

3rd INTERNATIONAL WORKSHOP ON INTERIM- PET IN LYMPHOMA

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POSTER SESSION

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PROGNOSTIC VALUE OF INTERIM 18FDG-PET/CT IN PATIENTS WITH HODGKIN'S LYMPHOMA USING DIFFERENT 5-POINT VISUAL SCALES

Findings of interim 18FDG-PET/CT examinations have great importance in prognosis of HL patients. Currently there is no standard definition of minimal residual uptake (MRU) using 5-point visual scales. The aim of our study was to compare the effect on prognosis of the currently applied MRU definitions.

Interim PET/CT examinations of 82 newly-diagnosed HL patients stage (IIB-IVB) (m: 40; f: 42; average age: 36 ys) were evaluated by London, Hutchings, Gallamini and Barrington criteria. All of control PET/CT studies were performed on the same camera according to the standard protocol. Two experienced specialists visually analysed the studies. All patients had six courses of ABVB/EBVD and received radiotherapy according to the protocol if it was necessary. The result of interim PET/CT did not affect the later used therapy. The median follow-up period was 24 months (range, 9-47m). Chemotherapeutic protocol was not changed based on interim PET-CT results. Kaplan-Meier analysis was performed to determine the overall survival (OS) and progression free survival (PFS) and Mantel-Cox probe was calculated to compare the outcome of the different groups.

During the follow up period 78% (64/82pts) of patients did not progress. Comparing the PET negative group to the PET positive group poor prognosis was measured on the basis of all four criteria. The Barrington and Gallamini methods were more robust in estimating prognosis. Using forward stepwise Cox regression analysis Barrington method has been proved the most effective among 4 criteria systems ($p < 0.0001$). However comparing PET negative groups there were not significant differences in OS or PFS in either defined MRU groups.

A 101 - J. Zaucha, B. Małkowski, M. Kobylecka, M. Dziuk, A. Warszevska, J. Tajer, E. Subocz, J. Dziętczenia, W. Kulikowski, E. Chmielowska, D. Woszczyk, R. Kroll, P. Piwkowski, J. Walewski-Polish Lymphoma Research Group, PL

INTERIM PET1 COMPARED TO PET2 IN PATIENTS WITH HODGKIN LYMPHOMA TREATED WITH ABVD-POLISH OBSERVATIONAL STUDY

Several data confirm the high prognostic value of interim FDG-PET/CT testing the chemosensitivity of patients with Hodgkin lymphoma (HL) treated with ABVD. We launched in Poland an observational study to test the usefulness of 5-point scale by PET centers naïve in interpretation of interim PET scans. We hypothesized that PET after 1 ABVD cycle (PET1) should have better negative (NPV) and comparable positive predictive value (PPV) as after 2 cycle (PET2). 124 patients: 38 with early unfavorable (N-ADV) and 86 with advanced (ADV) stage HL were enrolled. PET1 was scored locally. Only If PET1 positive (score 4-5, POS) or equivocal (3-MRU), PET2 was performed. Subsequently, all scans will be assessed by the Polish-Italian panel of reviewers and compared to the initial local score. Before the study, all Polish reviewers scored training PET scans and their Krippendorff's alpha coefficient was 0.59. At the time of abstract submission only local scores are available. Within N-ADV group PET1 was POS in 5(13%) pts, MRU and negative (NEG) in 9(24%) and 24(63%) pts, respectively. PET2 was POS in 3(8%) pts: 2 of them had PET1 POS, the 3rd one had PET1 MRU. All pts except 1 with PET1 NEG or MRU remain in CR. Within ADV group PET1 was POS in 30(35%) pts, whereas MRU and NEG in 19(22%) and 37(43%), respectively. PET2 was scored POS in 13(15%) pts but only in pts with PET1 POS. All pts with PET1 MRU had either PET2 NEG or MRU. They, together with PET1 NEG pts remain in CR. Within pts with PET1 POS and PET2 NEG/MRU only 2 pts progressed but the follow-up is short. Our data suggest the higher NPV of PET1 than PET2. Longer follow-up is needed to assess the PPV of PET1 compared to PET2

A 102 - Pavlovsky A, Pavlovsky S, Fernandez I, Prates MV, Pavlovsky M, Zoppegno L, Basquiera A, Cerutti I, Rodriguez A, Castano V, Sackmann F, Rudoy S, Lastiri F, Eleta M, Milone GATLA , IMAXE

TREATMENT FOR ALL STAGES OF HODGKIN LYMPHOMA ADAPTED TO THE RESULT OF PET-CT AFTER 3 CYCLES OF ABVD.

OBJECTIVES: Reduce therapy in pts. with Hodgkin Lymphoma (HL) who achieve early complete remission (CR). Intensify therapy in pts. with positive (+) PET-CT after 3 cycles of ABVD (PET-CT+3). **METHOD:** One hundred and ninety three pts. with HL were included in a prospective multicenter trial (LH-05) . Pts. received 3 ABVD and then performed PET-CT+3 . Pts with a negative (-) PET-CT+3 received no further treatment. Pts. with persistent hyper metabolic lesions completed 6 cycles of ABVD+IFRT on PET + areas.Pts. with less than PR received more aggressive chemotherapy. One hundred and fifty (77%) had localized stage (I-II) and 43 (23%) advanced stage (III-IV), 33 (17%) had bulky disease.**RESULTS:** One hundred an forty eight (83%) achieved early CR with a - PET-CT+3. Forty five (17%) were PET-CT +, 4 with progressive disease, 41 pts. were in PR and completed 6 ABVD+IFRT. Thirty achieved CR and 11 persisted with PET +, 3 died of progresive disease. After finishing treatment, 178 pts (92%) were in CR. With a follow up of 39 months the EFS and OS at 36 months is 80% and 97%. Pts. with - PET-CT+3 regardless their stage at diagnosis had an EFS of 86% compared to 61% for all pts. with + PET-CT+3 (P< 0.001). In a multivariate analysis for EFS which included age, stage (I-II vs. III-IV), areas involved, Bulky disease and result of PET-CT+3, this last paramenter was the only one with statistical significance (P= 0.001) . Comparing to our historical control (LH-96) there is no difference in EFS and OS at 36 months but in LH 05 only 17% received 6 ABVD plus IFRT vs. 61% and 100% in LH-96.**CONCLUSION:** Risk adapted ABVD to PET-TC+3 leads to a high EFS with less chemo and radiotherapy

A 103 - RO Casanovas, M Meignan, A Berriolo-Riedinger, V Edeline, C Ferme on behalf of GELA
CHU Dijon, CHU Creteil, CGFL Dijon, C R.Huguenin / I Curie, IGR, France

AHL2011: AN ONGOING PHASE III GELA STUDY OF A TREATMENT DRIVEN BY INTERIM [18]FDG-PET RESPONSE IN PATIENTS WITH ADVANCED HODGKIN LYMPHOMA

ABVD chemotherapy is currently widely used as standard treatment of Hodgkin lymphoma (HL) as well in USA as in Europe, but the escalated BEACOPP (BEACOPPesc) regimen, which delivers more drugs at a higher dose intensity appears to improve patient's outcome. BEACOPPesc provides a 10-years failure free and overall survival of 82% and 86% respectively (Engert A, JCO 2009; 27: 4548). The better efficiency of BEACOPPesc against HL is associated to a marked and frequent but manageable immediate hematologic toxicity and a higher risk of secondary myelodysplasia and leukemia. This toxicity is a real concern and encourages us to identify: -Early responding patients after BEACOPPesc treatment, able to benefit from a strategy of dose intensity decrease after upfront BEACOPPesc as well in term of treatment safety as in term of cure rate. - Patients requiring to maintain during the whole treatment a higher dose intensity than that provides by the ABVD regimen. [18]FDG-PET is currently the more convenient tool that could identify the population of patients which might benefit to a risk adapted strategy. In this setting, the AHL 2011 trial was designed to test in patients with Ann Arbor stage III, IV or high risk IIB according to the GHSg criteria, a treatment strategy driven by PET after 2 cycles of BEACOPPesc, delivering 4 cycles of ABVD for PET2 negative patients and 4 cycles of BEACOPPesc for PET2 positive patients, and compared to a treatment no monitored by interim PET. Interim PET will be interpreted according to modified 5 point scale criteria.

The design and the assumptions of the study along with the current accrual will be presented.

A 104 - EJ. Dann, O. Bairey, R. Bar-Shalom, M. Izak, A. Korenberg, D. Attias, K. Filanovsky, U. Abadi, R. Abdah- Bortnyak, N. Goldschmidt, R. Epelbaum, D. Lavie, JM. Rowe, O. Shpilberg, O. Paltiel

TAILORED HL THERAPY BASED ON PREDEFINED RISK FACTORS AND INTERIM PET/CT: PRELIMINARY REPORT ON 191 PATIENTS ON ISRAEL NATIONAL HODGKIN STUDY

This multicenter ongoing study prospectively evaluates the outcome of HL pts treated depending on baseline prognostic factors with further therapy tailoring based on PET/CT performed after 2 cycles of chemotherapy. Pts with classic HL aged 18-60 yrs, stages I-IV are eligible. After 2 cycles of ABVD, pts with early favorable HL and negative PET/CT undergo involved nodal radiation therapy (INRT) and pts with early unfavorable HL receive 2 more cycles of ABVD (total 4 cycles) followed by INRT. If interim PET/CT remains positive, pts are given 2 more cycles of ABVD (total 4-6 cycles) followed by RT. Pts with advanced HL including those with B symptoms or stages III and IV HL are assigned to treatment according to IPS. Standard risk pts (IPS 0-2) initially receive ABVD x 2 and pts with IPS \geq 3 receive escalated BEACOPP (EB) x 2. If interim PET/CT is negative or shows minimal residual uptake in no more than 1 site, further therapy with ABVD x 4 is given and RT to bulky mediastinal masses is omitted. If interim PET/CT is positive, therapy is escalated to EB with RT given to bulky mediastinal masses. To date, 12 pts progressed; 5 of them had primary refractory disease. 2 pts died - 1 during auto BMT and the other from acute MI. 11 of 12 relapsed pts had negative interim PET. 8 pts with early disease had therapy escalation following positive interim PET/CT and none of them had disease progression. 89% of pts with advanced disease had interim negative PET/CT and therapy was reduced in 89% of advanced high risk pts. At a short follow up (median 21 m), the 2-y PFS was 88% and NPV was 92%, demonstrating that de-escalation is feasible and safe for patients with negative interim PET/CT

A 105 - Kobe C(1), Engert A(2,3), Markova J(4), Haverkamp H(3), Zijlstra J(5), Eich HT(6), Mueller R-P(6), Dietlein M (1), Borchmann P(2,3), Diehl V(3)

ASSESSMENT OF RESIDUAL BULKY TUMOR USING FDG-PET IN PATIENTS WITH ADVANCED STAGES AFTER COMPLETION OF CHEMOTHERAPY. FINAL REPORT OF THE GHSG HD15 TRIAL

Introduction:

The role of additional radiotherapy after chemotherapy for advanced-stage Hodgkin lymphoma (HL) is unclear. The German Hodgkin Study Group (GHSG) thus performed the HD15 trial in which advanced-stage HL patients having residual disease after 6 - 8 cycles of BEACOPP were evaluated by 18F- FDG-PET following chemotherapy.

