had non organ saving surgery (en bloc resection, amputation) in first line treatment.

Results: 5y EFS was 81%, 81%, 73% and 22%; 5 y SUR was 90%, 89%, 70% and 22% for IRS Group I, II, III and IV pts., respectively (p<0.001 for localized vs. metastatic). Univariate analysis revealed the following risk factors for localized disease: Tumor size <5cm vs >5cm (5y EFS 63% vs. 91%, p=0.001; 5y SUR 69% vs. 96%, p=0.002); histology biphasic vs. monophasic (5y EFS 89% vs 69% p<.03 5y SUR 90% vs 76%, n.s.). Radiotherapy no/yes (5y EFS 56% vs. 85%, 5y SUR 59% vs. 90%). Site: extremeties vs. trunk vs. head/neck (5y EFS 81% vs. 67%, vs. 60%, n.s.; 5y SUR 85% vs. 88%, vs. 67%, n.s.). No difference for T1/2 and age </>10y. No difference in 5y EFS and 5y SUR in IRS group I or II pts. between ifosfamide and cyclophosphamide containing regimen. Response to chemotherapy (week 9-12) was >2/3 tumor volume reduction in 13/27 (48%), >1/3 and <2/3 in 3/27 (11%) and non response in 11/27 (41%). Overall local control rate for IRS group I-III was 88%, systemic control rate 89%. Multivariate analysis will be presented.

Conclusions: To our knowledge these results are superior to other published data concerning systemic control rate and EFS for patients with localized disease emphasizing the indication for systemic chemotherapy in SySa. Tumor size and initial metastases have a high impact on prognosis.

1043 ORAL

Results of the German multinational GPOH-HD 95 trial: analysis of risk factors in pediatric Hodgkin's disease after combination chemotherapy with and without radiation

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Purpose: The aim of the multicenter trial GPOH-HD 95 was to maintain the excellent treatment results of previous studies in pediatric Hodgkin's disease(HD), however to minimize the risk of potential late effects caused by radiation therapy(RT). Analysis of treatment failures should guide the planning of new protocols in the future.

Methods: Children below the age of 18 years were treated according to risk factors (stage,B-symptoms,extranodal extension) within 3 different treatment groups(TG) with 2,4 or 6 cycles of chemotherapy(CTx).When a complete remission could be achieved no consolidating RT followed.When a tumor reduction of >75% was obtained the RT-dose to involved fields(IF) was 20Gy,otherwise 30Gy, remaining lymphomas of >50ml were treated locally to 35Gy.Quality assessment of radiation therapy with review of radiaton protocols, planning and verification films was carried out centrally, as well as the analysis of treatment failures.

Results: From August 1995 to March 2001 a total of 956 eligible patients were registered from 126 institutions in European countries. At a median follow-up time of 34 months relapse free survival for the low risk group TG1(stage I/IIA) is 95%; for the intermediate risk(TG2) and advanced cases(TG 3) RFS is 94% and 92% with RT after chemotherapy induced PR and 79% after achieving a CR and no adjuvant RT, this difference is now statistically significant with a p-value of 0.006.However, overall survival is excellent with 97% for all pts., 99% for TG1 and 96% for TG3.- 71 events occurred, 65 of them were treatment failures (29 progressive disease during CTx, before,during or shortly after RT and 36 relapses). Risk factors for early failures were advanced stages, extranodal extension of disease, B-symptoms and nodular sclerosis type 2 histology.Risk factors for relapses were different for irradiated and not irradiated pts.Of importance seems to be the time lag between end of CTx and start of RT. Minor protocol violations in RT techniques did not show a major impact on treatment failures.

Conclusion: The omission of RT after achieving a CR with CTx causes an increased risk of treatment failures in advanced cases, however the total incidence of failures is low and has no impact on survival. The potential gain by reducing radiation dose and volume with respect to treatment induced long term toxicity might be considerable for the young patient population.

