Chonnam National University Hwasun Hospital, Jeollanam-do, Korea, Republic of

^{18}F-fluoro-2-dexoy-D-glucose-positron emission tomography (FDG-PET)/computerized tomography (CT) has been used for staging and monitoring responses to treatment in patients with diffuse large B cell lymphoma (DLBCL). The sequential interim PET/CT was prospectively investigated to determine whether it provided additional prognostic information and could be a positive predictable value within patients with the same international prognostic index (IPI) after the use of rituximab in DLBCL.

Patients and Methods: One hundred and sixty-one patients with newly diagnosed DLBCL were enrolled between August 2004 and December 2009 in a single institution. The assessment of PET/CT was performed at the time of diagnosis, the mid-treatment and completion of R-CHOP chemotherapy. The clinical stage and response of the patients were assessed according to revised response criteria for aggressive lymphomas (Cheson, J Clin Oncol, 2007). Patients that had mild or diffuse FDG uptake at any site were considered negative for intensities lower than or equal to that of the mediastinal blood pool structures with SUVmax cut-off value of 3.0.

Results: Sixty-seven patients (41.6%) presented with advanced stage disease and 27 (16.8%) had bulky lesions. At diagnosis, 53 patients (32.9%) were classified as high/high-intermediate risk by the IPI and two patients could not check the interim response due to treatment-related mortality (TRM). Forty-three patients (26.7%) continued to have positive metabolic uptakes with a significantly high relapse rate (62.8%) compared to the patients with a negative interim PET/CT (12.1%) (P<0.01). After a median follow-up of 30.8 months, the positivity of interim PET/CT was found to be a prognostic factor for both OS and PFS, with a hazard ratio of 4.07 (2.62 – 6.32) and 5.46 (3.49 – 8.52), respectively. In the low-risk IPI group, the 3-year OS and PFS rate was significantly different in the patients with positive (53.3 and 52.5%) and negative (93.8 and 88.3%) interim PET/CT, respectively (P<0.01). These significant prognostic differences of interim PET/CT responses were consistent with the results of the patients with high-risk IPI group (P< 0.01).

Conclusions: Interim PET/CT scanning had a significant predictive value for disease progression and survival of DLBCL in post-rituximab treatment; it might be the single most important determinant of clinical outcome in patients with the same IPI risk.

223 PREDICTIVE VALUE OF INTERIM PET IN ELDERLY PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): A SUB-GROUP ANALYSIS OF THE LNH03-6B GELA STUDY

R. Delarue[1], M. Meignan[2], M. Fournier[3], V. Safar[4], B. Coiffier[5], S. Bologna[6], O. Casasnovas[7], S. Picard[8], A. Bosly[9], H. Tilly[10]
[1]Hematology, Hopital Necker, Paris, France, [2]Nuclear Medicine, Hopital H. Mondor, Creteil, France, [3]Biostatistics, GELARC, Pierre Benite, France, [4]Hematology, Hopital H. Mondor, Creteil, France, [5]Hematology, CH Lyon Sud, Pierre Benite, France, [6]Hematology, CHU, Nancy, France, [7]Hematology, CHU, Dijon, France, [8]Clinical Research, GELARC, Pierre Benite, France, [9]Hematology, UCL Mont-Godinne, Yvoir, Belgium, [10]Hematology, Centre H. Becquerel, Rouen, France

Introduction: Use of PET in response assessment after completion of immunochemotherapy for patients with DLBCL is now a standard. In contrast, predictive value of interim PET is a major issue and is still under investigation. We report here the prognostic value of interim PET, i.e. after C4, in the prospective LNH 03-6B protocol.

Methods: 602 pts between 60 and 80 years old with DLBCL and aaIPI≥1 were randomized between R-CHOP14 and R-CHOP21 for 8 cycles. Response assessment was planned after C4 and at the end of treatment, based on CT scans and IWG response criteria 1999. Within the database, 180 patients were identified with a post-C4 PET evaluation. Result of this interim PET was recorded, based on local interpretation, with visual assessment (positive or negative). The primary endpoint of this analysis was to evaluate PFS according to interim PET result.

