84 INVITED

Response assessment in new drug trials

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The conventional method for assessing response in solid tumours is serial measurement on anatomical imaging, usually CT or MRI. This approach has disadvantages: the size of the tumour is likely to decrease later than the response at a cellular level and assessment does not take account of the fact that the whole mass may not be viable tumour. New imaging techniques, commonly grouped under the term functional imaging, are increasingly addressing these problems by probing tissue properties rather than anatomical structure.
There are two main technological approaches to functional imaging, one based on extensions of magnetic resonance imaging and the other based on advances in nuclear medicine.
Advanced magnetic resonance imaging methods have the advantage that they can be readily coupled to conventional MR imaging investigations with little additional equipment required. There are several complimentary techniques and they are commonly being used together in a multimodality approach. Magnetic resonance spectroscopy provides a quantitative profile of metabolites and lipids. Clinical studies have already identified markers of tumour response, in particular total choline. Animal studies have shown polyunsaturated fatty acids to be a very early marker of apoptosis. Diffusion weighted imaging provides a useful marker of cellularity and correlates with cell death. Studies have shown diffusion weighted imaging can be an early maker of tumour response. Perfusion may be studied by a number of techniques, the most common being dynamic contrast enhanced MRI. These techniques have become of particular relevance with the interest in anti-vascular and anti-angiogenic treatments. Perfusion imaging gives a direct measure of drug action and studies have shown alterations when these agents are effective. Dynamic nuclear polarization is an emerging method for producing molecular tracers of metabolism which can be detected by magnetic resonance spectroscopy. Pyruvate is a promising tracer for tumour response and is entering clinical trials. Molecular imaging may be undertaken by the addition of gadolinium atoms to molecules designed to attach to specific targets allows them to be visualized on conventional MRI. Molecular imaging is of particular relevance to novel targeted agents and is likely to become of increasing interest in the future. Nuclear medicine techniques are well established and the advent of single photon emission computerized tomography (SPECT) and positron emission tomography (PET) has allowed multi-slice images to be produced. Combining these techniques with CT and MRI allows the functional images to be registered accurately with high quality anatomical imaging revolutionizing their use in cancer. 19F-deoxyglucose PET has become well established as a marker of active tumour. However, more specific markers are becoming available and the exquisite sensitivity of PET currently makes this the targeted molecular imaging modality of choice. PET tracers can also be made from drugs making in vivo pharmacokinetics available. Combining MRI and PET in a single scanner allows high quality structural and multimodality functional imaging and promises to revolutionize response assessment of new drugs.

86 INVITED

Ethical aspects of early phase clinical trials in children

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The objective of a phase I trial in paediatrics is to determine the recommended dose of a new treatment in children while evaluating its toxicity. These trials are proposed when no effective curative treatment is available. The probability of a benefit in terms of disease control is certainly very low, but greater than zero.
We will present the work conducted by a collaborative group of parents, healthcare personnel and a philosopher which concludes that phase I therapeutic trials can be considered to be an ethically acceptable proposal provided the criteria and risks of inclusion in such a trial are clearly defined. We will discuss the main elements of this inclusion process and try to provide guidelines for healthcare personnel and parents. Furthermore, we will present specific preliminary information from a current prospective study about information and consent process for early phase clinical trials. The need for information provided gently but honestly, the importance of a sufficient time to think about the proposed trial, a two-sided dialogue and partnership between the various actors, and the priority given to the child's best interests, constitute the decisive elements to guide the proposed inclusion in an early phase trial. These conditions help to ensure that a decision is reached which appears to be morally founded for all parties, while allowing the child to remain alive up until the end, i.e. a human being capable of relating. This decision allows parents and healthcare personnel to retain a good self-image; if the child dies, it is by keeping their self-esteem that parents can live with their bereavement and healthcare personnel can reinvest in other patients.

Advocacy Session (Mon, 21 Sep, 16:15−17:45)
Access to clinical trials

87 INVITED

Clinical trials registries and databases

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In 2005 a World Health Assembly resolution called for the establishment of "a platform linking a network of international clinical trial registers to ensure a single point of access and the unambiguous identification of trials". This resulted in the establishment of WHO's International Clinical Trials Registry Platform (ICTRP), the core principle of which is that the registration of clinical trials in a publicly accessible registry is a scientific, ethical and moral responsibility. In 2007 the ICTRP published its online Clinical Trials Search Portal which allows users to search the data sets provided by registries that meet WHO's standards for quality control and content. Registries that currently meet these criteria are based in Australia, China, Germany, India, Iran, the Netherlands, Sri Lanka, the UK and USA. On 3rd July 2009 the portal contained records relating to 86978 trials, of which 15742 were identifiable as being trials in cancer. A more detailed search reveals that there has been a significant increase in the number of registered trials recruiting participants with cancer over a 5 year period with 703 being registered in 2004 compared with 2780 registered in 2008. Although the need to register trials in a publicly accessible database has become accepted by many there are still barriers to achieving full compliance, particularly in developing countries. We need to consider how we may better use the information these registries contain, how we might make the data they contain more accessible, and the opportunities they give us to build better systems for clinical trials oversight.

90 INVITED

The patient perspective

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The patient advocacy view of clinical trials goes beyond the crucially important aspects of information about trials and access to them which are commonly presented as primary patient interests. The presenter has been treated on a trial, helped and advised other patients considering or entering trials, taken part in the development and review of new studies, is involved in funding review, and has used trial evidence to support advocacy cases in regulatory review. He has also worked with strategic management and has developed a deep understanding of how the evidence from trials informs (or sometimes fails to inform) treatment and service development, through guidelines and health technology appraisals. He draws on his own wide-ranging experience to present a fresh and challenging view of clinical research and what can be developed to help clinical trials deliver greater benefit to patients.

Tuesday, 22 September 2009

Scientific Symposium (Tue, 22 Sep, 09:00−11:00)
Researching complex clinical issues in cancer care

91 INVITED

Nursing-sensitive outcomes: what are they and should we be measuring them?

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Background: Nurses, like all health professionals, are being asked to assume greater accountability for the improvement of health care system costs and outcomes. Accountability means answering for one's actions and the consequences of those actions. Accountability is one of the hallmarks of the professions. Patient outcome is a measure of the consequences of health care actions. Nursing sensitive patient outcomes are those that are