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^2 over 24 h every 3 weeks or 3 g/m^2 per day administered over 4 h on 3 consecutive days every 3 weeks. Second-line patients had received either doxorubicin 75 mg/m^2 or epirubicin 150 mg/m^2. 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 alkycycline 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^2, with cycles repeated every 21 days. The MTD was 14 and 16 mg/m^2 in heavily and minimally/not pretreated patients, respectively, and therefore the recommended doses for phase II studies were 12 and 14 mg/m^2, 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_{max} of PNU-159548. Phase II studies are now underway.

Forthcoming papers

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