Silmitasertib

Cat. No.: HY-50855
CAS No.: 1009820-21-6
Molecular Formula: C₁₉H₁₂ClN₃O₂
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)
H₂O : < 0.1 mg/mL (insoluble)
* “≥” means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.8590 mL</td>
<td>14.2951 mL</td>
<td>28.5902 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5718 mL</td>
<td>2.8590 mL</td>
<td>5.7180 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2859 mL</td>
<td>1.4295 mL</td>
<td>2.8590 mL</td>
</tr>
</tbody>
</table>

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 IC₅₀ values of 1 nM against CK2α and CK2α'.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>IC₅₀</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 nM</td>
<td>CK2α</td>
</tr>
<tr>
<td>1 nM</td>
<td>CK2α'</td>
</tr>
</tbody>
</table>

In Vitro
Silmitasertib (CX-4945) causes cell-cycle arrest and selectively induces apoptosis in cancer cells relative to normal cells, attenuates PI3K/Akt signaling, 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 mm³, 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 × width²)/2.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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REFERENCES


