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Commentary: Resected pulmonary sarcomatoid carcinoma—a defined treatment paradigm, or just the end of the beginning of the search?

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Events at a cellular level help to explain the behavior of pulmonary sarcomatoid carcinoma (PSC). This rare tumor is a form of non-small cell lung cancer (NSCLC) characterized by a change from an epithelioid subtype to a sarcomatoid subtype. Spindle and/or giant cells are seen. At least 10% of the tumor must have undergone such sarcomatoid change for it to be classified as PSC according to the World Health Organization.¹ Because this change represents a form of high-grade tumor progression, the survival is correspondingly poor stage for stage when compared with more common forms of NSCLC.

Members of lung cancer multidisciplinary teams, including thoracic surgeons, are not often called on to

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CENTRAL MESSAGE

Adjuvant chemotherapy should be offered to patients with resected stage II and III pulmonary sarcomatoid carcinoma, but the search for more targeted therapies continues.

make management decisions regarding PSC. Attitudes about treatment and prognosis may tend toward nihilism. This is not altogether unreasonable given the poor prognosis and the lack of a firm evidence base for treatment. In unresected disease, patients often respond poorly to first-line chemotherapy.²

In an attempt to improve the lot of patients with PSC who have undergone lung resection, adjuvant chemotherapy is often recommended. Until now, there has been little evidence to back this up. This raises questions about such patients being exposed to unnecessary harm. Abdallah and colleagues³ have clearly had similar reservations and have performed a retrospective study using the National Cancer Database, identifying patients with resected PSC. Following some statistical manipulations, including propensity matching, they found that adjuvant chemotherapy appears to confer a long-term survival advantage in stage II and III disease. No such benefit is seen in stage I disease. The study has

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obvious strengths. It is multi-institutional and among the largest studies of PSC ever reported. It is also likely to be the largest study to look at the effects of adjuvant chemotherapy following lung resection. Its inevitable weaknesses (such as selection bias for chemotherapy, no information on chemotherapy type, and missing pathological stage data) have been largely identified by the authors and attempts made to mitigate these effects.

Given the rarity of PSC, any randomized controlled trial will almost certainly find it impossible to recruit adequate cohorts. This study will probably represent the limit of the evidence available for the role of conventional adjuvant chemotherapy in PSC. As with the more common NSCLC variants, it will not be the last word in perioperative treatment. With advances in immunohistochemical and molecular methods, it is becoming evident that PSCs have similar immunophenotypes and molecular signatures to other NSCLCs, including high-grade adenocarcinomas.⁴ Unfortunately, targetable mutations such as *EGFR* and *ALK* are not often seen. *MET* mutations and amplification show potential for treatment with targeted tyrosine kinase inhibitors. *PD-L1* overexpression is common and raises the prospect that immune checkpoint inhibitors may have an important role to

play. There also appear to be important differences in mutations expressed in the tumors of smokers and nonsmokers, leading to the identification of further possible targets.⁵

On the basis of the work presented here, patients with resected stage II and III PSC should be considered for adjuvant chemotherapy. Now there is a new challenge for the management of this unfortunate and rare disease: Catch up with the advances seen in the treatment of conventional NSCLC.

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