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patient, having several café-au-lait spots, developed a mediastinal T-cell lymphoblastic lymphoma at age 6. Following chemotherapy, she relapsed and underwent haematopoietic stem cell transplantation from a matched sibling donor. By the age of 13, she was referred for genetic counselling due to the diagnosis of colorectal cancer. Her consanguineous parents reported on colorectal cancer at age 42 in a paternal uncle married to the sister of the index patient's mother, but LS or MMRCS was not yet considered. **Results.** The index patient's colon cancer showed high-grade microsatellite instability (MSI). Immunohistochemistry demonstrated a loss of MSH6 both in normal and cancer cells. Sequence analysis of MSH6 detected the homozygous germline mutation c.691delG (p.Val231TyrfsX15). Subsequently, the parents of the index patient and the affected paternal uncle, whose synchronous colorectal carcinomas also displayed MSI and loss of MSH6, were shown to be heterozygous carriers of the frame shift mutation. **Conclusions.** We report here on a novel MSH6 mutation and provide clinical information on a further family with LS and MMRCS. Although LS is well known, up to now there are only few reports on MMRCS. This report further emphasizes how important it is to be aware of MMRCS in pedigrees with Lynch syndrome-associated cancer, e.g. early-onset colon cancer, and childhood leukaemia / lymphoma and / or brain tumour. The synchronous colorectal carcinomas of the affected uncle, retrospectively the first evidence of a mismatch repair defect in the reported family, were diagnosed one year before the lymphoma relapse of the index patient and six years before she was diagnosed with colorectal cancer. Up to now, no evidence-based screening recommendation exists for patients with constitutional mismatch repair deficiency. Nevertheless, early diagnosis of this severe cancer susceptibility syndrome may improve the clinical management of affected individuals and their relatives at risk.

0426

DOSE-DENSE THERAPY WITH NON-PEGYLATED LIPOSOMAL DOXORUBICIN, CYCLOPHOSPHAMIDE, VINCRISTINE, PREDNISONE AND RITUXIMAB (R-COMP) IS FEASIBLE AND EFFECTIVE IN ELDERLY PATIENTS WITH NEWLY DIAGNOSED AGGRESSIVE B-CELL NON-HODGKIN LYMPHOMA: R-COMP 14 VS R-COMP 21. INTERIM ANALYSIS FROM AN ITALIAN MULTICENTRE

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The toxicity and efficacy of nonpegylated liposomal doxorubicin (Myocet™) when substituted for conventional doxorubicin in the CHOP 14 or 21 regimen (Doxorubicin, Cyclophosphamide, Vincristine, Prednisone given every 2 or 3 weeks) were evaluated in the treatment of elderly patients with newly diagnosed aggressive B-cell non-Hodgkin's lymphoma. Forty-eight patients with aggressive B cell non-Hodgkin lymphoma at diagnosis were enrolled so far in the study. Patients were split in 2 groups according to the Multidimensional Geriatric Assessment (MDGA). Patients with an Activities of Daily Living (ADL) = 6 were addressed to receive dose-dense R-COMP every 2 weeks (14), whereas patients with an ADL > 7 were addressed to receive R-COMP every 3 weeks (21). Starting from this background, 30 patients were enrolled in the R-COMP 21 arm and 18 in the R-COMP 14 arm. The study was planned as a double phase II according to a single-step Fleming design using 3 years event-free survival as primary endpoint. The characteristics of patients enrolled in the study were as follows: the median age was 72 years (range: 67-80) in the R-COMP 14 group and 75 years (range: 66-89) in the R-COMP 21. At baseline 13/18 (72%) patients had stage IV disease in the R-COMP 14 group, whereas 13/30 (43%) in the R-COMP 21. Median performance status and median number of comorbidities were comparable between the 2 groups. Thirteen out of 18 (72%) patients had an intermediate or high risk International Prognostic Index score in the R-COMP 14 group, compared to 12/30 (40%) in the R-COMP 21. The median left ventricular ejection fraction (LVEF) before starting chemotherapy was comparable between the two groups (59% vs 60%). A total of 261 cycles of chemotherapy were administered (96 R-COMP 14 and 165 R-COMP 21). Of the cycles administered, 9 (9%) were delayed by haematological toxicity in the R-COMP 14 group and 11 (7%) in the R-COMP 21 group, with a relative dose intensity for the regimens of 91% and 93%, respectively. Toxicity was mainly haema-