Results: Baseline patients characteristics did not differ from the overall LNH 03-6B population: median age (69y), Ann-Arbor stage III-IV (88%), elevated LDH (67%), aaIPI 2-3 (63%). Among baseline characteristics, only bulky mass (>10 cm) was predictive of positive interim PET (p=0.001). After C4, based on CT scans, 65% of pts were in CR or CRu, among them 66% were PET negative. There was no correlation between response according to CT scans and PET results. Response according to IWG response criteria 1999 (CR or CRu vs. PR) was not statically significantly associated with outcome (PFS or OS). In contrast, with a median follow-up of 44 months, PET negativity after C4 was strongly associated with PFS (median not reached vs. 41.3 months; HR 0.523; CI 95% 0.326-0.838; p=0.006) and also OS (median not reached vs. 68.6 months; HR 0.57 CI95% 0.324-0.996; p=0.046).

Conclusion: In the context of a local and visual evaluation, negativity of interim PET was a powerful predictor of PFS and OS for elderly patients receiving immunochemotherapy for DLBCL, justifying on going studies with a PET-driven strategy.

224 ^{18}FDG PET / CT AFTER INTENSIFIED CHEMO-IMMUNOTHERAPY IN DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL), AGED 18-65 YEARS WITH AAIPI 2-3. POSITIVE OR INDETERMINATE LESIONS HAVE A LOW POSITIVE PREDICTIVE VALUE. A NORDIC PHASE II SUBSTUDY

H. Holte[1], T. Bogsrud[2], S. Leppä[3], M. Laukka[4], M. Björkholm[5], H. Jacobsson[6], S. Jyrkkiö[7], M. Seppanen[8], M. Jerkeman[9], E. Brun[10], Ø. Fluge[11], L. Möller Pedersen[12]
[1]Oncology, Oslo University Hospital, Oslo, Norway, [2]Nuclear Medicine, Oslo University Hospital, Oslo, Norway, [3]Oncology, Helsinki University Hospital, Helsinki, Finland, [4]Radiotherapy, Helsinki University Hospital, Helsinki, Finland, [5]Medicine, Karolinska University Hospital, Stockholm, Sweden, [6]Nuclear medicine, Karolinska University Hospital, Stockholm, Sweden, [7]Oncology, Turku University Hospital, Turku, Finland, [8]PET centre, Turku University Hospital, Stockholm, Sweden, [9]Oncology, Lund University Hospital, Lund, Sweden, [10]Oncology, Lund University Hospital, Lund, Sweden, [11]Oncology, Haukeland University Hospital, Bergen, Norway, [12]Medicine, Roskilde University Hospital, Roskilde, Denmark

In a phase II study for patients with DLBCL aged 18-65 and high-risk disease, (aaIPI 2-3), we evaluated end-therapy FDG PET analysis at five of the centres and a score using internal standards.

Methods: ^{18}FDG PET / CT were scored as negative, indeterminate or positive. Retrospectively, PET intensity was scored as follows (Barrington protocol): 1: no uptake, 2: uptake ≤ mediastinum, 3: uptake > mediastinum and ≤ liver, 4: moderately- and 5: markedly increased uptake compared to liver.

Results: PET scan was done in 53 patients post-therapy out of 156 eligible patients. Median observation time for live patients: 30 months. Radiotherapy given: 9 patients. OS and FFS at 30 months: 91.3% (95% CI 82.7-99.9%) and 88.4% (95% CI 78.0-98.8%), respectively. ^{18}FDG PET / CT were originally considered negative in 39 cases (1 relapse), indeterminate in 6 cases (1 relapse) and positive in 8 cases (2 relapses, 1 secondary cancer). Only 1 of 17 cases had a positive biopsy, 3 were undetermined (necrotic). 48 of the cases were scored according to the Barrington protocol: 1: 14 cases, 2: 17 cases, 3: 8 cases, 4: 3 cases, 5: 6 cases. For 1-3 scored as negative and 4-5 as positive, there were 2 out of 39 and 2 out of 9 relapses, respectively. Four of the 17 cases with PET score 3 or higher were given radiotherapy, all these patients are in CR_1. The original and the Barrington score dichotomising for neg. and pos. cases between 3 and 4 were equally effective in predicting FFS ($p < 0.03$).

Conclusions: Patients with a negative FDG PET / CT have an excellent prognosis. PET positive lesions have a low positive predictive value although, in a few patients, radiotherapy may have prevented relapse. The Barrington score seems useful for multicenter analysis. Positive lesions should be documented with a biopsy or with a follow-up PET before further chemotherapy is initiated.

