

## This issue's topics



### *Mixed response*

#### **Mixed response following ifosfamide treatment for advanced STS**

The European Organization for Research and Treatment of Cancer Soft-Tissue and Bone Sarcoma Group (EORTC STBSG) using ifosfamide to treat advanced soft-tissue sarcoma (STS) patients, in both the first- and second-line settings, report in this issue that the response rates differed according to the schedule used. They enrolled 182 patients (103 first-line, 79 second-line) and randomised them to treatment of 5 g/m<sup>2</sup> over 24 h every 3 weeks or 3 g/m<sup>2</sup> per day administered over 4 h on 3 consecutive days every 3 weeks. Second-line patients had received either doxorubicin 75 mg/m<sup>2</sup> or epirubicin 150 mg/m<sup>2</sup>. In evaluable first-line patients, they observed five Partial Responses (PR) (11%) in the 5 g group and 12 PR (28%) in the 3 g group. The corresponding rates for second-line patients were one Complete Response (CR)+1 PR (6%) and 1 CR + 2 PR (8%), respectively. The toxicity overall was acceptable despite some leucopenia. Thus, with the exception of the first-line patients in the 3 g group, the responses were disappointing and the authors state that this may be partly due to the large proportion of leiomyosarcomas in the study group, as these are known to be relatively resistant sarcomas. The 28% rate observed for the first-line patients in the 3 g group is comparable to single agent doxorubicin treatment if it is given at an optimal dose. However, this rate did not translate into either a progression-free or survival advantage, although this could be due to a lack of power as the study was not specifically designed to examine these parameters. The authors therefore suggest that novel agents should be examined to try to improve survival rates in these rare sarcomas.

#### **Nordic immigrant populations—attractive subject groups to study possible aetiological factors of cancers?**

This is the conclusion of a study by Hemminki and Li, who examined the risk of cancer amongst Nordic immigrants and their offspring in Sweden. The immigrants migrated to Sweden in their 20s and subsequently became parents whilst living in Sweden. The authors calculated standardised incidence rates (SIRs) and either 90 or 95% Confidence Intervals (CIs) for 26 cancer sites using the Swedish population as a reference group. They found that the cancers in the first-generation immigrants predominantly followed the rates of their country of origin. Three sites, breast, ovary and urinary bladder, showed some protection among the offspring where one parent was from the immigrant country. However, this was not reinforced when both parents were from this country- which is inconsistent with heritable effects. Lifestyle and habits—influencing cancer patterns—are likely to have already been set in the immigrants before they reached their 20s as the differences to the Swedes persisted in cancers that predominate in old age. The authors propose that such study groups are useful to examine the aetiological causes of poorly understood cancers such as testicular cancer.

#### **Phase 1 studies of the novel alkylcycline PNU-159548**

In this issue, de Jonge and colleagues examine the maximum tolerated dose (MTD), dose-limiting toxicity (DLT) and pharmacokinetics (PKs) of the novel cytotoxic agent, PNU-159548, and its metabolite, PNU-169884, in two parallel phase I studies. PNU-159548 is an agent that has been modified from idarubicin to have an increased lipophilicity and improved stability. It has a unique mechanism of action that combines DNA intercalation and alkylation of guanine in the DNA major groove. It has shown activity in several human tumour cell lines and xenografts. 69 patients with advanced solid tumours were given the drug intravenously either over 10 or 60 min and the dose was escalated from 1 to 16 mg/m<sup>2</sup>, with cycles repeated every 21 days. The MTD was 14 and 16 mg/m<sup>2</sup> in heavily and minimally/not pretreated patients, respectively, and therefore the recommended doses for phase II studies were 12 and 14 mg/m<sup>2</sup>, respectively. Toxicities included thrombocytopenia, hypersensitivity reactions and nausea and vomiting. There was a significant correlation between a decrease in the platelet count and both the area under the plasma concentration–time curve (AUC) and C<sub>max</sub> of PNU-159548. Phase II studies are now underway.