Methods:

Entry criteria for the PET question in HD15 were partial remission after the end of chemotherapy with at least one involved nodal site measuring more than 2.5 cm in diameter by CT. A total of 2182 patients with de novo HL were included in HD15 of whom 740 were qualified for the PET question. An expert panel performed the assessment of response and PET. The negative-predictive value (NPV) of PET was defined as the proportion of patients without progression or relapse within 12 months.

Results:

The full analysis set included 740 patients of whom 712 had at least 12 months of follow-up. 74% were PET-negative and 26% PET-positive. In the PET-negative group, a total of 31 patients relapsed or had radiotherapy resulting in a negative prognostic value of 94%. Overall, only 12% of patients had additional radiotherapy as compared to 70% in our prior HD9 trial. In addition, there was no difference in PFS or overall survival as compared to our earlier trials in advanced-stage HL.

Discussion:

The NPV of PET of 94% suggests that indeed only patients with residual disease after chemotherapy who are PET-positive need additional radiotherapy. PET-negative patients at least after BEACOPP can be spared from additional radiotherapy.

A 106 - R.Kluge, D.Hasenclever, L.Kurch, A.Elsner, L.Tchavdarova, F. Montravers, M. Hoffmann, C.Kobe, O.Sabri, C.+D.Körholz; Universities of Leipzig, Paris, Vienna, Cologne, Halle, Hermes Med.Sol.,Stockholm

SEMIAUTOMATIC METHOD FOR DISCRIMINATION BETWEEN ADAEQUATE AND INADAEQUATE EARLY RESPONSE IN FDG PET/CT OF PAEDIATRIC HODGKIN LYMPHOMA(HL) PATIENTS

For interim response assessment in HL visual comparison of FDG uptake in residual tumour lesions vs. liver and mediastinal blood pool (MBP) is recommended. This approach can be problematic especially in case of small residua or enhanced background activity. A semiautomatic algorithm for calculation of the quotients between SUV_{peak} in the lesion with worst local response and mean liver (Q_{resid/liver}) and MBP uptake (Q_{resid/med}) was developed and tested in 152 children with HL. Mean uptake in MBP and liver were proportional (mean factor 0.68), with higher signal-to-noise ratio in the liver. Therefore, in order to project residua of all patients on a uniform scale Q_{resid/liver} was used for further evaluation. Histogram of Q_{resid/liver} in 152 cases suggests a mixture model of a roughly normal "negative" part including 78% of cases with mean value of 0.95 and an abnormal "positive" part including 22% of cases with a median of 2.0; a value of 1.3 could be suggested as best cut-off. 78/152 cases were in addition visually interpreted by four readers; (resid=liver) was documented in median at Q_{resid/liver} of 1.3, suggesting a biologically meaningful cutpoint in good agreement with visual criteria. We interpret the first peak as residual signals of responsive lesions representing inflammation or cell debris elimination processes while the residuals of the abnormal positive part may be indicative of inadequate response to chemotherapy. In contrast, use of MBP as cutpoint corresponds to a Q_{resid/liver} of about 0.9 (0.68 * 1.3) which is in the range of the peak of the "negative" part. This could be a reason for the low PPV observed in several clinical studies using MBP as reference.

A 107 - J. Radford, M. O'Doherty, S. Barrington, W. Qian, R. Pettengell, S. Coltart, D. Culligan, J. Wimperis, E. Bessell, B. Popova, D. Linch, D. Cunningham, A. Lister, B. Hancock, P. Hoskin, P. Johnson, T. Illidge

UK NCRI RAPID TRIAL IN PATIENTS WITH CLINICAL STAGE IA/IIA HODGKIN LYMPHOMA: AN UPDATE FOLLOWING ATTAINMENT OF THE RECRUITMENT TARGET

In limited stage HL abbreviated chemotherapy (CT) followed by involved field radiotherapy (IFRT) is the current standard of care but some pts may be cured by CT alone. 18FDG-PET provides an opportunity to identify patients (pts) with an excellent prognosis after CT but the impact of PET determined treatment de-escalation on disease control requires careful assessment.

For pts with stages IA/IIA HL taking part in RAPID a PET scan is performed after 3 cycles standard ABVD. If this is reported -ve (score 1 or 2 on 5 point scale) following central review at the Core Lab in London, pts are randomly allocated either IFRT or no further treatment. Pts with a +ve PET scan (score 3, 4 or 5) have a 4th cycle ABVD and IFRT. With 400 PET-ve pts randomised the trial is powered to exclude $\geq 7\%$ difference in PFS. At the time of data-lock in 05/11, 602 pts (320 male, 282 female; median age 34 yrs) had been registered. Following 3 cycles ABVD, 571 had a PET scan allocated a score of 1 (n=301, 52.7%), 2 (n=125, 21.9%), 3 (n=90, 15.8%), 4 (n=32, 5.6%) or 5 (n=23, 4.0%) giving an overall PET-ve rate (scores 1 and 2) of 74.6%. 420 of 426 PET-ve pts have been randomised to receive IFRT (n=209, 49.8%) or no further treatment (n=211, 50.2%) and 6 pts have not been randomised. After a median 34.1 months from randomisation and combining both arms, 389 of 420 (92.6%) pts are alive and progression free, 24 (5.7%) have progressed and 6 (1.4%) have died giving a combined 3 year progression-free survival of 92.2% and overall survival of 98.2%.

This update confirms a PET+ve rate after 3 cycles ABVD at the upper end of the expected range, a low event rate and no reason to halt the trial early.

A 108 - J Markova (1) D Kahraman (2) C Kobe (2) M Skopalova (3) H Mocikova (1) K Klaskova (1) K Dedeckova (4) HT Eich (5) B Böll (6, 7) M Dietlein (2) T Kozak (1)

THE ROLE OF FDG-PET IN EARLY AND LATE THERAPY ASSESSMENT OF PATIENTS WITH ADVANCED HODGKIN LYMPHOMA TREATED WITH BEACOPP

Introduction:

The prognostic value of positron emission tomography (PET) in early therapy response assessment, after completion of chemotherapy, and 3 months after the end of treatment, in advanced Hodgkin lymphoma (HL) remains to be defined.

Methods:

We report the results of 69 patients with first presentation of advanced HL. FDG-PET scan was performed after 4 cycles (PET-4), on completion of chemotherapy after 6/8 cycles (PET-6/8) and 3 months after completion of chemotherapy (PET 3-months).

Results:

Median follow-up was 55 months. The NPV for PET-4, PET-6/8 and PET 3-months were 98%, 95% and 97%, respectively. The 4-year PFS for PET-4 negative (n=51) and PET-4 positive (n=18) patients were 96% and 78%, respectively (p=0.016). The 4-year PFS for PET-6/8 negative (n=59) and positive PET-6/8 (n=9) patients were 95% and 78%, respectively (p=0.046). Patients with large mediastinal mass contributed to nearly all of the PET-4 positive (16/18) and PET-6/8 positive (8/9) patients. After radiotherapy of PET-6/8 positive patients, PET 3-months was negative in 64 (97%) and positive in 2 (3%) patients.

Conclusion:

The PET 3 months after end of chemotherapy is of limited value when interim PET-4 is negative. Interim PET after 4 cycles of BEACOPP is a strong prognostic marker for PFS in advanced HL.

A 109 - Zsófia Simon¹, Edit Páyer¹, Sándor Barna², Ferenc Magyar¹, Ildikó Garai², Zsófia Miltényi¹, Árpád Illés¹
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2 ScanoMed Ltd.

INTERIM PET/CT IN HODGKIN'S LYMPHOMA-THE HUNGARIAN EXPERIENCES

The role of the interim 18FDG-PET/CT in Hodgkin's lymphoma's treatment is obvious. The authors has enrolled 89 new Hodgkin lymphoma patients to the prospective CHEAP study (chemotherapy effectiveness assessed by PET) in Hungary. They examined 89 Hodgkin-lymphoma patients between 2007 January and 2011 March. Forty seven women and forty two men underwent staging and interim PET/CT. The mean age was 36.7 (17-79) years at the time of the diagnosis. Nodular sclerotic was the most common histological subtypes (37 % of the patients). 47 % of the patients were diagnosed in early stage, 53 patients had B symptoms. The first-line therapy was ABVD or EBVD, and radiotherapy if it was necessary. We made the interim PET/CT after the second cycle of the chemotherapy. Two experienced specialists visually analysed the scans, based on the Gallamini criteria. Kaplan-Meier analysis was performed to determine overall - and event-free survival (EFS). 55 % of the patients were in complete metabolic remission (CMR), we detected minimal residual uptake (MRU) in 28 %, and stabile disease or progression was seen in 17 %. The 3-years overall-, and eventfree survival is 100 % and 84 % in the CMR and MRU group, 78 % and 20 % in the PET positive group. Restaging PET/CT was done in 73 patients up to now. Based on the interim PET/CT results: in the CMR group 87 % of the patients remained in CMR, in the MRU group 80 % of the patients got into CMR at the restaging. There were 5 progression in the interim CMR group at the restaging, they underwent autologous stem cell transplantation. Interim 18FDG-PET/CT is an useful and independent predictor of EFS in Hodgkin-lymphoma. It could be possible to avoid und

A 110 - Mounier N, Bower M, Spina M, Besson C, Schiantarelli C, Re A Bonnet F, Hentrich M, Schommers P, Van Den Neste E, Costagliola D, Borsatti E, Tirelli U for the GECAT.

EARLY DETERMINATION OF TREATMENT SENSITIVITY IN HIV-RELATED HODGKIN LYMPHOMA BY FDG-PET/CT AFTER TWO CYCLES OF ABVD CHEMOTHERAPY.

Introduction:

The high prognostic value of FDG-PET/CT performed after two cycles of chemotherapy for HIV negative Hodgkin lymphoma (HL) is well known. However, experience with PET scanning in HIV-related HL needs to be further studied as nodal FDG uptake can be observed in various opportunistic infections and AIDS-related conditions (i.e. false positive results).

