Molecular 'portraits' of tumours match patients with trials in everyday clinical practice

November 8 2012

Researchers in France are taking advantage of the progress in genetic and molecular profiling to analyse the make-up of individual cancer patients' tumours and, using this information, assign them to particular treatments and phase I clinical trials—an approach that could become part of everyday clinical practice.

In research presented at the 24th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Dublin, Ireland, today, Dr Christophe Massard, a medical oncologist and senior consultant in the early drug development unit at the Institut Gustave Roussy in Villejuif, France, describes how he and his colleagues have successfully incorporated "molecular triaging" into their phase I clinical trial unit, with results of patients' molecular analyses being made available within three weeks of a sample being taken.

"Advances in our ability to characterise the genomic changes that drive an individual patient's tumour have led to successes in phase I trials that select patients on the basis of the molecular make-up of their tumours," said Dr Massard. "So we set up a prospective molecular triage trial in which fresh tumour biopsies were taken from patients with advanced cancer referred to our phase I unit. The study aims at offering patients a molecular portrait of their tumour. This allows us to rationally direct those patients to the relevant phase I trial, i.e. the one with an anti-cancer drug targeting the tumour's molecular driver that has been identified by

the analysis."

The trial is called MOSCATO 01 (MOlecular Screening for CAncer Treatment and Optimisation) and since October 2011 more than 120 patients have been enrolled. Tumour samples were taken with the aid of computerised tomography (CT) or ultra-sound guidance. The researchers analysed the biopsies using comparative genome hybridisation (CGH) to identify changes in the DNA of the tumour, such as mutations, gene deletions or amplifications, or other molecular alterations, and results were available within three weeks. An expert panel of scientists and clinicians reviewed the results to decide on the biological significance of the molecular changes and then referred the patients to the relevant phase I trial where it was available.

Over 95% of patients agreed to join the MOSCATO trial. Molecular analysis has proved feasible in more than 85% of patients, molecular alterations have been detected in half of them and 30% of patients have been allocated so far to a specific trial on the basis of the analysis.

"The most important findings at the moment are that this approach is feasible in the context of daily practice, and the patients are very keen to participate to this programme. A hundred patients were enrolled in seven months. They intuitively know that rational choice of their therapies is key to their future. For some patients, the results of the analyses changed the phase I trials and treatments for which they were being considered," said Dr Massard.

The researchers are continuing the trial and aim to enrol a total of 900 patients. Dr Massard says the approach could be used by other cancer centres but it requires a good, multidisciplinary team, including clinicians, interventional radiologists, pathologists, biologists, bioinformaticians and statisticians, who are available to meet on a regular basis to discuss the results of the molecular analyses.

Professor Stefan Sleijfer, the scientific chair of the EORTC-NCI-AACR Symposium, from Erasmus University Medical Centre (The Netherlands), commented: "This study is interesting because it shows the feasibility of performing complex molecular characterisation of tumours in daily clinical practice. Such approaches are key to reaching a more personalised treatment approach for cancer patients."

Examples of targeted anti-cancer drugs where phase I trials have demonstrated the success of selecting patients on the basis of the molecular make-up of their tumour include: olaparib, a PARP inhibitor, which was used successfully in phase I trials against tumours involving mutations in the BRCA 1/2 genes; vemurafenib used in melanomas with mutations in the BRAF gene; crizotinib in non-small cell lung cancers with translocations in the ALK gene; and vismodegib used in basal cell carcinoma with mutations in the SMO gene.

More information: Abstract no: 612. Poster session, Phase I trials, 09.00 hrs, Friday 9 November.

Provided by ECCO-the European CanCer Organisation