Silmitasertib

Cat. No.: HY-50855

CAS No.: 1009820-21-6

Molecular Formula: $C_{19}H_{12}ClN_3O_2$

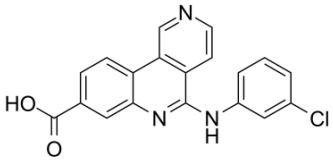
Molecular Weight: 349.77

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)

0.1 M NaOH : 33.33 mg/mL (95.29 mM; ultrasonic and adjust pH to 9 with NaOH)

* "≥" 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.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (5.95 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (5.95 mM); Suspended solution; Need ultrasonic

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 PS-341 treatment prevents leukemic cells from engaging a functional UPR in order to buffer the PS-341-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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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):eaan4368.
- Nat Cell Biol. 2021 Mar;23(3):257-267.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- EMBO Mol Med. 2020 Aug 7;12(8):e11987.
- Oncogene. 2017 Aug 24;36(34):4943-4950.

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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 PS-341 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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