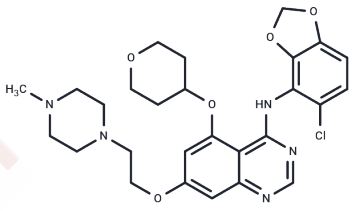
Data Sheet (Cat.No.T6078)

TargetMol

Saracatinib

Chemical Properties



CAS No. : 379231-04-6

Formula: C27H32ClN5O5

Molecular Weight: 542.03

Appearance: no data available

Storage: store at low temperature,keep away from moisture
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Saracatinib (AZD0530) (AZD0530) is an effective Src inhibitor (IC50: 2.7 nM), and effective to Lck, Fyn, Lyn, Blk, Fgr and c-Yes.
Targets(IC50)	EGFR,BTK,Autophagy,Src
In vitro	Saracatinib (AZD0530) potently inhibited the in vitro proliferation of Src3T3 mouse fibroblasts and demonstrated variable antiproliferative activity in a range of human cancer cell lines containing endogenous Src. Sub-micromolar growth inhibition of five of the human cancer cell lines tested with AZD0530 (tumor types: colon, prostate, lung, and leukemia) was observed with IC50 values of 0.2–0.7μM. In 3-day MTS cell proliferation assays, AZD0530 inhibited in vitro proliferation of the Bcr-Abl-driven human leukemia cell line K562 with an IC50 of 0.22μM [1]. VS cells were cultured with cabozantinib (2 μmol/L) and saracatinib (2 μmol/L), alone or in combination, for 48 hours. For both VS01 and VS02, the combination treatment reduced VS cell viability by approximately 35%–40% compared with vehicle (0.3% DMSO) and was significantly more effective than saracatinib alone [2]. In DU145 and PC3, AZD0530 inhibited Src activation in a dose-dependent manner. Src inhibition by AZD0530 was also rapid, within 5 min of treatment. A single treatment with AZD0530 resulted in a dose-dependent decrease in the number of cells in all cell lines. LAPC-4 is the most resistant against AZD0530 among prostate cancer cell lines. Immortalized nonmalignant cell lines PZ-HPV7 and RWPE-1 are also on average more resistant to Src inhibition than cancer cell lines [3].
In vivo	AZD0530 treatment potently inhibited the proliferation of subcutaneously transplanted Src3T3 fibroblasts in mice and rats in a dose-dependent manner. In both models, significant inhibition of tumor growth was seen at doses ≥6mg/kg/day (60% inhibition in mice and 98% inhibition in rats versus animals treated with vehicle) and, at the maximum doses investigated, complete tumor growth inhibition was observed (100% inhibition at 25mg/kg/day in mice and 10mg/kg/day in rats) [1]. Mice were assigned into vehicle, cabozantinib (12.5 mg/kg/day), saracatinib (25 mg/kg/day), and combination (cabozantinib and saracatinib at 12.5 mg/kg/day and 25 mg/kg/day, respectively) treatment cohorts. bioluminescence imaging (BLI) showed that grafts in the combination-treated group had a significantly slower growth rate compared with those in the single-agent groups. Although the vehicle-treated allografts had a 160-fold increase in BL signal over 14 days, the grafts treated with saracatinib or cabozantinib had a 50- and 60-fold increase in BL signal, respectively. Significantly, the allografts