225 PROGNOSTIC VALUE OF RESIDUAL CT SCAN MASS IN AGGRESSIVE LYMPHOMAS PATIENTS WITH PET NEGATIVE AFTER CHEMO+/-RADIOTERAPY

M. Magagnoli[1], K. Marzio[2], M. Balzarotti[3], M. Rodari[2], L. Giordano[4], F. R. Lutman[5], A. Chiti[2], A. Santoro[1]
[1]Cancer Center, Istituto Clinico Humanitas, Rozzano, Italy, [2]Nuclear Medicine Department, Istituto Clinico Humanitas, Rozzano, Italy, [3]Department of Medical Oncology and Hematology, Istituto Clinico Humanitas-Cancer Center, Rozzano, Italy, [4]Biostatistic Unit., Istituto Clinico Humanitas-Cancer Center, Rozzano, Italy, [5]Department of Radiology, Istituto Clinico Humanitas, Rozzano, Italy

Background: Positron emission tomography (PET) with 2-[18F]fluoro-2-deoxy-D-glucose (18F-FDG) currently rapresents the most accurate tool for the assessment of treatment response in some lymphoma subsets. Infact, the revised response criteria (Cheson, 2007) for FDG avid lymphoma require Pet negativity to define complete remission (CR), independently from the persistence of residual masses of computed tomography (CT scan). Nevertheless, some reports suggested a slightly lower prognosis among PET patients (pts) with CT scan residual masses.

Material and methods: To evaluate the negative predictive value (NPV) of residual CT scan masses in pts with DLCL and HL patients with PET negative at the end of treatment. The NPV was defined as the proportion of patients without progression, relapse, or need for irradiation within 12 months after PET.

Results: From February 2004 to February 2008, PET negative was observed in 219 pts (128 with DLCL and 91 with HL, respectively). One hundred seventy-seven pts were evaluated after first line treatment program, while 42 pts after salvage therapy program. Residual CT scan disease (PET-/CT scan +) of at least 2.0 cm in the largest diameter was assessed in 139 pts. Ninety-six had only one side with residual mass, while 43 pts more than one sides. As of March 2009, 44 pts relapsed, and 27 of these had previous CT scan positive. The disease-free survival (DSF) was 77.9% for PET-/CT scan- pts and 79.4%

for PET- /Ct scan + pts (P=0.722). Among other prognostic factors analyzed, (histology, number or size of masses, first vs salvage treatment program) no correlation with DSF or overall survival (OS) emerged. With a median follow-up of 3 years, the DSF and OS were 79.2% and 89.1 %, respectively.

Conclusions: In our study we did not observe any significant difference in DFS among PET negative pts with or without CT scan residual masses after lymphoma therapy. This suggest that residual disease at CT scan is not a prognostic factor for relapse/progression disease. Further analysis will be performed in order to identify a possible dimensional cut-off at CT scan predictive for disease progression. This could imply the submission to consolidative radiotherapy on largest residual masses.

226 EARLY INTERIM ^{18}F-FDG PET IN EARLY AND ADVANCED STAGE HODGKIN'S LYMPHOMA: EVALUATION ON 304 PATIENTS

P.L. Zinzani[1], L. Rigacci[2], V. Stefoni[1], A. Broccoli[1], B. Puccini[1], L. Gandolfi[1], S. Fanti[3], A. Castagnoli[4], C. Pellegrini[1], F. Quirini[1], L. Vaggelli[5], E. Derenzini[1], L. Argnani[1], A. Bosi[2], M. Baccarani[1]
[1]Institute of Hematology and Medical Oncology, University of Bologna, Bologna, Italy, [2]Hematology Department, Azienda Ospedaliero Universitaria ''Careggi'', Florence, Italy, [3]Department of Nuclear Medicine, Policlinico ''Sant'Orsola-Malpighi'', Bologna, Italy, [4]Nuclear Medicine, Ospedale ''Misericordia e Dolce'', Prato, Italy, [5]Nuclear Medicine, Azienda Ospedaliera ''Careggi'', Florence, Italy.

Background: The use of early (*interim*) positron emission tomography (PET) restaging during front-line therapy in Hodgkin's lymphoma (HL) has considerably increased in clinical practice as an early recognition of treatment failure allows patients to be addressed to more intensive treatment regimens.

Patients and Methods: Between June 1997 and June 2009, 304 newly-diagnosed Hodgkin's lymphoma patients (147 early-stage and 157 advanced-stage) were treated with the ABVD regimen at two Italian institutions. Patients underwent to a PET staging and restaging at baseline, after 2 cycles of therapy and at the end of the treatment.

