

This issue's topics

Current perspective of the new 'magic bullet' STI 571

With advances in the understanding of molecular and biological pathways, new selective and targeted drugs are being designed and tested. One such agent is STI 571. This drug is a highly selective, synthetic inhibitor of the protein tyrosine kinase family, a group of enzymes involved in the regulation of cell proliferation, growth and function. In this issue, Verweij and colleagues discuss current studies of its use in chronic myeloid leukaemia (CML), acute lymphoblastic leukaemia (ALL) and gastrointestinal stromal tumours (GIST) patients. These studies show the drug to have activity with generally limited side-effects, although as Verweij and colleagues point out data on long-term effects are lacking and thus cumulative toxicity can not be assessed. The Food and Drug Administration (FDA) approved on 9 May this year its use in patients with CML and the authors, although urging caution in its widespread use until further experience has been acquired, state that "in their opinion, STI 571 is one of the most important agents recently developed".

Use of a mistletoe lectin as an immunoadjuvant in IL-2-based therapy

Interleukin-2 (IL-2) therapy has been shown to be effective in a range of animal and human cancer models. However, such therapy is associated with a life-threatening side-effect known as 'capillary leak syndrome'. The syndrome is characterised by rapid fluid accumulation in the tissue spaces and severe hypotension and is thought to result from an overproduction of nitric oxide (NO), as it can be ameliorated by the use of NOS inhibitors. Plant lectins, derived from mistletoe, have recently been proposed to have antitumour activities despite, at present, no clear clinical validation of such claims. Indeed, data from animal models have provided evidence of both detrimental and beneficial effects of these compounds. In this issue, Timoshenko and colleagues have examined whether the addition of a galactoside-specific lectin from *Viscum album* L., VAA, at non-toxic and immunostimulatory concentrations, is able to increase the anti-tumour and anti-metastatic properties of IL-2, without any increase in adverse side-effects. Their results suggested that the addition of VAA to IL-2 to treat C3L5 mammary adenocarcinomas in C3H/HeJ mice did not further decrease tumour growth and the number of metastases compared with IL-2 treatment alone. Moreover, VAA treatment alone resulted in an increase in these parameters compared with controls confirming that the translation of these compounds to the clinic should be viewed with caution.

A structural homologue of mitoxantrone with cytotoxic activity in cisplatin-resistant ovarian and osteogenic sarcoma cell lines

Imidazoacridinone C1311, a structural homologue of mitoxantrone, has potent activity in animal models and murine and human experimental models for colorectal cancer *in vitro* and is shortly to enter testing in clinical trials. In this issue, Zaffaroni and colleagues study the activity of this compound in two ovarian cancer cell lines, A2780 and OAW42, and one osteogenic sarcoma cell, U2-OS. They looked at the growth of these cell lines and their experimentally induced cisplatin-resistant sublines following a 1 h incubation with the drug. They showed the drug had cytotoxic activity against these cells and also induced the accumulation of cells in the G2/M phase. Apoptosis was also induced in a small percentage of the U2-OS cell lines. The authors state that "their findings should stimulate further studies into the preferential targets of C1311 in human tumours".

Forthcoming papers

Current Perspective

Studies on supportive care in oral mucositis: random or randomised
C.C.D. van der Rijt, L. van Zuijlen

Meeting Highlight

EORTC Laboratory Research Division Workshop on the Role of *in vivo* preclinical models in the development of contemporary cancer Therapeutics
H. Newell

Review

What have we learnt from previous phase II trials to help in the management of childhood brain tumours?
P. Chastagner, E. Bouffet, J. Grill, M.D. Kalifa

Original Papers

Clinical

Decrease of duration and symptoms in chemotherapy-induced oral mucositis by topical GM-CSF: results of a prospective randomized trial

M. Hejna, W. Köstler, M. Raderer, *et al.*

Local application of granulocyte-macrophage colony stimulating factor (GM-CSF) for the treatment of oral mucositis

G.M. Sprinzl, O. Galvan, A. de Vries, *et al.*

Double-blind, placebo-controlled cross-over study of oral pilocarpine for the prevention of chemotherapy-induced oral mucositis in adult patients with cancer

A. Awidi, U. Homsy, K. Rasul, *et al.*

Phase II study of pegylated liposomal doxorubicin (Caelyx) as induction chemotherapy for patients with squamous cell cancer of the head and neck

K.J. Harrington, C. Lewanski, A.D. Northcote, *et al.*

A hypothesis about tumour development and the clinical features of hereditary breast cancers

H. Olsson

Neoadjuvant chemotherapy for osteosarcoma of the extremity: long-term results of the Rizzoli's 4th protocol

G. Bacci, A. Briccoli, S. Ferrari, *et al.*

Ovarian carcinoma cells in serous effusions show altered MMP-2 and TIMP-2 mRNA levels

B. Davidson, R. Reich, A. Berner, *et al.*

Pre-operative chemoradiation with raltitrexed (Tomudex) for T2/N+ and T3/N+ rectal cancers: a phase I study

V. Valentini, G.B. Doglietto, A.G. Morganti, *et al.*

Paediatric

Evaluation of an oral care protocol intervention in the prevention of chemotherapy-induced oral mucositis in paediatric cancer patients

K.K.F. Cheng, A. Molassiotis, A.M. Chang, W.C. Wai, S.S. Cheung

Angiogenic profile of childhood primitive neuroectodermal brain tumours/medulloblastomas

H. Huber, A. Eggert, A.J. Janss, *et al.*

Paediatric Update

Second tumours

A. Meadows

Commentary

M. Hawkins

Epidemiology and Cancer Prevention

Large regional differences in the frequency of *BRCA1/BRCA2* mutations in 517 Dutch breast and/or ovarian cancer families

L.C. Verhoog, A.M.W. van den Ouweland, E. Berns, *et al.*

Dietary fibre and the risk of colorectal cancer

F. Levi, C. Pasche, F. Lucchini, C. La Vecchia

Experimental

Tumour-associated antigen (TAA)-specific cytotoxic T cell (CTL) response *in vitro* and in a mouse model, induced by TAA-plasmids delivered by influenza virosomes

P. Correale, M.G. Cusi, M. Sabatino, *et al.*

Chemopreventive allylthiopyridazine derivatives induce apoptosis in SK-Hep-1 hepatocarcinoma cells through a caspase-3-dependent mechanism

M.-Y. Jung, S.-K. Kwon, A. Moon

Expression of vascular endothelial growth factor in mouse tumours subjected to photodynamic therapy

M. Uehara, T. Inokuchi, K. Sano, W. ZuoLin

An evolutionary-game model of tumour-cell interactions: possible relevance to gene therapy

L.A. Bach, S.M. Bentzen, J. Alsner, *et al.*

Rapamycin increases the cellular concentration of the BCL-2 protein and exerts an anti-apoptotic effect

A. Calastretti, F. Rancati, M.C. Ceriani, *et al.*

A novel gene on human chromosome 2p24 is differentially expressed between androgen-dependent and androgen-independent prostate cancer cells

G.T.G. Chang, M. Steenbeek, E. Schippers, *et al.*

Letter

Something old, something new, something hot, something blue

R.D. Macmillan, R.S. Rampaul, R.D. Blamey