Chairperson's Introduction

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Novel, molecular targeted therapies are starting to fulfil their promise, changing how patients with cancer are treated and altering the natural history of many types of cancer. It was, perhaps, over-optimistic to expect they could do this alone, and many such agents are best used in combination with chemotherapy and/or radiotherapy. Likewise, we were maybe naive if we imagined that major therapeutic benefits could be gained at no cost in terms of toxicity.

Cytotoxic chemotherapy is usually associated with predictable anti-proliferative toxicities, in particular, myelosuppression; specific classes of cytotoxics have other side-effects, but acute neutropenia remains their hallmark, reflecting their "target". The potential value, and challenge, of using the newer molecularly targeted agents lies in the novelty and diversity of their targets, and this is reflected in the breadth of the toxicities with which they are associated. Pre-clinical data, and emerging experience from clinical trials, indicate that optimal use of novel targeted agents may require their administration to disease progression or beyond. The time-course of the toxicities caused by novel molecular targeted agents is, therefore, potentially chronic rather than acute. Chronic toxicity is a particular issue in the adjuvant setting for patients who may be cured or have a life expectancy of several years. Another characteristic of novel targeted therapies is that many are oral and taken by the patient at home; this brings new challenges in terms of compliance, greater potential for drug–drug interactions and the involvement of community physicians.

Dr. Carles and colleagues address the issue of renal toxicity, which is a particular issue for inhibitors of angiogenesis targeting the vascular endothelial growth factor (VEGF) pathway. To date, most experience has been gained with bevacizumab but small molecule kinase inhibitors of this pathway are already in the clinic and others are in development. Diarrhoea is associated with monoclonal antibodies targeting the epidermal growth factor receptor, but Dr. Perlemuter and colleagues also describe gastro-intestinal and hepatic toxicities seen with other targeted therapies. Dr. Tejpar and colleagues describe the cutaneous toxicities seen increasingly with the widespread use of epidermal growth factor receptor (EGFR) inhibitors and other targeted therapies. This is especially important as patients on EGFR inhibitors who develop skin toxicity appear to have better outcomes so it is important we develop strategies to avoid treatment interruption or discontinuation. Finally, Dr. Siu guides us through cardiovascular toxicities, in particular, hypertension related to the use of agents targeting the VEGF pathway. Many patients are either already on anti-hypertensive therapy before starting, or found to be hypertensive when screened for, anti-VEGF therapy with others subsequently hypertensive; the management of hypertension will, therefore, be increasingly relevant for oncologists.

That we are facing these new challenges in identifying and treating a new spectrum of toxicities is to be welcomed. A generation ago, cisplatin revolutionised the treatment of testicular cancer but at a considerable cost in terms of toxicity. The real challenge in using cisplatin, and one that was successfully overcome, was how to make treatment tolerable. Likewise, the treatment of potentially life-theatening myelosuppression has been central to the effective use of other cytotoxics. Now, our patients are being exposed to new molecular targeted drugs with an entirely different spectrum of toxicities affecting the kidney, cardiovascular system, skin and gastro-intestinal tract. Therefore, not only will patients gain optimal benefit from these novel targeted therapies if we are able to prevent toxicities where possible, but also if we are able to recognise and treat those toxicities if and when they arise.

Conflict of interest statement

None declared.