The Promise and Perils of Measuring Circulating Tumor Cells

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One of the more obvious and clinically relevant differences between the management of hematologic malignancies and solid tumors is the common presence in the former of circulating cancer cells which can be routinely sampled and studied. Disease response and progression can be documented with relative ease, evaluated regularly, and with sophisticated molecular techniques the extent of regression or quite early demonstration of therapeutic resistance can lead to rapid modifications in management.

In an attempt to establish a disease assessment paradigm similar to hematologic malignancies, investigators in the solid tumor arena have spent considerable effort over the past decade attempting to document the presence and clinical meaning of malignant cells within the systemic circulation, both to assist in providing a more accurate assessment of prognosis and also to more easily monitor response to therapy. It has been speculated that circulating cancer cells are almost certain to be present in many patients with apparently localized tumors as the subsequent documentation of metastatic spread is unfortunately common in association with particular clinical features of the disease process (e.g., high grade cancers or lymph node involvement).

Unfortunately, it has not been a simple task to document the existence of such cells or to distinguish low concentrations of cancer within the blood from other non-

malignant cell populations. For example, the mere presence of a cell with an epithelial signature does not make the cell malignant. And even if the cells are malignant the finding does not necessarily mean they are either viable or are capable of successfully growing in metastatic sites.

However, increasingly solid evidence generated over the past several years has provided strong support for both the presence of circulating tumor cells in several malignancies (breast, colon, and prostate cancers) and the documentation of this population in individual patients has been shown to be of negative prognostic significance [1–3].

In this issue of *Oncology*, de Albuquerque et al. [4] present preliminary data regarding a novel multigene strategy to document the presence of circulating malignant cells in patients with pancreatic cancer. Recognizing the limited sample size ($n = 34$ patients), circulating tumor cells were apparently successfully identified in 47% of their population and in none of the non-malignant control group ($n = 40$ patients).

Further, and of potential clinical relevance, the patients with cancer cells present in the blood were found to experience a substantially shorter time to disease progression (median 66 days) compared with individuals who tested negative for this population (median 138 days). While these results certainly require confirmation in a much larger prospective study, the data suggest

that, conceptually, the presence of circulating tumor cells may be employed not only to evaluate prognosis, but also to monitor the extent of treatment response as well as assist in the documentation of time to disease progression.

Finally, one can anticipate that future efforts will specifically explore the potential to discover unique molecu-

lar features associated with the circulating tumor cell population. It is possible that identification of particular genetic signatures present at baseline and/or modified following anti-neoplastic therapy may ultimately permit the delivery of appropriately targeted and far more effective therapy based on the molecular profiles of individual cancers.

References

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