observed in 25 pts (57%). Hypersensitivity reactions occurred in 12 pts (27%); in 2 cases (4%) the reaction was severe (gr. 3 and 4). Partial bowel obstruction occurred within 30 days from TXL administration in 6 pts (14%): the relationship with chemotherapy was uncertain. Overall 8 pts (18%) stopped TXL treatment because of adverse events: 5 hypersensitivity reactions, gr. 3 paresthesias in one case, partial bowel obstruction in 2 cases. In our opinion pts with constipation or bowel subobstructive condition at the beginning of TXL treatment should be carefully selected and monitored.

524 PUBLICATION

**CISPLATIN (C) + IFOSFAMIDE (I) FOR PATIENTS WITH OVARIAN CARCINOMA (O.C.) WITH PRIOR CARBOPLATIN (CBT) + CYCLOPHOSPHAMIDE (CTX) CHEMOTHERAPY**

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Thirty patients (pts) aged 55 (45–68) 8/30 with refractory and 22/30 with recurrent O.C. received C:100 mg/m$^2$ day 1 and I: 5 g/m$^2$ over 3 days as second line therapy. Staging at first diagnosis was: stage III 24 cases, stage IV 4 cases. After primary surgery all pts were treated with CBT + CTX for six courses. Eight pts had early tumor recurrence within 6 months while 22/30 had tumor recurrence 1–2 years after first line chemotherapy. Objective response was achieved after 4 courses in 2/8 pts with resistant tumors (PRS of 4 and 6 mo duration) while 8/22 pts with tumor recurrence responded with 2 pathology CRS and 6 clinically and laboratory confirmed $\geqslant$ PRS. Time to progression was 8 mo (6–12) all pts expired within 16 months. Myelotoxicity was moderate because of GCSF or GM-CSF post chemotherapy administration. Neurotoxicity was moderate also except for one case with Grand-mal most probably due to (I). With a (33%) response rate C + I as second line is at least as effective as newer drugs. However, the major determinant of response to C + I was the progression free interval from first line chemotherapy. This interval may be an indicator for deciding Cisplatin Taxanes or both drug administration in recurrent O.C.

# Paediatric oncology

525 SIOP Award lecture

**THE CONSEQUENCES OF THE TREATMENT OF CHILDREN WITH CANCER. SUCCESS OR FAILURE/DO WE YET KNOW THE ANSWERS?**

*P. Morris Jones*

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Survival rates for children treated for cancer have continued to rise from the 1950's to the present day and for most diagnoses are now in excess of 50%, reaching 90% in some categories. These results have not been achieved without unwanted consequences which have long term implications for the health status of the survivors and health care costs for the community. Patients treated in the 1950's and 1960's demonstrate the long term effects of surgery and radiation therapy while more recently chemotherapeutic sequelae have increased in importance and frequency. The interaction of radiation and chemotherapy was poorly understood in the earlier decades but is now well documented.

As more intensive protocols are introduced using many different drugs it is likely that the long term survivors of the future will have as yet unrecognised complications. Even the survivors from the earlier years continue to develop new problems and need ongoing regular surveillance. The psychological problems associated with the diagnosis, long periods of intensive life threatening treatment and continuing uncertaintity of outcome add to the sequelae. A multidisciplinary approach to follow up is as necessary as it is in the initial treatment period. The optimum method of insuring that this monitoring is effective is still being evolved and requires repeated revision. Guidelines have been developed which require clinicians to check each patient on an individual basis and provide a simple method of regular review. If used systematically they should reduce the chance of missing as yet undescribed problems and allow these essentially healthy young adults to control and modify their own lifestyle.

526 ORAL

**THE SIOP WILMS' TUMOR (WT) TREATMENT (TRT) STRATEGY AND RESULTS: A REPORT OF THE SIOP WILMS' TUMOR TRIAL AND STUDY COMMITTEE**

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The advantage of a preoperative Trt, in non metastatic WT, in terms of surgical tumor rupture (< 5%) and chances for a favorable stage (stage I rate >50%), avoiding the need for rediotherapy (Rth) to cure, have been proven through the SIOP trials 1 and 5 and the optimal duration of a 4 weeks Actinomycin D + Vincristine (AV) preoperative chemotherapy (CT) has been established in SIOP 9. Lymphnodes invasion and unfavorable histology (UH), known to be of pronostic value and still determinable in preop-treated tumors, were considered in scheduling SIOP 6 and 9 postoperative Trt. Through randomized trials risk adapted treatment groups have been defined. Stage I: 1 post-op. and 2 maintenance AV courses are sufficient, 3-year disease free survival (DFS) = 85% and survival (S) = 95%. Stage II N0 non UH: no Rth needed, 3-drug CT using AV + Epirubicin (AVE), abdominal recurrence rate <4%, DFS = 84%, S = 92%. Stage IIN1 and III non UH: abdominal Rth and 3-drug AVE CT needed, DFS = 73%, S = 92% .Stage over I with UH: 4-drug CT using AVE + Ifosfamide DFS 49%.