1044 ORAL

Randomised trial comparing high-dose-methotrexate plus doxorubicine versus high-dose-methotrexate plus etoposide-ifosfamide as preoperative treatment for osteosarcomas

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Intensive high-dose-Methotrexate containing regimens (ie T10 protocol) produce the best results in term of EFS for the treatment of osteosarcomas. In the original T10, high-dose-Methotrexate was associated with Bleomycin-Cytoxan-Dactinomycin and Doxorubicin during the preoperative phase. Recently we have reported a 50% response rate with the combination of Etoposide-Ifosfamide in relapsing osteosarcoma patients.

Objectives: To improve the efficacy of the preoperative chemotherapy in osteosarcomas we have conducted a randomized trial comparing high-dose-Methotrexate 12gr/m2 (7 courses) associated with Doxorubicin 70 mg/m2 (2 courses) or with Etoposide 75 mg/m2/day-Ifosfamide 3 gr/m2/day x 4 days. The main criteria was the percentage of good histological responses (<5% viable cells). To provide an 80% power to detect a 20% difference in good responder rates between the 2 groups, for an overall level 2a = 5%, requires 226 pts.

Methods: 227 non metastatic, limb, osteosarcoma patients, aged 3 to 19 years, have been randomized (Doxorubicin 113, Etoposide-Ifosfamide 114). Surgery was conservative in 214 patients and radical in 13.

Results: 47 pts had a good histological response in the Doxorubicin arm (42%) and 61 pts in the Etoposide-Ifosfamide arm (54%) (information missing in one patient). The observed difference between the percentage of good responders between the 2 arms is 12% (p=0.06, CI 95% -0.5% +25%). For the whole population, the EFS3y is 70%.

Conclusions: The12% difference in favor of Etoposide-Ifosfamide does not reach statistical significance. Taking into account the potential long term toxicity, Etoposide-Ifosfamide appears less toxic than Doxorubicin and will be considered as a better arm in future studies.

1045 ORAL

Children nasopharyngeal carcinoma

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Purpose: To report the epidemiological, clinical and therapeutic features of pediatric Nasopharyngeal carcinoma among Tunisian children.

Materials and Methods: Our retrospective study concerned patients aged less than 16 years affected by histological proven Nasopharyngeal carcinoma. Initial work-up included: clinical examination with measures (cervical nodes square), chest-x ray, abdominal ultrasonography, bone scintigraphy. We used the UICC-AJC 1987 classification.

Results: We collected 34 patients (20 M/14 F) from 1980 to 1998, with a mean age of 13.7 years (10 to 16) and a 1.4 sex-ratio. Mean delay to consultation is 5.8 months (1 to 51) and symptoms dominated by cervical nodes (91%) or more rarely rhino logic (56%), neurological signs (38%) of otologic signs (29%). Paraneoplastic syndromes were seen in 9 cases (26%). Tumors are mainly posterior (61%) and fun gating (62%). Nodes are predominantly in the high and posterior cervical area with a mean diameter of 4.8 cm (1 to 10) and mean surface of 22.5 cm2 (2 to 80). 74% of patient presented with T3–4 tumors and 82% with N2–3 nodes. Undifferentiated histological type predominate representing 94.2% of cases. All patients received loco - regional radiotherapy while 27 received chemotherapies mainly neoadjuvant and cisplatin based. With a median follow-up of 58 months (10 to 168), 5-years survival and disease-free survival are 58% and 55% while loco-regional control rate is 90%. Failures were dominated by metastases observed in 10 patients (37%) mainly in bones and loco-regional relapses ate observed in 2 patients (7.5%). Multifactor analysis showed a prognostic value for loco-regional control of delay to consultation (p = 0.001), nodal surface > 20 cm2 (p = 0.04) and cranial nerve palsies (p = 0.02), for overall survival the importance of delay to consultation (p = 0.05), sex (p = 0.03), neoadjuvant chemotherapy (p = 0.03) and cervical nodes surface (p = 0.05), for metastasis-free survival the impact of delay to diagnosis (p = 0.05) and nodal surface (p = 0.05) and for disease-free survival the impact of delay to consultation (p = 0.04).

Conclusion: The child's nasopharyngeal carcinoma is relatively frequent in Tunisia. The clinical presentation is often comparable adult nasopharyn-

geal carcinoma with a bulky tumoral volume. The more better results were obtained by combined therapy but posed the problem of the risk of long term sequelae.

