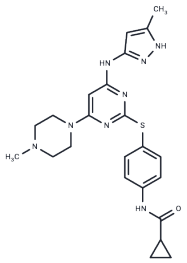
Data Sheet (Cat.No.T2509)

TargetMol

Tozasertib

Chemical Properties



CAS No. : 639089-54-6

Formula: C23H28N8OS

Molecular Weight: 464.59

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Tozasertib (MK-0457) is a pan-Aurora kinase inhibitor (Kis: 0.6/18/4.6 nM for Aurora A/Aurora B/Aurora C). It shows selectivity against more than 190 different kinases.
Targets(IC50)	Aurora Kinase,Autophagy
In vitro	Tozasertib (VX-680) is a potent inhibitor of all three Aurora kinases, with apparent inhibition constant (Ki(app)) values of 0.6, 18 and 4.6 nM for Aurora-A, Aurora-B, and Aurora-C, respectively. VX-680 caused accumulation of cells with 4N DNA content and potently inhibited the proliferation of a wide variety of tumor cell types with IC50 values ranging from 15 to 113 nM [1]. Treatment of the different ATC cells with VX-680 inhibited proliferation in a time- and dose-dependent manner, with the IC50 between 25 and 150 nM. The VX-680 significantly impaired the ability of the different cell lines to form colonies in soft agar. Analysis of caspase-3 activity showed that VX-680 induced apoptosis in the different cell lines [2].
In vivo	In nude mice treated with Tozasertib at 75 mg/kg, twice a day intraperitoneally (b.i.d. i.p.) for 13 d, mean tumor volumes were reduced by 98% in comparison with the control group. In four of ten animals, the final tumor volume was lower than the initial volume before treatment. Tumor growth reduction was dose-dependent and significant at a dose of 12.5 mg/kg b.i.d. Tozasertib was well tolerated, with a small decrease in body weight observed only at the highest dose (5% decrease at 75 mg/kg b.i.d.). Tozasertib also induced tumor regression in pancreatic and colon xenograft models. In an established human pancreatic (MIA PaCa-2) xenograft model, Tozasertib at 50 mg/kg b.i.d i.p. induced regression in seven of ten tumors, with a 22% decrease in mean tumor volume relative to initial tumor size before treatment [1].
Kinase Assay	Recombinant Aurora-1 (62-344), Aurora-2 (1-403) and Aurora-3 (1-309) were expressed as N-terminal, His6-tagged fusion proteins using a baculovirus expression system. The proteins were purified by affinity chromatography using Ni-NTA agarose, followed by size exclusion using a Superdex 200 26/60 column. Inhibition of kinase activity was assessed using a standard enzyme-coupled system or a radiometric, phosphocellulose-peptide capture assay as previously described [1].
Cell Research	Logarithmically growing MCF-7 cells were incubated with either VX-680 or DMSO for 48 h. Single-cell suspensions were fixed in 70% ethanol for 15 min, incubated with RNase (1 mg/ml) at 37 °C for 30 min, labeled with 400 µl propidium iodide (50 µg/ml) for at least 15 min at room temperature. Cell-cycle profiles were determined by flow cytometric

	analysis [1].
Animal Research	For the HL-60 study, female athymic NCr-nu mice were inoculated subcutaneously with 10^7 HL-60(TB) leukemia cells into the right axillary area. Treatment was administered i.p. b.i.d. after tumors reached 150-200 mm^3. VX-680 was prepared in a vehicle of 50% PEG 300 in 50 mM phosphate buffer. Cisplatin, formulated in saline, was administered i.p. q.4.d. for a total of three injections, at a dose of 5.4 mg/kg. For the MIA PaCa-2 studies, female MF1 nude mice were inoculated with 10^7 MIA PaCa-2 cells into the dorsal flank. Treatment was administered i.p. b.i.d. after tumors reached 175 mm^3. VX-680 was prepared in a vehicle of 50% PEG 300 in 50 mM phosphate buffer. 5-fluorouracil, formulated in saline, was administered i.v. q.4.d. at a dose of 50 mg/kg. For the HCT116 study, female Hsd RH rnu/nu rats were inoculated with 10^7 HCT116 cells into the right flank. Treatment was administered once the tumors reached 700-950mm^3. VX-680 was administered continuously through an indwelling femoral catheter, followed by a saline infusion for 4 d before repeating the dose cycle. For all studies, tumor volume was determined by caliper measurements three times a week [1].

Solubility Information

Solubility	DMSO: 40 mg/mL (86.1 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1524 mL	10.7622 mL	21.5244 mL
5 mM	0.4305 mL	2.1524 mL	4.3049 mL
10 mM	0.2152 mL	1.0762 mL	2.1524 mL
50 mM	0.043 mL	0.2152 mL	0.4305 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

Harrington EA, et al. VX-680, a potent and selective smallmolecule inhibitor of the Aurora kinases, suppresses tumor growth in vivo. Nat Med. 2004; 10:262-7.

Cheng S, Jin P, Li H, et al. Evaluation of CML TKI Induced Cardiovascular Toxicity and Development of Potential Rescue Strategies in a Zebrafish Model. Frontiers in Pharmacology. 2021: 2866.

Arlot-Bonnemains Y, et al. Effects of the Aurora kinase inhibitor VX-680 on anaplastic thyroid cancer-derived cell lines. Endocr Relat Cancer. 2008 Jun;15(2):559-68.

Shao Y, Li H, Wu Y, et al.The feedback loop of AURKA/DDX5/TMEM147-AS1/let-7 drives lipophagy to induce cisplatin resistance in epithelial ovarian cancer.Cancer Letters.2023: 216241.

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