

clinical meaningfulness. This increased symptom burden did not translate into a difference in overall QOL. These data suggest that either females enjoy a higher QOL despite experiencing more symptoms, or, conversely, that both genders enjoy the same QOL because the symptom burden is in fact equal but females are more likely to report their symptoms. As previously reported, females described more abdominal symptoms. However, in distinction to previous reports, these symptoms were not the result of abdominal thrombosis suggesting that abdominal symptoms in females are multifactorial and worthy of additional investigation. Though higher rates of macrothrombosis have been previously documented in females, the high rates of microvascular symptoms and platelet counts suggests females may also suffer from higher rates of microthrombosis.

Hodgkin lymphoma - Clinical

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OUTCOME OF PATIENTS AGED OVER 60 WITH CLASSICAL HODGKIN LYMPHOMA TREATED WITH ABVD

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Background: Approximately twenty percent of classical Hodgkin's Lymphoma (cHL) patients are aged over 60 years. There is no standard of care in this age group. ABVD (Doxorubicin, bleomycin, vinblastine and dacarbazine), proposed for younger patients, is also used in elderly patients but little is known about its toxicity and efficacy. Recently, the German group published his experience for early-stage cHL treated within their trials with ABVD and concluded that four cycles were associated with substantial toxicity leading to dose reduction, delay and mortality.

Aims: In order to evaluate our everyday life practice, we reviewed patients referred to three French hematological departments.

Methods: We retrospectively analyzed efficacy and toxicity of ABVD in 147 patients aged over 60 years referred to Hôpital Saint-Louis in Paris, Institut Paoli Calmette in Marseille and Centre Henri-Becquerel in Rouen between January 1997 and September 2012.

Results: Median age was 68 years (60-88), sex ratio 82M/65F. According to Ann Arbor, stage was I-II-III-IV in 16-47-42-42 patients, respectively. Performance status was 0 in 61 patients, 1 in 50, 2 in 24, and >2 in 5. B symptoms were present in 84 patients. All patients received at least 1 ABVD (1-8), 50 patients received additional radiotherapy. 120 patients achieved a CR (82%), 5 a PR, 15 had refractory disease and 7 couldn't be evaluated. Twenty-five patients relapsed and 11 of them achieved a CR2. Pulmonary toxicity occurred at a median delay of 5 months from the first cycle (range: 1-31). Early pulmonary toxicity (32 patients) led to a treatment regimen modification in 24 patients. There was no significant correlation between pulmonary toxicity and pulmonary history, tobacco use, age, G-CSF, and radiotherapy. Overall survival for the whole group at five years was estimated at 67% (95% CI 58-74). Overall survival was significantly influenced by age ≤ 70 vs >70, stage I-II vs III-IV and PS 0 vs ≥ 1. With a median follow-up of 58 months, 52 patients died, 18 from disease progression, 17 from toxicity, 11 from secondary tumors and 6 from unknown cause.

Summary and Conclusion: Our study confirms the efficacy of ABVD in elderly patients. The high frequency of pulmonary events let us to propose either to remove bleomycin from the regimen or to reduce the dose as no factor appears to predict the occurrence of this toxicity.

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EVALUATION OF THE PROGNOSTIC ROLE OF TISSUE ASSOCIATED MACROPHAGES (TAM) IN HODGKIN LYMPHOMA AND CORRELATION WITH EARLY FDG-PET ASSESSMENT

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Background: Hodgkin Lymphoma (HL) is a highly curable malignancy that mostly affects young adults; despite satisfactory results, about 20% of patients still die of relapsed/refractory disease and late toxic effects rate, often due to over treatment, continue to rise with time. Consequently, the optimal treatment should be designed based on prognostic models, but currently all of them predict outcome with scarce accuracy. Since in the last few years "early FDG-PET" and tissue macrophages infiltration in diagnostic specimens (TAM) emerged as powerful independent prognostic predictors, we previously conducted a pivotal analysis aimed to confirm these issues and looking for a possible link between the 2 tools, concluding that only early FDG-PET was a reliable prognostic factor.

