Indolent NHL

418 FOLLICULAR LYMPHOMA, IMMUNOCYTOMA, AND MANTLE CELL LYMPHOMA: RANDOMIZED EVALUATION OF CURATIVE RADIOTHERAPY IN LIMITED STAGE NODAL DISEASE

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On behalf of the study group
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Background: Indolent lymphomas in early stage nodal disease can be treated effectively by radiotherapy (RT). In Follicular lymphoma grade I/II (FL), optimum target volumes are controversial: involved field (IF) RT risks out-field relapse, large field RT implies higher toxicity. In Immunocytoma (IC) and Mantle Cell Lymphoma (MCL), experience is limited. This study aims to determine adequate age-adapted RT volumes in FL patients (pts) (randomised trial, HD) and to evaluate standardised RT in IC and MCL pts (prospective observation trial, OBS).

Methods: In FL stage I-II, limited stage III disease, pts aged 18-65 years (ys) were randomised to Extended field (EF) or Total lymphatic RT (TLI), basic dose 30 Gy + boost to macroscopic lymphoma. Pts aged 66-75 ys were treated by EF. In IC / MCL pts aged 18-75 yrs stage I-II, modified EF RT was given. All pts >75 ys received IF RT.

Results: A total of 269 pts was recruited to the completed study. In the RD trial, 203 pts with IC/MCL randomised to TLI, median age 53 (33-65) yrs, stage I, II and III were 57%, 34% and 9%. In the OBS trial, 67 pts, median age 70 (30-85) yrs, were included, 54 with FL, 2 with IC, 11 with MCL. In the updated combined analysis of RD and OBS trials, overall survival is 96%, median follow-up 24 months. In FL, complete remissions (CR) were 179/191 (94%), relapses occurred in 37/179 pts (21%, median interval 21 months). In IC and MCL, 2/5 and 6/6pts reached CR, 1/2 and 4/5 relapsed. RL were strictly nodal (81%), combined with spleen and/or liver (19%), involved skin/soft tissue (7%) or were gastrointestineal (9%). In 74% of RL, histology was obtained; 12% of these were secondary aggressive lymphoma, 88% remained indolent.

Conclusions: In the randomised FL pts, EF, TLI induced high rates of CR. The analysis of relapse histology and patterns contributes to the definition of optimal irradiation volumes in early stage disease and provides the basis for further treatment improvements. In MCL, local therapy does not seem to be able to control the disease.

419 SAFETY AND EFFICACY OF RADIOIMMUNOTHERAPY WITH 90Y-ritzuximab IN PATIENTS WITH RELAPSED OR REFRACTORY CD 20+ B CELL NON HODGKIN'S LYMPHOMA: A PILOT STUDY

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Background: Both anti-CD20 antibodies (rituximab, Zevalin® and tositumomab, Bexxar®) used in daily practice for radioimmunotherapy (RIT) of B cell NHL are murine immunoglobulins. The use of chimeric antibodies (such as rituximab) for radioimmunotherapy may potentially increase immunised-based anti-tumour activity, improve pharmacokinetics, and reduce immunogenicity. The aim of this pilot single arm phase I-II study (in a single centre) is to evaluate the safety and efficacy of RIT with 90Y-rituximab.

Materials and Methods: At present, 5 patients with B-cell non-Hodgkin’s lymphoma (CD20+) in partial remission or progressive disease after at least 2 lines of therapy have been included in this study, with a follow-up of at least 3 months after therapy. We evaluated the safety and efficacy of RIT with 90Y-rituximab, using the same doses and treatment schedule as actually approved by the European Medicines Agency for the treatment with 90Y-rituximab tiuxetan (Zevalin®). Response assessment with 90Y-rituximab was performed 3 months after the treatment and/or when progressive disease was clinically suspected.

