Conclusion: RT alone for limited stage FL is associated with long-term relapse-free survival. Relapse after 10 years is uncommon, suggesting that cure is possible. Reduction in RT field size to INRT≤5cm was not associated with significantly different outcomes.

9203 ORAL

Accelerated total lymphoid irradiation (TLI)-containing salvage regimen for patients with refractory and relapsed Hodgkin lymphoma (HL): 20 years outcome with multivariate analysis

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Background: An increasing number of patients with HL fail after receiving chemotherapy alone. We report the long-term results of a program that maximized the benefit of radiotherapy by integrating accelerated involved-field radiotherapy (IFRT) followed by TLI into the high-dose salvage regimen followed by autologous stem-cell transplantation (ASCT).
Materials and Methods: From 11/1985 to 07/2008, 186 previously unirradiated patients with relapsed or refractory HL underwent TLI as part of a high-dose therapy (HDT) salvage regimen prior to ASCT. All were treated on a consecutive series of 4 IRB-approved protocols; 98 (53%) had primary refractory HL, 88 (47%) relapsed after complete response (CR) to chemotherapy alone (58% of those relapsed in <1 year). All refractory or relapsed disease was biopsy proven. Median age at salvage was 30 years. After standard-dose salvage, accelerated IFRT (18−20 Gy) was given to sites of refractory or relapsed disease, followed by TLI of 15−18 Gy and HDT with cyclophosphamide/etoposide. 36% underwent an autologous bone marrow transplantation, 61% a peripheral ASCT, 5 had a double transplant. Overall (OS) and event-free survival (EFS) were analyzed by Cox analysis and disease-specific survival (DSS) by competing risk regression.
Results: With a median follow-up of 57 months, 5- and 10-year OS was 68% and 56%, 5- and 10-year EFS was 62% and 56%, and 5- and 10-year cumulative incidence of HL-related deaths was 21% and 29%, respectively. 116 patients (62%) were alive with no evidence of disease at end of follow-up. On multivariate analysis, CR to salvage chemotherapy predicted for improved OS, EFS and DSS. Primary refractory disease and extranodal disease at relapse predicted for poor EFS. OS improved after introducing peripheral ASCT in 1995 ($p = 0.06$); further improvement was observed following initiation of risk-adapted HDT. Early mortality from ASCT decreased over time ($p = 0.02$); since 1998, only 1 early death from ASCT (1.2%) has occurred. Grade ⩾3 toxicity had no impact on outcome. 8 patients had grade ⩾3 cardiac toxicity; 3 of them died. 11 patients developed second malignancies [AML (2); MDS, DLBCL, NHL, thyroid, lung, stomach, colon, and unknown primary (1 each)]; 5 of them died.
Conclusions: Integrating accelerated IFRT followed by TLI into HDT salvage for previously unirradiated patients with refractory or relapsed HL is effective, feasible and safe. It resulted in excellent long-term OS, EFS and DSS in a heavily pretreated patient population. On multivariate analysis, CR to salvage chemotherapy predicted for improved OS, EFS and DSS.

9204 ORAL

Toxicity of high-dose methotrexate (HDMTX) based chemotherapy in primary CNS lymphoma (PCNSL): preliminary experience from a randomized phase III study (G-PCNSL-SG1, NCT00153530)