Aims: The primary endpoint of this study was to investigate, in a larger cohort of patients with a longer follow-up, the prognostic role of both early-FDG PET and TAM, while the secondary endpoint was to test if early-FDG PET positivity could correlate with high TAM in diagnostic specimens.

Methods: A cohort of 200 patients (M/F: 105/95; median age 33.5 yrs) diagnosed and treated at 6 Italian hematology institutions between March 2005 and December 2012 was retrospectively analyzed. All patients, diagnosed with classic HL, completed staging with whole body CT scan, FDG-PET and bone marrow biopsy. Eleven patients had stage I disease, 92 stage II, 55 stage III and 42 stage IV. Induction treatment plan consisted, according to staging, of 2-6 courses of ABVD and, if indicated, involved field radiation therapy. Patients repeated CT scan and FDG-PET after 2 cycles and after the completion of therapy. TAM in paraffin embedded diagnostic specimens were determined by immunohistochemistry with a monoclonal antibody (anti-CD68 KP1, Dako®) and classified in 3 groups, based on the percentage of CD68+ cells, as previously reported by Steidl and coworkers (NEJM; 2010).

Results: Overall, 168 out of 200 (84%) patients achieved a complete remission (CR), while 32 (16%) failed first line treatment, with 10 partial responses (PR) and 22 non-responders (NR); among responders 20 pts (10%) relapsed. After 2 cycles of ABVD, FDG-PET was negative in 163 patients (81.5%) and positive in 37 patients (18.5%), showing a high negative predictive value of 93% (95% CI=88-96%) and a significant correlation with the achievement of CR ($p < .0001$ by Fisher exact probability test). After a median follow-up of 40 months 194/200 patients were alive, progression free survival (PFS) was significantly better for PET negative patients ($p < .0001$). CD68 expression in diagnostic specimens was low, intermediate or high in 26 (13%), 100 (50%) and 74 (37%) cases respectively; moreover TAM score among responders was low in 23/168 cases (13.7%), intermediate in 85 (50.6%) and high in 60 (35.7%), while in non-responders was low in 3/32 cases (9.4%), intermediate in 15 (46.9%) and high in 14 (43.7%). PFS analysis showed no significant difference in any score group. Analysis aimed to evidence a possible role of TAM as prognostic factor and its possible correlation with early FDG-PET resulted not statistically significant performing the Freeman-Halton extension of the Fisher exact probability test. We observed the same results when we separately analyzed both early (I and IIA) and advanced stage disease.

Summary and Conclusion: The results of this study confirm that early FDG-PET has a high prognostic power, while TAM score doesn't seem to influence the outcome of patients with HL; moreover, in contrast to our original hypothesis, doesn't correlate with FDG-PET assessment.

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ROLE OF BONE MARROW BIOPSY IN HODGKIN LYMPHOMA STAGING IN THE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY ERA

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Background: In recent years, several studies investigated the role of routine bone marrow biopsy (BMB) in newly diagnosed classic Hodgkin's lymphoma (cHL) staged with positron emission tomography (PET/CT): recently, a meta-analysis reported data of 955 cases in 9 different studies, to determine whether BMB is still necessary in patients (pts) staged at diagnosis with PET/CT.

Aims: We report data of pts with cHL assessed at diagnosis with both BMB and PET/CT in order to evaluate their concordance in the detection of bone marrow involvement from cHL.

Methods: Data from pts with cHL diagnosed consecutively since 2007 to 2013 at 14 haematology centers of the Fondazione Italiana Linfomi (FIL) were retrospectively collected, excluding those who did not performed both baseline BMB and PET/CT; Ann Arbor stage assessed only with PET/CT was then compared to stage resulting from PET/CT combined to BMB. The predictive significance of PET/CT was determined in terms of positive (PPV) and negative predictive value (NPV), sensitivity and specificity.

