

Dramatic Responses in a Rare Type of Sarcoma

Positive results in an early trial for rare sarcoma have spurred a multicenter randomized registration trial.

“Most oncologists have probably never seen a patient with alveolar soft part sarcoma (ASPS),” explained Shivaani Kummar, M.D., Head of the Developmental Therapeutics Clinic within CCR and NCI’s Division of Cancer Treatment and Diagnosis. “So, it is treated like regular sarcoma, but it doesn’t respond to the regimens.” A rare and highly vascularized form of cancer for which radical surgery is the only known cure, ASPS has recently been the subject of a promising prospective phase 2 clinical trial conducted by Kummar and her colleagues. Their recent publication in the *Journal of Clinical Oncology* details the response of 46 patients to treatment with cediranib, an inhibitor of vascular endothelial growth factor receptors (VEGFRs).

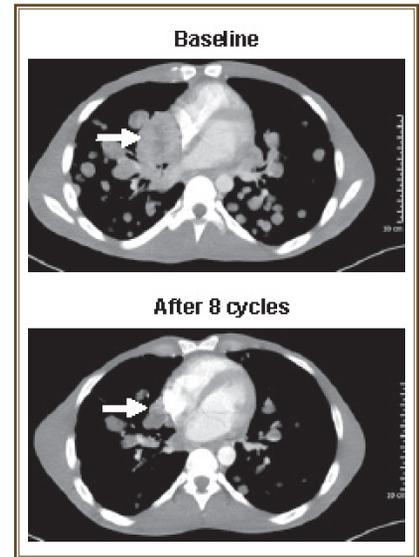
Kummar was excited to test cediranib in this patient population after a phase 1 clinical trial in the U.K. gave the first signs of the drug’s effectiveness in this patient population. She worked with NCI’s Cancer Therapy Evaluation Program (CTEP), which had access to the drug through a Cooperative Research and Development Agreement (CRADA) with its maker AstraZeneca, to get the necessary approvals. They started judiciously, enrolling only nine patients at first, before bringing in additional patients as encouraging initial responses emerged. Eventually, 24 patients were enrolled in one cohort and an additional 22 in a replicate cohort, making this the largest prospective

trial of a systemic drug to treat ASPS.

The paper reports results in which 15 of the first 43 patients saw at least a 30 percent reduction in the diameters of their tumors (measured along the longest dimension). For 26 patients, the cancer stabilized. At 24 weeks into the treatment, disease was under control in 84 percent of patients. “It was a very satisfying response,” said Kummar. “Both the high response rate and the durability of the response. We now have patients three years out on this drug.”

On the strength of these results, an open-label, multicenter randomized phase 2 trial has begun, comparing cediranib with sunitinib, a drug that acts to inhibit several receptor kinases including VEGFRs. The study will include M.D. Anderson Cancer Center, Dana-Farber Cancer Institute, Memorial Sloan-Kettering Cancer Center, and Santa Monica Oncology Center. As always, patient recruitment will be a challenge for a disease that accounts for less than one percent of cancers affecting supporting and connective tissues. “When we first began this work, it was hard to get the word out,” said Kummar. Support groups like iCureASPS have made a large difference in educating patients and oncologists alike about this unusual sarcoma.

In addition to monitoring tumor shrinkage, the clinical researchers also took tumor biopsies from patients to study changes in gene expression. Consistent with VEGFR inhibition, they found downregulation of the angiogenesis-related gene *ANGPT2*



(Image: S. Kummar, CCR)

CT scan from 25-year-old patient with newly diagnosed metastatic ASPS; top scan is cross-section of the chest at the start of the trial and bottom scan is post-treatment, with significant tumor shrinkage.

and the gene encoding VEGFR-1. These gene expression analyses give insight into the mechanism of action of the drug, as well as suggest combination therapies that could be tried in the future.

To learn more about Dr. Kummar’s research, please visit her CCR Web site at <http://ccr.cancer.gov/staff/staff.asp?name=skummar>.