FT-LSJ010

CX-4945 (Silmitasertib)

Potent and selective ATP-competitive small molecule protein kinase CK2 inhibitor with a Ki and an IC50 of 0.38 and 1 nM for recombinant human CK2α, respectively.

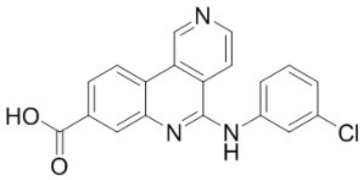
Product Description

Catalog #: LSJ010, 5 mg LSJ011, 10mg LSJ012, 50mg LSJ013, 100mg LSJ014, 250mg LSJ015, 1g

Name: **CX-4945**

Silmitasertib

Purity : >98%
CAS: [1009820-21-6]
MW: 349.77
$C_{19}H_{12}ClN_3O_2$



Solubility : 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)
H_2O : < 0.1 mg/mL (insoluble)

IC_{50} : CK2α : 1 nM CK2α' : 1 nM

Storage:

Powder	-20°C (3 years)
	4°C (2 years)
In solvent	-80°C (6 months)
	-20°C (1 month)

Technical and Scientific Information

Silmitasertib (CX-4945) is an orally bioavailable, highly selective and potent CK2 inhibitor, with IC50 values of 1 nM against CK2α and CK2α'.

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].

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Protocol (Extracted from published papers and Only for reference)

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.

AnimalAdministration [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.

Ordering information

Catalog size quantities and prices may be found at http://www.interchim.com.
Please inquire for higher quantities (availability, shipment conditions).
Please contact InterBioTech – Interchim for any other information
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