## Forthcoming papers

#### **Editorial Comment**

Calcium channel blockers, verapamil and cancer risk  
C. La Vecchia, C. Bosetti

#### **Current Perspective**

Changing concepts in Multiple Myeloma: from conventional chemotherapy to high-dose treatment  
P. Sonneveld, C.M. Segeren

#### **Review**

A systematic review of molecular and biological markers in tumours of the Ewing's sarcoma family  
R.D. Riley, S.A. Burchill, K.R. Abrams, D. Heney, A.J. Sutton, D.R. Jones, P.C. Lambert, B. Young, A.J. Wailoo, I.J. Lewis

## Original Papers

### Clinical

- Response to first-line chemotherapy and long-term survival in patients with multiple myeloma: results of the MM87 prospective randomised protocol  
A. Riccardi, O. Mora, C. Tinelli, C. Porta, M. Danova, S. Brugnatelli, D. Grasso, B. Tolca, R. Spanedda, A. De Paoli, L. barbarano, L. Cavanna, M. Giordano, C. Delfini, G. Nicolette, C. Bergonzi, E. Rinaldi, Piccinini
- Angiogenesis and invasive recurrence in ductal carcinoma *in situ* of the breast  
N.B. Teo, B.S. Shoker, C. Jarvis, *et al.*
- Shortened irradiation scheme, continuous infusion of 5-fluorouracil and fractionation of mitomycin C in locally advanced anal carcinomas. Results of a phase II study of the European Organization for Research and Treatment of Cancer. Radiotherapy and gastrointestinal cooperative groups  
J.F. Bosset, F. Roelofsen, D.A.L. Morgan, *et al.*
- Core biopsy versus FNAC for palpable breast cancers. Is image guidance necessary?  
T. Agarwal, B. Patel, P. Rajan, *et al.*
- Exercise reduces fatigue in chronic fatigued Hodgkin's disease survivors—results from a pilot study  
L.M. Oldervoll, S. Kaasa, H. Knobel, J.H. Loge
- Advanced soft-tissue sarcoma: a disease that is potentially curable for a subset of patients treated with chemotherapy  
J.-Y. Blay, M. van Glabbeke, J. Verweij, A.T. van Oosterom, A. Le Cesne, J.W. Oosterhuis, I. Judson, O.S. Nielsen
- Immunisation of metastatic cancer patients with MAGE-3 protein combined with adjuvant SBAS-2: a clinical report  
M. Marchand, C.J.A. Punt, S. Aamdal, *et al.*
- Phase II study of carboplatin in patients with advanced or recurrent endometrial carcinoma (a trial of the EORTC Gynaecological Cancer Group)  
F.H. van Wijk, C. Lhomme, G. Bolis, *et al.*
- Heparanase gene expression and its correlation with spontaneous apoptosis in hepatocytes of cirrhotic liver and carcinoma  
M. Ikeguchi, Y. Hirooka, N. Kaibara

### Paediatric

- Patterns of childhood cancer by ethnic group in Bradford, UK 1974–1997  
P.A. McKinney, R.G. Feltbower, R.C. Parslow, I.J. Lewis, A.W. Glaser, S.E. Kinsey

### Epidemiology and Cancer Prevention

- Verapamil is associated with an increased risk of cancer in the elderly  
A.B. Beiderbeck-Noll, M.C.J.M. Sturkenboom, P.D. van der Linden, *et al.*
- Geography of clinical cancer research publications from 1995 to 1999  
F. Grossi, O. Belvedere, R. Rosso

### Experimental

- Cellular determinants of oxaliplatin sensitivity in colon cancer cell lines  
S. Arnould, I. Hennebelle, P. Canal, *et al.*
- Retroviral transfer of MRP1 and gamma-glutamyl cysteine synthetase modulates cell sensitivity to L-buthionine-S, R-sulphoximine (BSO): new rationale for the use of BSO in cancer therapy  
G. Rappa, M.P. Gamsik, R.L. Mitina, *et al.*
- The Death Associated Protein (DAP) kinase homologue DLk/ZIP kinase induces p19ARF- and p53-independent apoptosis  
D. Kogel, C. Reimertz, H. Dussmann, P. Mech, K.H. Scheidtmann, J.H.M. Prehn