Results: 3 patients had follicular lymphoma, 1 had mantle cell lymphoma and 1 diffuse large B cell lymphoma. Toxicities related to 90Y-rituximab were mild (grade 2 or less) and acceptable. Hematological and gastrointestinal toxicities were low and manageable. Nadir blood counts occurred at 6 weeks following therapy for platelets and at 8 to 9 weeks for white and red blood cells. Response assessment with 90Y-rituximab showed complete metabolic response in 3 out of 5 patients, one patient had minimal residual disease and one had progressive disease.

Conclusion: The preliminary results of this study suggest that radioimmunotherapy with 90Y-rituximab in patients with relapsed CD20+ B-cell non-Hodgkin’s lymphoma is safe, well tolerated and efficient when using the Zevalin® treatment schedule.

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420 RADIOIMMUNOTHERAPY OF NEWLY DIAGNOSED, ADVANCED, LOW-GRADE LYMPHOMA WITH 131I-rituximab: THE INITIAL STUDY

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Introduction: Radioimmunotherapy (RIT) with 131I-labelled tositumomab has previously been shown to be safe and effective first-line therapy for low-grade Non-Hodgkin lymphoma (NHL), with a CR of 73% and five-year PFS of 39%. We report a phase I dose escalation study to determine the safety and efficacy of 131I-rituximab in patients with newly diagnosed, advanced, low grade NHL.

Methods: Eligibility criteria comprised CD20+ low-grade NHL, ECOG status 0-2 and adequate haematopoietic function (neutrophils > 1.0 x 10^9/L, platelets > 70 x 10^9/L, Hb >100g/L) and no prior NHL treatment. Administered therapeutic activities of 131I-rituximab limited the whole body absorbed radiation dose to 0.75 Gy.

Results: To date 23 patients have been enrolled; 3 are awaiting therapy. 20 patients have follicular NHL, 2 have lymphoplasmacytoid lymphoma and one low-grade NHL (NS). The median FLIPI score for patients with follicular NHL was 3. Disease assessment by PET-CT scan at three months showed an ORR of 92% with a CR of 62%. Haematological toxicity was minimal with a mean neutrophil nadir of 1.39 x 10^9/L at week 7 and a mean platelet nadir of 89 x 10^9/L at week 4. One patient experienced grade 4 haematological toxicity requiring a single prophylactic platelet transfusion. There were no episodes of neutropenic sepsis or renal or hepatic toxicity. Seven patients were assessable at 12 months; 4 of 5 patients in CR at 3 months remained in CR. Both patients with a PR at 3 months had progressive disease, although only one has required subsequent chemotherapy. Both of these patients had a baseline FLIPI score of 4.

Conclusion: 131I rituximab radioimmunotherapy is safe and effective as first-line therapy for advanced low grade lymphoma. The achievement of a CR on PET-CT criteria at three months confers an excellent prognosis at 12 months.

421 QUALITY OF LIFE (QOL) ANALYSIS FROM THE PHASE 3 RANDOMIZED FIRST-LINE INDOLENT TRIAL (FIT) IN PATIENTS WITH ADVANCED-STAGE FOLLICULAR LYMPHOMA RECEIVING CONSOLIDATION OF FIRST REMISSION WITH 90Y-IBRITUMOMAB TIUXETAN (ZEVALIN)

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Background: The QoL impact of consolidation therapy with Zevalin® was compared with no further treatment (control) was evaluated as one of the secondary end points of the recent international phase 3 FIT study.

Methods: Health-related QoL was measured using EORTC QLQ-C30 (version 2), which specifically assesses QoL in patients with cancer, and EuroQol-5D (EQ-5D, version 2), a generic instrument to assess health-related QoL that includes a visual analogue scale (VAS). Questionnaires were administered at screening and days 1, 14, 28 and 84 and at 6 months thereafter, and at the final follow-up visit. Descriptive statistics were used to compare scores across treatment groups. The change in scores from baseline was also assessed by gender, age, and first-line treatment.

Results: Mean scores for EQ-5D and VAS at screening and final visits are shown in the Table. An exploratory analysis of factors associated with final VAS scores showed that only baseline VAS scores affected final VAS scores (P<0.0001). No treatment differences were observed in EORTC QLQ-C30 (all domains) scores across time points or changes from baseline. Results of subgroup analyses by baseline characteristics will be presented.