Materials and Methods:

A total of 44 HIV-related HL patients were enrolled in 9 centers from the GECAT (European Cooperative Study Group on AIDS and tumors). There were 41 male, median age 46 yo. Median CD4 count was 394/mm³. Viral load was negative in 37 patients. 42 received concomitant HAART. Stage III-IV disease was present in 24 patients. S_IPI scored 3-5 in 23. All PET/CT study after 2 cycles were scored blinded to treatment outcome by experienced PET readers, according to the 5-point Deauville criteria (1-3 vs 4-5).

Results:

Overall, 77% of patients achieved a complete remission after first-line ABVD. At a median FU of 18 months, 3 patients had experienced a PFS event. PET was negative in 39 patients (88%) after the second cycle (2-year PFS = 100%) and 5 (12%) were PET positive (2-year PFS = 60%, p=0.003). All patients who were PET-negative after the 2nd cycle stayed PET-negative after the 4th cycle and entered a durable CR.

Conclusions:

Patients responding well to HL chemotherapy can be accurately identified by PET/CT after 2 cycles of chemotherapy. De-escalation treatment strategies may be better tailored to well responding individuals based on PET/CT results after two cycles of chemotherapy.

A 111 - Vassilakopoulos TP, Angelopoulou M, Datseris I, Dadakaridou M, Prassopoulos V, Chatziioannou S, Tsirkinidis P, Variami E, Panayiotidis P, Meletis J, Pangalis G, Rontogianni P, Athens, Greece

INTERIM PET-SCAN FOR EARLY RESPONSE ASSESSMENT AFTER 2 ABVD CYCLES (PET-2) IN ADVANCED STAGE HODGKIN LYMPHOMA (HL)

A positive PET-2 following ABVDx2 is a strong unfavorable prognostic factor in advanced HL. The evaluation of PET-2 is based on well defined, though arbitrary, criteria, requiring prospective validation. Early treatment intensification might improve prognosis. We present a retrospective study of 26 pts with advanced HL according to GHSg definition (25/26 <60 years). PET-2 was evaluated by the established 5-grade scale. Pts' median age was 28 years (19-72), 69% were men, 3,10 and 13 had stage II,III,IV, 70% B-symptoms; median IPS was 2.5 (0-5). 21/26 pts (81%) had negative PET-2: It was completely negative in 10; 8 pts had residual uptake <liver; 3 developed new sites with alternative explanation available and regression of the initial disease sites. PET-2-Neg Pts: A final PET was available in 15 pts (too early for 6): 14/15 were PET-neg, but 1/15 had frankly progressive disease. After 13 months median follow up, 1/14 PET-neg pts relapsed. Overall 2/21 pts have failed so far: 1/10 with completely negative PET-2 and 1/8 pts, who had mild (<liver) residual uptake. PET-2-Pos Pts: Among 5 PET-2 pos pts, only 1 switched to BEACOPP-escalatedx6 (continuous CR for 16 months) and 4 continued on ABVD (2 converted to PET-neg and remain in CR and 2 progressed at 4 and 7 months). If all the 26 pts had been treated with B-escx6-8, they would have had received 156-208 chemo cycles. According to our preliminary data, current criteria for PET-2 evaluation appear valid. During this initial phase of PET-2 incorporation, a negative result appeared to be reassuring. However, treating physicians tended to be reluctant to make early modifications of treatment plan, in the case of positive PET-2.

A 112 – ¹A. Gallamini, ²C. Tarella, ³C. Patti, ⁴AM. Gianni, ⁵S. Bolis, ⁶L. Trentin, ⁷G. La Nasa, ⁸A. Olivieri, ⁹F. Fiore, ¹⁰F Di Raimondo, ¹¹F. Ciceri, ¹²A. Biggi, ¹³S. Chauvie, ¹⁴M.R. Mennitto, and ¹⁵A. Rambaldi

MULTICENTRE CLINICAL STUDY WITH EARLY TREATMENT INTENSIFICATION IN HIGH-RISK HODGKIN LYMPHOMA (HL) PATIENTS, WITH A POSITIVE FDG-PET SCAN AFTER TWO ABVD COURSES - GITIL HD0607 STUDY

Background: Interim PET scan after 2 CT courses (PET-2) is the most powerful predictor of treatment outcome in advanced-stage, ABVD-treated HL patients (pts.). Although retrospectively demonstrated, the overall efficacy of a PET response-adapted treatment for ABVD-treated advanced-stage HL is still prospectively unproven. **Methods:** In the HD 0607 study, after 2 ABVD PET-2+ pts are randomized to BEACOPP escalated (Be) plus BEACOPP baseline (Bb) (4+4 courses) versus Be+Bb (4+4) plus Rituximab. PET-2 negative pts continue with 4 ABVD +/- consolidation radiotherapy on the sites of initial bulky disease. All the non-negative PET-2, defined as scans with any residual FDG uptake in any site outside the physiological areas of the tracer concentration, are uploaded in a website for review by a panel of 6 nuclear medicine experts. Scans are interpreted by visual assessment according to the Deauville 5-point scale. **Results** From 07/2008 till 07/2011, 365 advanced-stage (IIB-IVB) pts were consecutively enrolled and 315 performed PET-2. Overall, 130/315 PET-2 were considered non-negative and reviewed: 51/130 turned out positive (score 4-5) and 79/130 negative (score 1-3). In the 51 PET-2+ pts, 32 showed a single site, 19 \geq 2 sites of persistent FDG uptake. In the 32 single site-PET-2+ pts, the most frequent site was mediastinum (25), laterocervical (3), lung (2), supraclavicular (1), and iliac (1) nodes. The median time from PET uploading in the website to review was 1.22 days. The binary concordance rate among reviewers was very good, and ranged from 0.75 to 0.92 (Cohen's k coefficient); overall concordance rate was 0.83 (Krippendorff's alpha). 122/315 pts completed the scheduled treatment and are suitable for the analysis after a mean follow-up of 403 days from the end of treatment: 17 with a positive and 105 with a negative PET-2. 13/17 PET-2+ pts became negative at the end of treatment. The 1-y PFS was 76.5%, 96.2% and 93.4% for PET-2+, PET-2- p, and for the entire population, respectively. **Conclusions** These preliminary findings seem to show that 1) PET scan online review system is feasible and timely available; 2) concordance rate among reviewers is very good; 3) most PET-2+ pts after 2 ABVD courses could enter a sustained CR if promptly rescued with BEACOPP.

A 113 - C. Furth, H. Amthauer, H. Hautzel, I. G. Steffen, J. Ruf, J. Schiefer, S. Schönberger, G. Henze, R. Grandt, P. Hundsdorfer, M. Dietlein, C. Kobe
Magdeburg / Jülich / Düsseldorf / Berlin / Cologne

EVALUATION OF INTERIM PET RESPONSE CRITERIA IN PAEDIATRIC HODGKIN'S LYMPHOMA--RESULTS FOR DEDICATED ASSESSMENT CRITERIA IN A BLINDED DUAL-CENTRE READ.

Background: The aim of this study was to evaluate the use and reliability of the new positron emission tomography (PET)-based response criteria for interim positron emission tomography (iPET) in patients with paediatric Hodgkin's lymphoma (pHL). Particular emphasis was put on interobserver variability and on identification of a visual cut-off defining patients with very low risk for relapse.

Patients and methods: The iPET scans of 39 pHL patients were evaluated in two independent centres by two PET-experienced specialists in nuclear medicine (blinded read, centre consensus) each. The iPET scans were interpreted using a 5-point scale and were compared with the outcome. Cohen's kappa-test (kappa) was used to analyse the interobserver agreement.

Results: Concordant ratings were assessed in 19 patients with iPET-negative findings, in 11 patients with iPET-positive findings and in 2 patients with inconclusive ratings. A 'substantial agreement' between attended centres was achieved (kappa = 0.748). All patients suffering relapse were concordantly identified, taking mediastinal blood pool structures (MBPS) as visual cut-off between PET-positive and PET-negative findings, respectively. All pHL patients with uptake lower than or equal to MBPS remained in complete remission.

Conclusion(s): The iPET interpretation assured low interobserver variability. High sensitivity for identification of pHL patients suffering relapse is achieved if [18F]-fluorodeoxyglucose uptake above the MBPS value is rated as a PET-positive finding.

A 114 - M. Meignan, M. Hutchings, A. Versari, P. Olivier, R. Ricci, I. Hristova, C. Fortpied, T. Vander Borgh, S. Bardet, M. Federico, M. Bellei, J. Raemaekers, O. Reman, M. André. on behalf of GELA/EORTC/FIL

SOFTWARE AND VIEWER EFFECTS ON INTERIM PET REPORTING IN THE H10 TRIAL

The H10 trial is an EORTC/GELA/FIL randomized trial with a treatment adaptation based on interim PET after two cycles of ABVD in stages I/II Hodgkin's lymphoma. IHP criteria were used for interim PET reporting. A centralized reading (CRd) was performed using slightly different approaches by Groups 1(GELA) and 2 (EORTC/FIL), respectively G1: 6 experts; an online centralized network and PET reporting on dedicated workstations linked by a VPN. G2: 5 experts; PET reporting on a web based, non-dedicated software. An interim analysis (IA) was scheduled after approximately 34 events. In this IA, 1137 patients were analyzed; 80% were PET negative.

Aim of this study: Evaluate the impact of the two different ways of CRd on the results.

Methods: A new review was performed on 85 baseline scans and corresponding iPET scans. Half of patients had events. The scans were blindly reviewed on the same workstation, two experts from G2 reviewed the G1 scans, and vice versa. Agreements and differences in PET positivity were assessed between the new and original reviews.

Results: Less than 9% discrepancies between the two reviewers within each group. The agreement between new review and original was almost perfect for G2 experts reading G1 scans, ($k=0.82$), but moderate for G1 experts reading G2 scans, ($k=0.54$). Six patients from this group considered negative in the first review turned positive in the new review by both reviewers, but this had no potential significant impact on the outcome of the IA. Conclusion: The use of the same dedicated software for all experts for iPET reporting is mandatory in clinical trials to reduce the risk of missing residual activity.

