Saracatinib

Cat. No.: HY-10234

CAS No.: 379231-04-6

Molecular Formula: $C_{27}H_{32}ClN_5O_5$

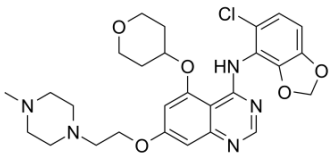
Molecular Weight: 542.03

Target: Src; Autophagy

Pathway: Protein Tyrosine Kinase/RTK; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (59.04 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8449 mL	9.2246 mL	18.4492 mL
	5 mM	0.3690 mL	1.8449 mL	3.6898 mL
	10 mM	0.1845 mL	0.9225 mL	1.8449 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Saracatinib (AZD0530) is a potent Src family inhibitor with IC_{50}s of 2.7 to 11 nM for c-Src, Lck, c-YES, Lyn, Fyn, Fgr, and Blk. Saracatinib shows high selectivity over other tyrosine kinases[1].

IC_{50} & Target

IC50: 2.7 nM (Src), 30 nM (v-Abl), 66 nM (EGFR), 200 nM (c-Kit)[1]

In Vitro

Saracatinib (AZD0530), an orally available Src inhibitor, demonstrates potent antimigratory and anti-invasive effects in vitro, and inhibits metastasis in a murine model of bladder cancer. Antiproliferative activity of Saracatinib varies between cell lines (IC_{50} of 0.2-10 μM). Saracatinib potently inhibits the proliferation of Src3T3 mouse fibroblasts and demonstrates 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 Saracatinib (tumor types: colon, prostate, lung, and leukemia) is observed with IC_{50} values of 0.2-0.7 μM. In 3-day MTS cell proliferation assays, Saracatinib inhibits proliferation of the Bcr-Abl-driven human leukemia cell line K562 with an IC_{50} of 0.22 μM. In the microdroplet migration assay, Saracatinib reduces the migration of human lung cancer A549 cells in a concentration-dependent manner (IC_{50} 0.14 μM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Saracatinib (AZD0530) treatment potently inhibits the proliferation of subcutaneously transplanted Src3T3 fibroblasts in mice and rats in a dose-dependent manner. In both models, significant inhibition of tumor growth is seen at doses ≥6 mg/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 is observed (100% inhibition at 25 mg/kg/day in mice and 10 mg/kg/day in rats)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Investigation of the reversibility and the mechanism of Saracatinib inhibition is conducted using a full-length activated human Src in a continuous, coupled assay. ATP and peptide substrate (Src II peptide) concentrations are varied in turn (ATP 40-1280 μM; Src II peptide 100-800 μM), in conjunction with Saracatinib (0-30 nM), at saturating concentrations of the non-varied substrate (ATP 1.6 mM; Src II peptide 1.0 mM). The binding affinity of Saracatinib for inactivated Src (phosphorylated at tyrosine 527, not tyrosine 416) is measured using a BIAcore inhibition-in-solution assay. The assay followed competition binding between Saracatinib and an immobilized ureidoquinazoline for binding to Src. Data analysis is performed by unweighted nonlinear regression using GraFit, version 5 and an F-test is used to identify the most suitable equation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cell proliferation is assessed using a colorimetric 5-bromo-2'-deoxyuridine (BrdU) Cell Proliferation ELISA kit. Briefly, cells are plated onto 96-well plates (1.5×10^4 cells/well), the following day 0.039-20 μM Saracatinib in DMSO (at a final concentration of 0.5%) is added and the cells are incubated for 24 h. The cells are pulse labeled with BrdU for 2 h and fixed. Cellular DNA is then denatured with the provided solution and incubated with antiBrdU peroxidase for 90 min. Following three washes with phosphate-buffered saline, tetramethylbenzidine substrate solution is added and the plates are incubated on a plate shaker for 10-30 min until the positive control absorbance at 690 nm is approximately 1.5 absorbance units[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice and Rats[1] Female athymic mice (nu/nu) and rats (RH-rnu/rnu) are used. Animals are treated once daily by oral gavage with either vehicle alone or Saracatinib 6.25-50 mg/kg for 10-91 days. Tumor growth inhibition is calculated. For pharmacokinetic and pharmacodynamic analysis animals are humanely sacrificed and samples (plasma and tumor) are collected. Tumor samples are homogenized with 5 volumes of water and extracted with chloroform. Plasma and tumor samples are analyzed for Saracatinib concentration using high-performance liquid chromatography with tandem mass spectrometric detection after solid-phase extraction. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Leukemia. 2012 Oct;26(10):2233-44.
- Cell Death Dis. 2020 Aug 7;11(8):652.
- Mol Cancer Ther. 2017 Nov;16(11):2387-2398.

- Cancer Sci. 2018 Jun;109(6):1949-1957.

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REFERENCES

[1]. Green TP, et al. Preclinical anticancer activity of the potent, oral Src inhibitor AZD0530. Mol Oncol, 2009, 3(3), 248-261.

[2]. 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.

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