Results: 53 patients showed a positive *interim* PET and only 13/53 (24.5%) achieved a complete response (CR), whereas 251 patients showed a negative PET and 231/251 (92%) remained in CR. Comparison between *interim* PET-positive and *interim* PET-negative patients indicated a significant association between PET findings and 10-year progression-free survival (p=0.0000) and 10-year overall survival (p=0.0000), with a median follow-up of 37 months.

Among the early-stage patients, 19 had a positive *interim* PET and only 4 (21%) achieved a CR; among the 128 negative *interim* PET patients, 122 (97.6%) obtained a CR. In the advanced-stage subset, 34 patients showed a persistently positive PET (with only 9/34, 26.4% in CR), whereas 123 showed a negative *interim* PET, with 109 (88.6%) remaining in CR.

Conclusions: Our results confirm the role of early PET as a significant step forward for the management of both early and advanced-stage HL patients, offering the potential for an immediate switch to high-dose treatments, if required.

227 RESPONSE ASSESSMENT AFTER 4 CYCLES OF BEACOPP USING FDG-PET IN PATIENTS WITH ADVANCED-STAGE HODGKIN LYMPHOMA

J. Markova[1], C. Kobe[2], M. Skopalova[3], K. Dedeckova[4], H. Mocikova[1], K. Klaskova[1], D. Kahraman [2], M. Dietlein [2], T. Kozak[1]
[1]Department of Clinical Hematology, University Hospital Kralovske Vinohrady, Third Faculty of Medicine, Charles University, Prague, Czech Republic, [2]Department of Nuclear Medicine, University of Cologne, Cologne, Germany, [3]Department of Nuclear Medicine, PET Center, Na Homolce Hospital, Prague, Czech Republic, [4]Institute of Radiation Oncology, University Hospital Na Bulovce, First Faculty of Medicine, Charles University, Prague, Czech Republic

Background: Positron emission tomography (PET) has been proven to be a powerful prognostic marker during the treatment of Hodgkin lymphoma with ABVD. Here, we analysed the prognostic value of PET after 4 cycles of BEACOPP in patients with advanced-stage Hodgkin lymphoma.

Patients and Methods: Between January 2004 and February 2008, 69 patients with newly diagnosed HL in clinical stages IIB with large mediastinal mass or extranodal disease, III and IV were treated in or according to the HD15 protocol of the German Hodgkin Study Group. In addition to the protocol of the HD15 trial all patients received a PET scan after 4 cycles of BEACOPP (PET-4) in the treatment consistent of 6-8 cycles of BEACOPP.

Results: Of the overall group (n=69), 18 patients had a positive PET-4 while 51 had a negative PET-4. At a median observation time of 55 months, 4 of the 18 patients with a positive PET-4 had progressed or relapsed, while there was one relapse in the group of PET-4 negative patients. The negative predictive value of PET-4 was 98%; the positive predictive value of PET-4 was 22%. There was a significant arm difference between PET-4 negative and positive patients concerning the time to progression or relapse starting from the point of diagnosis (p=0.004).

Conclusion: The results of the present analysis underline the clinical impact of PET-4 scan in advanced-stage Hodgkin lymphoma. A negative PET-4 scan has a high negative predictive value and predicts a significant longer non-progression than PET-4 positive patients.

228 PET/CT SURVEILLANCE IN PATIENTS WITH HODGKIN LYMPHOMA IN FIRST REMISSION

T. C. El-Galaly[1], M. Hutchings[2], A. Bukh[1], V. Iyer[3], M. Boegsted[1], H. Johnsen[1], I. Christiansen[1]
[1]Department of Hematology, Aalborg Hospital, Aalborg, Denmark, [2]Department of Hematology, Rigshospitalet, Copenhagen, Denmark, [3]Department of Nuclear Medicine, Aalborg Hospital, Aalborg, Denmark

Background: Although controversial, surveillance imaging is widely used during follow-up of Hodgkin Lymphoma (HL). Recent studies indicate that PET surveillance detects preclinical relapse in a number of patients.

Patients and Methods: We performed a single center retrospective study. HL patients entering follow-up after first-line treatment were included if PET/CTs were performed at some point during follow-up.