A 115 - ¹Borra A, ²Marchetti M, ³Biggi A, ^{4,5}Chauvie S, ⁴Stancu A, ⁴Cerello P, ¹Cavallo A, ¹Gallamini A ¹Hematology, ³Nuclear Medicine, ⁵Medical Physics S. Croce e Carle Hosp. Cuneo, ²Hematology C. Massaia Hosp., Asti, ⁴National Institute of Nuclear Physics, Turin,

COST - EFFECTIVENESS OF INTERIM PET RESPONSE - ADAPTED THERAPY IN ABVD - TREATED, ADVANCED - STAGE HODGKIN LYMPHOMA

Interim PET performed early during chemotherapy is considered a surrogate test for chemosensitivity assessment in lymphoma. In ABVD-treated (AT) Hodgkin Lymphoma (HL) patients, interim PET after two courses (PET-2) is the best predictor of treatment response. PET-2 positive patients show a very dismal prognosis and a more aggressive treatment is required. In advanced-stage, ABVD treated HL, a PET response-adapted strategy with a shift to BEACOPP in PET2 positive patients (A/B-T) was shown to increase the 2-y Failure Free Survival (FFS) of this patients subset from 12% to 62%, and to improve the disease control in the overall patient population by indirect retrospective comparison (Gallamini Br. J. Haematol 2011). Since PET is an expensive diagnostic procedure, a careful cost-benefit evaluation of an overall PET-based flexible therapeutic strategy such as A/B-T compared to standard AT is mandatory. The present report was built on a decision model based on Markov arrays, comparing A/B-T with AT for advanced HL. The model is based on a retrospective cohort of 154 advanced-stage HL patients in which PET2 was performed after 2 ABVD courses. PET-2 negative continued with ABVD x 4 and consolidation RxT in presence of bulky disease at baseline; PET-2 positive shifted to BEACOPP escalated x 4 + BEACOPP baseline x 4. Patients failing either AT or A/B-T were treated with IGEV x 4 and ASCT. In case of ASCT failure, DHAP re-induction therapy and allogeneic SCT (alloSCT) was given whenever possible. The decision model included 12 health-states: each health state last 1 month and the overall time horizon at baseline was 5 years. We considered severe toxicity in patient care (morbidity) and transplant-related mortality. Quality of life was reduced by 20% for chemotherapy, 30% for transplant and 40% for relapse. The model assessed the following endpoints: survival, quality of life - adjusted survival (QALY) and costs (in the perspective of the health-care system) as the principal end-points. TreeAge SW (2008) was run. National charges were used as estimators of unitary costs. 1st and 2nd order sensitivity analysis was performed. A/B-T reduced the overall percentage of patients failing treatment (refractory and relapsing) from 27% to 14%. This clinical advantage induced a prolongation of quality-adjusted survival from 53.20 to 55.63 quality-adjusted months, that is a gain of 0.18 QALYs (90% CI: -0.1;+1.4). The number of interim PET needed to avoid one ASCT was 8.3. The cost of universal interim PET (€1,546) was offset by the reduced number of ASCT procedures (€36,575). Consequently, health-care costs were €27,861 for A/BT versus €29,050 for AT strategy, which is a €1189 (90%CI: -41,208; +13,240) saving. At sensitivity analysis we verified that the results were mildly sensitive to the costs of PET and ASCT: A/B-T was not cost saving if PET would cost > €3,031 and ASCT < €20,200. A/B-T would cost > € 40,000/QALY only at a PET cost > €16,300. The results were also sensitive to the portion of PET-2 positive patients: A/B-T wouldn't turn out cost saving if the portion was > 22%. The results were not sensitive to the rate of severe adverse events during chemotherapy. The results were overall robust, since A/B-T cost < €30,000/QALY in > 80% out of 100,000 simulations (MonteCarlo analysis). In conclusion, this study suggests that the routine clinical use of a A/B-T strategy is cost-effective and could even improve treatment efficacy of standard AT in advanced-stage HL, while sparing toxicity to most of them.

A 116 - A. Biggi (1); S. Chauvie (3); A. Stancu (3); F. Fallanca (4); A. Chiaravalloti (5); M. Gregianin (6); U. Ficola (7); U. Guerra (9); Rambaldi (10); O. Schillaci (5); A. Cavallo (2); A. Gallamini (2)

(1) Nuclear Medicine Unit, (2) Hematology Unit and (3) Medical Physics S. Croce e Carle Hospital, Cuneo (4) Nuclear Medicine Unit, Institute of Cancer Research San Raffaele, Milan; (5) Nuclear Medicine Unit, University Tor Vergata, Rome; (6) Nuclear Medicine Unit, Ospedale Policlinico, Padova; (7) Nuclear Medicine Unit, Ospedale La Maddalena, Palermo; (9) Nuclear Medicine Unit (10) Hematology Unit Ospedali Riuniti, Bergamo

CONCORDANCE IN INTERIM PET REPORTING IN THE PROSPECTIVE HD 0607 CLINICAL TRIAL IN ABVD-TREATED, ADVANCED-STAGE HODGKIN LYMPHOMA

ackground: Interpretation rules for interim-PET (PET-2) reporting are still lacking. As a consequence, an expert review panel for PET interpretation has been implemented in the HD-0607 trial (NCT Identifier: NCT00795613). The latter was aimed at assessing the role of chemotherapy intensification in ABVD-treated Hodgkin Lymphoma (HL) patients with PET-2 positive after 2 cycles. **Patients and methods:** 370 advanced-stage HL patients have been consecutively enrolled in the Italian GITIL (Gruppo Italiano Terapie Innovative nei Linfomi) prospective multicenter clinical trial HD-0607. HL patients, after baseline PET (PET-0), are first treated with 2 ABVD courses and PET-2 was performed afterwards. All non-negative PET-2 scan (defined as a scan with any residual FDG uptake outside the physiological areas) are uploaded along with PET-0 in the web site. Hence the scans distributed to a panel of six independent expert reviewers. The latter interpreted the scans according to the 5-point semiquantitative score (Deauville criteria) (positive lesion: FDG uptake higher than liver uptake). The first three reviewers replying within 72 hours from PET upload determined the panel final decision; the remaining three reviewers reported the scans later. Patients with a positive PET2 shifted to BEACOPP or Rituximab-BEACOPP escalated treatment; patients with a negative PET2 continued with ABVD. Patients with bulky lesion (nodal mass > 6 cm) were treated with consolidation radiotherapy. **Results:** According to the results of the reviewed 338 of the patients that already underwent PET-2, 57 (16,8%) were scored as positive and 281 (83,2%) were scored as negative. The 57 PET-2 positive scans showed a single residual focus in 36 cases and multiple foci of residual FDG uptake in 21 (in 9 of them the attributed score was 5). Thirty-six showed lesions in the mediastinum, 19 in superficial lymph nodes and 2 in the lung. In 23/36 (64%) patients the single residual FDG uptake was within a bulky lesion and in 13/36 (36%) was outside. The agreement among reviewers was automatically calculated by WIDEN. The concordance between couples of reviewers (Cohen's Kappa) ranged between 0.78 and 0.84. The overall concordance among all the six reviewers (Krippendorff's Alpha) was 0.803. The concordance based on score was 0.422 considering the 1-5 scoring system and 0.585 scoring 1 as negative, 2 as above mediastinum and 3 above liver. Lower concordance among reviewers was found in scans showing FDG residual uptake in anatomical structures not clearly related to lymphoma (brown fat, large vessels, bowel, tonsil and inflammatory lung lesions). **Conclusions:** (1) the online review process for PET-2 scan is feasible and simple (2) a very high binary and overall concordance rate among reviewers is obtained using the Deauville score for PET-2 reporting; (3) most of the positive PET-2 scan showed a residual FDG uptake in the site of bulky disease, mostly in mediastinum.

A 117 – E. Brusamolino, A. Castagnoli, G. Rossi, U. Vitolo, F. Zaia, A. Pulsoni, V. Pavone, G. Ciccone, U. Riccardi, A. Santoro, A. Levis, P.L. Zinzani, on behalf of the Fondazione Italiana Linfomi (F.I.L.)

PET-BASED EARLY SALVAGE WITH HIGH-DOSE CHEMOTHERAPY AND STEM CELL TRANSPLANTATION IN ADVANCED STAGE HODGKIN LYMPHOMA

The role of FDG/PET functional imaging to demonstrate the chemosensitivity of Hodgkin lymphoma and to predict outcome has recently been emphasized. Patients who become PET negative after two courses of ABVD (PET-2) have shown a very low probability of relapse, whereas patients who remain PET positive are at high risk of progression. Accordingly, we adopted a treatment strategy tailored on early response to ABVD, evaluated with PET after two courses of chemotherapy. In this trial, PET-2 negative patients will complete the ABVD program (six courses), while PET-2 positive patients will switch to early salvage therapy with four courses of IGEV (ifosfamide, gemcitabine, vinorelbine) for debulking and stem cell harvesting. At restaging after IGEV, PET negative patients will receive BEAM conditioning followed by autologous rescue, while PET positive patients with an HLA-identical donor will receive an autologous followed by a reduced-intensity conditioning allogeneic transplant. Patients with no identical donor, will receive a double autologous transplant, with high-dose melphalan and BEAM, respectively. This trial is on-going and the sample size of 300 patients is being achieved. Data on interim PET and on early rescue efficacy will be illustrated and discussed.

B 100 - Deok-Hwan Yang¹, Byun Byung Hyun², Jung-Joon Min², Jae-Sook Ahn¹, Yeo-Kyeong Kim¹, Hee-Seung Bom², Ik-Joo Chung¹, Hyeoung-Joon Kim¹, Won Seok Kim³ and Je-Jung Lee¹

INTERIM PET/CT-BASED PROGNOSTIC MODEL FOR THE TREATMENT OF DIFFUSE LARGE B CELL LYMPHOMA IN POST-RITUXIMAB ERA

FDG-PET/CT has been used for staging and monitoring responses to treatment in patients with diffuse large B cell lymphoma (DLBCL). We investigated the prognostic accuracy of interim PET/CT using three different methods of the response assessment during R-CHOP chemotherapy in patients with DLBCL. Patients and Methods: One hundred and twenty-four patients with newly diagnosed DLBCL were enrolled. The assessment of PET/CT was performed at the time of diagnosis, the third or fourth cycle and the completion of R-CHOP chemotherapy. The response of interim PET/CT was assessed based on the combination with three parameters of the Deauville five-point scale (5-PS), the reduction rate of maximal standardized uptake value (Δ SUVmax), and the reduction rate of metabolic tumor volume (Δ MTV2.5). Results :Over the median follow-up of 23.8 months, both the positivity in Deauville 5-PS and the optimal cutoff value of Δ SUVmax could predict the prognostic difference in patients with DLBCL after R-CHOP chemotherapy. The response of interim PET/CT based on 5-PS, Δ SUVmax, and Δ MTV2.5 showed a significant potential as a prognostic value in PFS, respectively. Furthermore, when divided the patients into four groups according to the sum of score for three adverse factors; consisted of grade 4-5 by Deauville 5-PS, Δ SUVmax \leq 91.8% and Δ MTV2.5 \leq 99.3%, the clinical outcome of patients with factor 0 was significantly superior than that of patients with factor 3 or even with factor 1 or 2. Conclusion: The combined evaluation with three parameters using visual, quantitative SUV-based and MTV-based assessment could have a more differential potential for predicting the prognosis in patients with DLBCL.

