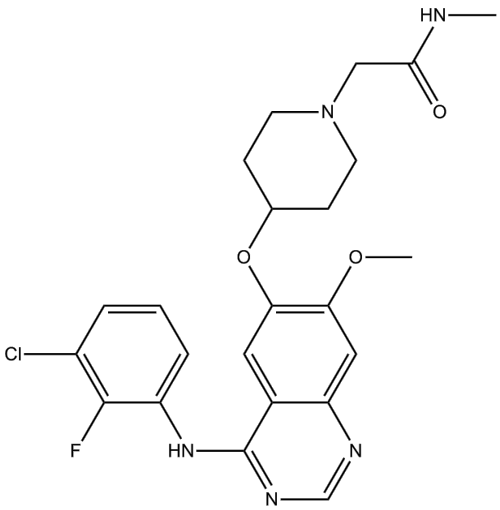
Product Data Sheet

Product Name: AZD8931 (Sapitinib)
Cat. No.: GC13761

Chemical Properties

Cas. No.	848942-61-0		
Chemical Name	2-[4-[4-(3-chloro-2-fluoroanilino)-7-methoxyquinazolin-6-yl]oxypiperidin-1-yl]-N-methylacetamide		
SMILES	CNC(=O)CN1CCC(CC1)OC2=C(C=C3C(=C2)C(=NC=N3)NC4=C(C(=CC=C4)Cl)F)OC		
Formula	$C_{23}H_{25}ClFN_5O_3$	M.Wt	473.93
Solubility	≥ 23.7 mg/mL in DMSO, ≥ 57.8 mg/mL in EtOH with gentle warming	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	A panel of NSCLC and SCCHN cell lines, MCF-7 cells, KB cells
Preparation method	The solubility of this compound in DMSO is >23.7mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting condition	96 h
Applications	AZD8931 showed great inhibition of ligand-stimulated EGFR phosphorylation in KB cells. AZD8931 also inhibited erbB2- and erbB3-mediated signaling in parental MCF-7 cells and in MCF-7 cl24 cells. AZD8931 showed a distinct pattern of tumor cell growth inhibition in NSCLC and head and neck squamous cell carcinoma cell panels.

Animal experiment [1]:

Animal models	BT474c (breast), Calu-3 (NSCLC), LoVo (colorectal), FaDu (SCCHN), and PC-9 (NSCLC) tumor xenograft mouse model
Dosage form	oral gavage,6.25-50 mg/kg, twice daily (bid)
Application	AZD8931 inhibited the growth of EGFR-sensitive and erbB2-sensitive human tumor xenograft models. AZD8931 led to pharmacodynamic changes in proliferation and apoptosis markers in human tumor xenograft models。

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Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Mu Z, Klinowska T, Dong X, 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]. Journal of Experimental & Clinical Cancer Research, 2014, 33(1): 47.

Background

Description:
IC50: AZD8931 showed equipotent, reversible inhibition of EGFR (IC50, 4 nmol/L), erbB2 (IC50, 3 nmol/L), and erbB3 (IC50, 4 nmol/L) phosphorylation in cells
The erbB receptor family is composed of four related receptor tyrosine kinases [epidermal growth factor receptor (EGFR, erbB1), erbB2 (human epidermal growth factor receptor 2, HER2), erbB3 (HER3), and erbB4 (HER4)]. AZD8931 is a novel small-molecule equipotent inhibitor of EGFR, HER2, and HER3 signaling.
In vitro: In a previous in vitro study, the authors investigated the antitumor activity of AZD8931 alone or in combination with paclitaxel using preclinical models of EGFR-overexpressed and HER2 non-amplified IBC cells. Results showed that AZD8931 significantly suppressed cell growth of IBC cells and induced apoptosis of human IBC cells in vitro [2].
In vivo: In a previous study, the authors investigated the antitumor activity of AZD8931 alone or in combination with paclitaxel IBC cells were orthotopically transplanted into the mammary fat pads of immunodeficient mice. AZD8931 was given by daily oral gavage at doses of 25 mg/kg, 5 days/week for 4 weeks. Paclitaxel was subcutaneously injected twice weekly. Results showed that AZD8931 monotherapy inhibited xenograft growth and the combination of paclitaxel + AZD8931 was demonstrably more effective than paclitaxel or AZD8931 alone treatment at delaying tumor growth in vivo in orthotopic IBC models. These results suggest that AZD8931 may provide a novel therapeutic strategy for the treatment of IBC patients with HER2 non-amplified tumors [2].
Clinical trial: A phase I/II clinical trial is conducted to determine if AZD8931 can improve the efficacy

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of standard chemotherapy for the treatment of advanced breast cancer. This study will be conducted in 2 parts: the first part (phase I) will determine a dose of AZD8931 that can be safely administered with paclitaxel chemotherapy. The second part (phase II) will determine the efficacy and safety of AZD8931 in combination with paclitaxel chemotherapy in breast cancer (https://clinicaltrials.gov/ct2/show/NCT00900627).

References:

[1] Hickinson DM, Klinowska T, Speake G, Vincent J, Trigwell C, Anderton J, Beck S, Marshall G, Davenport S, Callis R, Mills E, Grosios K, Smith P, Barlaam B, Wilkinson RW, Ogilvie D. 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;16(4):1159-69.

[2] Mu Z, Klinowska T, Dong X, Foster E, Womack C, Fernandez SV, Cristofanilli M. 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. doi: 10.1186/1756-9966-33-47.

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