tological in both groups. Grade 3/4 neutropenia occurred in 10% and 24% of cycles in the R-COMP 14 and 21 groups respectively, with an incidence of febrile neutropenia of 3% and 5% respectively. It is of note that patients addressed to receive dose-dense chemotherapy were treated with pegfilgrastim on day +2 during the entire study treatment, with a notable reduction in the incidence of both severe and febrile neutropenia. Regarding cardiotoxicity, only 1/18 patients presented a grade II-IV WHO toxicity (atrial fibrillation) in the R-COMP 14 group, whereas 4/30 in the R-COMP 21 group (one congestive heart failure, two ischemic heart failure, one reduction of 20% in the LVEF). All patients were evaluable for response between the two groups. In the R-COMP 14 group, 15/18 patients (83%) obtained a CR, 2/18 (11%) achieved a PR, and 1/18 (6%) did not respond to therapy and rapidly died due to progressive disease. In the R-COMP 21 group, 20/30 patients (67%) obtained a CR, 7/30 (23%) achieved a PR, and 3/30 (10%) did not respond to therapy and rapidly died due to progressive disease. With a median follow-up of 7 months (range 2-12) and 10 (range 4-24) as of January 2009, 15/18 patients (83%) and 25/30 (83%) are alive and disease free in the R-COMP 14 and in the R-COMP 21 group, respectively. In conclusion, the stratification of patients according to the MDGA allows elderly and fit patients with aggressive B-cell NHL with poor prognosis (high IPI score) to receive dose dense chemotherapy which might favorably impact on response rate and survival. The increased response rate obtained with dose-dense R-COMP 14 might impact on long-term event-free survival. A longer follow-up is warranted to better define the impact of dose-dense R-COMP regimen on overall survival of patients with high-intermediate or high IPI score.

0427

ALLOGENEIC STEM CELL TRANSPLANTATION IN NON-HODGKIN'S LYMPHOMA PATIENTS WHO PROGRESSED AFTER HIGH DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANTATION: A RETROSPECTIVE STUDY BASED ON DONOR AVAILABILITY

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Background. There are few treatment options in non-Hodgkin's lymphoma (NHL) patients who progressed after high dose chemotherapy (HDC) with autologous stem cell transplantation (auto-SCT). The role of allogeneic stem cell transplantation (allo-SCT) in these patients has not yet been clarified. **Aims.** The objective of this study was to investigate the role of allo-SCT in NHL patients who progressed after HDC with auto-SCT. **Methods.** Retrospective analyses were performed on NHL patients who underwent human leukocyte antigen (HLA) typing after failure of HDC with auto-SCT between February 1998 and November 2008. We compared patients who received salvage allo-SCT (allo-SCT group) with those who did not have a suitable donor and received salvage chemotherapy only (chemotherapy group). Analyses of clinical outcomes of allo-SCT were also performed. **Results.** A total of 30 patients (male, 20) were included. Median age was 38 years (range, 17-61). During a median follow-up of 43.3 months (range, 3.9-103.4), 20 patients (allo-SCT group) received allo-SCT from a suitable donor: 15 HLA-identical siblings (75.0%) and 5 matched unrelated donors (25%). The other 10 patients (chemotherapy group) did not have a donor and received salvage chemotherapy only. In allo-SCT group, 11 patients received conventional conditioning (CC) and 9 patients received reduced intensity conditioning (RIC). Median overall survival (OS) from the time of failure after HDC with auto-SCT was 11.9 months (95% confidence interval (CI), 3.2-20.6). Allo-SCT group (21.5 months (95% CI, 7.9-35.1)) had significantly longer OS than chemotherapy group (3.4 months (95% CI, 0.5-6.3); $p=0.002$). In allo-SCT group, median event-free survival (EFS) and OS from allo-SCT were 2.8 (95% CI, 0.0-6.5) and 19.0 months (95% CI, 4.0-34.0), respectively. Estimated 5-year survival rate of allo-SCT group was 33.8%. There was no significant difference in EFS and OS between CC group and RIC group. Median number of CD34⁺ cells infused was $4.36 \times 10^6/\text{kg}$ (range, 1.26×10^6 - 10.37×10^6). Median time to recovery of neutrophil ($>500/\text{microliter}$) and platelet ($>20,000/\text{microliter}$) was 17 and 27 days, respectively. Median duration of hospitalization after allo-SCT was 26 days (range, 2-54). Acute graft-versus-host disease developed in 4 patients (20.0%). There were 5 transplant-related deaths (25.0%). Incidence of transplant-related mortality (TRM) in CC group tended to be higher than that in RIC group (36.4% vs. 11.1%; $p=0.319$). Patients with low baseline serum albumin level ($<3.0 \text{ g/dL}$) had significantly higher TRM (75.0% vs. 12.5%; relative risk 21.0 (95%