B 101 - Silvia Park¹, Seok Jin Kim¹, Joon Young Choi², Seung Hwan Moon², Won Seog Kim¹/
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INITIAL TLG AND SUVTOTAL CAN PREDICT THE OUTCOME OF DLBCL

Taking a step forward from the IPI, attention is focused on the role of 18F-FDG PET as a tool for guidance in risk stratification. We attempt to investigate the most appropriate PET parameter for prediction of disease progression in patients with an IPI score of 1, 2, or 3.

Method: 120 patients with newly diagnosed DLBCL between January 2008 and February 2010 were assessable for SUV and TLG at baseline and interim PET/CT in a retrospective chart review. SUVtotal, SUVmax, and TLG were collected for initial PET parameters, and Δ SUVtotal, Δ SUVmax, and Δ TLG were used as interim PET parameters.

Results: The median number of RCHOP cycles was 6 (range, 2-9), and interim PET/CT was performed after 2 to 5 (median, 3) cycles. IPI showed strong predictive value for PFS in all patients with DLBCL ($p < 0.01$). When comparing PFS according to initial PET parameters, initial SUVtotal and TLG showed significant difference in prediction of PFS in all patients ($p < 0.01$ and $p = 0.03$) and in patients with an IPI score of 1, 2, or 3 ($p = 0.05$ and $p = 0.02$). No significant difference in PFS was observed between patients with higher initial SUVmax and those with lower SUVmax. In regard to the interim PET parameters, none of the PET parameters, including Δ SUVtotal, Δ SUVmax, and Δ TLG showed a significant difference in PFS in all patients and in patients with an IPI score of 1, 2 or 3.

Conclusion: Parameters from initial PET/CT, rather than interim PET/CT, and TLG or SUVtotal, rather than SUVmax, appeared to have a better value in prediction of PFS, and would be worthy of further evaluation for its use in clinical practice as an adjunct to IPI in patients with an IPI score of 1, 2, or 3.

B 102 - Pardal E, Grande C, Martín A, Marín-Niebla A, Panizo C, Conde E, Bello JL, Hernández M, Pérez E, González-Barca E, Arranz R, Bargay J, Ramírez MJ, Salar A, Canales M, Caballero MD.

***UTILITY OF INTERIM PET FOR TREATMENT DEESCALATION IN POOR RISK
DIFFUSE LARGE B CELL LYMPHOMA (DLBCL). A PHASE II GELTAMO TRIAL***

Background: Treatment results for patients with high-risk DLBCL are unsatisfactory even in the rituximab era. In order to improve outcomes, autologous stem cell transplantation (ASCT) is still considered in prospective trials. The aim of our study is to assess the role of early PET in stratify ulterior treatment. Patients and method: This a prospective multicenter phase II trial. Patients (pts) with an age-adjusted IPI \geq 1 or equal to 1 with high beta2 microglobulin level were included. All pts received 3 cycles of R-MegaCHOP. A PET scan was performed at diagnosis and after the third cycle (PET3). PET3 negative pts received 3 additional R-MegaCHOP cycles. PET3 positive pts received salvage therapy with 2 R-IFE cycles and responding pts underwent ASCT with BEAM. Primary endpoint was progression-free-survival (PFS). Results: A total of 73 pts with a median age of 54 years (25-65) were included. 66 pts were evaluated after 3 R-MegaCHOP cycles: 0.7% of pts progressed; 54% achieved PET3 negative complete remission and received 3 additional cycles. 44.9% achieved PET3+ partial response and received R-IFE and 90% of them ASCT. At a median follow up of 19 months, 3 years PFS and OS were 68% and 77%, respectively. 3 year PFS and OS were 79% and 87%, respectively, in the R-MegaCHOP group (6 relapses, 4 deaths) and 59% and 73%, respectively, in the R-IFE/ASCT group (6 progressions, 6 deaths) ($p>0.1$ in both cases). Comments: In pts with high risk DLBCL good results can be obtained after induction with R-MegaCHOP with or without ASCT. Our preliminary results show that a treatment deescalation based on early PET could be an option, offering ASCT only to patients with a positive PET.

B 103 - S. Barna (1), F. Magyari (2), Zs. Miltényi (2), L. Váróczy (2), L. Gergely (2), Zs. Simon (2), J. Varga (1), Á. Illés (2), I. Garai (1)

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2: Internal Medicine Department, University of Debrecen

THE ROLE OF SUVMAX REDUCTION IN THE PROGNOSIS OF DIFFUSE LARGE B-CELL LYMPHOMA BASED ON INTERIM 18FDG PET/CT

The aim of the study was to assess the effect of Δ SUVmax in association with the progression-free, the event-free and the overall survival in east-Hungarian patients with DLBCL. The clinical value of the decrease of Δ SUVmax in relation to the prognosis of DLBCL has not been validated in the literature yet. Interim PET/CT scans were performed in 50 patients (21 f/29 m, mean age 54y) with newly-diagnosed DLBCL. 3 patients were diagnosed with stage I, 20 patients with stage II, 7 patients with stage III and 20 patients with stage IV DLBCL. The mean follow-up time was 581 days (60-1140). After 4 cycle R-CHOP both staging and interim PET/CT scans were done in all cases. The assessment was based on the decrease of Δ SUVmax between staging and interim PET/CT scans. Cox regression analysis with forward stepwise (likelihood ratio) method identified one single significant factor influencing the outcome variable defined as the relapse-free survival of patients: the relative change of SUVmax ($p=0.022$). Beyond this none of the other observed variables (baseline SUVmax, interim SUVmax, the absolute change of SUVmax and the age) had significant effect. Kaplan-Meier analysis showed that the relapse-free survival was significantly different in the subgroups of patients with relative SUVmax change in each quartile of the range by Breslow (Generalized Wilcoxon) test ($p=0.033$). The most relevant difference was found between the subgroups with Δ SUVmax below and over 80%.

B 104 - PREGNO P.¹, CHIAPPELLA A.¹, BELLO' M.¹, PASSERA R.¹, BOTTO B.¹, FERRERO S.¹, FRANCESCHETTI S.¹, GIUNTA F.¹, LADETTO M.¹, MENGA M.¹, NICOLOSI M.¹, PUCCINI B.², RIGACCI L.², VAGGELLI L.², SALVI F.¹, BISI G.¹ and VITOLO U.¹

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THE OUTCOME OF DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) PATIENTS TREATED WITH R-CHOP IS NOT PREDICTED BY INTERIM-18-FDG-POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY (PET) EVALUATION.

The role of Interim-PET in DLBCL is controversial. Aim of the study was to determine the predictive value of interim (I-PET) and final PET (F-PET) on Progression Free Survival (PFS) in a cohort of DLBCL patients treated with R-CHOP. Between April 2004 and October 2009, 88 DLBCL patients at diagnosis, were included and treated with 6-8 R-CHOP regardless of Interim-PET results. PET were performed at diagnosis, after 2-4 courses and at the end of therapy with centrally reviewing according to visual dichotomous criteria according to First Consensus Conference (Deauville 2009). Clinical features were: median age 55 years (18-80); stages I-II/III-IV 29/59; L/LI-I/IH/H IPI score 53/35. I-PET was performed after 2 R-CHOP in 58 patients, after 3 or 4 in 30. Results were: Interim-PET 72% negative, 28% positive; final-PET 88% negative, 12% positive; clinical complete response 90%. Concordance between clinical response and final-PET negativity was 97% due to 2 false positive. With a median follow-up of 26.2 months, 2-year OS and PFS were 91% and 77%. 2-year PFS rates for Interim-PET negative vs positive and for Final-PET negative vs positive were: I-PET 85% vs 72% (p.0475); F-PET 83% vs 64% (p<.001). Two Cox-models were tested for PFS. In model 1 Final-PET retained its value compared to Interim-PET (HR 5.03, 95%CI 1.37-18.43, p=.015 vs 1.27, 95%CI 0.40-4.03, p=.691); in model 2, Final-PET (HR 4.54, 95% CI 1.68-12.31) and IPI score (HR 5.36, 95% CI 1.91-15.05, p=.001) remained independent prognostic factors. In conclusion, positive interim-PET is not predictive of worse outcome in DLBCL patients treated with R-CHOP. Larger prospective studies and harmonization of criteria reading for Interim-PET are needed in DLBCL.

B 105 - RO Casasnovas*, M Meignan, A Berriolo-Riedinger, S Bardet, A Julian, C Thieblemont, P Vera, S Bologna, JP Jais, C Haioun, B Coiffier, F Morschhauser on behalf of the GELA, *CHU Dijon, France.

INTERIM [18]-FDG PET SUVMAX REDUCTION IS SUPERIOR TO VISUAL ANALYSIS BASED ON DEAUVILLE CRITERIA TO PREDICT EARLY PATIENT'S OUTCOME IN DLBCL

Interim PET could predict treatment outcome in DLBCL provided that suitable interpretation criteria are used. We previously demonstrated that visual analysis based on IHP criteria was related to an excess of false positive results compared to a semiquantitative approach using the reduction of maximal SUV (DSUVmax) at interim PET (Blood 2011;118: 37). In order to assess the clinical usefulness of the visual Deauville criteria (5PS) we compared the impact of interim PET interpretation according to 5PS and DSUVmax on the outcome of 84 patients (pts) included in the LNH2007-3B GELA trial. PET was done at baseline (PET0) and after 2 (PET2) and 4 cycles (PET4) of R-ACVBP or R-CHOP14. All PET scans were centrally reviewed and interpreted using 5PS criteria and DSUVmax values between PET0 and PET2 (DSUVmaxPET0-2) or PET4 (DSUVmaxPET0-4). According to 5PS, a PET scan was considered positive if greater than liver uptake. Pts with DSUVmaxPET0-2 >66% and DSUVmaxPET0-4 >70% were considered as good responders after 2 and 4 cycles respectively. Using 5PS criteria, respectively 46% and 65% of pts achieved a negative PET2 and PET4. 36 of 48 PET2+ pts had a DSUVmaxPET0-2 >66% and 22 of 30 PET4+ pts reached a DSUVmaxPET0-4 >70%. PET2 and PET4 results assessed by the 5PS criteria had no influence on PFS and OS. Conversely, DSUVmaxPET0-2 (>66% v ≤66%) identified 2 groups of pts with different 2 year PFS (77% v 57%; p=0.028) and OS (60% v 93%; p<0.0001) and DSUVmaxPET0-4 (>70% v ≤70%) was also more accurate to identify pts with different 2 year PFS (83 v 40%) or OS (94% v 50%) (p<0.0001). In summary, DSUVmax analysis of interim PET better predicts outcome than visual analysis based on 5PS criteria.

