Gy respectively following WART (10 Gy). A statistical procedure known as generalized estimating equations (GEE), which treated the flank and beyond flank recurrences as binary variables without regard to time of recurrence, was used to handle the potential correlation between the two outcomes for the same patient. The odds ratios for tumor recurrence in relation to RT dose and doxorubicin were determined.

Results: Among 450 patients there were 33 who had relapses in the abdominal cavity (11-flank only, 13-beyond flank only, 9-both). The 4-yr. relapse free survival rates (RFS) among patients who received different RT doses were not significantly different: 86% (0 Gy), 91% (10 Gy-flank), 96% (10 Gy- WA), 94% (20 Gy-flank) and 94% (20 Gy WA). This conventional analysis did not give an accurate assessment of RT effects as 'BF' recurrences were counted as relapses against flank-only RT fields.

The results of treating 'F' and 'BF' recurrences separately showed that BF relapse occurred at only half the rate as flank relapses (6.2% vs 12.4%) when neither area was irradiated (0Gy). 10 Gy reduced the relapse risk by about 75% and 20 Gy completely eliminated the risk of flank recurrence. The odds ratio (OR) measured by GEE for abdominal recurrence for 10Gy vs no RT was 0.35 (p 0.01), whereas for 20Gy vs no RT it was 0.08 (p 0.01). Thus 10 Gy reduced the risk about three fold and 20 Gy by a factor of 12. The OR for recurrence following the use of 3 drugs relative to 2 drugs was 0.39 (p 0.01). However, after adjusting for RT site and dose, the effect of doxorubicin was not significant (p 0.37).

Conclusions: This report demonstrates that the addition of RT to the flank or whole abdomen (10 Gy and 20 Gy) in FH WT patients with tumor spillage resulted in significantly better tumor control rates compared to chemotherapy alone. The present policy of omitting RT for stage II patients with spillage needs to be reconsidered.

40 Local Control Using Radiotherapy for Non-Metastatic Ewing's Sarcoma: Is There a Dose Response?

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Purpose/Objective: The purpose of this study is to determine prognostic factors for local control in the radiotherapeutic management of non-metastatic Ewing's sarcoma

Materials/Methods: From 1976 to 2001, 40 patients (pts) with localized Ewing's sarcoma (ES) were treated with definitive RT after biopsy at 1 institution. There were 19 male and 21 female pts with a median age of 14 years (range, 2 to 58 years). Tumor location was extremity in 19 (47%), pelvis in 10 (25%), spine in 5 (13%), trunk in 4 (10%) and head and neck in 2 (5%). Tumor size was $\leq$ 8 cm in 23 (58%) and $>$ 8 cm in 17 (42%). Median RT dose was 55.8 Gy (range, 25.5 to 76 Gy). Beam energy was 1.25 mv photons in 12, 4 mv in 9, 10 mv in 8, 6 mv in 3 and 24 mv in 2. Four were treated with 250 kv photons while 2 received 15 MeV electrons. RT volume was whole bone followed by involved field (tumor + 2 to 4 cm margin) in 19 (47%) or involved field in 21 (53%). RT was started within 12 weeks of treatment in 31 (78%) and $>$ 12 weeks in 9 (22%). Chemotherapy was given to 34 pts (85%). The most common regimen employed was vincristine, dactinomycin, cyclophosphamide, doxorubicin alternating with ifosfamide and etoposide (VACA +IE) in 10 of 34 pts (29%). Median follow-up for surviving pts was 12.3 years (range, 1.7 to 26.4 years).

Results: The 5- and 10-year Kaplan-Meier overall survival estimates were 55.5% and 45.1%. Cox regression analysis showed that tumor size was the only factor found to impact on overall survival. The 5- and 10-year local control rate was 78.2%. On multivariate analysis, RT dose was found to be the only prognostic factor for local control. The 5- and 10-year local control rate was 88.7% for RT dose $\geq$ 49 Gy and was 37.5% for RT dose $<$ 49 Gy ($p = 0.0002$, log-rank test). For tumors $\leq$ 8 cm, the 5- and 10-year local control rate was 94.1% for RT dose $\geq$ 49 Gy and 50.0% for RT dose $<$ 49 Gy ($p = 0.01$, log-rank test). For tumors $\geq$ 8 cm, the 5- and 10-year local control rate was 85.7% for RT dose $\geq$ 54 Gy and 26.7% for RT dose $<$ 54 Gy ($p = 0.006$, log-rank test). For the 19 pts who survived at least 5 years after RT, 10 did not have documented late effects. For the remaining 9 pts, late effects included decreased limb length growth in 5, decrease range of motion of a joint in 3, scoliosis in 2, fracture in 2 and ovarian failure in 1. Two patients developed secondary malignancies, both in the RT field: osteosarcoma at 9.6 years and breast cancer at 26 years after RT.