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<tr>
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<th>Zev screening</th>
<th>Zev final</th>
<th>Control screening</th>
<th>Control final</th>
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<tr>
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<td>0.84</td>
<td>0.83</td>
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<tr>
<td>VAS</td>
<td>77.52</td>
<td>77.64</td>
<td>76.57</td>
<td>78.60</td>
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422 HIGH RESPONSE RATES FOR STAGE I-II IDIOLENT B-CELL LYMPHOMA WITH YTTRIUM-90 IBRITUMOMAB TIXETAN (ZEVALIN)

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Background: Yttrium-90 (90Y) ibritumomab tixetan (Zevalin) is an effective treatment for patients with relapsed follicular lymphoma. There is no standard treatment for stage I and stage II indolent lymphomas.

Methods: Patients with CD20-positive lymphomas, including follicular lymphoma grades 1 to 2 and marginal zone B-cell lymphoma of the mucosal associated lymphoproliferative tissue (MALT) were included. Staging was calculated via computer tomography (CT) scanning of the neck, thorax, abdomen, and pelvis, PET/CT scanning, and bone marrow biopsy. Eligibility criteria were a performance status of 2 or less, a white blood count greater than 1500/mL, a platelet count greater than 100,000/mL, and at least a 1.5 cm in the transverse dimension. Response evaluation of bowel disease required repeat biopsies of involved tissues after therapy was completed. Patients were treated with rituximab and Zevalin (0.4 mcg 90Y/kg capped at 32 mcg) at day 8 following the imaging dose on day 1.

Results: Ten patients who had completed therapy and were evaluable for response had a median age of 58 y (range: 36–76 y), with five male, 7 having follicular lymphoma, and 3 having marginal zone lymphoma. Ten patients have had follow-ups of at least 3 months, of which 10 have achieved a CR (1 patient has stable disease in a site of a recent surgical procedure). Patients experienced a median platelet count nadir of 50,000 (range: 20,000–170,000), at 4 weeks and a neutrophil count nadir of 1,323 (range: 360–1,366). There were no neurotoxicity-related infections. Nonhematologic toxicity included a rash associated with Rituximab90Y ibritumomab tixetan administration.

Conclusions: Yttrium-90 ibritumomab tixetan is a highly active therapy that is completed in 8 days for early stage follicular and marginal zone B-cell lymphoma with minimal toxicity.

423 90-YTTRIUM-IBRITUMOMAB TIXETAN CONSOLIDATION FOLLOWING 3 CYCLES OF FC-R IN ELDERLY PATIENTS WITH RELAPSED LYMPHOMA: A DOSE-FINDING STUDY

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Background: Phadariane-based Tx followed by Y-90 ibritumomab tixetan (RIT) consolidation may improve PFS in patients (pts) with CD20+ NHL. 4 to 6 cycles of FC-R and then RIT at standard activity lead to severe prolonged pancytopenia. Brief chemoimmunotherapy and RIT at lower Y-90 activity may alleviate this problem.

Methods: Rituximab- (anthracycline-pretreated pts unavailable for autotransplant) received 3 cycles of FC-R. If 2 stable disease was achieved and blood counts normalised, RIT was given. Y-90 activity levels were predefined at 11/15 MBq/kg. 1st endpoint was the rate of dose-limiting toxic events (DLT) induced by RIT per level of Y-90 activity. 1 DLT in two of three pts per level was acceptable. DLT was defined as grade 4 neutropenia or thrombocytopenia for >14 days or non-hematxicity of > grade 2 for >7 days.

