

## This issue's topics



### Translating response rates into survival

#### Translating response rates into survival benefits

It is intuitively thought that a good response to therapy should be a prerequisite to subsequent survival. However, this relationship has often been difficult to establish. In this issue Riccardi and colleagues report on the response of 258 evaluable multiple myeloma (MM) patients treated between January 1987 and March 1990 on protocol MM87. After a median follow-up of 134 months, the median survival was 40 (6–162 months) in the whole group and median survival did not differ significantly between those experiencing complete response (CR), partial response (PR) or stable disease (SD) whilst receiving first induction chemotherapy. Only patients who progressed had a significantly shorter median survival 13.6 (6–135 months) and the causes of death in this patient group were also more frequently related to MM than in the other response groups. The authors suggest that the questionable correlations observed between CRs and PRs and survival in previous MM studies and meta-analyses could be explained (at least partly) by the inclusion of the SD group in the non-responders. They point out that this could be a large proportion of the patient group (in their study 36.8%). They also note that response is subjectively measured in contrast to survival—which is an objective measure—making any translation from one to the other more difficult. Other factors such as tumour grade and performance status are also likely to play their part in this translation. In an accompanying Current Perspective, Sonneveld and Segeren outline the changing concepts in the treatment of MM. The state that high dose therapy has become the standard treatment for those aged 65–70 years whereas conventional chemotherapy is still considered the treatment of choice in elderly, more fragile populations. They propose that “the role of conventional chemotherapy will be further replaced by tumour debulking using high dose therapy combined with new drugs that are specific for malignant myeloma cells”.

#### Loss of heparanase in hepatocellular carcinomas is associated with a poor prognosis

Heparanase is an endoglycosidase that is involved in cell signalling pathways. Conflicting reports have been published with regard to its role in malignancy. Some studies have suggested that its overexpression is correlated with the metastatic potential of cells and is associated with a poor prognosis whilst others have suggested it may downregulate cell growth signals in tumours. Ikeguchi and colleagues using a real-time quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) have examined the expression of *heparanase* in 48 liver samples from patients with hepatocellular carcinoma (HCC). This expression was then compared with that in the corresponding non-cancerous tissues. The results were presented as the mean expression ratios of *heparanase* and the housekeeping gene glyceraldehyde-3-phosphate dehydrogenase (*GAPDH*). The expression in the non-cancerous tissues was significantly higher than that in the cancerous tissues. There was also a lower expression in the non-cancerous tissues that had more severe liver fibrosis. A correlation between the expression ratios and the apoptotic indices was also observed. 5 year disease-free survival was significantly better in those patients with a higher heparanase expression in their tumour tissues. The authors suggest that their results “indicate that heparanase expression may be lost during the malignant transformation of hepatocytes”. Their data contrasts with some previous studies and the authors propose that this may be due to differences in the methodology used.

#### Calcium channel blockers and their association with cancer in the elderly

Data from the literature has suggested that the long-term use of calcium channel blockers (CCB), given for the treatment of hypertension and symptomatic coronary artery disease, is associated with cancer, possibly through the inhibition of apoptosis. However, reports are conflicting and such associations have been proposed to be due to selection bias or due to misclassification in exposure. In this issue Beiderbeck-Noll and colleagues have investigated this further in 3204 participants, aged 71 years and older, from the Rotterdam study, a prospective population-based cohort study. They used three different models; the first similar to that previously reported in the literature, the second taking into account all the risk factors that were univariately associated with cancer in the Rotterdam study and the third including exposure to CCB as time-varying covariates with adjustment for potential confounders. They found that verapamil was significantly associated with cancer in all three models and stated that “it is too early to conclude that CCB are not associated with cancer” and “more detailed studies with larger numbers are required to shed more light on this issue”. In an accompanying editorial, La Vecchia and Bosetti agree that the current state of knowledge on CCB and cancer risk and the drawbacks of observational epidemiological studies makes it difficult to draw any firm conclusions particularly given that the different biological mechanisms of CCB remain largely undefined.

## Forthcoming papers

### Editorial Comment

Editorial  
R. Leake

### Current Perspective

What's new in the treatment of advanced prostate cancer?  
C. Sternberg

### Review

Insights into the molecular biology of germ cell tumours and what it has taught us about chemo-sensitivity  
R.H. Jones, P. Vasey

### Original papers

#### Clinical

Osteosarcoma over the age of forty  
R.J. Grimer, S.R. Cannon, A.M. Taminiau *et al.*  
Use of Serum 5-S-CD and S-100B protein levels to monitor the clinical course of malignant melanoma  
T. Banfalvi, K. Gilde, M. Gergye *et al.*  
Ultrasound-guided fine needle aspiration cytology of axillary lymph nodes in breast cancer patients. A preoperative staging procedure  
V. Kuenen-Boumeester, M. Menke-Pluymers, Y. de Kanter *et al.*  
Dynamic lymphoscintigraphy and image fusion of SPECT and pelvic CT-scans allows mapping of aberrant pelvic sentinel lymph nodes in malignant melanoma  
L. Kretschmer, G. Altenvoerde, J. Meller *et al.*  
Elevated levels of circulating platelet microparticles, VEGF, IL-6 and RANTES in patients with gastric cancer: possible role of a metastasis predictor  
H.K. Kim, K.S. Song, Y.S. Park *et al.*  
Favourable pathological stage after neoadjuvant radiochemotherapy in patients with initially irresectable rectal cancer correlates with a favourable prognosis  
O. Reerink, R.C.J. Verschueren, B.G. Szabo *et al.*  
Altered clearance of unbound paclitaxel in elderly patients with metastatic breast cancer  
C.H. Smorenburg, J. Verweij, M. Bontenbal, K. Mross, D.M. van Zomeren, C. Seynaeve, A. Sparreboom

#### Paediatric

No excess fatigue in young adult survivors of childhood cancer  
N.E. Langeveld, M.A. Grootenhuis, P.A. Voute, R.J. de Haan, C. van den Bos

### Epidemiology and Cancer Prevention

Long-term survival of women with breast cancer in New South Wales  
R. Taylor, P. Davis, J. Boyages  
Skin cancer and non-Hodgkin's lymphoma as second malignancies: markers of impaired immune function?  
K. Hemminki, Y. Jiang, G. Steineck

### Experimental

Chemopreventive agents induce senescence-like phenotype in rat mammary tumours  
K.T. Christov, A.L. Shilkaitis, E.S. Kim, V.E. Steele, R.A. Lubet  
Defective mismatch-repair in patients with multiple primary tumours including colorectal cancer  
K. Ericson, B. Halvarsson, J. Nagel *et al.*  
Dihydropyrimidine dehydrogenase circadian rhythm: comparison between enzyme activity and gene expression  
B. Porsin, J.-L. Formento, E. Filipinski *et al.*  
*In vivo* expression of the whole HOX gene network in human breast cancer  
M. Cantile, G. Pettinato, A. Procino *et al.*

### Letter

Second primary cancers in laryngeal cancer patients  
F. Levi, L. Randimbison, V.-C. Te, C. La Vecchia