Conclusions: Radiotherapy dose was found to influence local control in ES. In particular, pts who received RT doses $\geq$ 49 Gy for tumor size $\leq$ 8 cm and $\geq$ 54 Gy for tumor size $>$ 8 cm had better local control.

41 Treatment Results of 165 Pediatric Patients with Non-Metastatic Nasopharyngeal Carcinoma: A Rare Cancer Network Study

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Purpose/Objective: This study was performed retrospectively in pediatric (age $<$ or $=$ 17 years) nasopharyngeal carcinoma (NPC) patients to evaluate the role of chemotherapy, the optimal dose of radiotherapy, and the differences in outcomes in regard to prognostic factors.

Materials/Methods: The study included 165 (109 male and 56 female) pediatric patients with the diagnosis of non-metastatic NPC treated between 1978 and 2003 from 16 centers. Only patients evaluated either with CT and/or MRI were included and staged according to AJCC 1997. The median age is 14 years old (Range 7–17 years). Histopathological classification revealed 23 (13.9%) patients with WHO II and 142 (86.1%) patients with WHO III.. There were 3 (1.8%) patient with stage I, 1 (0.6%) with IIa, 10 (6.1%) with IIb, 60 (36.4%) with III, 44 (26.7%) with IVA, and 47 (29%) with IVB. While 21 (12.7%) patients treated with radiotherapy alone, 144 (87.3%) patients received chemotherapy (neoadjuvant $\pm$ concomitant $\pm$adjuvant) beside radiotherapy. Chemotherapy schedule was non-cisplatin based mono therapy in 1 (0.8%), cisplatin based mono therapy in 10

(6.9%), non-cisplatin based multi regimen in 29 (20.1%) and cisplatin based multi regimen in 104 (72.2%) patients. The median follow-up time for all patients was 48 months (Range, 5–249 months).

Results: The actuarial overall 5-year survival (OS) was 77.4%, whereas the actuarial 5-year local relapse free survival (LRFS), loco-regional relapse free survival (LRRFS), distant metastasis-free survival (DMFS) and disease-free survival (DFS) rates were 87.8%, 81.9%, 80.5% and 68.8%, respectively. While 19 patients (11.5%) developed local recurrence, 14 (8.5%) developed regional failure, and 30 (18.2%) developed distant metastases. Overall, 32 patients died during follow up (27 due to disease, 2 due to chemotherapy complications and 3 due to inter current disease). In univariate analysis, statistically significant unfavourable factors were male gender for DMFS ($p=0.01$), T3&T4 disease for LRFS ($p=0.01$), presence of cranial nerve palsy at diagnosis for LRFS ($p=0.02$) and LRRFS ($P=0.01$), stage IV for DFS ($p=0.02$), N3 disease for DFS ($p=0.004$) and OS ($p=0.03$), total nasopharyngeal EBRT dose of less than 66 Gy for LRRFS ($p=0.01$) and patients treated with radiotherapy alone for LRFS ($p=0.001$) and LRRFS ($p=0.02$). In multivariate analysis, statistically significant unfavourable factors were age older than 14 years for LRC ($p=0.04$); male gender for DMFS ($p=0.03$); T3,T4 disease for LRFS ($p=0.01$); N3 disease for DFS ($p=0.002$) and OS ($p=0.002$); total nasopharyngeal EBRT dose of less than 66 Gy for LRFS ($p=0.02$) and LRRFS ($p=0.002$); and patients treated with radiotherapy alone for LRFS ($p=0.0001$), LRRFS ($p=0.007$) and DFS ($p=0.02$).

Conclusions: We have defined favourable prognostic factors in our pediatric NPC cohort as younger age (age < 14), female gender, early T1,T2 and N0-2 status, total nasopharyngeal EBRT dose > 66 Gy, and the treatment schedule incorporating chemotherapy with radiotherapy. This data suggests that high dose RT combined with multiagent chemotherapy is effective in achieving satisfactory results. However, research in dose and field reductions of radiotherapy in selected patients besides the optimal chemotherapy schedule and timing should be encouraged to achieve a lesser amount of late sequels.