Results: 22 pts entered the trial (10 follicular, 10 mantle cell, 2 other). Median age was 69 years. Median no. of pre-Tx was 1.9 pts went off treatment before RIT due to persistent cytopenia or progression. 13 received RIT. Nadirs occurred at median 7 weeks post-RIT. Median ANC nadir was 0.6/6, with 1 pt in the 11 and 2 in the 15 MBq activity level sustaining DLT neutropenia. Median PLT nadir was 37/4. Grade 4 thrombocytopenia was found in 1 pt at each level but did not require transfusion. Only 3 pts had thrombocytopenia > grade 1 at week 12. Non-hem toxicities were rare and < grade 3. At med. 19 months follow-up in RIT-treated pts, only 1 in SD and 2 in PR before RIT have progressed.

Conclusions: RIT delivered after 3 cycles of FC-R at Y-90 activity of 15 MBq/kg may induce more severe neutropenia than at lower activity. Nevertheless, the incidence of infections, transfusions, hospital admissions and late cytopenias is low. RIT at standard activity may be regarded safe in this setting. The long PFS observed may either be due to selection bias or the result of consolidation of RIT.

424 REGISTRY OF RADIOMUNOTHHERAPY, ANALYSIS OF OUTCOMES OF RECURRENT OR FRACtORY NON-HODGKIN LYMPHOMA PATIENTS TREATED WITH 90Y IBRITUMOMAB TIXETAN

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Background: The aim of this registry is to collect data of Non-Hodgkin Lymphoma patients (p) treated with 90Y ibritumomab tixetan in the clinical practice setting, to retrospectively analyze treatment outcome.

Methods: Endpoints analyzed: objective response rate (ORR), time to progression (TTP) overall survival (OS) and safety. Clinical prognostic factors were also studied.

Results: 169 p from 51 centres (treated since commercial availability in Spain and Portugal until August 2007) were registered: M/F 57.7%-42.3%; mean age 59.6 years (19-83); ECOG 0-1 79.7%; 113 had FL (66.9%). ORR was 66.9% (95%CI:59,8, 74,0). Median follow-up time was 6.6 months; median TTP, 10.1 months (95%CI:6,8, 13,3) and median OS has not been achieved. Estimated OS at 1 and 2 years: 74.1% and 51.0%, respectively. Intermediate and high FLPI score were significantly associated with worse response rate and more risk for progression than lower score: Odds Ratio 0.29 (95%CI:0.09-0.88) and 0.25 (95%CI:0.08-0.77), respectively; Hazard Ratio 3.01 (95%CI:3.6-6.66) and 4.33 (95%CI:1.9-9.40), respectively. More than 2 previous treatments was also related with a worse response rate for FL: p Odds Ratio 2.49 (95%CI:87-7.08). Interventions required were: hospitalization 26.6%, G-CSF 43.8%, red blood cell/platelet transfusion 29.0/30.8%. Toxicity analysis is summarized in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Toxicity % (G3-4%)</th>
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<tbody>
<tr>
<td>Anemia</td>
</tr>
<tr>
<td>Neutropenia</td>
</tr>
<tr>
<td>Leucopenia</td>
</tr>
<tr>
<td>Neutropenia</td>
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</table>

425 MAINTENANCE THERAPY IN FOLLICULAR NON HODGKIN LYMPHOMA: EXPERIENCE WITH 6 MONTHS RITUXIMAB BASED SCHEDULE

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Follicular non-Hodgkin’s lymphoma (F-NHL) is rarely curable with standard chemotherapy, the natural history of disease is characterized by successive relapses. The addition of Rituximab to different chemotherapy regimens increases the response rate and progression-free survival (PFS), without significantly increase of toxicity. The administration of Rituximab as maintenance therapy is an useful and safe option for patients in complete remission after induction therapy with regimens based in immuno-chemotherapy, nevertheless the best maintenance schedule is not yet defined.

Objective: To present our experience with an homogeneous maintenance schedule with Rituximab administrate every 4 months for F-NHL.