527 ORAL

**MOPP/ABVD AND RADIOTHERAPY IN THE TREATMENT OF PEDIATRIC HODGKIN'S DISEASE (HD)**

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The aim of this paper is to assess: (1) results of combined approach (MOPP and/or ABVD and radiotherapy) in the treatment of HD in childhood and (2) factors proved to be prognostically significant. *Patients and methods:* During the period 1980–1984, 163 children aged 3 yrs–19 yrs (Me = 12 yrs) were treated for HD. There were 102 boys and 61 girls, in clinical stage I: 31 pts; II 88 pts; III 35 pts. and IV 9 pts. Histologically, the majority of children were diagnosed to have mixed cellularity (53) and nodular sclerosis (49). Mediastinal involvement was noticed in 58.5% pts and presence of systemic symptoms in 41.5%. All children received MOPP and/or ABVD and radiotherapy in "sandwich" regimen or after chemotherapy. Six cycles of chemotherapy where given in 106 pts, four in 45, and more than six cycles in 12 pts. Radiotherapy was applied on supervoltage units (TCT or Linear accelerator 10 MeV) using various techniques—the most often extended fields. *Results and conclusions:* During the follow up period from 1 yrs up to 15 yrs (Me = 8.1 yrs) overall survival rate is 96.5% and disease-free survival rate is 88.5%. In multivariate analysis, among 6 factors (age, sex, presence of systemic symptoms, bulky mediastinum, number of involved areas, hystologic subtype), advanced clinical stages and mediastinal involvement are deemed to be of the most importance for outcome. Based on these factors favourable and unfavourable subgroups are defined. Combined therapy (more or less intensive) should be designed according to subgroups. In pts with good prognosis (majority in our group) main goal is to decrease the risk of long-term treatment-related toxicity without

losing survival benefit. In poor prognosis group the aim is to obtain the highest remission rate at the lowest side effects of therapy.

528 ORAL

## RESULTS OF HM91 PROTOCOL OF THE FRENCH PEDIATRIC ONCOLOGY SOCIETY (SFOP) FOR CHILDREN WITH LARGE CELL ANAPLASIC LYMPHOMA

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*On behalf of the SFOP*

Between February 1991 and September 1994, 43 patients newly diagnosed with a large cell anaplastic lymphoma (LCAL) were enrolled in the HM91 study. After a cytoreductive phase COP course (Vincristine-Cyclophosphamide-Prednisone) were administered 2 induction courses (COPADM) with methotrexate, cyclophosphamide, adriamycine, vincristine and prednisone. Maintenance treatment consisted of 8 alternate courses of VEBBP (vinblastine, VPI6, bleomycine and prednisone) and séquence 1 (vincristine, methotrexate, cyclophosphamide, adriamycine and prednisone. Total length of the treatment was 7 months. There were 21 boys and 22 girls aged 3 to 16.5 years (median age 10 years). Immunohistochemistry data are available for 41 pts with positivity for Berh2 in 41/41, for EMA in 32/36. Cytogenetic analysis was performed in 19 cases and revealed a t (2; 5) in 14 cases. Lymphadenopathies were present in 42/43 patients, skin lesions in 34, visceral involvement in 22 and bone marrow involvement in 4. No patient had CNS involvement at diagnosis; 26 patients had B symptoms. Initial chemotherapy resulted in a complete remission in 39/43 patients. 2 patients failed to achieve CR and died, 2 patients achieved CR with the second line treatment and are alive disease free with 36 and 42 months follow up. 8 patients relapsed 7 to 12 months after diagnosis (3 of them died, 5 are alive with no evidence of disease), 33 patients are in first complete remission (including the 2 patients in CR only after the second line treatment) with a median follow-up of 20 months. Event free survival is 72% and crude survival 84% with a median follow up of 20 months.

529 ORAL

## COMBINED POSTOPERATIVE RADIO-CHEMOTHERAPY OF MALIGNANT BRAIN TUMOURS IN CHILDHOOD: RESULTS OF THE PILOT STUDY HIT '88/89

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*Objective:* Improvement of survival with postoperative additional chemotherapy before radiation therapy in medulloblastoma, ependymoma and glioma.

*Materials:* Chemotherapeutic agents: Procarbazine, Ifosfamide/VP16, MTX, Cis-Platinum, ARAC.