B 106 - Luca Ceriani, Sergio Suriano, Teresa Ruberto, (*) Emanuele Zucca and Luca Giovanella - Nuclear Medicine Dpt. and (*) Oncology - Oncology Institute of Southern Switzerland (IOSI) - Bellinzona (Switzerland)

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

AIM -To assess the inter- and intra-subjects variability of 18FDG mediastinum blood pool (MBP) and liver (L) uptake in patients (pts) with DLBCL treated with Rituximab (R)-based regimens.

MATERIALS AND METHODS -Fifty DLBCL pts undergone 18FDG PET-CT at baseline, after half of cycles (interim-PET) and after the end of therapy (final-PET) were enrolled retrospectively. 27 pts received R-CHOP and 23 R-MACOP-B/R-VACOP-B treatment. SUVmean and SUVmax values for L and MBP, their differences (L-MBP SUVmean and SUVmax) and their changes were calculated, respectively.

RESULTS-The inter-subjects variability (SD/mean x100) of MBP and L SUV values ranged from 20 to 26%. The L SUVmean and SUVmax significantly increased in the interim as compared with baseline-PET and decreased at the final-PET. Viceversa, the MBP SUV values showed no significant changes. The difference (L-MBP SUVmean) ranged -0.62 -1.21, 0.13 - 1.36 and -0.10 - 0.95 in basal, interim and final-PET with an inter-subjects variability of 97,46 and 49%, respectively. In six cases the MBP SUVmean was higher than L value and in 31 the difference was ≤ 0.25 . An increase in this difference was found in final and, particularly, in the interim-PET ($p < 0.05$). Comparable results were also obtained for L MBP SUVmax values. Different R-based regimens did not show significant impact.

CONCLUSIONS - Our data suggest that both L and MBP 18FDG uptake may be inadequate as references for the evaluation of different degrees of early response to R-based regimens. Particularly, the intra-subject variability of the L uptake during chemotherapy recommends great caution in employing it as gatekeeper in risk-adapted therapeutic strategies.

B 107 - Izutsu K, Kwong YL, Kim WS, Kodama T, Maeda Y, Hashimoto C, Suh C, Yamaguchi M, Suzumiya J, Nakamura S, Hyo R, Oshimi K, Suzuki R on behalf of The NK-cell Tumor Study Group (NKTSG)

PET AFTER 2 CYCLES OF SMILE IN A PHASE 2 STUDY FOR NEWLY-DIAGNOSED STAGE IV, RELAPSED OR REFRACTORY EXTRANODAL NK/T-CELL LYMPHOMA. NASAL TYPE

Background] Extranodal NK/T-cell lymphoma, nasal type (ENKL) is FDG-avid (Kako, Ann Oncol 2007). The role of PET in post-treatment or mid-treatment assessment, however, has not been extensively evaluated for ENKL. Therefore, using data of a phase II study of SMILE (SMILE-P2), we retrospectively evaluated the role of mid-treatment PET in ENKL. SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide) is a promising regimen for newly-diagnosed stage IV, relapsed or refractory ENKL (Yamaguchi, ASCO 2010, abstract 8044). [Patients & Methods] In the SMILE-PII, the responses after two cycles of SMILE were assessed by the Central Imaging Review Board according to CT-based criteria modified from the WHO response criteria. PET after two cycles, which had not been defined in the protocol, was performed in 16 pts out of 28 pts who completed the protocol. In the SMILE-PII, patients could undergo additional treatment at physician's discretion including additional cycles of SMILE and/or hematopoietic stem cell transplantation (HSCT). [Results] All of the 16 pts were responders (CR 9, PR 7) according to the CT-based criteria. PET after 2nd cycle of SMILE was positive in 5 pts, all of whom were in PR. All of the 16 pts but one had additional treatment including HSCT (10 pts). For overall survival (OS), there was a trend in favor of a group with negative PET after two cycles of SMILE with 1-y OS of 81.8% vs 40.0% (log rank, P=0.09). [Conclusions] In patients with newly-diagnosed stage IV, relapsed or refractory ENKL, mid-treatment PET might predict prognosis and deserves further evaluation. PET is a useful tool for judging the response of ENKL.

B 108 - Stefan P. Müller¹, Hong V. Ngo¹, Ulrich Dührsen², Andreas Bockisch¹, Andreas Hüttmann². 1. Nuclear Medicine,
2. Hematology, Universitätsklinikum, Essen, Germany

FDG-PET IN AGGRESSIVE NON-HODGKIN LYMPHOMA (NHL): Δ SUV VS. LYMPHOMA-TO-REFERENCE TISSUE RATIOS IN THE GERMAN MULTICENTRIC PETAL STUDY

In the German multicentric PETAL study the SUV reduction in lymphoma, Δ SUV, after 2 cycles of R-CHOP therapy (interim PET) compared to a baseline scan is used to intensify treatment in non-responders (Δ SUV \leq 66%). We are investigating whether interim PET alone may provide similar classification of non-responders using ratios of SUV in lymphoma to typical reference tissues commonly employed for comparison in visual scales.

For 145 of 261 patients studied so far in our center we calculated the ratios of maximum interim SUV in lymphoma to maximum and mean SUVs in spherical reference ROIs with 2 cm \emptyset in mediastinal blood pool, liver, and spleen. The ratio-based response was compared to the Δ SUV-based classification as the gold standard. Therefore, the sensitivity describes the agreement of the resulting study populations with the non-responder group of the PETAL study.

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

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

B 109 - Nathalie Nols, Nicolas Mounier, Salima Bouazza, Renaud Lhommel, Thierry Vanderborght, Anne Sonet, Marc André, André Bosly, Eric Van Den Neste. UCL, Belgique; Nice , France

QUANTITATIVE AND QUALITATIVE ANALYSIS OF METABOLIC RESPONSE AT INTERIM PET-SCAN IS HIGHLY PREDICTIVE OF OUTCOME IN DLBCL

We investigated whether interim metabolic response using adapted criteria had prognostic value in DLBCL. 74 pts (median 60 y; 47M/27F; IPI: low, 32%; low-int, 18%; high-int, 26%; high, 24%) treated with anthracyclin-cont. regimen, with baseline and mid-treatment (after 3 or 4 cycles) pet, were included. Qualitative analysis of response was done using Deauville's criteria, and quantitative analysis by comparing baseline to interim pet (Δ SUV(max)). Survivals are at 2 y. Deauville's score was 1 in 34%, 2 in 23%, 3 in 15%, 4 in 18%, and 5 in 10% of pts. Median Δ SUV(max) was 85% (-9% to 98%). Pts with score 1 to 3 had a better outcome than patients with score 4 or 5 in term of EFS (79% vs 36%, $P < .0001$), PFS (83% vs 47%, $P = .0006$), and OS (91% vs 58%, $P = .0003$). In pts with a Δ SUV(max) \geq or $<$ 66%, EFS (73% vs 41%, $P = .009$), PFS (78% vs 50%, $P = .02$), and OS (88% vs 56%, $P = .008$) were significantly different. Pts with a positive interim pet (score 4 or 5) and a Δ SUV(max) $<$ 66% had a particularly poor outcome (OS: 20%). Pts combining aaIPI 0 or 1, and negative interim pet either by Deauville's or Δ SUV(max) criteria, had particularly good outcome (EFS: 85%, PFS: 88%, OS: 94%). Deauville's response at interim pet and Δ SUV(max) independently predicted for EFS (HR 4.3, $P = .001$; HR 4.3, $P = .003$), PFS (HR 3.2, $P = .01$; HR 3.5, $P = .02$), and OS (HR 3.6, $P = .01$; HR 4.2, $P = .01$, respectively). aaIPI did not retained independent prognostic value. In this retrospective study, quantitative or qualitative analysis of metabolic response at mid-treatment was highly and independently predictive of any outcome (EFS, PFS, OS).

B 110 - Deok-Hwan Yang¹, Byun Byung Hyun², Jung-Joon Min², Jae-Sook Ahn¹, Yeo-Kyeong Kim¹, Hee-Seung Bom², Ik-Joo Chung¹, Hyeoung-Joon Kim¹, Won Seok Kim³ and Je-Jung Lee¹

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

We prospectively investigated the sequential interim PET/CT to determine whether it provided additional prognostic information for the treatment of PTCL. **Patients and Methods:** Fifty-nine patients with newly diagnosed PTCL were enrolled. The response of interim PET/CT was assessed based on the combined evaluation with visual assessment by Deauville five-point scale (5-PS), quantitative assessment of the maximal standardized uptake value reduction rate (Δ SUVmax) and quantitative assessment of metabolic tumor volume reduction rate (Δ MTV2.5). **Results:** 35 patients (59.4%) presented with advanced stage disease and 14 (23.7%) had bone marrow involvements. 52 patients could be assessed the interim response based on Deauville 5-PS and 18 patients (34.6%) remained positive metabolic uptakes. After following median 12.9 months (range, 0.5-75.0), the positivity of interim PET/CT was significantly prognostic factor in PFS with a hazard ratio of 3.19 (1.48 - 6.89). The 2-year PFS rate was significantly different in the patients with interim PET-positive (27.8%) and interim PET-negative (56.7%) interim PET/CT ($P=0.004$). Among the patients, we re-analyzed the 34 patients who were available for the interim response based on three parameters of the visual, SUVmax, and MTV2.5. Both Deauville 5-PS and the optimal cutoff value of Δ SUVmax could predict the prognostic difference in patients with PTCL. However, the percentage of MTV2.5 reduction failed to differentiate the patients for predicting the progression. **Conclusions:** The combined assessment using Deauville 5-PS, SUV-based and MTV-based interim PET/CT could have a differential potential for predicting the prognosis in PTCL.