Patients and methods: Prospective, observational study in 41 F-NHL patients in complete remission after first line therapy with immuno-chemotherapy (R-CHOP, R-FC, R-MCF) since January 2002 to July 2006. Maintenance schedule: Rituximab 375 mg/m2 weekly × 4 every 6 months two years in an outpatient protocol of fast infusion (24 hours before the patient received anti H1 and H2 orally and steroids 40 mg, desclofenamin 5mg and paracetamol 1 g IV previously to administration every Rituximab dose in a total volume of 250 mL. The first 50 mL is administered in 30 and 200 mL in 60 minutes), patients with severe previous reactions were excluded of this schedule and received Rituximab in slow infusion. Patients were evaluated previous to start maintenance and two months after 4 courses, CT scan, PET and molecular study of (114)18 in bone marrow were performed. Side effects according to common toxicity criteria were evaluated. Overall survival and relapsed free survival were analyzed according Kaplan-Meier and Cox regression study.

Results: 37 valuable patients (25 F/12 M); Mean age 53.1(35.77); ECOG (0-0,8); 1/34,7%, 2/4,3%; At diagnosis: B symptoms 43,4%; FLPI 0.18,1%, 1,14,3%; 2,80,4%, 8,13,7%; stage I/II, 53,9%; III (19,1%), IV (34,3%); grade I/II (43,5%), II/III (56,5%); Bulky 14%; extra node disease 14%; Hb<9 g/dL (14,9%, LDL increased 14%; B2M increased 14%. R-CHOP (69,5%), R-CHOP+Bical Rx (8,7%), R-FC (17,3%), R-FC (4,3%). 90% of patients have received maintenance fast infusion.
Material and methods: We here present long-term results from a randomized trial conducted in the period 1988–1989 by the Danish LYFO Study Group comparing CHOP with CHL in patients with advanced stage indolent lymphoma.

Background: Indolent lymphomas are characterized by a chronic course with a median survival of 7–10 years. Very long-term follow-up data are needed, but rarely available. We here present long-term results from a randomized trial conducted in the period 1988–1989 by the Danish LYFO Study Group comparing CHOP with CHL in patients with advanced stage indolent lymphoma.

Material and methods: 146 patients with indolent lymphoma were randomized to either 9 cycles of CHOP (4 weeks intervals) or CHL (10 mg daily for 6 weeks, followed by 2 mg daily for 9 months). Patients were originally diagnosed according to the Kiel classification: CC/CB follicular 69%, CB follicular 1%, CC/CB diffuse 15%, small lymphocytic 12%, and unclassifiable low-grade 3%. Median age (range) was slightly lower for the CHOP as compared to the CHL cohort, 51.5 (29-76) yrs and 58.5 years (34–78yrs), respectively, (p=0.12). Male gender was 50% vs 38% (p=0.15), and stage IV disease 69% vs 62% (p=0.39). Histological subtype, nodal vs extranodal disease, B symptoms, LDH, and performance score were all equally distributed.

Results: The data table shows event free (EFS) and overall survival (OS).

<table>
<thead>
<tr>
<th>Treatment arm/end point</th>
<th>5 years</th>
<th>10 years</th>
<th>15 years</th>
<th>20 years</th>
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<tbody>
<tr>
<td>CHOP (EFS %)</td>
<td>37</td>
<td>26</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>CHL (EFS %)</td>
<td>26</td>
<td>17</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>CHOP (OS %)</td>
<td>71</td>
<td>46</td>
<td>33</td>
<td>21</td>
</tr>
<tr>
<td>CHL (OS %)</td>
<td>57</td>
<td>37</td>
<td>24</td>
<td>18</td>
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</table>

No statistical differences between the two groups were found in terms of EFS or OS.

Conclusion: In the pre-rituximab era, more intensive combination chemotherapy (CHOP) was not superior to oral monotherapy with regard to EFS or long-term OS.

427 PHASE I DOSE ESCALATION STUDY OF FLUDARABINE, BORTEZOMIB, AND RITUXIMAB FOR RELAPSED/REFRACTORY INDOLENT AND MANTLE CELL NON-HODGKIN LYMHPMA

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Background: Fludarabine (F) and bortezomib (B) have both demonstrated tolerability and efficacy in patients (pts) with non-Hodgkin lymphoma (NHL). Despite potential synergy between these agents, the combination remains untested.

