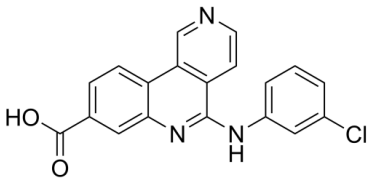
Data Sheet

Product Name:	Silmitasertib
Cat. No.:	CS-0563
CAS No.:	1009820-21-6
Molecular Formula:	$C_{19}H_{12}ClN_3O_2$
Molecular Weight:	349.77
Target:	Autophagy; Casein Kinase
Pathway:	Autophagy; Cell Cycle/DNA Damage; Stem Cell/Wnt
Solubility:	DMSO : ≥ 35 mg/mL;0.1 M NaOH : 33.33 mg/mL (ultrasonic;adjust pH to 9 with NaOH)



BIOLOGICAL ACTIVITY:

Silmitasertib (CX-4945) is an orally bioavailable, highly selective and potent **CK2** inhibitor, with **IC_{50}** values of 1 nM against CK2α and CK2α'. IC50 & Target: IC50: 1 nM (CK2α), 1 nM (CK2α')[1] ***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]. ***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 (Extracted from published papers and Only for reference)

Cell Assay: Silmitasertib (CX-4945) is dissolved in DMSO at a concentration of 5 mM.[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. **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.

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.

CAIndexNames:

Benzo[c]-2,6-naphthyridine-8-carboxylic acid, 5-[(3-chlorophenyl)amino]-

SMILES:

O=C(C1=CC=C2C3=C(C(NC4=CC=CC(Cl)=C4)=NC2=C1)C=CN=C3)O

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