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Background: The optimal primary therapy for PCNSL has not been defined thus far. This ongoing phase III multicenter study was designed to determine the role of whole-brain radiotherapy (WBRT) after high-dose methotrexate (HDMTX) based first-line chemotherapy. In this preliminary analysis toxicity data for primary chemotherapy are presented.
Patients and Methods: Immunocompetent adult patients with newly diagnosed PCNSL were randomized to consolidating WBRT with 45 Gy (1.5 Gy fractions) or no further therapy in case of complete response (CR) to primary chemotherapy or to rescue WBRT with 45 Gy (1.5 Gy fractions) or high-dose cytarabine in case of non-CR and stratified according to age (< or ⩾60 years) and treating institution. Initial treatment consisted of up to 6 courses HDMTX on day 1 as monotherapy from May 2000 to October 2006, and, from November 2006 according to a protocol amendment, of HDMTX on day 1 and ifosfamide 1.5 g/m^2 over 2h i.v. day 3−5. HDMTX was administered at a dose of 4 g/m^2 over 4h i.v. with an adjustement to creatinine clearance in all patients. Dexamethasone 3×8 g/m^2 was given only in course 1.
Results: At the last evaluation, 498 patients with a median age of 63 years (18−82) and a median Karnofsky Performance Status of 70% (30−100%) evaluable for toxicity have been included. HDMTX alone was given to 394 patients and HDMTX/Ifosfamide to 104 of these patients. Hematologic toxicity was the most common side-effect with leukopenia WHO grade 3−4 in 19.8% (10.7% on HDMTX alone and 54.8% on HDMTX/Ifosfamide; $p < 0.0005$), infections in 20.9% (18.3% on HDMTX alone and 32.7% on HDMTX/Ifosfamide; $p = 0.003$) and thrombocytopenia in 9.7% (8.4% on HDMTX alone and 15.4% on HDMTX/Ifosfamide; $p = 0.041$) of patients. Organ toxicities were infrequent (<10%). Sixty-three (12.6%) patients died on therapy: 12.9% on HDMTX alone and 11.5% on HDMTX/Ifosfamide.
Conclusions: HDMTX based chemotherapy is feasible in a context of a multicenter randomized phase IV study even in older patients when the HDMTX dose is adjusted to creatinine clearance. As expected the combination of HDMTX with ifosfamide was more toxic than HDMTX alone, however, with similar death rate on therapy. At the meeting actualized data will be presented.

9205 ORAL

Pralatrexate treatment response by key baseline parameters in the pivotal, multi-center, phase 2 study in relapsed or refractory peripheral T-cell lymphoma (PROPEL)

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Background: The rationally designed antifolate pralatrexate has increased selectivity for cells expressing reduced folate carrier-1 (RFC-1) and is retained within cancer cells for longer time periods due to more efficient polyglutamation by folypolyglutamyl synthase (FPGS). PROPEL (NCT00364923) was an international phase 2 study of pralatrexate in patients (pts) with relapsed or refractory peripheral T-cell lymphoma (PTCL). Overall response rate (ORR) was 27% (29/109) by central review and 39% (42/109) by investigator assessment; median duration of response by central review was 287d. We report here efficacy results in PROPEL by baseline subsets of age, gender, and prior therapy.
Materials and Methods: Pralatrexate 30 mg/m^2 IV was administered weekly for 6 of 7 weeks. Vitamin B_{12} and folic acid were administered to all pts. Eligibility criteria included histologically confirmed PTCL, disease progression after ⩾ 1 prior treatment, and ECOG performance status ⩽ 2. Central reviewers confirmed pathology and assessed response using the International Workshop Criteria (IWC).
Results: 109 pts were evaluable for response. ORR by central review was 31% (12/39) among elderly pts (⩾ 65y) and 24% (17/70) among younger pts (<65y); 27% (20/74) among male pts and 26% (9/35) among female pts; and 26% (6/23), 21% (6/29), and 30% (17/57) among pts with 1, 2, and 3+ prior regimens, respectively. ORR by investigator assessment was 46% (18/39) among elderly pts and 34% (24/70) among younger pts; 38% (28/74) among male pts and 40% (14/35) among female pts; and 39% (9/23), 34% (10/29), and 40% (23/57) among pts with 1, 2, and 3+ prior regimens, respectively. 111 pts were evaluable for safety, including 40 pts ⩾ 65y and 71 pts <65y, and 76 male pts and 35 female pts. Common adverse events by demographic subset (⩾ 65y vs <65y; male vs female) were stomatitis (58% vs 44%; 47% vs 51%), mucosal inflammation (53% vs 28%; 30% vs 51%), and thrombocytopenia (35% vs 28%; 24% vs 46%).
Conclusions: The PROPEL study demonstrated the activity of pralatrexate in pts with relapsed or refractory PTCL. Pralatrexate activity in this study seemed independent of age, gender, or number of prior therapies, with a trend for improved response in the elderly compared to the younger cohort, suggesting pralatrexate may provide a therapeutic option in the management of relapsed refractory PTCL in this age cohort.