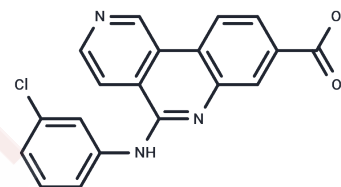


Silmitasertib

Chemical Properties

CAS No. :	1009820-21-6
Formula:	C ₁₉ H ₁₂ ClN ₃ O ₂
Molecular Weight:	349.77
Storage:	Store at low temperature Powder: -20°C for 3 years In solvent: -80°C for 1 year <small>Actual storage temperature shall be subject to the COA.</small>



Biological Description

Description	Silmitasertib (CX-4945) is a potent, orally bioavailable inhibitor of casein kinase 2 (CK2; Ki: 0.38 nM).
Targets(IC50)	Casein Kinase, Autophagy
In vitro	The antiproliferative activity of Silmitasertib (CX-4945) against cancer cells correlated with expression levels of the CK2 α catalytic subunit. CX-4945 caused cell-cycle arrest and selectively induced apoptosis in cancer cells relative to normal cells. In models of angiogenesis, CX-4945 inhibited human umbilical vein endothelial cell migration, tube formation, and blocked CK2-dependent HIF-1 α transcription in cancer cells [1]. Adding CX-4945 after bortezomib treatment, prevented leukemic cells from engaging a functional UPR in order to buffer the bortezomib-mediated proteotoxic stress in ER lumen. Bortezomib/CX-4945 treatment inhibited NF- κ B signaling in T-ALL cell lines and primary cells from T-ALL patients, but, in B-ALL cells the drug combination activated NF- κ B p65 pro-apoptotic functions [2]. CX-4945 was found to potently inhibit endogenous intracellular CK2 activity with an IC ₅₀ of 0.1 μ M in Jurkat cells. CX-4945 induced dephosphorylation of Akt(S129) and a rapid dephosphorylation of the Akt substrate p21 (T145). CX-4945 induced apoptosis in multiple cancer cell lines [3].
In vivo	When administered orally in murine xenograft models, CX-4945 was well tolerated and demonstrated robust antitumor activity with concomitant reductions of the mechanism-based biomarker phospho-p21 (T145) [1]. Mice bearing subcutaneous PC3 tumors were treated with CX-4945 (25 mg/kg, 50 mg/kg, and 75 mg/kg, po, bid). Tumor growth inhibition compared to vehicle-treated control, and a dose-responsive efficacy was observed. Last, CX-4945 was well tolerated in mice as assessed by minimal changes in body weight during the course of treatment compared to vehicle control [3].
Kinase Assay	The 238 kinase selectivity panel was conducted using the Kinase Profiler service, which utilizes a radiometric filter-binding assay. The percent inhibition of each kinase was estimated using 0.5 μ mol/L CX-4945 at ATP concentrations equivalent to the K _m value for ATP for each respective human recombinant kinase. The determination of IC ₅₀ values was done at ATP concentrations equivalent to the K _m for ATP for each kinase using 9 concentrations of CX-4945 over a range of 0.0001 to 1 μ mol/L. The K _i value (inhibition constant) for CX-4945 against recombinant CK2 was determined by graphing the IC ₅₀ values of CX-4945 determined in the presence of various concentrations of ATP

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Kinase Assay	against the concentration of ATP. The K_i value is equivalent to the Y-intercept according to the Cheng-Prussoff equation ($K_i = IC_{50}/(1+[ATP]/K_m)$), where K_i is the inhibition constant and K_m is the Michaelis constant [1].
Cell Research	Various cell lines were seeded at a density of 3000 cells per well 24 h prior to treatment, in appropriate media, and then treated with indicated concentrations of CK2 inhibitors. Suspension cells were seeded and treated on the same day. Following 4 days of incubation, 20 μ L of Alamar Blue (10% of volume/well) was added and the cells were further incubated at 37 °C for 4-5 h. Fluorescence with excitation wavelength at 530-560 nm and emission wavelength at 590 nm was measured [3].
Animal Research	Xenografts were initiated by subcutaneous injection of BxPC-3 cells into the right hind flank region of each mouse or BT-474 cells were injected into the mammary fat pad of mice implanted with estrogen pellets. When tumors reached a designated volume of 150-200 mm ³ , animals were randomized and divided into groups of 9 to 10 mice per group. CX-4945 was 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 were measured twice weekly. The length and width of the tumor were measured with calipers and the volume calculated using the following formula: tumor volume = (length \times width ²)/2. Percent tumor growth inhibition (TGI) values were calculated on the final day of the study for CX-4945-treated compared to vehicle-treated mice and were calculated as $100 \times \{1 - [(TreatedFinal\ day / TreatedDay\ 1) / (ControlFinal\ day / ControlDay\ 1)]\}$. The significance of the differences between the treated versus vehicle groups were determined using 1-way ANOVA [1].

Solubility Information

Solubility	H ₂ O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 17 mg/mL (48.6 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.859 mL	14.2951 mL	28.5902 mL
5 mM	0.5718 mL	2.859 mL	5.718 mL
10 mM	0.2859 mL	1.4295 mL	2.859 mL
50 mM	0.0572 mL	0.2859 mL	0.5718 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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