B 111 - H Lanic, S Mareschal, F Mechken, JM Picquenot, P Bertrand, P Ruminy, C Bastard, H Tilly, P Vera, S Becker, F Jardin.
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GENE EXPRESSION PROFILE AND INTERIM TEP SCAN ARE TWO COMPLEMENTARY AND INDEPENDENT TOOLS TO PREDICT THE OUTCOME OF DLBCL

The aim of the study was to assess the relationship between molecular classification and PET scan features in DLBCL. 57 cases treated by CHOP/CHOP-like+R were retrospectively analysed (median age = 65y, aaIPI 0-1 = 30%, 2-3 =70%). PET scan results at diagnosis (SUVmax), following 3/4 cycles of chemotherapy (interim PET) and at the end of treatment (final PET) were correlated to molecular features. Expression profile of 18 genes related to GCB/ABC signatures and 5 genes coding for glucose transporters (GLUT) was determined. Gene expression profiling classified 30 DLBCL in the GCB (2-year PFS=76%) and 27 in the ABC subtypes (2-year PFS=51%, p=0.03). Expression of GLUT2 was significantly higher in DLBCL with SUVmax \geq third quartile, regardless the GCB/ABC subtype. At base-line, SUVmax was higher in the GCB subtype (p = 0.029) but was not predictive of the outcome. Using semi-quantitative assessment of SUV decrease at interim PET (DSUV) fast (n=36) and slow (n=9) responders (DSUV \geq or $<$ 70%) were defined. In multivariate analysis, GCB/ABC(OR=5.1), aaIPI(OR=7.1) and slow/fast responses (OR=0.1) were independently correlated with PFS and OS. Using the GCB/ABC classification and interim PET, we identified patients with a very favourable outcome (2-year OS/PFS = 100%) characterized by a GCB phenotype and a fast metabolic response. Conversely, in the GCB group, slow responders display a very poor prognosis (2-year OS=33%). DLBCL with fast metabolic responses but belonging to the ABC subtype displayed an unfavourable outcome (2-year OS = 57%). In conclusion, Molecular classification and interim TEP scan are two strong complementary and independent prognostic factors in DLBCL

B 112 - E González-Barca, M Canales, MJ Vidal, A Oriol, A Salar, J Bargay, M Cortés, J Coya, JF Tomas, A López, JJ Sánchez, E Donato, A Llorente, S Ferrer, D Caballero, on behalf of GEL/TAMO

PREDICTIVE VALUE FOR EVENT-FREE SURVIVAL (EFS) OF INTERIM PET IN PATIENTS WITH DLBCL TREATED WITH 6 CYCLES OF DOSE-DENSE R-CHOP-14

Background: the role of an interim PET to early identify patients with poor survival after chemotherapy in DLBCL patients is controversial.

Aim: to evaluate the predictive value for EFS of an interim PET (after 2 cycles) in patients with DLBCL treated with 6 cycles of dose-dense R-CHOP-14 chemotherapy.

Methods: prospective clinical trial for patients with DLBCL older than 65 with IPI 0-5 or younger than 65 with IPI 0-2. Treatment consists on 6 cycles of R-CHOP administered every 14 days followed by pegfilgrastim on day 2. Interim PET results did not change the planned treatment.

Results: 124 patients were included in the trial, over 105 who completed 6 cycles of treatment, 69 with complete PET evaluation (at diagnosis, after 2 cycles, and at the end of therapy) were included in the analysis. Characteristics of the population: median age 61.6 yo (18.2-82.8); males: 37 (53.6%), ECOG 0-1: 59 (85.5%), stage III-IV: 45 (65.2%), bulky disease: 17 (24.64%), >2 extra-nodal sites: 4 (5.8%), B symptoms: 18 (26.1%), elevated LDH: 36/67 (53.7%), elevated beta-2-microglobulin: 23/62 (37.1%), IPI 3-5: 23 (33.3%). Thirty-four (49.3%) patients achieved a negative PET evaluation after 2 R-CHOP cycles and 57 (82.6%) at the end of therapy. With a median follow-up of 29 months (limits 6-49), EFS was 64.4% for patients with positive interim PET and 91% for patients with negative interim PET (p=0.025). EFS was 25% for patients with positive end-of-treatment PET and 89.7% for patients with negative end-of-treatment PET (p<0.001).

Conclusions: a negative interim PET is highly predictive of a good outcome and patients with a positive interim PET have significantly worse EFS.

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COMPARISON OF QUANTITATIVE & QUALITATIVE RESPONSE CRITERIA IN THE UK-NCRI PET STUDY IN DLBCL- AN INTERIM ANALYSIS

Background: Various criteria for interim PET response assessment are currently being investigated in Diffuse Large B-cell Lymphoma (DLBCL). We compared 3 sets of criteria in a cohort of patients who underwent blinded FDG-PET after 2 cycles of RCHOP as part of an ongoing UK-NCRI study.

Method: The "PET after 2 cycles in NHL" study is aiming to recruit 200 "eligible" patients (with baseline and post-cycle 2 PET) & is expected to reach its target later in 2011. In June 2011, 197 patients were enrolled, of whom 171 were eligible. Of these 125 have completed treatment & were included in this analysis. We compared the original response criteria of the study (SS), the Deauville criteria (DS) & Δ SUV. We also compared 2 definitions of DS 5; 2 times & 3 times the liver activity.

Results: 54 patients with excellent response who had SS 1(no uptake), 2a (MRU) & corresponding DS 1, 2 were classified as responders with Δ SUV >66%. Only 3 pts had SS 2c (stable) who were classified as 1 DS 4 and 2 DS 5. No patients had SS 2d (progression). 69 patients had SS 2b (partial response) and were distributed in DS 2-5, with the majority being DS 3 (25) and 4 (32). 25/28 DS 3 had >66% Δ SUV with the 2 classified as non-responders having baseline SUVmax of 4.1 & 5.6. In DS 4, 32/36 patients had Δ SUV >66%. Overall, only 14/125 pts (11%) had Δ SUV <66%.

Conclusions: There is good concordance between the 3 criteria in patients with excellent response (DS 1+2) & poor response (DS 5). Patients with PR are classified differently by different criteria & most of DS 3+4 classify as responders by Δ SUV. DS 5 defined as 2 times changes 7 pts from DS 4 to 5. Outcome data is awaited to define the best criteria.

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THE IMPACT OF R-VACOP-B AND THE PROGNOSTIC SIGNIFICANCE OF INTERIM FDG-PET/CT ON THE OUTCOME IN PRIMARY MEDIASTINAL LYMPHOMA

The choice of a rituximab-based regimen and the prognostic significance of interim FDG-PET/CT in primary mediastinal lymphoma (PMBCL) are still debatable issues. We evaluated the clinical features and outcomes of 95 consecutive patients with PMBCL who were treated in Sheba Medical Center between 1985 and 2009. 43 patients received rituximab-based chemotherapy: R-VACOPB (n=30) or R-CHOP21 (n=13), whereas 52 patients were treated with VACOPB (n=47) or CHOP21 (n=5) in the pre-rituximab era. Radiotherapy was not given following initial chemotherapy. Patients who received rituximab as part of treatment had 5-yr PFS of 79% and OS 97% compared with 58% (p=0.06) and 88% (p=0.2), respectively, without rituximab. Notably, 5-yr PFS in patients treated with R-VACOPB, R-CHOP21, VACOPB or CHOP21 were 83%, 69%, 62% and 20%, respectively (P=0.039). However, direct survival comparison showed that the difference between PFS rates in patients receiving R-VACOPB compared to R-CHOP21 was not statistically significant (p=0.3). Mid-interim FDG-PET/CT scans were performed in 30/43 patients who received R-VACOPB (n=19) or R-CHOP21 (n=11). The negative predictive values of mid-PET activity were high (100% for R-VACOPB and 86% for R-CHOP21), while the positive predictive values (PPV) were relatively low (30% and 75%, respectively). Despite the low PPV, overall, the 5-yr PFS for mid-PET negative patients (n=16) was significantly higher (94%) than for mid-PET positive (n=14) patients (57%, P=0.015). Conclusions: 1) The superiority of VACOPB over CHOP21 for treatment of PMBCL disappears once rituximab is included. 2) mid-PET activity has a prognostic impact on the outcome of patients with PMBCL.

B 115 - LH Sehn, P Hoskins, R Klasa, KJ Savage, T Shenkier, RD Gascoyne, T Pickles, J Morris, F Benard, D Wilson, JM Connors
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PHASE II TRIAL INVESTIGATING TAILORING INITIAL THERAPY FOR ADVANCED STAGE DLBCL BASED ON INTERIM PET RESULTS - A PRELIMINARY REPORT

Currently, approximately 70% of all patients with DLBCL can be cured with R-CHOP. Despite increasing biologic insight, the ability to predict outcome with clinical and biologic predictors remains limited. The use of interim PET may provide a functional predictor of response to therapy to enable a tailored approach before further resistance develops. We are currently performing a phase II trial investigating interim PET in patients with advanced stage DLBCL in British Columbia. Patients >17 years of age with biopsy proven de novo DLBCL, planned for curative therapy with R-CHOP, with an ECOG PS <3, and no significant co-morbidities are potentially eligible. In an attempt to capture patients treated across the province, patients could be enrolled at any time prior to cycle 4 of R-CHOP, provided they meet all eligibility criteria and had routine staging investigations performed and were treated with standard dose R-CHOP. Interim PET scans are performed following cycle 4 (between day 21 to day 28 to minimize false positive scans). PET negative patients complete therapy with 2 additional cycles of R-CHOP, while PET positive patients are switched to receive 4 cycles of R-ICE. This trial is ongoing and a preliminary report will be provided at the meeting.

C 100 - Louisa Barré 1, Martine Dhilly 1, Ahmed Abbas 1, Charles Dumontet 2, Michel Leporrier 3.

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A NOVEL PET PROBE FOR LYMPHOMA IMAGING: [18F]FLUDARABINE

Lymphoma represents a very heterogeneous pathologic disease group and its initial assessment, treatment strategy and prognosis is closely related within each histological subtype. [18F]-FDG PET a functional and metabolic imaging tool has taken a major position in the pretreatment staging, restaging, therapy monitoring as well as post-therapy surveillance of lymphoma. However, the observed results remain sometimes equivocal, depending, among other criteria, on the histological subtype of the lymphoma, leading to false negative results in low grade lymphomas (SLL, MALT). Moreover, the lack of specificity of [18F]-FDG leads to false positives in the case of increased glycolysis.

The aim of our work was to develop from fludarabine, a drug used in low-grade non-Hodgkin's lymphoma treatment, a novel PET radiopharmaceutical ([18F]-fludarabine) and evaluate its potential in preclinical studies. Fludarabine was labeled with [18F]-KF. After purification and formulation of [18F]-fludarabine, a preliminary study was conducted using normal mice (control), tumor-free SCID (Severe Combined Immuno Deficient) mice and SCID mice bearing RL lymphomas. Animals were injected via the tail vein with [18F]-fludarabine and microPET imaging study was performed during 60 min. The results suggest that [18F]-fludarabine possesses specific affinity for lymphoid tissues. This is supported by the observation that this compound is preferentially localized in spleen and in tumors. The preliminary biological evaluation as a new PET tracer for lymphoma is very promising. A comparative study with [18F]-FDG will be presented.

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"TUMOR-FINDER" AND "RESPONSE-CONTROLLER" - SEMIAUTOMATIC ALGORITHMS FOR DETECTION AND QUANTIFICATION OF TUMOR LESIONS IN LYMPHOMA

Aim: Compared to malignant solid tumours with usually no or little metastasis Hodgkin's lymphoma (HL) do show a lot of involved sites. Thus, initial staging and especially response evaluation of PET/CT studies is a time consuming process. Therefore we are developing a semi automatic software tool to identify VOIs to be most likely manifestations of HL in the initial PET. These can directly be projected on follow up PET to gain an efficient visual and semi quantitative restaging process. In this abstract we would like to describe the methodical approach and our first results.

