

AstraZeneca	AZD0530 (saracatinib)
Mechanism of Action	Src tyrosine kinase inhibitor http://www.ncbi.nlm.nih.gov/gene/6714
Overview	AZD0530 (saracatinib) is a potent orally bioavailable v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog (avian) inhibitor. Src is a non-receptor protein tyrosine kinase that is involved in the regulation of numerous cellular functions such as growth, adhesion, migration and embryonic development and has been linked to the development of numerous cancers. In pre-clinical studies AZD0530 has an IC ₅₀ at isolated v-Src of 5 nM and isolated v-Abl of 30 nM. It has sub-micromolar activity in cell models of human tumor cell proliferation and produces inhibition of tumor growth in murine and rat allografts and xenografts at 25 and 10 mg/kg, respectively.
Safety/Tolerability	The safety assessment package includes pivotal reproductive toxicity studies and general toxicity studies of 6 month duration in rat and dog. Multiple target organs for toxicity are identified with a focus on gastrointestinal, liver, kidney and bone marrow. NOEL's exist to all identified changes apart from embryofetal toxicity. In healthy human volunteer studies, AZD0530 was tolerated in single ascending dose studies at up to 1000 mg and in 14 day multiple ascending dose studies at up to 250 mg. A maximum tolerated dose in oncology patients of 175 mg per day has been determined in advanced solid tumors with patients remaining on drug for extended periods. Adverse events in patients include: anemia, nausea, anorexia, asthenia, pyrexia, vomiting, diarrhea, and pneumonitis-type events.
Additional Information	AZD0530 has been studied in a range of cancers either alone or in combination with chemotherapy, hormonal therapies, bisphosphonates and other novel agents including a Phase 2b clinical trial in ovarian cancer. There are on-going, non-AstraZeneca sponsored Phase 2b trials in renal, prostate and breast cancer.
Suitable for and Exclusions	The reproductive toxicology package indicates that AZD0530 can induce effects on embryofetal survival and fetal development, therefore, the inclusion of women of child-bearing potential would need to be assessed for any proposal based on the risk benefit and the use of appropriate contraception. No data are available as yet to support use in pediatrics. AZD0530 is a moderately potent CYP3A4 inhibitor and concomitant administration of medicines that are metabolized by this route should be avoided. Dependent on a thorough risk/benefit assessment, proposals for the use of AZD0530 may be supported for chronic indications. Proposals for use in orphan indications would be particularly welcome. Studies in tumor biology, ophthalmology or dermatology are not of interest.
Clinical Trials	http://clinicaltrials.gov/ct2/results?term=AZD0530
Publications	http://www.ncbi.nlm.nih.gov/pubmed?term=AZD0530%20or%20saracatinib