6013 POSTER

Risk factors for premature menopause following treatment for Hodgkin lymphoma

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Background: The long-term prognosis for Hodgkin lymphoma (HL) patients is nowadays favorable. Female HL survivors may, however, experience therapy-induced gonadal failure causing premature menopause, defined as cessation of menses before age 40. Although radiosensitivity of the human ovary has been studied in great detail, information on the effects of different chemotherapeutic agents is still limited.
Methods: We conducted a cohort-study among 518 female 5-year HL-survivors, aged 14 to 40 years (median 25 years) at treatment (1965–1995). In case the ovaries were situated in the radiation fields, the patients were excluded from analysis. Multivariable Cox-regression was used to quantify treatment effects on risk of premature menopause.
Results: After a median follow-up of 9.4 years, 97 women had reached menopause before age 40 (3 women had acute ovarian failure). Treatment with chemotherapy was associated with a 12-fold increased risk of premature menopause compared to radiotherapy only (Hazard ratio [HR] 12.3; 95% confidence interval [CI] 5.3−28.8). Women treated with mechlorethamine, vincristine, procarbazine, prednisone (MOPP; HR 5.7; 95% CI 3.6−9.1) or mechlorethamine, vincristine, procarbazine, prednisone/doxorubicine, bleomycine, vinblastine (MOPP/ABV; HR 2.9; 95% CI 1.6−5.2) were at increased risk for premature menopause, and these risks increased with higher dose. The chemotherapeutic agents responsible for the induction of premature menopause were the alkylating agents, and especially procarbazine (HR 8.1 95% CI 2.0−32.8) and cyclophosphamide (HR 3.5; 95% CI 2.0−5.9). The actuarial risk of premature menopause among women treated with high cumulative doses of procarbazine (>8.4 g/m^2) was 64% (95% CI 44%-78%), whereas the risk among those treated with low doses ($\leqslant$4.2 g/m^2) was 15% (95% CI 6%-23%) 10 years after their first treatment.
Conclusions: Alkylating chemotherapy (particularly with procarbazine and cyclophosphamide) induces menopause before the age of 40, which is in most cases not the result of acute gonadal failure. Although women treated with MOPP/ABV experience a lower risk for premature menopause compared to MOPP, treatment with MOPP/ABV is associated with a significantly increased risk for premature menopause compared to radiotherapy only. As long as alkylating agents (and especially procarbazine) will be used for curing HL, premature menopause will occur in these women, with various clinical implications.

6014 POSTER

G-CSF prophylaxis and neutropenic events in NHL patients receiving standard CHOP or R-CHOP – results from a retrospective study in the UK

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Background: In patients with non-Hodgkin lymphoma (NHL) receiving 21-day (R)CHOP chemotherapy, the incidence of febrile neutropenia (FN) is about 22% with current granulocyte colony stimulating factor (G-CSF) support. FN and related dose modifications can lead to poorer outcomes. We aimed to audit current practice neutropenia management in the UK and its impact on neutropenic events.
Methods: Consecutive NHL patients planned to receive full dose (R)CHOP chemotherapy at 12 UK centres during periods in 2001–5 were retrospectively studied. Patients were categorized by G-CSF use during chemotherapy: primary prophylaxis (PP), secondary prophylaxis (SP), treatment (T) and no G-CSF. Pegfilgrastim was considered to be 10 doses of daily G-CSF in number of doses calculation. Neutropenic events were recorded and included hospitalization due to FN, dose delays $\geqslant$1 week due to neutropenia and dose reductions $\geqslant$15% due to neutropenia. Relative dose intensity (RDI) was also calculated.
Results: 252/254 patients were analysed (59% male, mean$\pm$SD age: 60$\pm$14 yrs, 58% $\geqslant$ stage III disease) and 1548 cycles were delivered. The mean$\pm$SD number of G-CSF doses per cycle was 6.8$\pm$2.1, 4.4$\pm$2.2 and 1.7$\pm$1.3 in the PP, SP and T groups, respectively. Five or more G-CSF doses were used in just 20% of cycles. The incidence of neutropenic events in the different groups is shown (table). In cycle 1, 3% of PP patients were hospitalized for FN vs 12% of those receiving 'other' treatments. Furthermore, 97% of patients receiving PP had RDI $\geqslant$85% versus 83% of the 'other' treatment groups. Among those who had a neutropenic event, all PP patients achieved RDI $\geqslant$ 85% in contrast to just 70% of the 'other' treatment group.

	PP	Other			
	(n = 32)	SP (n = 42)	T (n = 67)	No G-CSF (n = 111)	All 'Other' (n = 220)
Hospitalization due to FN	4 (13%)	17 (40%)	32 (48%)	12 (11%)	61 (28%)
Dose delay $\geqslant$1 week due to neutropenia	2 (6%)	16 (38%)	29 (43%)	14 (13%)	59 (27%)
Dose reduction $\geqslant$15% due to neutropenia	0 (0)	8 (19%)	2 (3%)	2 (2%)	12 (6%)
All neutropenic events	4 (13%)	29 (69%)	43 (64%)	23 (21%)	95 (43%)

Conclusions: Relatively few (13%) NHL patients on 21-day (R)CHOP chemotherapy received PP G-CSF. Those receiving PP G-CSF had fewer neutropenic events than those receiving other neutropenia management and a greater proportion achieved RDI $\geqslant$ 85%. Half of those not planned to receive G-CSF subsequently required G-CSF SP or T. Results from studies such as these can aid implementation of new ASCO/EORTC guidelines which recommend PP with G-CSF when overall risk of FN is $\geqslant$20%.

6015 POSTER

FcgammaRIIIa and FcgammaRIIa polymorphisms do not influence overall survival in follicular lymphoma patients treated with rituximab

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Background: In follicular lymphoma (FL) genomic polymorphisms corresponding to the expression of valine (V) or phenyloalanine (F) in position 158 of Fc?RIIIa alter the binding affinity of immunoglobulin G1 (IgG1) and consequently response to rituximab. Recent data suggest that patients with FcγRIIIa-158V genotype have longer progression free survival (PFS) than those with 158F or 158 V/F genotypes. In contrast, the FcγRIIa-131 polymorphism is not associated with response to rituximab. In this study, we tested weather these polymorphisms may also influence overall survival (OS) in follicular lymphoma patients treated with rituximab.
Materials and Methods: DNA was extracted from the 2 ml of blood samples of 161 FL patients treated with rituximab. Polymorphisms were examined by PCR-RFPL method in a group. Median time of observation was 31 months (range 12–144 months).
Results: The study population consisted of 40% V homozygous, 20% F homozygous and 40% V/F heterozygous patients for gene FCGR3A and of 32% H homozygous, 16% R homozygous, 52% H/R heterozygous patients for FCGR2A. Fc?RIIIa-158 polymorphism did not influence overall survival. Although the differences in OS after 60 months and later were observed for FcγRIIa-131 polymorphism (95% for H, 90% for H/R but 58% for R), those differences were not statistically significant.
Conclusions: Although the presence of FcγRIIIa-158 V homozygous polymorphism elongate time to progression (TTP) in FL patients, our studies have shown that OS time is not influenced by any of the examined polymorphisms.

6016 POSTER

A novel organic arsenic S-dimethylarsino-glutathione (ZIO-101) experience in hematological malignancies

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Background: ZIO-101(S-dimethylarsino-glutathione), a novel organic arsenic, has a multifaceted mechanism of action which is mediated by