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Health-related Quality of Life of patients with malignant pleural mesothelioma treated with pemetrexed disodium

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In order to further describe the impact of pemetrexed disodium (ALIMTA®), health-related quality of life (HRQoL) assessment was included in a multinational phase II trial for patients with malignant pleural mesothelioma (MPM). Because no MPM-specific HRQoL instrument was available, a modified version of the Lung Cancer Symptom Scale (LCSS) form for patients was used. Separate data demonstrate that the modified LCSS is reliable and valid for MPM patients. Patients completed the LCSS two times before the start of therapy and then weekly while on-study. Patients with unresectable MPM who had not been previously treated with systemic chemotherapy received ALIMTA 500 mg/m2 every 3 weeks. LCSS data were averaged for baseline and for each cycle. Preliminary results from 62 patients were as follows: 87% male, median age=62 (range 40-80), median KPS=90 (range 70-100), 85% stage III-IV. Baseline median LCSS scores (scale 0-100, 0=best possible) were as follows: anorexia=20; fatigue=29; cough=8; dyspnea=35; hemoptysis=0; pain=22; symptom distress=27; activity level=44; and global QoL=26. Based on previously reported meaningful change of 10 points, using Cycle 3 data (after first on-study tumor assessment and 3 doses of ALIMTA), patients were grouped by best study response and categorized as improved, preserved or deteriorated for each LCSS item. Percentage of responding patients (N=9) with improved and preserved scores, respectively, were: anorexia (56%, 33%); fatigue (33%, 33%); cough (44%, 56%); dyspnea (33%, 67%); hemoptysis (0%, 100%); pain (33%, 44%); symptom distress (56%, 22%); activity level (56%, 33%); and global QoL (44%, 44%). Percentage of patients with stable disease (N=32) with improved and preserved scores, respectively, were: anorexia (16%, 37%); fatigue (23%, 35%); cough (22%, 53%); dyspnea (15%, 50%); hemoptysis (0%, 100%); pain (12%, 50%); symptom distress (13%, 35%); activity level (16%, 37%); and global QoL (6%, 50%). These preliminary LCSS results indicate that most patients receiving ALIMTA had stable or improved HRQoL during Cycle 3. Responders were more likely to report improvement, indicating that the modified LCSS is responsive to changes in clinical status.

Paediatric oncology

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Risk factors in malignant extracranial germ cell tumours (MGCTs) of childhood: Analysis of UKCCSG's GCII study

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Purpose: Most national groups now obtain high cure rates in paediatric extracranial MGCTs, mostly using cisplatin-based chemotherapy. In the UK carboplatin is preferred because it is less oto- and nephrotoxic. An analysis was performed to determine whether therapy should be based on risk factors.

Methods: Children aged 0–16 years with histologically verified extracranial MGCTs were excised if feasible without major morbidity, or biopsied. Chemotherapy with JEB (carboplatin, etoposide and bleomycin) was given if excision was incomplete or if tumour recurred after excision. Uni- and multivariate analyses of survival were performed.

Results: Between January 1989 and December 1997 192 patients were registered of whom 8 were excluded (no histology in 3, non-protocol chemotherapy in 5). The remaining 184 patients had germinoma (20), malignant teratoma (55), embryonal carcinoma (1), yolk sac tumour (107) or choriocarcinoma (1). Age, site and histology followed recognised patterns: yolk sac tumours in children aged <5 years; germinomas mostly in older children; malignant teratoma in all age groups; site of primary was also age related.

Univariate analysis of JEB treated patients showed 5 year EFS%

Testis	100	Stage I	100	Germinoma	100
Ovary	91	Stage II	94	Malignant teratoma	87
Vagina/uterus	80	Stage III	85	Yolk sac tumour	86
Sacrococcygeal	87	Stage IV	78		
Thorax	75			AFP < 10,000	95
Other	73			AFP ≥ 10,000	77

Surgery alone cured 47 patients and 137 required JEB. Overall 5 year survival was 93.2%. For JEB treated patients OS was 90.9% and EFS 87.8%

Multivariate analysis showed AFP level followed by stage and then site were the strongest risk factors and identified risk groups.

Conclusion: AFP level, stage, site and histology should be used to stratify patients for treatment.

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The prognostic value of histological subtype and tumor volume in localized unilateral nephroblastoma

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Today the prognosis of nephroblastoma is excellent. Questions arising in the management of children with nephroblastoma are mainly focusing on preventing late effects and in finding new prognostic risk factors.

Purpose: A retrospective analysis was performed to investigate the influence of histological subtypes and tumor volume on prognosis in nephroblastoma. Method: From April 1994 to December 2000 808 patients with a nephroblastoma were enrolled in the SIOP 93-01/GPOH study. 622 of them had stage I, II or III disease at diagnosis. In 352 of these patients tumor volume was measured by ultrasound at diagnosis and after preoperative chemotherapy. Histology was reviewed according to the Stockholm working classification.

Results: 10% had low risk, 78% intermediate risk and 12% high risk tumors. Relapse free survival after 5 years (RFS) for patients with localized unilateral nephroblastoma receiving preoperative chemotherapy is 93% for low risk, 91% for intermediate risk, and 79% for high risk tumors. Of the intermediate risk tumors epithelial and stromal predominant tumors show the best outcome with 98% RFS, compared to 81% for blastemal predominant tumors and 91% for all other subtypes of intermediate risk ($p<0.01$). In these patients a median tumor volume of 360 ml was measured at diagnosis and of 160 ml after preoperative chemotherapy. No tumor volume reduction was found in patients with low risk tumors (except completely necrotic tumors), in epithelial and stromal predominant tumors and in all high risk tumors (non-responsive tumors). In all other tumors (responsive tumors) a median tumor volume reduction of 180 ml did occur. The difference in tumor volume reduction between responsive and non-responsive tumors is highly significant ($p<0.01$). Patients with a localized unilateral nephroblastoma and a tumor volume of less than 500 ml after preoperative chemotherapy have a RFS of 89% compared to 72% for those with a larger tumor ($p<0.01$). By combining histological subtype and tumor volume after preoperative chemotherapy the intermediate risk tumors can be divided into 4 prognostic different subgroups: epithelial or stromal predominant (98% RFS), blastemal predominant (81% RFS), rest of intermediate risk and < 500 ml tumor volume (92% RFS), rest of intermediate risk and > 500 ml tumor volume (71% RFS).

Conclusion: Tumor volume after preoperative chemotherapy as well as the histological subtype can be used for further stratifying postoperative treatment.

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Synovial sarcoma in childhood and adolescence in the CWS 81-96 trials

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Objectives: To show event free and overall survival rates in Synovial Sarcoma (SySa) treated with a multimodal therapy concept. To define risk factors for future stratification for SySa, the third most common sarcoma in childhood and adolescence

Patients and Methods: We analyzed a group of 103 pts. enrolled in the CWS 81 to 96 studies (median age 13y, 0.1-20 years), minimum F/u of 30 months (for living pts.); median F/u 63 months (6-195). Postsurgical stage was IRS Group I in 34, II in 30, III in 30 and IV 9 pts. Sites: extremities 87 (21 upper, 62 lower limb), trunk 8, head/neck 8 pts.. 102 (99%) pts. received chemotherapy (VAIA, VACA, EVAIA or CEVAIE), 76 (74%) radiation therapy (16-60 Gy), 25 (24%) secondary surgery. Only 7