

## *The Liddy Shriver Sarcoma Initiative*

### **Grant to fund study of tissue samples in conjunction with a Phase II Trial of Dasatinib in patients with advanced sarcoma**

The Liddy Shriver Sarcoma Initiative is proud to announce that it has just awarded a grant of \$25,000 to help fund a SARC research study in which leiomyosarcoma, liposarcoma, MFH, malignant peripheral nerve sheath tumor, rhabdomyosarcoma and osteosarcoma patients will be eligible to participate. Dr. Scott Schuetze of the Department of Internal Medicine at the University of Michigan's School of Medicine, who is heading up the study, said that patients with alveolar soft part sarcoma, epithelioid sarcoma, chondrosarcoma, hemangiopericytoma, giant cell tumor of bone and chordoma will also be eligible to participate in the this study.

SARC, the Sarcoma Alliance for Research through Collaboration, is a non-for-profit consortium with a mission to conduct clinical trials to improve the diagnosis and treatment of sarcoma, and to ultimately find a cure for this disease. SARC includes participants from 20 institutions with many physicians from various diagnostic and therapeutic disciplines whose practices are limited to sarcoma. In addition, SARC is committed to providing accurate and up-to-date information about sarcoma to physicians, patients and families affected by the disease.

#### **SARC**

To participate in SARC, physicians must be part of a multidisciplinary sarcoma practice that includes expertise in diagnosis (pathology and radiology physicians) and treatment (pediatric, medical, radiation, surgical and orthopedic oncologist) of sarcoma. In addition, participants must have a commitment to research and a practice that sees at least 150 new sarcoma cases per year. SARC participants are committed to the CTOS (Connective Tissue Oncology Society) model and philosophy that sarcoma's are best studied and managed in a collaborative fashion. While pooling intellectual resources, SARC also strives to pool patient resources

Patients with advanced sarcoma will be enrolled into histology-specific cohorts for Phase II testing of dasatinib activity. The primary endpoint for defining potential activity of the drug will be objective tumor response or stable disease for 6 months or more. Dasatinib is an oral small-molecule inhibitor of the SRC, PDGFR, C-KIT receptor tyrosine kinases among others. Dasatinib will be taken orally, twice daily. Based on prior studies of imatinib (gleevec) in sarcoma and pre-clinical testing of sarcoma tumor samples for expression of the SRC kinase, patients with the sarcoma subtypes of leiomyosarcoma, liposarcoma, MFH, malignant peripheral nerve sheath tumor, rhabdomyosarcoma and osteosarcoma will be eligible to participate. Patients with alveolar soft part sarcoma, epithelioid sarcoma, chondrosarcoma, hemangiopericytoma, giant cell tumor of bone and chordoma will also be eligible to participate because identification of new drugs with the potential for anti-tumor activity in these rare subtypes is greatly needed.

Patients who are eligible to participate in the study will be registered into one of the following histology sub-type specific cohorts: leiomyosarcoma, liposarcoma, MFH, malignant peripheral nerve sheath tumor, rhabdomyosarcoma, osteosarcoma or “indolent sarcomas”. The indolent sarcoma sub-group will consist of alveolar soft part sarcoma, epithelioid sarcoma, chondrosarcoma, hemangiopericytoma, giant cell tumor of bone and chordoma. Each cohort will be analyzed for evidence of dasatinib activity. Enrollment in a cohort will stop if there is a low likelihood that patients with the sarcoma sub-type will benefit for treatment with dasatinib. A minimum of 9 subjects will be enrolled in the leiomyosarcoma, liposarcoma, MFH, malignant peripheral nerve sheath tumor, rhabdomyosarcoma and osteosarcoma cohorts. A minimum of about 20 subjects will be enrolled in the indolent sarcoma cohort.

Tumor samples (tumor blocks) from patients participating in the study will be collected and shipped to the University of Michigan. The Liddy Shriver Sarcoma Initiative’s research grant will be used to help fund the tissue analysis done by Dr. Schuetze. A minimum of 73 and a maximum of approximately 452 specimens will be collected. SRC and focal adhesion kinase (FAK) expression in tumor will be evaluated using immunohistochemical stains. FAK is a down-stream target of activated SRC, and inhibition of SRC may prevent activation of FAK. FAK is expressed in many of the sarcoma subtypes and may contribute to the malignant phenotype. The presence of activating mutations in the platelet-derived growth factor receptor (PDGFR) in tumor will be assessed by polymerase-chain reaction (PCR) methods. Testing for expression or activation of other kinases targeted by dasatinib may occur if significant anti-tumor activity is seen. It is our hypothesis that the presence of the known targets of dasatinib such as PDGFR and SRC and/or the downstream kinase FAK in sarcoma will predict tumor response to treatment. [Click here](#) to find out more information.

**[Editor's Note:** The funds for this research were a result of contributions made by numerous people to the [Team Sarcoma 2006 Initiative](#). In particular we wish to acknowledge the wonderful fund raising efforts of Deborah Buks and Denise Reinke, RN both of whom are associated with SARC.]

#### Comments and Questions

We would appreciate receiving any comments or questions regarding the contents of this column. [Click here](#) to send us a note.