9206 ORAL

Long-term follow-up of follicular lymphoma (FL) patients receiving single agent rituximab at two different schedules in trial SAKK 35/98

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Background: In FL, Rituximab as a single agent delivered in the standard schedule (4 times weekly) may induce a response rate of 50−70% with an event-free survival (EFS) of 1−3 years according to patients' characteristics. Prolonged Rituximab exposure seems to improve EFS at least in responding patients and to increase the rate of long-term responders. Here we report long-term results of a clinical trial comparing single agent Rituximab delivered in the standard schedule versus prolonged exposure, with focus on the proportion of long-term responders and their characteristics.
Material and Methods: Between 1998 and 2002, chemotherapy naïve (n = 64) or pre-treated (n = 138) FL patients received Rituximab in the standard schedule. Those responding or with stable disease were randomized to no further treatment (observation, n = 78) or 4 additional doses of Rituximab given at 2-month intervals (prolonged exposure, n = 73). EFS was calculated from the first dose of standard schedule until progression, relapse, second tumor or death.
Results: At a median follow up of 9.4 years and with all living patients having been followed for at least 5 years, the median EFS is 13 months for the observation and 24 months for the prolonged exposure arm (p = 0.0007). In the observation arm 13% had no event at 5-years and only 4% at 8 years, while in the prolonged exposure arm it was 27% at 5 years and remained 21% at 8 years. The only significant prognostic factor for EFS in a multivariate Cox regression was the prolonged Rituximab schedule (hazard ratio 0.58, CI 0.39−0.86, p = 0.007), whereas being chemotherapy naïve, presenting with stage <IV and showing a VV phenotype at position 158 of the Fc receptor RIIIA were not of significant prognostic value. No long-term toxicity from treatment was observed. There were 22 cases of second malignancy: 12 on observation, 10 on prolonged exposure. 5 patients developed myelodysplastic syndrome; all received previous chemotherapy treatment.
Conclusions: Our results confirm that the prolonged exposure to Rituximab significantly improves EFS as compared to the standard schedule. This benefit continues for many years after the end of therapy and the prolonged exposure seems to be the sole factor which may be considered of prognostic value. Patients treated with prolonged schedule (8 doses of Rituximab) may have approximately 25% and 20% chances to be in remission at 5 and 8 years respectively and to avoid subsequent chemotherapy treatment.

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Efficacy of 90Yttrium-ibritumomab tiuxetan in extranodal marginal-zone lymphoma

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Background: A prospective, single arm, open-label, pilot study was performed to evaluate clinical activity of ^{90}Y-Ibritumomab Tiuxetan in Extranodal Marginal-Zone Lymphoma.
Material and Methods: From May 2004 to April 2009 twenty-four patients affected by relapsed/refractory Marginal-Zone Lymphoma arisen at any extranodal site were enrolled to receive ^{90}Y-Ibritumomab Tiuxetan at the activity of 0.4 mCi/kg. Median age was 58 years (range 36−83 ys); 15 female and 9 male. Ten out of 24 patients had Helicobacter Pylori-negative gastric Mucosa-Associated Lymphoid tissue Non Hodgkin Lymphoma. The remaining 14 patients had extra-gastric Marginal-Zone Lymphoma. At time of treatment 10 out of 24 patients had disseminated disease (stage III/IV; Ann-Arbor Staging System); bone marrow involvement was detected in 4 patients. The median number of previous treatments administered was 1 with a maximum of 7; 23 patients had received prior chemotherapy (CT), 11 Rituximab, 3 radiotherapy, 2 surgery. Eleven out of 24 patients had received more than 2 treatments.
Results: Toxicities were primarily haematological and reversible. Twenty-one out of 24 patients are now evaluable for response: 16 patients experienced a complete response (CR); partial response was observed in 2 patients, while stable disease occurred in 3 patients. At the time of the analysis all patients are alive: the median duration of response (e.g. time to progression) was not estimable; however - with a median follow-up of 22 months - CR duration ranged from 3 to 59 months. In particular, 6 out of 16 CRs have been maintained at >3 years. There was no statistically significant associations between response to therapy and the occurrence of the MALT-1 translocation (p = 1.000).
Conclusions: ^{90}Y-Ibritumomab Tiuxetan seems to be very active in patients with Extranodal Marginal-Zone Lymphoma relapsed/refractory to conventional systemic treatment. The high rate of complete remission (76%) and the duration of response are clearly superior to those observed with conventional systemic approaches (CT, monoclonal Antibody alone or in combination with CT). If these preliminary results can be confirmed in a larger number of patients, a single shot of radioimmunotherapy could represent a valid alternative option for the treatment of relapsed Marginal-Zone Lymphoma.

Poster presentations (Tue, 22 Sep, 09:00−12:00)
Haematological malignancies and myeloma

9208 POSTER

Late sequelae of radiation therapy for malignant lymphoma of the thyroid

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Background: Malignant lymphoma of the thyroid (MLT) is an uncommon primary extranodal lymphoma. As many cases of this disease are detected at an early stage, and a common pathology of these lesions involves MALT lymphomas, which are considered low-grade malignancies, local control and overall survival exceed 70% with chemo-radiotherapy. Because of the long prognosis of this disease, late sequelae of radiotherapy (RT) have become a problem. In this study, we evaluated late sequelae of RT for MLT treated in our institute that have been followed up for three years or more.
Materials and Methods: Between May 1990 and March 2009, 91 cases of MLT underwent RT in our institute. Of these cases, 48 patients with 36 months or more of follow-up time were evaluated for late toxicity such as hypothyroidism (HT), decrease of the secretion of saliva (DS), and induration and/or fibrosis of skin and subcutaneous tissue around the shoulder (IS). We also investigated the relationship between the treatment dose and the rate of sequelae. The toxicity was estimated by Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.
Results: The mean age of the 48 cases was 61.8 years old; 36 cases were female, and 12 were male. All cases except for two underwent one to six courses of chemotherapy with the "CHOP" regimen (Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone). The median doses of RT were 46 Gy (range; 36−50.4 Gy). Median follow up time was 88.5 months (range; 36.3−195.8 months). Sixteen (57.1%) of 28 patients who had taken medicine for HT before RT were required to increase the medicine, and only three (15.0%) of 20 patients who had not been treated for HT before RT were required to start taking the medicine (p = 0.0051). Grade 2 or higher DS was observed in 13 cases (27.1%) three to 12 months after treatment. Three of these cases showed improvement of their symptoms 36, 64, and 128 months after irradiation. IS occurred in 28 patients (58.3%), 20 with Grade 2 and 8 with Grade 3, 12 months or more after RT. Late toxicity was shown in six cases (50.0%) of 12 who received less than 40 Gy irradiation, and in 23 cases (63.9%) of 36 who received 40 Gy or more (p = 0.3982). For IS, high doses of irradiation increased the rate of sequelae significantly (33.3% for low doses vs. 66.7% for high doses; p = 0.0479). For HT and DS, there was no significant relation between irradiation doses and toxicity rates.
Conclusions: Twenty-nine (60.4%) of 48 patients who underwent RT for MLT experienced late sequelae. IS was shown significantly in patients received 40 Gy or more irradiation.