Methods: Pts with relapsed/refractory indolent and mantle cell NHL were eligible. Dose levels of F and B were escalated to a maximum of 8 cycles. Dose levels of 5, 7.5, 10, 12.5, and 15 mg/m² were used for F and 0.7, 1.0, 1.3, 1.5, and 1.8 mg/m² for B. The dose of Rituximab (R) was fixed at 375 mg/m² at each dose level. The maximum tolerated dose was determined by the occurrence of dose-limiting toxicities (DLTs). Dose levels were then escalated to the next level if no DLTs were observed in at least 3 patients at a given dose level. Treatment cycles were repeated every 21 days for a maximum of 8 cycles.

Results: 23 pts have been enrolled to date. Patient characteristics include 12 with follicular, 4 with marginal zone, 3 with lymphoplasamcytic, 2 with small lymphocytic, and 2 with mantle cell NHL. Dose limiting toxicities were observed in cohorts 1 through 4. The addition of R in cohort 5 resulted in dose limiting hematologic toxicity. At dose level 5a and 5b, no further dose 3 or 4 hematologic toxicity has been observed with cycle 1 of the 17 pts currently evaluable for a response. 3 have achieved a CR, 4 have achieved a PR, 8 had stable disease, and 2 pts progressed on therapy. The median time of stable disease for the 8 pts was 9 months (range 3-30).

Conclusion: FBR is a well-tolerated and active regimen for pts with relapsed or refractory NHL. B may worsen the hematologic toxicity of a nucleoside analog and proteasome inhibitor containing regimen.

428 BENDAMUSTINE/MABthera IN PATIENTS WITH RELAPSED OR REFRACTORY AGGRESSIVE CD20+ B- CELL-LYMPHOMA

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Introduction: Bendamustine has been extensively studied in patients with indolent B cell neoplasms showing high response rates and moderate mostly hematologic toxicity. However, only one small study of patients with relapsed non-Hodgkin’s lymphomas (NHL) treated with bendamustine as a single agent has been published to date showing a response rate of approximately 40%. To further improve treatment results we initiated the following study.

Patients and methods: Adult patients (218 years) with relapsed or refractory aggressive CD20+ NHL, who had received at least one anthracycline based combination chemotherapy were eligible. The first course included mabthera 375 mg/m² on days 1,8,15 and 22 and bendamustine 60 mg/m² on days 1,8,15 and 15 of a 4-week cycle.

Results: Twelve patients aged 56 to 78 years (mean age 69.6 years) were included in this study. 10 patients had received one, 2 had had 2 prior therapies. 10 patients and 35 treatment courses are evaluable for response so far. Four patients had a complete, three a partial and one a minimal response. The overall response rate was 80%. Three of four patients are still in CR after 33, 18 and 6 months, respectively. One patient with a complete response had progressive disease after 2 months. Partial remission lasted for 2, 4 and 6 months in 3 patients. Two patients with high dose chemotherapy with autologous stem cell transplantation as first-line treatment had progressive disease after 1 and 2 courses, respectively. There was only one grade 3 leukopenia in one of 35 treatment courses and no further grade 3 or 4 hematologic toxicities. There were no toxicity-related treatment delays, interruptions or mortalities.

Conclusion: These preliminary results show that bendamustine/mabthera is a well-tolerated regimen with promising response rates also in patients with aggressive NHL. Larger patient numbers are needed to confirm our findings.
Background: The benefit of improved PFS for rituximab (R) maintenance in follicular lymphoma (FL) has been first reported by Hainsworth et al and was later confirmed in randomized trials by Ghielmini, van Oers, and others. The primary objective of the current study is to extend the safety database for rituximab maintenance following a wide range of induction therapies.