	from the combination group had only a 25-fold increase in BL signal after 14 days of treatment [2].
Kinase Assay	Inhibition of tyrosine kinase activity was examined using an ELISA with recombinant catalytic domains of a panel of receptor and non-receptor tyrosine kinases (in some cases only part of the catalytic domain was used). This method has been described previously. AZD0530 dose ranges varied depending on the activity versus the particular kinase tested, but were typically 0.001–10μM. Specificity assays against a panel of serine/threonine kinases were performed using a filter capture assay with 32P. Briefly, multidrop 384 plates containing 0.5μL AZD0530 or controls (DMSO alone or pH 3.0 buffer controls) were incubated with 15μL of enzyme plus peptide/protein substrate for 5min before the reaction was initiated by the addition of 10μL of 20mM Mg.ATP. For all enzymes the final concentration was approximated to the Michaelis constant (Km). Assays were carried out for 30min at room temperature before termination by the addition of 5μL orthophosphoric acid. After mixing, the well contents were harvested onto a P81 Unifilter plate, using orthophosphoric acid as the wash buffer. Microcal Origin software was used to interpolate IC50 values by nonlinear regression [1].
Cell Research	Cell proliferation was assessed using a colorimetric 5-bromo-2′-deoxyuridine (BrdU) Cell Proliferation ELISA kit, as described previously. Briefly, cells were plated onto 96-well plates (1.5×10^4 cells/well), the following day 0.039–20μM AZD0530 in DMSO (at a final concentration of 0.5%) was added and the cells were incubated for 24h. The cells were pulse-labeled with BrdU for 2h and fixed. Cellular DNA was then denatured with the provided solution and incubated with anti-BrdU peroxidase for 90min. Following three washes with phosphate-buffered saline, tetramethylbenzidine substrate solution was added and the plates were incubated on a plate shaker for 10–30min until the positive control absorbance at 690nm was approximately 1.5 absorbance units [1].
Animal Research	Female athymic mice (nu/nu: Alpk) and rats (RH-rnu/rnu) were housed and maintained as previously described. Src3T3 and human tumor lines (as indicated in Table 3) were inoculated subcutaneously in the left flank of animals. Tumor growth was monitored by bi-dimensional caliper measurements twice weekly. The tumor volume was calculated by the following formula: (length×width)×√(length×width)×(π/6) and supported by excision and weighing of tumors at the end of the studies. Dosing started when the average tumor volume reached 0.2–0.5cm3 (except MDA-MB-231 and HT29). Animals were treated once daily by oral gavage with either vehicle alone or AZD0530 6.25–50mg/kg for 10–91 days. Tumor growth inhibition was calculated as described previously. For pharmacokinetic and pharmacodynamic analysis animals were humanely sacrificed and samples (plasma and tumor) were collected. Tumor samples were homogenized with 5 volumes of water and extracted with chloroform. Plasma and tumor samples were analyzed for AZD0530 concentration using high-performance liquid chromatography with tandem mass spectrometric detection after solid-phase extraction [1].

Solubility Information

Solubility	DMSO: 65 mg/mL (119.92 mM),Sonication is recommended. Ethanol: 29 mg/mL (53.5 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8449 mL	9.2246 mL	18.4492 mL
5 mM	0.369 mL	1.8449 mL	3.6898 mL
10 mM	0.1845 mL	0.9225 mL	1.8449 mL
50 mM	0.0369 mL	0.1845 mL	0.369 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Green TP, et al. Preclinical anticancer activity of the potent, oral Src inhibitor AZD0530. Mol Oncol, 2009, 3(3), 248-261.
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Fuse MA, et al. Combination Therapy With c-Met and Src Inhibitors Induces Caspase-Dependent Apoptosis of Merlin-Deficient Schwann Cells and Suppresses Growth of Schwannoma Cells. Mol Cancer Ther. Mol Cancer Ther. 2017 Nov;16(11):2387-2398.
Li J, Liu X, Liu Y, et al.Saracatinib inhibits necroptosis and ameliorates psoriatic inflammation by targeting MLKL. Cell Death & Disease.2024, 15(2): 122.
Chang YM, et al. Src family kinase oncogenic potential and pathways in prostate cancer as revealed by AZD0530. Oncogene. 2008 Oct 23;27(49):6365-75.
Ma R, Bi H, Wang Y, et al.Low concentrations of saracatinib promote definitive endoderm differentiation through inhibition of FAK-YAP signaling axis.Cell Communication and Signaling.2024, 22(1): 1-18.

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