

SARC 012

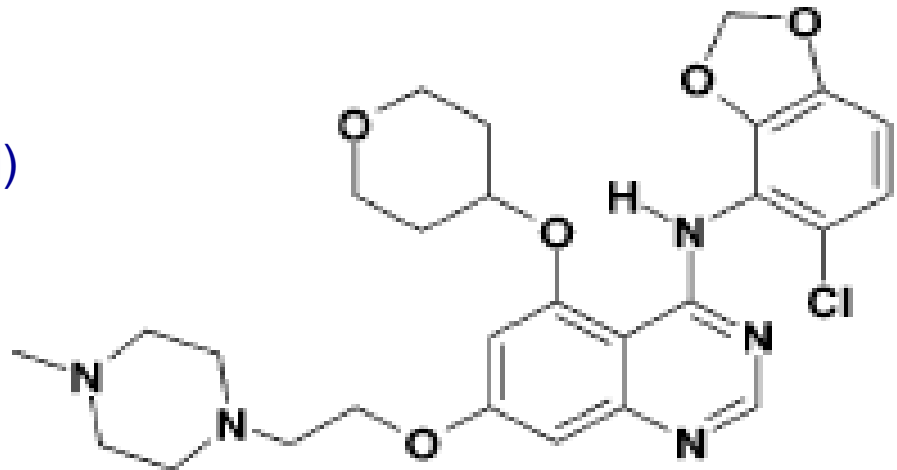
A Randomized, Double-Blinded, Placebo-Controlled, Multi-Institutional, Phase II.5 Study of AZD0530, a Selective Src Kinase Inhibitor, in Patients with Recurrent Osteosarcoma Localized to the Lung

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AZD0530

- AZD0530 is a potent Src inhibitor that modulates multiple key signaling pathways in cancer

Protein Kinase	IC ₅₀ (uM)
c-Src	0.0027
c-Yes	0.004
c-Lck	0.004
c-Fyn	0.01
v-abl	0.03



- 175 mg was the MTD in a Phase I study in adults with advanced cancer**

Primary Objective

- To determine if the addition of AZD0530 to pulmonary metastasectomy, versus placebo and pulmonary metastasectomy, results in an increase in progression free survival

Secondary Objectives

- To determine if the addition of AZD0530 to pulmonary metastasectomy, versus placebo and pulmonary metastasectomy, results in an increase in overall survival
- To perform microarray analysis of tumor samples to identify a gene signature that predicts for recurrence of osteosarcoma
- To evaluate tumor samples for biomarkers related to activation of Src and Src substrates
- To establish cell lines and murine xenografts from recurrent tumor samples

Eligibility Criteria

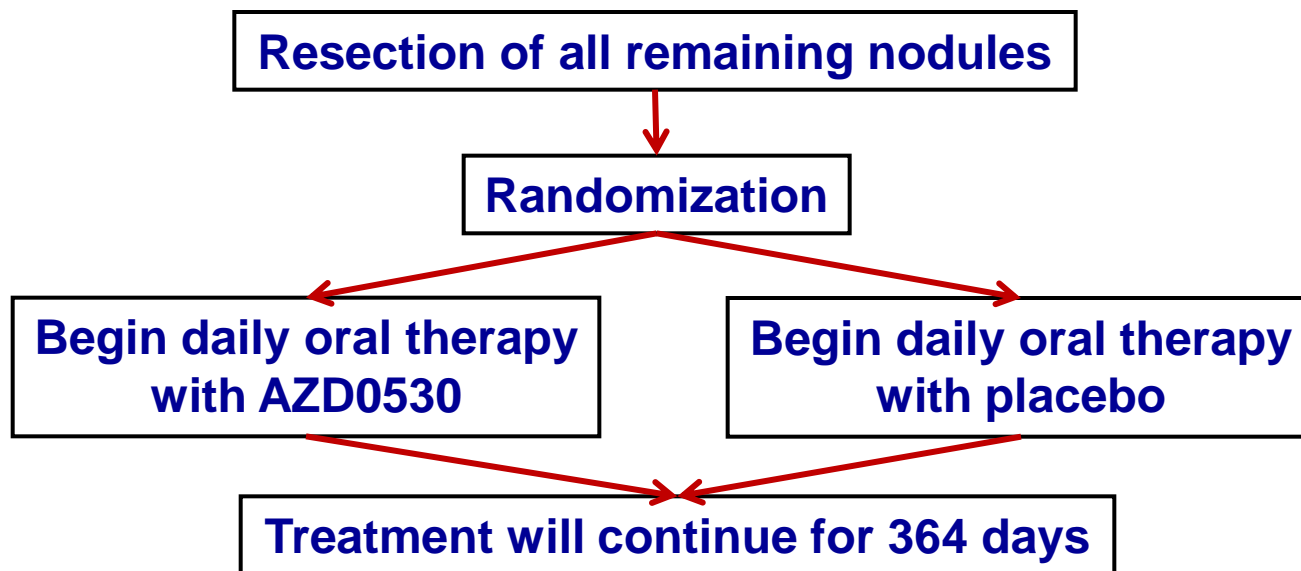
- Patients who have recurrence of osteosarcoma, localized to the lungs, who have had complete surgical removal of all lung nodules
- Histology of the recurrent sample must be one of the following:
 - Osteoblastic, chondroblastic, fibroblastic or telangiectatic
- Recurrence following standard front-line chemotherapy
- Age ≥ 15 and < 75 years
- Weight > 34 kg
- ECOG score 0, 1 or 2

Exclusion Criteria

- The presence of metastatic disease in other locations, in addition to the lung
- Disruption of the lung pleura by tumor
- Paget's disease
- Interstitial lung disease that is diffuse, bilateral or parenchymal, or any unstable or uncompensated respiratory condition

Treatment Design

- Patients with histological confirmation of recurrent osteosarcoma
- Stratification
 - Number of Recurrences
FIRST vs SECOND vs THIRD or MORE
 - Number of Nodules
ONE or TWO vs THREE or MORE



Follow-up Schedule

Start		Begin daily oral therapy with AZD0530 or placebo	
Week 1	labs *	(* may be with primary care physician)	
Week 3	labs	Thoracic CT	(due to several cases of
Week 6	labs	Thoracic CT	interstitial pneumonitis)
Week 9	labs *		
3 Months	labs	Thoracic CT	EKG
4 Months	labs *		
5 Months	labs *		
6 Months	labs	Thoracic CT	
7 Months	labs *		
8 Months	labs *		
9 Months	labs	Thoracic CT	
10 Months	labs *		
11 Months	labs *		
12 Months	labs	Thoracic CT	Bone scan
		Discontinue oral therapy	

Required Patient Accrual

Randomization	Surgery and AZD0530	Surgery and Placebo
Year 1	11 patients	11 patients
Year 2	11 patients	11 patients
Year 3	11 patients	11 patients
Year 4	11 patients	11 patients
Year 5	Follow-up	Follow-up

Participating Centers

OPEN	Stanford University	3-27-09
	Pennsylvania Oncology	3-30-09
	NCI / NIH	4-1-09
PENDING	Carolinas Hematology-Oncology Associates	
	Cedars Sinai	
	Johns Hopkins	
	MD Anderson	
	Memorial Sloan-Kettering	
	UCLA	
	University of Alabama-Birmingham	
	University of Iowa	
	University of Minnesota	
University of Pittsburgh		

All centers are welcome to refer children and young adult patients to the NIH for treatment