1046 ORAL

Statural growth impairment and growth hormone deficit as a late effect in childhood medulloblastoma: a comparison of hyperfractionated versus conventionally fractionated craniospinal radiotherapy

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Purpose: With more patients potentially living longer due to the improvement in survival in childhood medulloblastoma, the negative late effects of radiotherapy (RT) on statural growth become important factors to consider when treatment decisions are planned. Hyperfractionation can reduce the delayed effects of RT.

Methods and materials: The authors compared the incidence of growth alterations and GH deficit (GHD) after hyperfractionated craniospinal RT (Group A, n=13 patients; 1 Gy bid, 36 Gy CSI followed by 30 Gy posterior fossa boost) versus conventionally fractionated RT (Group B, n=22 patients; 36 Gy CSI followed by 18 Gy boost to the posterior fossa) in a group of children with medulloblastoma.

Results: The mean age at the time of tumor diagnosis was 8.1 years in Group A (10 patients were prepubertal, 2 were treated at the beginning of puberty and 1 at the end of puberty) and 8.9 in Group B (19 cases were prepubertal). Patients were followed for a mean of 6.2 years for Group A and 10.2 years for Group B. All prepuberal patients were evaluated yearly for standing height, height velocity (HV), sitting height (SH), subischial leg length (SLL) and bone age. GH secretion was evaluated 2 years after RT when HV fell below the 10th percentile. In the first year after RT growth was constantly impaired in all patients due to malnutrition. In the following years we observed among Group A patients treated during prepuberty or at the beginning of puberty a reduction of HV in 11/12 cases; in 6 cases GHD was noted 2-4 years after RT, while in 5 patients GH secretion was normal. In one patient treated at the beginning of puberty GHD was noted only very late (9 years after RT). SH was more reduced than SLL in 11/12 cases (selective growth impairment due to spine RT). The patient treated at the end of puberty showed normal GH secretion 6 years after RT. In all Group B patients GHD occurred between 2 and 6 years after RT. Analysis by cumulative incidence function showed a statistical significant difference (p=0.03) between the two groups; the probability of normal GH secretion at 4th year after RT was 60.6% (SE=13.8) in Group A and 9.1% (SE=6.1) in Group B patients.

Conclusions: The current study findings suggest that the use of hyperfractionated craniospinal RT is associated with a lower risk of statural growth impairment; in particular GHD is less frequent and longer deferred in the group treated with hyperfractionated than conventionally fractionated RT.

1047 ORAL

Ovarian function in young women treated for Hodgkin's disease in childhood

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Purpose; To review ovarian function in female long term survivors of childhood Hodgkin's Disease (HD).

Method: The records of young women attending our long term follow up clinic, who were treated with alkylating agents for HD in childhood, were reviewed. Information on age at diagnosis, age at menarche, number of pregnancies and hormone profile was extracted.

Results: Between 1974-95 21 females, median age at diagnosis 12y 8m (range 8y10m - 15y6m) were treated with a median of 6 courses (range 3-8) of Chlorambucil, Vinblastine, Procarbazine and Prednisolone (ChlVPP). Four patients had additional chemotherapy with other alkylating agents. One of these 4 patients has primary amenorrhoea and another secondary amenorrhoea. All other patients have a normal menstrual cycle with normal gonadotrphin levels. Fourteen patients were menstruating at the time of diagnosis of HD. There have been 29 pregnancies in 16 patients, median age at first pregnancy 26y (range 19-29y), resulting in 25 live births (1 twin), 3 terminations and 2 spontaneous abortions. Six pregnancies occurred in women over 30y. Median length of follow up is 19y (range 6-27y) and median age at follow up is 30y (range 19-36y). To date there is no evidence of premature menopause in our patients treated with ChlVPP alone.

Conclusion: Female patients treated with ChlVPP chemotherapy have good prospects of fertility, and do not appear to be at risk of menopause under 30y. Continuing follow up is important as these patients may still have an early menopause and be at risk of osteoporosis.