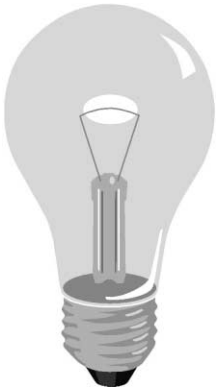
This issue's topics



Alternatives to BSA dosing—any bright ideas?
In a Current Perspective published in this issue, Sparreboom and colleagues review the evidence for using BSA dosing of drugs. They propose that "the use of BSA should be restricted to those agents for a which a relationship between BSA and clearance or with other pharmacokinetics (PK) parameters has been proven," such as paclitaxel or liposomal doxorubicin. The importance of accurate dosing is emphasised by the fact that most drugs have a narrow therapeutic window where small changes in dose can result in unacceptable toxicity or poor antitumour effects. The authors propose that it is inappropriate to try to identify a single variable that can be applied to all anticancer agents and that knowledge of the PK of each agent is essential in order to choose a suitable parameter to reduce interpatient variability. Indeed, this strategy has already been applied for carboplatin, where Calvert found that a formula for creatinine clearance accurately described both the drug's PK and also predicted dose-limiting toxicity. However, in the absence of such an alternative for other drugs, such as CPT-11, cisplatin and oral topotecan, where the data from literature suggest that BSA is an inadequate measure to employ, the authors of the perspective suggest using flat-fixed doses and adjusting the dose for subsequent cycles based on the toxicity observed in the individual patient. Other alternative methods are also discussed, such as enzyme phenotyping, i.e. differences in CYP3A4 activity have been used for docetaxel dosing. Nevertheless, given the woeful inadequacy of BSA dosing for many anticancer agents, it is likely that more bright ideas will need to be put forward to ensure that these agents are used in appropriates doses.

Chromosomal alterations and MSI are associated with different tumorigenic pathways in sporadic endometrial cancers?
This is the hypothesis suggested by data from a study by Muresu and colleagues. Since endometrial tumorigenesis is still poorly understood, the authors used fluorescence *in situ* hybridisation (FISH), microsatellite analyses and immunohistochemistry (IHC) to study chromosomal changes and microsatellite instability (MSI) in 86 sporadic endometrial cancers (ECs) from a Sardinian population and to compare the data with clinicopathological parameters. They found 24/74 (32%) of the tumours exhibited MSI and 38/86 (44%) displayed aneuploidy. However, the MSI+ cases were more commonly associated with late-stage (15/24; 63%) and poorly differentiated cancers, whereas those cases with aneuploidy were more frequently early stage patients (23/38; 61%). IHC staining suggested that inactivation of the *MLH1* mismatch repair gene may be associated with the development of the MSI+ ECs. However, neither MSI nor aneuploidy seemed to be of prognostic value. The authors conclude that "specific alterations in chromosome number and MSI seem to be associated with different tumorigenic pathways," but emphasise that their data should be confirmed in a larger group of sporadic EC patients.

Effective treatment of mantle cell lymphomas with reduced dose 2-CdA and mitoxantrone
Purine analogues, such as fludarabine and cladribine (2-CdA), have some activity as single-agent treatments for mantle cell lymphomas (MCL), but little impact on survival. Therefore, new treatments are needed to improve the prospects of patients with MCL. Due to the minimal toxicity associated with their use, it has been proposed that these analogues should be combined with other agents with activity in the treatment of these lymphomas. One such drug is the DNA-damaging agent mitoxantrone. In this issue, Rummel and colleagues have examined the efficacy and toxicity of reduced dose 2-CdA (5 mg/m^2/day as a 2 h infusion given over 3 days) and mitoxantrone (8 mg/m^2, days 1 and 2/12 mg/m^2, day 1, untreated/relapsed) in 62 patients with low grade lymphomas (including 18 with MCL). The overall response rate was 90% (95% Confidence Interval (CI) 80–96%) and this was 100% for those with MCL. Toxicity was generally mild with myelosuppression the most common side-effect. The authors conclude that the regimen is highly active, particularly for those with MCL.

Forthcoming papers

Editorial Comment
Tumour viruses: could they be an achilles heel of cancer?
P. Farrell

Position Paper
Measuring the clinical response. What does it mean?
P. Therasse

Reviews
Health related quality of life assessment methodology and reported outcomes in primary brain cancer randomised controlled trials
F. Efficace, A. Bottomley
Current status and future prospects for the treatment of chemotherapy-induced peripheral neurotoxicity
G. Cavaletti, C. Zanna

Original Papers
Clinical
p107 variations correlate with carcinogenesis and prognosis in colorectal tumours
F. Wu, J.Q. Li, H. Mike, *et al.*

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