Results: Fifty-three patients with classical HL and two patients with nodular lymphocyte predominant HL were included. Disease was characterized as early stage (15), intermediate stage (10) or advanced stage (30). During a median follow-up of 962 days (59-2722), 143 surveillance PET/CTs were performed, of which 127 were routine PET/CTs and 16 were evaluation of suspected relapse. Eighteen PET/CTs were suspicious for recurrent lymphoma while 125 PET/CTs showed continuous remission. Four patients with advanced stage disease relapsed during follow-up. In three patients, preclinical relapses were diagnosed by routine PET/CTs while the fourth patient was diagnosed due to reported symptoms. The PET/CT detected relapses all occurred within 7 month after response assessment and interim PET/CT was PET positive in two out of three patients. Fourteen PET/CTs incorrectly suggested relapse which was subsequently disproved by biopsy (4), additional imaging (3) and a clinical course incompatible with recurrent HL (7). The causes of false positive results were PET (11), CT (0) or concomitant PET and CT pathology (3). True and false positive PET/CT rates were 3 % and 10 %, respectively. Sensitivity and specificity of routine PET/CT were 100 % and 90 %, respectively. The positive predictive value (PPV) and negative predictive value (NPV) of routine PET/CT were 19 % and 100 %, respectively. PPV and NPV of PET/CTs performed on clinical indication were 50 % and 100 %, respectively. SUVmax in true and false positive PET/CTs did not differ significantly (p=0.18). The costs of detecting three preclinical relapses by use of routine PET/CT surveillance in our cohort were 97.856 USD per relapse.

Conclusions: Routine PET/CT surveillance detects preclinical relapse and has high NPV, but its general use is compromised by false positive results and high costs. Indiscriminate use of routine PET/CT surveillance for all patients is not efficacious, although it may be valuable in specific subgroups such as patients with advanced stage disease or interim PET positive.

229 FDG-PET IN THE STAGING AND PROGNOSIS OF T-CELL LYMPHOMA

C. Casulo[1], J. Maragulia[1], A. Zelenetz[1], H. Schoder[2], J. Feeney[2], S. Horwitz[1]
[1]Department of Medicine, Lymphoma Service, Memorial Sloan-Kettering Cancer Center, New York, United States, [2]Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, United States

Background: We have previously reported that fluoro-deoxy-glucose positron emission tomography scan (FDG-PET) is almost universally positive in patients with T-cell lymphoma (Feeney, Amer J Roentgenol, 2010 195: 333). In the current analysis we examined the role of FDG-PET in initial staging and at interim evaluation as a prognostic factor for patients with peripheral T-cell lymphoma (PTCL).

Methods: We reviewed the PTCL database at Memorial Sloan-Kettering Cancer Center to identify patients (pts) with mature T or NK lymphomas with PET scans as part of initial staging or relapse (N=91), and a subset of pts with repeat PET for interim restaging while treated with curative intent (N=50).

Results: The frequency of specific T-cell histologies included in this analysis were: PTCL-NOS (N=35); angioimmunoblastic T-cell lymphoma (N=17); anaplastic large cell lymphoma, ALK-1+ (N=10) and ALK-1- (N=11); HTLV-1 associated lymphoma (N=7); NK/T cell lymphoma (N=5); other (N=6). Seventy three pts were newly diagnosed, 18 had relapsed disease. FDG-PET during pre-treatment staging was positive in 97% of pts. Compared to CT-based evaluation, stage, if PET-based, would be altered in 10 pts (11%): 3 pts were upstaged and 7 pts downstaged. PET-based staging did not alter treatment for any pt. PET identified new disease sites in 46 pts (50%). Most frequently identified additional sites were: other nodal (N=24); bone (N=8); skin (N=7); nasopharynx (N=3); spleen (N=3); and lung (N=2). After a median of 4 cycles of chemotherapy, 50 pts underwent interim PET. Treatment regimens included CHOP (N=19); CHOP/ICE (N=24); other (N=7). At median follow up of 2.2 years, pts with negative interim PET had superior OS and PFS compared to pts with positive interim PET. Eighty five percent of pts with negative interim PET were alive at median follow up vs. 44% with positive interim PET, and 73% of pts with negative interim PET were progression free vs. 24.3% with positive interim PET.

Conclusions: In this data set, PET was positive at initial staging in most pts with PTCL. Additional disease sites were found by PET in 50% of pts but stage was impacted on in only 11% of pts, with no alteration in treatment. Interim FDG-PET predicted for both OS and PFS. The ability to achieve a negative interim PET seems to be an important predictor of outcome in pts with PTCL.