*Patients;* Eligible patients: n = 147, Follow-up: 6 years, mean 4 years.

*Results: Medulloblastoma (n = 94)*: 26/39 patients with residual tumour or meningeal dissemination responded to chemotherapy (CR/PR). In complete response the 5-year eventfree survival was 54% (±15%), in poor/non-responder 23% (± 9%) ($P = 0.02$). However, for all patients with residual tumour or meningeal spread the 5 year eventfree survival was 32% (± 7%), without residual tumour 58% (± 8%)($P = 0.004$).

*Ependymoma (n = 21)*: 5 year eventfree survival with residual tumour: 30%, without residual tumour: 53%

*Glioma (n = 22)*: 5 year eventfree survival WHO Gr III: 57%, WHO Gr IV: 0%

*Conclusions:* In medulloblastoma additional chemotherapy improved the survival for patients with residual disease who responded to chemotherapy. However, for the total group of patients with or without residual disease the survival was equal to postoperative radiation therapy only (i.e. SIOP II). Due to a low number of patients it is difficult to draw conclusions from our data on survival in ependymoma and glioma. At present, however, there is no firm evidence for an improvement of the therapeutic outcome.

530 ORAL

## CLINICAL ASPECTS AND SURGICAL TREATMENT OF POST-CHERNOBYL CHILDREN'S AND ADOLESCENT'S THYROID CANCER

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The cases of children's and adolescent's thyroid cancer treated in the Surgical Clinic of the Institute of Endocrinology and Metabolism during the period from 1980 to 1994 were reviewed retrospectively. 199 patients with thyroid cancer were operated on. The analysis has shown a substantial increase in thyroid cancer incidence among children in Ukraine after the Chernobyl accident (1990 to 1994) which differs by its clinical characteristics and a high level of aggression. Most of the thyroid cancers were well-differentiated papillary forms. The method to be used for treatment is total thyroidectomy with radical excision of cervical lymph collectors followed by ablation of thyroid remnants with $^{131}I$, if necessary, and life-long suppressive therapy with thyroid hormones.

531 ORAL

## RESULTS FOLLOWING RADIOTHERAPY AND/OR CHEMOTHERAPY OF ORBITAL RHABDOMYOSARCOMA

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The results of treatment of previously untreated patients younger than 17 years with primary localized rhabdomyosarcoma of the orbit were analyzed. In a multicenter study 46 patients with stage I–III orbital RMS were treated with chemotherapy (CT) (VACA: 1981–1985 or VAIA: 1986–1990)after initial tumour excision or biopsy. Patients with primary unresectable tumours were stratified after preoperative CT according to the result of second look surgery or degree of tumour volume reduction either to receive radiotherapy (RT) with 40 or 50 Gy using conventional fractionation, or 32 or 54.4 Gy (1.6 Gy/fraction BID). Sixteen patients were not irradiated, whereas 30 had RT. Forty patients were eligible for analysis. Local recurrence occurred in 0/1 stage I, 2/5 stage IIA, and 2/7 stage III patients without RT. The numbers in stage I to III after RT were: 1/1, 1/3 and 4/23, resp. Five year disease free survival (DFS) is 78% in the first study and 74% in the subsequent study. There is no significant difference in local control and DFS in patients treated with conventional or accelerated fractionation. The study demonstrates good local control with acceptable toxicity using either conventional or accelerated fractionation.

532 POSTER

## MALE FERTILITY FOLLOWING CHEMOTHERAPY IN CHILDHOOD

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205 patients treated by chemotherapy in the Institut Gustave-Roussy for childhood cancer between 1963 and 1990 have been assessed for fertility by serum basal FSH-LH level (200 pts), sperm count (22) and/or testicular biopsy (4) after the end of puberty and 1 to 21 years (m: 8 y) after the end of chemotherapy. They received various polychemotherapy including cyclophosphamide (129 pts), procarbazine (42 pts), CCNU (37 pts), D actinomycin (80 pts), doxorubicin (138 pts), methotrexate (69 pts), vincristine (182 pts). 127 pts (62%) had normal, and 78 abnormal results.

A multivariate analysis showed that pubertus status of the children at time of the treatment had no influence, but that cyclophosphamide, procarbazine and CCNU were significantly associated to abnormal results. 32 pts treated only with D-actinomycin, vincristine + adriamycine had normal results.

533 POSTER

## INFECTION WITH HEPATITIS B, C, AND HIV IN CHILDREN WITH CANCER IN TURKEY

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Turkey is considered to be an area of endemic hepatitis B virus (HBV) infection. Prevalence of HBV infection in the pediatric age group is 9.8%. Pediatric cancer patients are at an increased risk for hepatitis