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## High-dose Busulfan + Melphalan (BuMel) with autologous stem cell support for metastatic Ewing's tumor (ET). The experience of the French Society of Pediatric Oncology, EW91 study

O. Oberlin[1], K. Maincent[1], J. Michon[2], C. Bergeron[3], H. Rubie[4], D. Plantaz[5], H. Roche, E. Plouvier, O. Hartmann. [1] *Institut Gustave Roussy, Pediatrics, Villejuif, France;* [2] *Institut Curie, Pediatrics, Paris, France;* [3] *Centre Léon Bérard, Pediatrics, Lyon, France;* [4] *Hôpital Purpan, Pediatrics, Toulouse, France;* [5] *CHU, Pediatrics, Grenoble, France*

**Purpose:** Attempts to improve outcome of patients (pts) with metastatic ET have focused on chemotherapy dose intensification strategies.

**Patients and Methods:** Seventy-two metastatic ET pts were included in the study from 01.91 to 01.97. After induction chemotherapy (5 courses of cyclophosphamide/doxorubicin and 2 courses of VP16/Ifosfamide), pts in complete/good partial remission (CR/GPR) of their metastases received consolidation high dose chemotherapy by BuMel (busulfan 600 mg/m2, melphalan 140-180 mg/m2) followed by autologous stem cell support.

**Results:** Fifty five patients (76%) achieved CR/GPR at the metastatic sites following induction therapy and underwent BuMel. Twenty five patients remain disease-free with a follow-up of 13 to 111 months (median: 63 months).

For the whole group of 72 pts, 3-year EFS was 41% (29 - 52). Two pts died from interstitial pneumonitis after BuMel. Sixteen pts developed transient veino-occlusive disease. Fifteen pts had BM involvement at diagnosis. All died. There was no other identified risk factor.

**Conclusion:** As compared to the experience of conventional CT, high dose CT with BuMel is a feasible and promising treatment approach for patients with metastatic ET. For patients with isolated lung metastases, the present Euro-Ewing Intergroup study is assessing in a randomised trial the value of this strategy as compared to conventional chemotherapy and additional lung irradiation.

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## Temozolomide (TMZ) in the treatment of pediatric anaplastic astrocytomas (AA) and glioblastomas multiforme (GBM)

O. Geludkova[1], I. Tarassova[1], M. Belogourova[1], S. Gorbatykh[2], B. Kholodov[3], E. Koumirova[1]. [1] *Research Institute of Pediatric Hematology, Chemotherapy, Moscow, Russian Federation;* [2] *Morozovskaya Children's Clinical Hospital, Neuro-surgery, Moscow, Russian Federation;* [3] *Research-Practical Center for Pediatric Medical Care, Chemotherapy, Moscow, Russian Federation*

TMZ is a novel oral alkylating agent that crosses the blood-brain-barrier. Prospective clinical trials showed activity of this drug in adult newly diagnosed and recurrent AA and GBM. We performed a clinical trial with TMZ in 20 children: 6 patients - AA, 13 patients - GBM and 1 patient - malignant glioma. Eligible patients were given 10 cycles TMZ at a dose of 150/mg/m2/day (second line treatment) or 200/mg/m2/day (first line treatment) orally for 5 days every 28-day cycle. The efficacy of TMZ (CT/MRI) was evaluated every second cycle. 8 patients with newly diagnosed tumor (7 patients immediately after surgery and radiotherapy (RT) and 1 patient after surgery alone) and 12 patients with progressive disease (PD) after initial treatment (6 patients had prior surgery, RT, and chemotherapy and 6 - surgery and RT) were included in the present trial. The distribution of tumors by location: supratentorially (the majority of tumors) - 12 patients, brain stem - 5 patients, visual tuber - 2 patients, and cerebellum - 1 patient. 6-month PFS for the whole group was 58±12%; for newly diagnosed tumors - 56±20% with median follow-up 4,1 months; for PD - 68±15% with median follow-up 8,8 months. 15-month PFS for newly diagnosed tumors was 28±22%; for PD - 18±16%. 6-month OS for the whole group was 62±13% with median follow-up 11,7 months: for newly diagnosed tumors - 52±20% with median follow-up 4,8 months, and for PD - 67±16% with median follow-up 11,7 months. For 16 patients with GBM 6-month PFS was 60±13%, 12-month - 60±14%, median follow-up was 16 months. Response on TMZ (13 patients): complete response (CR) - 15% of patients, stable disease (SD) - 23%, progressive disease (PD) - 61%. Observed toxicity during 72 cycles: vomiting - in 6,94% of cycles, grade 4 hematological toxicity - 1,4%, infection complications - 1,4%. In the present clinical trial TMZ has shown activity in children with newly diagnosed and recurrent AA and GBM.

