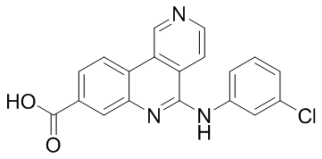
Silmitasertib

Cat. No.:	HY-50855
CAS No.:	1009820-21-6
Molecular Formula:	$C_{19}H_{12}ClN_3O_2$
Molecular Weight:	349.77
Target:	Casein Kinase; Autophagy
Pathway:	Cell Cycle/DNA Damage; Stem Cell/Wnt; 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 : ≥ 35 mg/mL (100.07 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8590 mL	14.2951 mL	28.5902 mL
5 mM	0.5718 mL	2.8590 mL	5.7180 mL
10 mM	0.2859 mL	1.4295 mL	2.8590 mL

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

BIOLOGICAL ACTIVITY

Description

Silmitasertib (CX-4945) is an orally bioavailable, highly selective and potent **CK2** inhibitor, with **IC_{50}** values of 1 nM against CK2α and CK2α'.

IC_{50} & Target

CK2α	CK2α'
1 nM (IC_{50})	1 nM (IC_{50})

In Vitro

Silmitasertib (CX-4945) causes cell-cycle arrest and selectively induces apoptosis in cancer cells relative to normal cells, attenuates PI3K/Akt signalingand, and the antiproliferative activity of Silmitasertib (CX-4945) is correlated with expression levels of the CK2α catalytic subunit, Attenuation of PI3K/Akt signaling[1]. Silmitasertib (CX-4945) with bortezomib treatment prevents leukemic cells from engaging a functional UPR in order to buffer the bortezomib-mediated proteotoxic stress in ER lumen, and decreases pro-survival ER chaperon BIP/Grp78 expression[2]. Silmitasertib (CX-4945) induces cytotoxicity and apoptosis, and exerts anti-proliferative effects in hematological

	tumors by downregulating CK2 expression and suppressing activation of CK2-mediated PI3K/Akt/mTOR signaling pathways[3].
In Vivo	Silmitasertib (CX-4945) (25 or 75 mg/kg, p.o.) is well tolerated and demonstrated robust antitumor activity with concomitant reductions of the mechanism-based biomarker phospho-p21 (T145) in murine xenograft models[1].

PROTOCOL

Cell Assay [1]	Various cell lines are seeded at a density of 3,000 cells per well 24 hours prior to treatment, in appropriate media, and then treated with indicated concentrations of Silmitasertib (CX-4945). Suspensions cells are seeded and treated on the same day. Following 4 days of incubation, Alamar Blue (20 μL, 10% of volume per well) is added and the cells are further incubated at 37°C for 4-5 hours. Fluorescence with excitation wavelength at 530-560 nm and emission wavelength at 590 nm is measured. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Xenografts are initiated by subcutaneous injection of BxPC-3 cells into the right hind flank region of each mouse or BT-474 cells are injected into the mammary fat pad of mice implanted with estrogen pellets. When tumors reach a designated volume of 150-200 mm^3, animals are randomized and divided into groups of 9 to 10 mice per group. Silmitasertib (CX-4945) is administered by oral gavage twice daily at 25 or 75 mg/kg for 31 and 35 consecutive days for the BT-474 and BxPC-3 models, respectively. Tumor volumes and body weights are measured twice weekly. The length and width of the tumor are measured with calipers and the volume calculated using the following formula: tumor volume=(length × $width^2$)/2. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Science**. 2017 Dec 1;358(6367). pii: eaan4368.
- **Sci Transl Med**. 2018 Jul 18;10(450). pii: eaaq1093.
- **Oncogene**. 2017 Aug 24;36(34):4943-4950.
- **Oncol Rep**. 2017 Feb;37(2):1141-1147.
- **Patent**. US20180263995A1.

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REFERENCES

[1]. Siddiqui-Jain A, et al. CX-4945, an orally bioavailable selective inhibitor of protein kinase CK2, inhibits prosurvival and angiogenic signaling and exhibits antitumor efficacy. Cancer Res. 2010 Dec 15;70(24):10288-98.

[2]. Buontempo F, et al. Synergistic cytotoxic effects of bortezomib and CK2 inhibitor CX-4945 in acute lymphoblastic leukemia: turning off the prosurvival ER chaperone BIP/Grp78 and turning on the pro-apoptotic NF-κB. Oncotarget. 2016 Jan 12;7(2):1323-40.

[3]. Chon HJ, et al. The casein kinase 2 inhibitor, CX-4945, as an anti-cancer drug in treatment of human hematological malignancies. Front Pharmacol. 2015 Mar 31;6:70.

Caution: Product has not been fully validated for medical applications. For research use only.

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