Targeted Therapy in Oncology: A Key Player in the Move towards Personalized Medicine

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Editorial

The past few years have witnessed huge changes in the approach to creating new anticancer agents, in part due to sophisticated new technologies and computer tools, and in part due to new ways of research focused on improving our understanding of the underlying genetic alterations and key molecular pathways driving the development of cancer, findings which are helping us to better identify which patients will benefit from a given targeted therapy and allow us to move towards a personalized therapeutic approach. This ever-growing knowledge base has also led to the identification of more molecular targets and the subsequent development of new targeted agents that may well shape the future treatment of cancer [1,2].

Targeted therapy is a drug that blocks the cancer cells growth by interfering with specific targeted molecules needed for carcinogenesis and tumors growth, [3] rather than by simply interfering with rapidly dividing cells (e.g. with traditional chemotherapy). Targeted therapy in oncology has been a major stimulus for the evolving field of pharmacogenomics. Also it is defined as pharmacogenomics can encompass germline and somatic (disease) gene and protein measurements used to predict the likelihood that a patient’s tumor will respond to a specific single-agent or multiagent chemotherapy regimen and the risk of toxic side effects [4]. Also the US Food and Drug Administration (FDA) has considered targeted therapy as a drug with an approved label in which there is a specific reference to a simultaneously or previously approved diagnostic test that must be performed before the patient can be considered eligible to receive the drug [5].

Targeted therapy has opened new questions about the development of cancer treatment to an individual patient’s tumor, the effect of drug and toxicity, and the economics of cancer care worldwide. As increased of diagnosed persons with cancer and as these patients live longer, primary care clinics will improve health care for patients who have received targeted cancer therapy [6].

Treatment with targeted therapy has improved outcomes for some diseases. Imatinib has had an excellent effect on chronic myeloid leukemia, and sunitinib, rituximab, trastuzumab and ipilimumab have revolutionized the treatment of renal cell carcinoma, non-Hodgkin’s lymphoma, breast cancer, and metastatic melanoma respectively [7-9]. In other instances, the degree of clinical benefit is more modest. In lymphoma, breast cancer, and metastatic melanoma respectively [7-9]. In other instances, the degree of clinical benefit is more modest. In instances, the degree of clinical benefit is more modest. In patients with advanced pancreatic cancer, the addition of erlotinib to standard chemotherapy increases the one-year survival rate from 17 to 24 percent, which correlates to an increase in median survival from 24 to 27 weeks [10].

In addition to prolonging survival in patients with certain cancers, targeted therapies provide treatment options for some patients who may not otherwise be candidates for anticancer therapy. For instance, non-small cell lung cancer and non-Hodgkin’s lymphoma primarily affect elderly patients, many of whom have medical comorbidities that limit the use of standard chemotherapy. Targeted therapies such as erlotinib and rituximab are often less toxic and better tolerated than traditional chemotherapy, offering these patients additional treatment options [6].

The era of targeted therapy has long since been upon us. However, far from being the magic bullet of cancer therapy that we once hoped it would be, we are now learning that our patients may be better served by our selective use of these agents based on the overexpression of specific molecules or presence of genetic alterations that make these agents particularly lucrative.

An advantage of micro-array technologies is that they may lead to new and unexpected insights into the background of drug resistance and may lead to new genes or pathways that may serve as therapeutic targets. The genome-wide gene expression profiling of apparently similar human tumors by traditional criteria have revealed consistent and large-scale differences in the expression pattern of hundreds of genes, which allowed definition of new molecular subtypes of cancer with distinct risks of metastasis, death, and response to therapy [11,12].

Oncology remains a very attractive therapeutic area for biopharmaceutical companies where the number of drugs in clinical development more than doubled between 2000 and 2010. In particular, it was the early stage pipelines that grew disproportionally, indicating that basic research continues to be translated into clinical drug development [13].

As personalized oncology turns out be an ever more challenging task on the continuing development, and indeed success, of these compounds will rely heavily on close collaborations between laboratory scientists and clinician researchers. Also it is important that payers, policy makers, and economists realize that the definition of the target population uses evolving methodology and is not static. Even during the drug approval process, technology becomes cheaper, especially with multiple platforms and development of alternative assays. As clinicians, we want to get the right treatment to the right patient at the right time. Payers and society want this as well, but also at the right cost. This varies by the magnitude of benefit, availability of alternatives, and the ability to afford the intervention [14,15].

To achieve the goal of personalized medicine it is necessary not only to have agents with defined molecular specificities, but to have minimally invasive biomarker and imaging tests that will identify which patients have the target in their tumor and the patient’s pharmacogenotype. A related objective is to have a way to measure the effect of a drug on its molecular target in the tumor to be able to answer...
important questions, such as how much drug is required to inhibit the target in a tumor and is there a benefit to giving more drug or will this only increase toxicity [15]. It is also desirable to have a test to assess early response so that non responding patients can be spared unnecessary treatment and be moved to alternate therapies.

References
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