42 Results of the First International Consortium on Low Grade Glioma (ICLGG)-Analysis of Radiotherapy Outcomes for UKCCSG Patients Treated in the LGG1 Study

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Purpose/Objective: To present an analysis of the outcomes for children with Low Grade Glioma (LGG) treated by radiotherapy (RT) in the LGG1 study and to evaluate the efficacy of RT in the following groups. 1) at diagnosis for progressive disease, severe symptoms or threat to vision; 2) progression following observation; 3) progression following chemotherapy and 4) progression after initial observation followed by chemotherapy.

Materials/Methods: All patients were considered for maximal debulking surgery. Patients with completely or incompletely resected tumours without severe or progressive symptoms were observed. First-line non-surgical treatment for radiological and/or clinical progression was RT for children aged 5 years or older and chemotherapy for children aged less than 5 years. The RT dose schedule was 54 Gy in 30 daily fractions. Children younger than 3 years and those with spinal cord primaries were treated with 50 Gy in 30 daily fractions. ICRU 50 definitions for target volumes were adhered to. Volumes were determined with the aid of MR and CT imaging modalities. To minimize treatment related morbidity limited margins were applied.

Results: Between February 1997 and April 2004 181 patients from UKCCSG centres were treated with RT and 139 were eligible for analysis. There were 71 males and 68 females (median age at diagnosis 8.4 years, range 0.3 to 16.3 years, median age at RT 9.0 years, range 0.6 to 18.8 years). 9 patients had neurofibromatosis at diagnosis. The majority of cases involved the following anatomical sites; supratentorial (fifty-four patients) (38.9%), brainstem (twenty-two patients) (15.8%), cerebral hemispheres (nineteen patients)(13.7%) and cerebellum (nineteen patients) (13.7%). The main histological diagnoses included pilocytic- 73 patients, low grade astrocytomas- 30 patients and fibrillary- 11 patients. The commonest presenting symptoms were headaches, lethargy, nausea and vomiting, unsteadiness, double or reduced vision and weakness.

The median follow-up period following RT is 3.1 years (range 0.1 to 7.1 years). For patients initially observed the median time to RT was 1.9 years (range 0.3 to 5.7 years). For all patients, from the date of radiotherapy the 3-year OS was 85.9% and EFS 74.6%. Sixty-four (46.0%) had RT at diagnosis with 3-year OS 82.1% and EFS 72.2%. Forty-two (30.2%) had RT after observation with 3-year OS 87.5% and EFS 71.9%. Twenty-two (15.8%) had RT for progression after chemotherapy with 3-year OS 94.4% and EFS 83.6%. Eleven (7.9%) had RT after observation followed by chemotherapy with 3-year OS 80.0% and EFS 78.8%. The majority of patients with visual symptoms had stabilisation following RT.

Conclusions: An analysis of the outcomes of patients treated with RT in the LGG1 study is presented. Patients treated at progression following observation and/or chemotherapy have a similar OS and EFS to those treated at diagnosis. With a high probability of long-term OS and EFS, it is important to utilize modern RT planning to minimise acute toxicities and late sequelae from therapy and optimise the therapeutic outcome.

43 Impact of TBI on Late Effects in Children Treated by Megatherapy for Stage IV Neuroblastoma: A Study of the French Society of Pediatric Oncology

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Purpose/Objective: To determine role of total body irradiation (TBI) to late sequelae in children treated with high dose chemotherapy and autologous bone marrow transplantation (ABMT) for stage IV neuroblastoma.

Materials/Methods: We compared 2 groups that were similar regarding age, stage, pre MGT regimen, period of treatment, follow up(F.U) (12 years), DFS, but differing in whether TBI was given. Group 1 ($n=30$), treated between 1985–92 without TBI, but 7 patients pts received radiotherapy to primary tumor site (1pt: 36Gy; 3pts: 35Gy; 2pts: 25Gy; 1pt: 30Gy). Before 1989 MGT was chosen according to response to induction regimen: 7 pts with complete response were treated with teniposide, BCNU, melphalan. 9 pts with partial response received cyclophosphamide, melphalan, busulfan. Group 2 ($n = 32$), received TBI as part of MGT (1982–1993). 25 pts received 12Gy (2Gy $\times$ 2x/j in 3 days), 4 pts: 8Gy, 1 pt: 7Gy, 1 pt: 10Gy, 1 pt: 4Gy