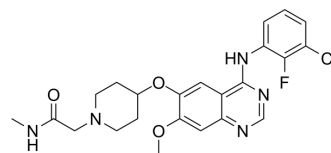


Sapitinib

Cat. No.:	HY-13050
CAS No.:	848942-61-0
Molecular Formula:	C ₂₃ H ₂₅ ClFN ₅ O ₃
Molecular Weight:	473.93
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	<div> Powder -20°C 3 years </div> <div> 4°C 2 years </div> <div> In solvent -80°C 1 year </div> <div> -20°C 6 months </div>



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 33 mg/mL (69.63 mM)
 * "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		2.1100 mL	10.5501 mL	21.1002 mL
	5 mM		0.4220 mL	2.1100 mL	4.2200 mL
	10 mM		0.2110 mL	1.0550 mL	2.1100 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
 Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sapitinib (AZD-8931) is a reversible, ATP competitive EGFR inhibitor of with IC₅₀s of 4, 3 and 4 nM for EGFR, ErbB2 and ErbB3 in cells, respectively.

IC₅₀ & Target

EGFR 4 nM (IC ₅₀)	ErbB2 3 nM (IC ₅₀)	HER3 4 nM (IC ₅₀)
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In Vitro	AZD8931 shows potent inhibitory effect on erbB2 in the ligand-independent MCF-7 cl24 cells, with IC ₅₀ of 59 nM ^[1] . AZD8931 (1 μM) has no significant effect on EGFR expression level, but significantly inhibits phosphorylation of Akt in a time- and dose-dependent manner in both SUM149 and FC-IBC-02 cells. AZD8931 (0.01, 0.1, 1, or 2 μM) inhibits proliferation and induces apoptosis in human IBC cells ^[2] . At the cellular level, AZD8931 inhibits EGF-stimulated phosphorylation of EGFR in the KB cell line (IC ₅₀ : 4 nM) and heregulin-stimulated phosphorylation of HER2 (IC ₅₀ : 3 nM) and HER3 (IC ₅₀ : 4 nM) in the MCF-7 cell line. However, AZD8931 exhibits no CYP P450 inhibition (IC ₅₀ > 10 μM against 1A2, 2C9, 2C19, 2D6, and 3A4) ^[3] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AZD8931 (6.25-50 mg/kg, p.o.) significantly inhibits BT474c (breast), Calu-3 (NSCLC), LoVo (colorectal), FaDu (SCCHN), and PC-9 (NSCLC) tumor xenograft growth. AZD8931 is active in xenograft tumor models responsive to EGFR inhibition alone (LoVo and PC-9) or EGFR or erbB2 inhibition (BT474c, Calu-3, and FaDu). AZD8931 causes pharmacodynamic changes in proliferation and apoptosis markers in human tumor xenograft models ^[1] . AZD8931 (25 mg/kg, p.o.) significantly inhibits the growth of SUM149 and FC-IBC-02 cells in vivo in SCID mice ^[2] . AZD8931 displays favorable oral pharmacokinetics in rat and dog (low clearance and good bioavailability) and low human hepatocyte turnover (Clint < 4.5 μL/min/106 cells). In nude mouse after oral administration at 50 mg/kg, AZD8931 shows improved exposure, and at 100 mg/kg oral dose once daily, it shows potent tumor growth inhibition activity in the LoVo mouse xenograft model ^[3] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[1]	Cells are incubated for 96 h with a suitable range of concentrations of drug to ensure accurate estimation of the inhibitor concentration required to give 50% growth inhibition (GI ₅₀ ; typically between 0.001-10 μM). Viable cell number is determined by 4 h of incubation with MTS Colorimetric Assay reagent and absorbance measured at 490 nm on a spectrophotometer. Each experiment is carried out in triplicate for each drug concentration and data are presented as geometric means. Sensitivity groupings of GI ₅₀ data are <1 μM, 1 to 7 μM, and >7 μM. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration ^[1]	Swiss nude (nu/nu genotype) and severe combined immunodeficient mice are used. AZD8931, GW572016, and ZD1839 are suspended in a 1% (v/v) solution of polyoxyethylenesorbitan monooleate (Tween 80) in deionized water. Animals are given AZD8931 (6.25-50 mg/kg), GW572016 (100 mg/kg), ZD1839 (100-150 mg/kg), or vehicle control once (qd) or twice daily (bid) by oral gavage. The duration of each study is determined by tumor growth characteristics, with studies ending once tumors reach ~1 cm ³ . Tumor volume and percentage tumor growth inhibition are calculated and statistical analysis of any change in tumor volume is carried out using a standard t test (P value of lower than 0.05 is considered to be statistically significant). 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.
- Cell Rep. 2023 May 29;42(6):112570.
- J Transl Med. 2021 Jan 23;19(1):43.
- Mol Cancer Res. 2019 Jan;17(1):20-29.
- Molecules. 2023 Mar 2.

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REFERENCES

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- [1]. Hickinson DM, et al. AZD8931, an equipotent, reversible inhibitor of signaling by epidermal growth factor receptor, ERBB2 (HER2), and ERBB3: a unique agent for simultaneous ERBB receptor blockade in cancer. Clin Cancer Res. 2010 Feb 15;16(4):1159-69.
- [2]. Mu Z, et al. AZD8931, an equipotent, reversible inhibitor of signaling by epidermal growth factor receptor (EGFR), HER2, and HER3: preclinical activity in HER2 non-amplified inflammatory breast cancer models. J Exp Clin Cancer Res. 2014 May 30;33:47.
- [3]. Barlaam B, et al. Discovery of AZD8931, an Equipotent, Reversible Inhibitor of Signaling by EGFR, HER2, and HER3 Receptors. ACS Med Chem Lett. 2013 May 31;4(8):742-6.
- [4]. Wang R, et al. Endothelial Cells Promote Colorectal Cancer Cell Survival by Activating the HER3-AKT Pathway in a Paracrine Fashion. Mol Cancer Res. 2018 Aug 21. pii: molcanres.0341.2018.
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