Method: The software consists of two modules, "*Tumor-finder*" for initial staging and "*Response-Controller*" for response evaluation. The "*Tumor-finder*" module creates VOIs of potential tumor lesions in PET by a source-to-background ratio based segmentation. The threshold is defined by $(SUV_{\text{meanLiver}} + 3 \text{ SD})$ using a cuboid VOI of 30ml for liver background. This criteria is based on PERCIST for tumor burden estimation [1]. While PERCIST is defined for solid tumors, it has also proven as a stable criteria in our test for HL. Candidate VOIs in close distance are grouped by applying clustering techniques. For identification of skeletal lesions, bone segmentation is performed in CT studies and transferred into the co-registered PET after applying a hole filling filter. Based on histogram analysis, a different background value is used for identifying skeletal bones. Statistics ($SUV_{\{\text{max, mean, peak}\}}$, MTV, lesion glycolysis) for all lesions is automatically calculated, summarized and displayed in a table. Each possible lesion is also projected on a PET-MIP for quality control. False positive findings can be removed manually by selecting them in the table or directly in the PET-MIP. Finally, the lesion set is exported as DICOM RT structure set. The "*Response-controller*" module first automatically coregisters initial-CT with follow-up CT. After this step, follow-up PET is coregistered with follow-up CT. For coregistration quality control, initial PET and follow-up PET are shown in a fused display. The initial lesion VOI-set is then projected in the follow-up PET. For all VOIs of the initial study, SUV_{peak} based on a VOI_{peak} consisting of the hottest four voxel is automatically calculated to avoid variability compared to single-voxel. This value is then normalized to $SUV_{\text{meanLiver}}$ and compared to the value of the initial study VOI. All VOI_{peak} created are sorted by the highest residual uptake and presented to the user in a table of potential residual pathological uptake. They also act as bookmarks and allow jumping to each VOI_{peak} for inspection of the residual uptake automatically detected.

Results: The given approach was evaluated on 33 patients with newly diagnosed paediatric HL and compared to the results of conservative reading process. In the "*Tumor-Finder*" module, separation of the skeleton from the CT performed correctly in 22/33 patients. In 11 PET/CT studies positive oral contrast agent had been used, resulting in additional separation of parts of the intestine, which had to be removed manually. Lesion segmentation correctly identified 157 of 170 lesions. Areas with physiologically increased uptake (bladder, heart, e.g.) could be easily removed manually. An automatic approach to remove common areas of physiologically increased uptake is still in development. First tests of the "*Response-Controller*" module are promising, results on a pilot group of 50 patients will be presented. If the implemented tools for follow-up studies will turn out to be sufficient as well, this software could be very helpful and time efficient in investigating follow-up PET/CT studies in direct comparison to initial staging studies.

Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: Evolving Considerations for PET response criteria in solid tumors. J Nucl Med. 2009 May;50 Suppl 1:122S-50S.

C 102 - Alain Rahmouni (1), Sarah Toledano (1), Chieh Lin (1), Emmanuel Itti (2), Corinne Haioun (3), Alain Luciani (1). Department of Medical Imaging, Nuclear Medicine and Hematology, CHU Henri Mondor (France)

WHOLE-BODY MR DIFFUSION IN PATIENTS WITH LARGE B-CELL LYMPHOMA: A PRELIMINARY ADC MAPPING STUDY AT 3T

Purpose: to evaluate the feasibility of whole-body MR diffusion imaging in patients with large B cell lymphoma before and after four cycles of chemotherapy

Material and Methods: From the cervical region to the inguinal region, axial single-shot echo-planar images were acquired at $b = 50, 400, \text{ et } 800 \text{ s/mm}^2$ with chemical fat suppression and respiratory gating. MR imaging technique included surface phased-array coils covering the patient allowing parallel acquisition and a roller plat-form table allowing 24 5mm-thickness images per station. ADC mapping was generated for all images. Image quality, total acquisition time, ADC values of nodal lesions were measured before and after four cycles of chemotherapy. Results were compared with those of combined FDG-TEP-CT.

Results: On a 1 to 4 scale, image quality was 3.4. Mean total time of acquisition was 19 min. Mean ADC was $0.792 \times 10^{-3} \text{ mm}^2/\text{s}$ (SD: 0.236) before treatment and increased to $1.303 \times 10^{-3} \text{ mm}^2/\text{s}$ (SD: 0.793) after treatment. Seven patients had no FDG uptake after treatment with increased ADC value of all residual nodes. One patient had a persistent FDG uptake of one nodal region with a restricted ADC equal to $0,599 \times 10^{-3} \text{ mm}^2/\text{s}$.

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

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TUMOR VOLUME EVALUATION: COMPARISON BETWEEN CT AND PET/CT IN PHANTOMS AND PATIENTS WITH HODGKIN LYMPHOMA

Aim: the tumor burden is an important prognostic tool in pts with Hodgkin lymphoma (HL) but the definition on CT images is complex and time consuming. FDG PET/CT is accurate in staging pts with HL. Aim of this study is to compare CT and PET/CT in calculating the tumor volume (VL).

Methods: twelve fillable objects characterized by different VL (range 0.5-1700 cm³), shape and complexity were filled with a solution of water and 18F and then acquired with PET/CT. The VL was calculated on CT (manually) and PET images separately and blindly by a radiologist and a nuclear medicine physician. A semiautomatic segmentation software (PET VCAR - Volume Computer Assisted Reading - GE) was used for PET VL calculation using for contouring different thresholds (35-40-45-50-55-60%). CT and PET VLs were compared with the actual VLs. We compared also MDCT and PET/CT tumor VLs in 16 pts with HL.

Results: compared with the actual object VLs, CT and PET global VL was +4% and +1%, respectively. The best PET threshold for segmentation was 45%. Dividing the VLs in "small"(five: range 0.5-26.5 cm³) and "big"(seven: range 70-1700 cm³) CT VL was -28% and +4% and PET VL +4% and +1%, respectively.

In HL pts the CT VL range was 13-840 cm³. PET VL was comparable (+/-20%) in 7/16 pts while in the other 9 pts the discordance range was from -47% to +86%. The best threshold for pts is variable and often a visual evaluation needs. VL calculation time/pt was 10' (range 5'-15') with PET, much less than CT.

Conclusions: PET/CT is a valid tool for VL evaluation. The prognostic value of functional tumor VL needs to be evaluated in clinical studies.

C 104 - S. Chauvie (3); A. Stancu (3); A. Biggi (1); P. Cerello(4); A. Cavallo (2); A. Gallamini (2);

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WIDEN : A NEW ONLINE TOOL FOR IMAGING-BASED CLINICAL TRIALS MANAGEMENT

Background: Recently a novel clinical trial generation for lymphoma treatment was launched in which a flexible therapeutic strategy is adapted to tumour chemosensitivity. The latter is assessed by a functional imaging technique such as PET scan, performed early during treatment. As a consequence, a central review of the images became necessary. A new web-based online tool called WIDEN (Web-based Imaging Diagnosis by an Expert Network) was developed to allow PET images exchange and review within the prospective multicenter Italian clinical trial HD 0607, in which Hodgkin Lymphoma (HL) treatment is tailored on results of interim PET scan performed after 2 chemotherapy cycles. **Methods:** In the HD 0607 clinical trial patients affected by advanced-stage HL are treated by standard ABVD therapy for 2 courses, followed by an interim PET scan (PET-2). PET-2 along with the baseline scan (PET-0) is uploaded to a dedicated web site thanks to WIDEN and hence distributed to reviewers. Reviewers report the scans within 72 hours from the upload and determine the choice whether intensify or not the treatment intensity (NCT identifier 00795613). **Results:** The average (median) time per scan upload and download were 14'33" (3'23") and 6'56" (3'34") respectively. The average (median) PET scan size were 133.3 MB (120.7 MB), with a minimum size of 51.2 MB and a maximum size of 469.8 MB. The average (median) time frame between the case files upload by the submitting centre and the case review reporting was 84h 21' (47h 06'). 10% of the cases were reviewed among the fourth and the fifth days. 12% cases were reviewed after the fifth days. In cases of a delayed scan review beyond three days the delay depended on the presence of a week-end or other holiday time. If one excludes the "training period" of the first three months just after the protocol start, the average (median) time frame between the files upload by the submitting centre and the availability of the review results was 54h 24' (39h 42'). 7% of the scans were reviewed among in days 4 and 5; 7% of the cases were reviewed after the fifth day. **Conclusions:** WIDEN proved to be an effective tool for medical imaging exchange and review. Data security, simplicity, low cost, feasibility and prompt scan review were demonstrated. Its applicability in any clinical trial in which imaging is decisional for treatment modulation is warranted.

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METABOLIC TUMOR BURDEN (MTB), TUMOR SUVMAX AND WHOLE BODY SUVMAX (WBSUVMAX) IN PATIENTS WITH DLBCL IN THE LNH07-3B TRIAL: A PRELIMINARY ANALYSIS

Objective: To investigate the feasibility of MTB measurement and its relationship with tumor and whole body SUVmax in DLBCL.

Materials and Methods: the baseline PET/CT of 56 patients included in the LNH07-3B trial was analysed with MT measurement of each hypermetabolic mass done with a semi automatic method using various volume shapes (cube, sphere, cylinder) and systematic thresholding of 41% of the maximum SUV. The best fitting was decided visually by the operator. The interobserver reproducibility was tested on 10 patients. The MTB was calculated as the sum of the individual MT. Patients were divided in three subgroups :1- predominant abdominal mass, 2- predominant mediastinal mass 3- diffuse involvement. WBSUVmax was determined as previously described (Blood 2011; 118; 37).

Results: 129 tumoral masses were selected in 56 patients. The best fitting for MT measurement was obtained with a cubic shape especially for abdominal masses. Median MT was 57cc (0.6-776) with a high dispersion of size (skewness=1.6, p=0.0001). Median SUVmax of the tumors was 17.3 (2.5-49.2). Correlation between MT and tumor SUVmax was very weak, some cases with small MT being associated with high SUVmax or conversely. Median MTB was 230cc (12.5-1208) and median WBSUVmax was 22 (2.9-49.2). Median MTB and SUVmax were 258 (12.5-856) and 20 (3.7-49) in subgroup 1 (n=19), 265 (65-637) and 19.9 (10.8-31.9) in subgroup 2 (n=18) and 158 (31-1208) and 22.8 (2.9-38.1) in subgroup 3 (n=19) respectively. There was no correlation between MTB and WBSUVmax in both the whole cohort or in each patients subgroup. In conclusion, there was no correlation between MTB and either tumor SUVmax or WBSUVmax.