Results: In this survey we included 1180 pts; 152 were excluded due to the lack of baseline BMB or PET/CT. 1028 cases were evaluated, median age 33 (range, 14-80 years), 542 male (53%). Nodular sclerosis (70%) and mixed cellularity (20%) were the most common histotypes; bulky disease and B symptoms were present in 27% and 42% of pts, respectively. 148 pts (14%) presented one or more focal skeletal lesions at PET/CT and 53 (5%) had a positive BMB; other patients' characteristics are summarized in table. In 33/53 pts focal skeletal lesions evidenced by PET/CT revealed a positivity of BMB, while in 860/975 pts the absence of skeletal lesions or a diffuse skeletal FDG uptake combined with a negative BMB. Based on these data, PPV and NPV resulted to be 22% and

98%, respectively; sensitivity and specificity were 62% and 88%, respectively. Moreover, a total of 9 patients (1%), one in stage II (0.1%) and 8 in stage III (0.8%) according to PET/CT were upstaged by BMB to stage IV, inducing a change in treatment only in 1 patient (0.1%). Central revision of PET/CTs in BMB-positive cases is ongoing, and will be ready for June 2014.

Table 1.

Correlation between PET/CT-assessed staging and BMB results				
	Patients with negative BMB (n=974)		Patients with positive BMB (n=53)	
	No	%	No	%
PET/CT Ann Arbor stage				
I	52	6	0	0
II	520	53	1	2
III	284	29	9	17
IV	188	19	41	81
Focal skeletal PET/CT lesions				
Unifocal	38	4	1	2
Multifocal	34	3	2	4
No focal lesions	84	8	34	64
Non-specific diffuse skeletal FDG uptake	860	88	20	38
Overall	117	12	8	15

Summary and Conclusion: Consistently to data previous reported, in stages I-II according to PET/CT, positive BMB were occasional; moreover, the NPV of PET/CT for bone marrow involvement was very high. Furthermore, the influence of BMB on the planning of treatment was minimal. On these grounds, BMB may be omitted in cHL patients staged with PET/CT.

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Abstract withdrawn

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A RANDOMIZED TRIAL OF ROUTINE SURVEILLANCE IMAGING PROCEDURES: ULTRASONOGRAPHY PLUS CHEST RADIOGRAPH vs FDG PET/CT FOR DETECTING RELAPSE IN PATIENTS WITH ADVANCED STAGE HODGKIN LYMPHOMA

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Background: Despite the high complete response (CR) rate to induction therapy with ABVD or ABVD-like regimens, about one-third of Hodgkin lymphoma (HL) patients with extensive disease at presentation are expected to relapse over time upon treatment discontinuation. Usually, 30%>50% of relapses are clinically asymptomatic, lacking any physical and/or laboratory sign. For patients at high risk of relapse, a close monitoring plan based on imaging procedures is justified, since early detection of recurrence allows a timely administration of appropriate salvage therapy. Nevertheless, only few clear indications for monitoring such patients are presently available. The existing guidelines are not evidence-based, and post-treatment follow-up is still left to "expert opinions". New imaging approaches are now available, and require validation in a randomized fashion.

Aims: This randomized study compared the benefits and pitfalls of [¹⁸F] fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) vs. ultrasonography (US) plus chest radiograph (CXR) to systematically follow-up patients with high risk HL. This study was designed as an equivalence trial.

Methods: From January 2001 to December 2009, in this single centre trial, after institutional review board approval and informed consent, patients with advanced stage HL, completely responding to first-line treatment, were randomly assigned (1:1) to either PET/CT-based or US+CXR-based follow-up. Follow-up imaging procedures in the US+CXR group comprised ultrasonographic scans for the evaluation of superficial-anterosuperior mediastinum-abdominal-pelvic (S-M-A-P) lymph nodes, and frontal and lateral CXR for the evaluation of mediastinum compartments. In the PET/CT group, total-body FDG PET/CT scans were carried out using a combined in-line system. The surveillance schedule for each arm implied 12 checkpoints, including clinical and imaging procedures, at 4, 8, 12, 16, 20, 24, 30, 36, 48, 60, 84 and 108 months after treatment discontinuation. When clinical and/or imaging procedures were positive, recurrence was histologically confirmed. The primary end-point was to compare the sensitivity of the two follow-up imaging approaches. Secondary endpoints were their specificity, positive and negative predictive values, time to recurrence detection, radiation risks and costs.

Results: Overall, 300 patients were randomized in the two arms. The study was closed after a median follow-up of 60 months, with a relapse rate of 27%.