Methods: The sample size of this trial was calculated to detect at least one rare event with an incidence of 0.3% with 80% power. Patients with FL having achieved a CR or PR after R-containing induction therapy were eligible to receive standard-dose R every 8 weeks for up to 2 years. Primary endpoint is safety, with standard secondary efficacy endpoints.

Results: 349 patients with FL have been enrolled at clinical cut-off for whom follow up through 2005. Patients had to have more than 5 lymph nodes sites involvement is significantly associated with unfavorable 5-year DFS 58% vs 50%). LDH elevation, hypoproteinaemia, abdominal mass and more than 5 lymph nodes involvement in 30/56 (55%) FL patients, less in 7/56, the same extension in 15/56 and 4

Results: 349 patients with FL have been enrolled at clinical cut-off for whom follow up through 2005. Patients had to have more than 5 lymph nodes sites involvement is significantly associated with unfavorable 5-year DFS 58% vs 50%). LDH elevation, hypoproteinaemia, abdominal mass and more than 5 lymph nodes involvement in 30/56 (55%) FL patients, less in 7/56, the same extension in 15/56 and 4

Results: 349 patients with FL have been enrolled at clinical cut-off for whom follow up through 2005. Patients had to have

Conclusion: R maintenance q 8 weeks in FL after rituximab containing induction therapy can be safely administered. Rapid-infusion appears to be safe in this setting.

Conclusion: BR was effective in the treatment of relapsed NHL, achieving high remission rates and PFS for about 1 year. Furthermore, safety data indicate that B toxities are manageable and the drug is well tolerated even in elderly patients.

430 SAFETY IN PATIENTS RECEIVING MAINTENANCE RITUXIMAB (MABTHERA®) IN FOLLICULAR LYMPHOMA: RESULTS FROM THE PHASE IIIIB MAXIMA TRIAL


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Background: Over 10,000 cases of FL were diagnosed in 2007 in the United States. The direct medical costs attributable to FL are not clearly documented.

431 COST OF FOLLICULAR LYMPHOMA (FL) IN MEDICARE PATIENTS

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Background: Median age was 69 years (47-85). Patients had received one (34), two (11) or three (3) prior treatment regimes. After induction chemotherapy the ORR in this primary analysis population was 85%, including 42.5% CR, 42.5% PR, and 2% SD. The median EFS was 9 months (0-39), the median PFS 12 months (0-39), and the median OS 14 months (0-40).

432 REMARKABLE PROGNOSTIC VALUE AND CONTRIBUTION IN STAGING OF F-18-FLUORODEOXYGLUCOSE EMISSION TOMOGRAPHY IN FOLLICULAR LYMPHOMA

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Introduction: F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) is a powerful tool for the imaging of aggressive Non Hodgkin’s lymphomas and Hodgkin’s lymphoma. In contrast, there is relatively little data on FDG-PET in follicular lymphoma (FL) in spite of its high FDG uptake.

Methods: A retrospective analysis of 127 FDG-PET scans was performed among 100 patients with FL (93% grade I or II). FDG-PET was obtained at initial staging (n=56) and results were compared with conventional staging. Post-treatment scans (n=71), in 87 patients treated by conventional therapy were compared with clinical follow-up.

Results: FDG-PET compared with CT and clinical examination showed more foci of involvement in 30/56 (55%) FL patients, less in 7/56, the same extension in 15/56 and 4 patients revealed discordant founds on PET or CT only (p<0.001). FDG-PET upstaged essentially FL in 15 patients (from stage 0-2 to 3-4). Including results of trephine biopsy the stage was substantially changed in 15/56 (23%) patients, which was projected into treatment strategy. Post-treatment PET-positive patients (11/71) had shorter progression free survival (9/11 relapsed in median of 6 months) compared with PET-negative patients (56/71), 9 of whom relapsed in median of 10 months, 47 of them remain in remission (median follow up 19 months) (p<0.001). All of remaining 4/71 patients with PET-positivity of undetermined significance (close to cut-off) are in long-term remission (median follow up 39 months).

