(150–180 cGy/fraction/day). Post-operative radiotherapy was omitted for 2 patients on POG-9354 who had complete resection of the primary tumors.

No patients had metastatic disease at presentation. 13 patients had gross total resection of the primary tumors prior to enrollment on chemotherapy. Surgical margins were negative (10), microscopic (2), and indeterminate (1). The patient who had biopsy only received induction chemotherapy followed by definitive surgical resection and post-operative local radiotherapy.

The median follow-up was 77 months (range 17–111 months). None of the patients developed local recurrence or distant metastasis. Five patients developed treatment-related sequelae.

Cutaneous and subcutaneous ES are associated with an indolent course and a favorable prognosis with multimodality treatment. The hypothesis that complete wide excision resulting in adequate local control without the use of post-operative radiation is being tested in the POG-9354 protocol to eliminate the potential risk of radiation-induced toxicity. The next goal is to tailor treatment to minimize toxicity while maintaining a high cure rate.

398 ORAL

Recommended age for total thyroidectomy in children with MEN-2a syndrome

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Introduction: Since the introduction of RET proto-oncogene as the disease related gene in MEN-2a syndrome total thyroidectomy is usually performed at an age of 4 to 5 year. Up to that time an abnormal calcitonin stimulation test in children of an affected parent was the indication for thyroidectomy. The risk of surgical treatment in these young children is scarce in the literature. Therefore we evaluated our experience and results of management.

Patients and Methods: Since 1989, eight children from MEN-2a parents with an abnormal pentagastrin test and/or proven mutated RET gene underwent a total thyroidectomy.

Results: In seven children with an abnormal pentagastrin test and in one patient with a possible abnormal pentagastrin test total thyroidectomy was performed at the age of 14, 11, 11, 10, 7, 5, and 4 years. Microscopic examination showed C-cell hyperplasia in two patients (10 and 7 yr), C-cell hyperplasia with in situ carcinoma in three pts (12, 5, 4 yr) and invasive carcinoma in the remainig two children (14, 11 yr). One of these last children (14 yr) also had nodal metastases. The recurrent nerve function after surgery was normal in all patients. One patient (11 yr) developed a hypoparathyroidism after dissection of the central region

Conclusion: Medullairy thyroid cancer can be found at an early age of 4 years in children of parents with MEN-2a. The recommended age for starting diagnostic test (RET proto-oncogen mutation) is 4 year and even at that age total thyroidectomy seems to be a save procedure.

399 ORAL

Second malignant neoplasms (SMNs) in retinoblastoma (RB)

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Genetic alterations in RB may predispose patients to the development of secondary malignant neoplasms. Overall survival and the development o SMNs was determined for RB cases identified from the SEER Cancer Incidence Public-Use Database 1973–1994. Out of 457 cases, 326 (71%) were unilateral, 121 (27%) were bilateral, and 10 (2%) were unknown. Results showed actuarial survival to be superior for unilateral versus bilateral RB ($p < 0.01$) with 15 year survival of 92% versus 70%. Approximately half of this difference could be attributed to excess deaths from SMNs. At fifteen years the risk for developing an SMN in unilateral versus bilateral RB was 0.6% versus 15.8%, respectively ($p < 0.01$). Eight out of nine SMNs had received radiation therapy (RT) and four tumors could be considered in the field of RT. The standardized incidence ratio for developing an SMN in bilateral RB was 565. Germline deletion or mutation of the RB gene appears to confer increased susceptibility to neoplastic transformation. Surveillance for SMNs in bilateral RB is warranted.

Years	Unilateral No. at Risk	% SMN (SE)	Bilateral No. at Risk	% SMN (SE)
0	326	0 (0)	121	0 (0)
5	181	0 (0)	60	2.1 (1.5)
10	122	0.6 (0.6)	34	4.6 (2.6)
15	68	0.6 (0.6)	17	15.8 (6.8)
20	15	0.6 (0.6)	4	45.8 (18.2)

SE = Standard Error.

400 ORAL

Early prophylactic treatment with high-dose recombinant human erythropoetin (rHuEPO) in children with solid tumors

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Purpose: Children with solid tumors who are treated with chemotherapy (CT) frequently develop anemia and may need to be transfused. Avoidance of transfusion is the goal in pediatric cancer patients and rHuEPO has been shown to be effective in ameliorating anemia in adult solid tumor cancer patients on CT. A pilot study to assess the benefit of rHuEPO as prophylaxis for anemia in children with solid tumors was designed.

Methods: In an open, nonrandomized trial we studied 41 children, median age 13.5 years (range 5 months–26 years), with solid tumors (osteosarcoma: 44%; Ewing's sarcoma: 24.4%; rhabdomyosarcoma: 12.2%; others: 19.4%) and CT-induced anemia. Treatment with rHuEPO (Erypo® (epoetin alfa), Janssen-Cilag, Austria) was started during the first course of CT before anemia was observed. The patients received 150 international units (IU)/kg rHuEPO 3 times weekly if the hemoglobin value was 12 g/dL or greater, and 300 IU/kg if the hemoglobin value was 12 g/dL or less. All patients received oral iron supplementation. During the study, rHuEPO responders did not receive packed red blood cell (RBC) transfusion in any 2-week time period, while a non-responder was defined as a person who received packed RBCs during 2 consecutive weeks. Such patients were therefore excluded from further receiving rHuEPO.

Results: The median observation time was 6 months (range 1-11 months). 36/41 (88%) patients were responders to rHuEPO; 16/41 (39%) did not receive packed red blood cells at any time during the course of chemotherapy. 25/41 (61%) received a median of 3 units of packed red blood cells (range 1–15 units).

Conclusion: In our study, early prophylactic treatment with high-dose rHuEPO seems to have a major benefit to prevent CT-induced anemia in children with solid tumors. Therefore, we suggest that a randomized study with rHuEPO in children with solid tumors should be initiated.

401 POSTER

Results of first multicentric studies of therapy children and adolescents with acute lymphoblastic leukemia in Ukraine

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Purpose: General level of pediatric oncology-hematology in post-sovjet countries was extremely low only some years ago. Introduction of modern treatment strategy for the most frequent oncologic disease in childhood (ALL) in frame of controlled multicentric study was used for achieving progress in this field.

Methods: In 1993 6 (later on 8) pediatric hematologic centers in Ukraine organized Cooperative Group of Pediatric Leukemias and Lymphomas (GPLLU). 117 pts were enrolled in the first prospective ALL-GPLLU-93 Study which was based on Protocol ALL-BFM-90 with some modifications (1 g/m^2 MTX instead of 5 g/m^2); 275 pts were included into the second ALL-GPLLU-95 Study (with ALL-BFM-95 stratification for Risk Group) till 1.01.99.

Results: I first Study 5-years pEFS was 0.68 (SD = 0.06) with pS = 0.72 (SD = 0.06); in second Study pEFS for 43 month was 0.78 (SD = 0.07) with pS = 0.79 (SD = 0.05). The incidence of Early Deaths (1.8% vs 3.4%) and Deaths in remission (4.7% vs 7.7%) markedly decreased in second Study comparatively to the first one.

Conclusions: Introducing of modern therapeutical strategy in frame of controlled cooperative Studies resulted in dramatic improvement in outcome of patients with ALL and therapy results became compatible with data of analogous western Studies. At the same time cooperation between different oncohematologic centers helps them in achieving fast professional development.