Comments Regarding Lung Metastasis Surgery for Sarcoma

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In this issue of ONCOLOGY, Kon and Martin review the difficult issue of lung metastasis from sarcoma and its management. This article is timely as a reminder that we still have a long way to go before we understand and treat metastatic cancer more effectively.

Biological factors appear to predominate in the management of patients with this difficult development, whether it arises from osteosarcoma, from other bone tumors, or from soft-tissue sarcomas. It is not surprising that patients with a smaller number of lung metastases appearing at a later time after primary therapy fare better than those with a larger number of nodules appearing at a short interval after the completion of primary therapy.[1] The latter patients in turn fare better than those who have unresectable disease; as I have been taught, “those who do better, do better.” While there continue to be studies examining and quantitating the outcomes for people with lung metastatic disease, there are no randomized data examining the role of surgery in this setting, nor are there likely to be any data comparing surgery and no surgery for people with small numbers of resectable metastases, given that there is a known cure rate for surgery alone.

The data are equally inadequate with regard to the role of chemotherapy in the setting of resection of metastatic disease. Certainly, retrospective analyses from MD Anderson and Memorial Sloan-Kettering that look at the outcomes for patients who receive chemotherapy either before or after surgery for lung metastases are not particularly rousing, with overall survival around 20% at best, whether or not chemotherapy is employed.[2,3] Unfortunately, there is such variation in the diagnoses of patients treated with chemotherapy, in the use of adjuvant chemotherapy as part of primary therapy, and in variables such as time from initial diagnosis and number of nodules resected that it is impossible to say whether chemotherapy might be beneficial or not. This remains one area ripe for study in a prospective fashion.

What is new under the sun? In osteosarcoma, an attempt is being made to randomly assign patients to use of an SRC inhibitor or placebo after resection of lung metastases, a study that has been slow to accrue due to the rare nature of the diagnosis and the relative success achieved with primary adjuvant chemotherapy (clinicaltrials.gov # NCT00752206). With respect to an immunotherapeutic approach to the problem, a multicenter study is examining the utility of a ganglioside vaccine with carrier compared to the carrier alone in patients with resected lung metastases (clinicaltrials.gov # NCT01141491). These studies will provide more conclusive data regarding at least some potential interventions we clinicians can offer patients with this otherwise usually lethal condition.

We are also on the verge of being able to assess patients for circulating sarcoma cells, a finding that may serve as a surrogate for metastatic disease for at least some patients with sarcoma. Such analyses are hampered by the lack of surface markers such as EpCAM (used in analysis of circulating epithelial cancer cells), but may help point the way regarding new interventions we can offer to both people destined to develop metastatic disease and those with overt metastatic disease. One might wish to be a bit more sanguine than the authors regarding the use of anti-chemokine–based therapy to treat metastases. While Kon and Martin are of the opinion that this therapy likely has no such role in the treatment of existing metastases, the self-seeding hypothesis put forth by Norton and Massagu suggests that intervening along these lines could be useful in the treatment of existing metastases.[4,5]

Although sarcomas are rare, lung metastases and other metastatic disease arising from sarcomas remain all too common. By understanding model systems better and intervening based on the findings of these models, we hope to see true progress made in this difficult clinical scenario in the near future.

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