Spotlight on Clinical Response: Introduction

Studies in target-based treatment

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In this issue, *Molecular Cancer Therapeutics* inaugurates a new feature—The Cutting Edge: Spotlight on Clinical Response—whose objective is the rapid publication of breaking discoveries regarding target- or mechanism-based clinical responses in cancer.

Targeted molecules are poised to alter the landscape of clinical cancer treatment. For example, because they can distinguish cancer cells from their normal counterparts, agents such as imatinib mesylate, a Bcr-Abl and Kit kinase inhibitor, can result in remarkable responses with minimal host toxicity in patients suffering from diseases characterized by abnormalities in the targeted kinases. Indeed, studies of imatinib mesylate in early-stage chronic myelogenous leukemia, whose hallmark is the aberrant Bcr-Abl, show response rates of more than 90%. Furthermore, gastrointestinal stromal tumors (GIST), a notoriously chemotherapy-refractory sarcoma, characterized by activating Kit kinase mutations, can show dramatic metabolic responses within days after initiation of treatment.

With the wealth of new knowledge in this field, and numerous novel targeted molecules entering clinical trials, the above examples are likely to represent the tip of the iceberg. Indeed, in this issue, a paper by Senzer et al. documents, for the first time, successful use of adenoviral p53 therapy to treat a tumor in a patient with Li Fraumeni Syndrome, a hereditary cancer syndrome caused by the mutation of the p53 tumor suppressor gene. Some of the features of this response, such as the early disappearance of metabolic activity on fluorodeoxyglucose–positron emission tomography scans, are reminiscent of those of GIST responses to imatinib. These findings have important implications for patients with this syndrome, who are prone to develop numerous tumors and often succumb at a young age. In addition, because mutations in p53 are one of the more common aberrations in cancer in general, identification of these mutations and exploration of this approach is warranted in patients with sporadic cancers.

In summary, the era of ''molecular cancer therapeutics'' has begun. Even so, results in the laboratory and in animals often do not translate into salutary effects in patients. However, when they do, it is important that the information be made quickly available to the investigative community. *Molecular Cancer Therapeutics* believes that providing a forum for the rapid dissemination of cutting-edge findings of successful, albeit early, clinical research should stimulate further study and will ultimately benefit patients with cancer.

Objective

The goal of this feature is rapid publication of breaking discoveries regarding mechanism- or target-based treatment responses in cancer. Appropriate papers should describe one or more patients or pilot/early-phase studies that show significant responses. The responses must be mechanism based. For the response to be mechanism based, it must meet the following criteria:

- Either the tumor of the patient(s) has been shown, via experimentation documented in the manuscript, to have a specific molecular aberration, or it must already be known, through citable literature reports, that that molecular aberration characterizes the type of tumor reported.
- Either the treatment used must be shown, via experimentation documented in the manuscript, to target the specific molecular aberration found in the patient(s)' tumor, or it must already be known, through citable literature reports, that that treatment impacts the molecular target.
- The response must be documented by tumor markers, imaging, and/or analogous modalities as appropriate.

Appropriate papers should be brief.

- <1,500 words for text (Abstract, Introduction, Methods, Results, and Discussion; does not include references, tables, and figures)
- ≤20 references
- ≤3 figures plus tables

All papers must include a statement regarding the patients' treatment and data collection being done in accordance with the guidelines of an appropriate surveillance committee.

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