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## Neonatal neuroblastoma: our experience in 15 years

I. Astigarraga[1], A. Fdez-Teijeiro[1], A. Navajas[1], L. Martín[2], C. Castro[2], C. Centeno[2]. [1] *Hospital de Cruces, Pediatric Oncology Unit, Bilbao-Vizcaya, Spain;* [2] *Hospital de Cruces, Neonatal Unit, Bilbao-Vizcaya, Spain*

Neuroblastoma(NB)is the most common malignant tumour in neonates.Spontaneous differentiation,favourable biology and good prognosis are characteristics in infants.The optimal strategy for treatment has not yet been defined.The aim of the study is the review of the diagnosis,treatment and follow-up of infants with NB diagnosed in the first month of life in our hospital.From Jan/1986 to Jan/2001,7 neonates were diagnosed of NB(23% of the total NB).Prenatal diagnosis of left suprarenal cystic mass by routine maternal ultrasonography(US)at 34 weeks gestation was done in the last patient(p).They were delivered naturally without complications.The initial clinical presentation was abdominal mass palpated in the first 3 days of life in 5 p,associated with huge hepatomegaly in 1,tachypnea in 1 and paraplegia with sphincters disorder at 23 days in another.Diagnosis was casual in US in one p in the study of urinary tract infection.Each mass was confirmed by US in all p,CT in 5 and MRI in 2.The location was left adrenal in 4 cases.Intraspinal extension was found in 2 p.Bone marrow analysis and MIBG scan were performed.Surgical resection was complete in 4 and partial in 2 cases.One p underwent neurosurgical decompression.Diagnosis was based on histology and biological studies including N-myc amplification,DNA content and 1p chromosome deletion.No cases with unfavourable prognosis factors were found.According to INSS,the diagnosis was stage 1 in 4, 2A in 2 and 4-S in 1.One p with partially resected tumor,treated in 1994,received chemotherapy (CH)with complete remission but in other similar case regression without treatment was obtained.An infant with 4-S NB received minimal CH and liver radiotherapy.The outcome is favourable with an event free survival of 100%(follow-up 1,5-11,5 years).As late effects we found unilateral kidney atrophy attributed to surgery in 3 p and neurological sequellae and scoliosis in the child with spinal compression at diagnosis.

**Comments:**The increasing use of obstetric US has made possible prenatal diagnosis of NB.The most common clinical presentation of neonatal NB is localized abdominal mass.Surgical resection of the tumour, even partial, is curative in most cases and prognosis is excellent.Due to the possibility of spontaneous tumour regression,aggressive treatment with early surgical excision may not always be necessary.The follow-up of this particular NB population is important to define the optimal strategy to avoid late effects.

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## Partial nephrectomy in unilateral wilms - yes or no ?

M. España. *Hospital D. Estefania, Pediatric Surgery, Lisbon, Portugal*

**Purpose:** To demonstrate the feasability, safety and advantages of nephron sparing surgery in Unilateral Nephroblastomas.

**Methods:** Since 1972, after looking at the operative specimens following radical nephrectomies for unilateral tumours, it was evident that partial nephrectmy on (normal renal tissue) could have been safely performed, with the significant advantage of preserving normal kidney tissue Enucleation was not considered adequate surgery. All patients, had, pre-operatively, polychemotherapy, for an average of 4 weeks, what, by reducing tumour size, made feasable an otherwise impossible partial nephrectomy. Polychemotherapy was also used post-operatively, for 2 or 4 cycles according to histology. Diagnoses was always based on clinical, laboratory and imaging grounds, fine needle biopsy not being used.

**Results:** A total of 29 patients with unilateral Wilms tumours (around 20% of all patients treated) and of 20 patients with bilateral tumours were analized. In the unilateral group 27 patients are alive and well and 2 died of lung metastases (but with no local recurrence, at autopsy). In the bilateral group 16 patients are alive (one required later total nephrectomy) and 4 died, 2 with lung metastases and 2 of renal failure.

**Conclusions:** Nephron sparing surgery, is possible, safe (with no increased risks of local recurrence) and useful, and is advisable also for unilateral Nephroblastomas after 4 weeks of neo-adjuvant polychemotherapy