Conclusions: Our results indicate that FDG-PET is accurate and reliable method for staging of FL. Post-treatment PET-positive patients are likely to relapse prior to PET negative patients. Surprisingly, presented data are very similar to those observed in studies with aggressive lymphomas.

433 CLINICAL FEATURES AND OUTCOME OF FOLLICULAR LYMPHOMA PATIENTS WITH BONE MARROW INVOLVEMENT

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Background: Approximately 40-45% of patients (pts) with follicular lymphoma (FL) have bone marrow (BM) involvement. In some cases clusters of malignant cells are found next to trabeculae, in others – circulating malignant cells detectable on peripheral blood. The aim of study is to explore the clinical features and outcomes of pts FL with different types of BM involvement.

Methods: From 1985 to 2005, 65 pts FL with BM involvement were included in the study. In 35 pts (54%) the BM involvement was accompanied with clinical and hematological manifestation of leukemia, in 30 pts (46%) – malignant cells detected only by the morphological examination. The clinical parameters and treatment options were balanced between the two groups. There were 33 (51%) men and 32 (49%) women, median age 53 years (range 21-73). 30 pts (46%) had FL grade 1, 15 (32%) presented B symptoms, LDH was increased in 21 (32%), 33 pts (46%) had ECOG 2. According to FLIPIL, 5 pts (8%) ranked in the low risk, 26 (40%) in intermediate and 34 (52%) in high risk category. 37 pts (57%) had widespread disease at diagnosis, including abdominal lymph nodes 45 (70%), liver 15 (23%) and spleen 22 (34%).

Results: The efficacy of the first-line treatment (R-CHOP, R-ACVPP) was poor: CR was achieved in 28 pts (43%), while 21 (32%) were resistant to chemotherapy. The 5-year DFS and PFS were 24% and 22% respectively. There were no significant difference in OS and PFS of pts with two different type of BM involvement (7-year OS 58% vs 62%, 5-year DFS 58% vs 50%). LDH elevation, hyperproteinemia, abdominal mass and more than 5 lymph nodes sites involvement is significantly associated with unfavorable prognosis.
Conclusion: The two types of BM involvement, with or without symptoms of leukemia, occur equally, do not have prognostic significance in FL, but the BM failure at diagnosis is associated with widespread disease, poor efficacy of first-line therapy and high risk of relapse. The future studies of the FL with BM involvement can help to develop the optimal therapeutic approach to this group of patients.

434 INITIAL PROGNOSTIC PROFILE OF FOLLICULAR LYMPHOMA PATIENTS WITH POOR OUTCOME

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Background: Follicular lymphoma is the most common type of low grade Non-Hodgkin Lymphoma and it accounts for about 30% of all NHL. All widely accepted prognostic indices such as Follicular Lymphoma International Prognostic Index (FLIPI) and Italian Lymphoma Intergroup (ILI) identify different risk groups of patients, but great heterogeneity in the outcome within these groups is still present.

Methods: We have identified 25 pts treated at the Institute of Hematology from 2002 up to the end of 2007 who did have poor outcome. We have defined poor outcome as death within 5 years of diagnosis, stable or progressive disease on initial therapy, or relapse within one year after the completion of initial treatment. FLIPI index was determined for all the pts.

Results: The mean age was 57.04±9.94 yrs, range 37-71 (52% of pts were <60 yrs). Advanced clinical stadium (III or IV) was recorded in 22 pts (88%), 11 pts (44%) had anemia, 19 pts (76%) had ≥4 regions affected, 15 out of 25 pts (60%) had elevated LDH, and 17 pts (68%) had high risk according to FLIPI. There was no statistical significance regarding the age of patients, level of Hgb and LDH, and low/intermediate and high FLIPI. The advanced clinical stadium (p=0.0001) and the number of affected regions (p=0.009) did show statistical significance.

Conclusion: In our group of pts FLIPI did not show a prognostic significance in terms of outcome. Therefore, further subgrouping of pts using additional parameters seems to be necessary to identify pts with high risk of poor outcome.