

Early Clinical Trials Forum - Novel Methodologies in Early Clinical Trials.

Peter Ho (Glaxo SmithKline, USA) highlighted how biomarker discovery and development in industry now starts in Phase 0, anticancer compounds generated in industry are now expected to show evidence of antitumour activity as early as Phase 1 in order to progress through to further development and combination therapies are being developed in greater number and earlier as new agents and targets enter the clinic at greater pace.

Hilary Calvert (Northern Institute of Cancer Research, Newcastle) explained the different Phase 1 trial designs; traditional, pharmacokinetically-guided (Collins), continual reassessment (O'Quigley), accelerated Phase 1 design (Simon), and the relative advantages and disadvantages of each (*Eur. J. Cancer* 44 (1) 19-24).

Janet Dancey (National Cancer Institute (NCI), USA) explained the NCI Clinical Trials Evaluation Programme's approach to Intellectual Property and regulatory issues in the process of combining investigational agents from different sponsors for use in clinical trials (<http://ctep.cancer.gov/industry>). The importance of the consideration of scientific issues such as appropriate target, agent and patient selection in the set up of novel combination therapies were also highlighted.

Peter Johnson (Cancer Research UK & Southampton General Hospital Southampton) discussed novel approaches in antibody therapy. He highlighted antibodies used as curative agents in Non-Hodgkins Lymphoma (Rituximab). Additionally, the rationale for antibody combinations emphasising the potential synergy between immunostimulatory antibodies which may result in stronger and/or more specific immune responses was discussed.

John Griffiths (Cambridge Research Institute, Cancer Research UK) described the need for the development of better and more quantitative imaging biomarkers by which therapeutic efficacy can be assessed and which may eventually be used as surrogate endpoints. The importance of the validation of novel imaging methods in animal models and the clinical trials training needs of imaging professionals involved in clinical trials were also highlighted.

Afternoon workshops

Immunotherapeutics workshop

This session discussed the use of immunotherapy and novel immunotherapeutic techniques.

Issues highlighted in the session;

- The importance of establishing the correct viral dose, delivery route and treatment regimen when using virotherapy in combination with radiotherapy or chemotherapy treatments.
- Radiolabelled antibody therapy enables haematological tumours to be specifically targeted with radiotherapy without the side effects usually seen in patients treated with standard radiotherapy.
- Immunostimulatory monoclonal antibodies (mAbs) can be used to boost the body's ability to reject cancer cells.
- There is a need to develop biomarkers to enable differentiation between tumour expansion by tumour cell division and tumour expansion by immune cell infiltration.
- Intramuscular or intratumour delivery of DNA encoding anti-cancer vaccines, including the delivery of genes encoding full antibody molecules, allows longer lasting more stable protein expression compared with conventional systemic recombinant protein or mAb delivery therapies.

Translational radiotherapy and innovations in radiotherapy workshop

This session discussed the use of intensity modulated radiotherapy and the use of radiotherapy in conjunction with chemotherapeutic or signal transduction targeted agents.

Issues highlighted in the session;

- The enormous potential for further benefits from combining new molecularly targeted agents with radiation.
- The shortage of research staff to support radiotherapy trial activity in the UK especially in technically challenging trials such as those involving intensity modulated radiotherapy.
- Investment in research assessing the potential of radiotherapeutic toxicity (grade 1-3), as opposed to solely high grade toxicity (grade 3), as a surrogate for late effects would facilitate and expedite the development of innovative radiotherapy trials.
- The importance of having access to a clinical trial unit with experienced staff available to support setting up innovative trials and facilitate the collection of high quality (i.e. complete) data.
- The importance of pre-clinical research to provide a rationale for innovative drug radiation combinations and scheduling.
- Phase I single agent activity does not necessarily predict for a positive interaction with radiation and agents lacking single agent activity may show efficacy in combination with radiotherapy.
- The need to educate pharmaceutical companies to understand the strategic importance of early drug radiation interaction work.
- The workshop finished by highlighting the importance of translational research in early phase trials and the need to consider translational research early in trial development. The importance of funding radiation biomarker development was stressed.

A more detailed description of the Translational Radiotherapy workshop can be found at <http://www.ncri.org.uk/ectf/includes/RadiotherapyWorkshopExtendedSummary.pdf>.

Cancer Research UK Phase 1/2 committee and Drug Development Office Trials workshop

Cancer Research UK's Drug Development Office (DDO) held a workshop on 'Trial Design, Findings and Exploring Novel Methods of Measuring Endpoints'. The workshop was chaired by Professor Hilary Calvert and included a brief overview of DDO activities and initiatives and a number of presentations and discussions from clinical investigators on several recently closed or almost completed DDO trials.

Trials highlighted in the session;

- CR-UK trials of Antibody-Directed Enzyme Prodrug Therapy (ADEPT): methods of response assessment, results & proposed Phase II - Richard Begent, UCL
- The CR-UK trial of I131-CHT25 radioimmunotherapy: CHT25 is effective in relapsed Hodgkin's and T-cell lymphomas, results & future potential – Dr Gairin Dancey, Royal Free Hospital
- Combining antivasular therapy & radioimmunotherapy: results of the CR-UK Phase I trial of I131-A5B7 combined with Combretastatin A4P – Dr Tim Meyer, Royal Free Hospital
- PK-directed drug development: the CR-UK Phase I trial of CB1954 combined with EP0152R (NQ02) – Dr Mark Middleton, Oxford Radcliffe Hospital
- PD-directed drug development: the Phase I & II trials of Patrin 2 (Lomeguatrib) – Dr Mark Middleton, Oxford Radcliffe Hospital.