Veliparib dihydrochloride

Cat. No.: HY-10130
CAS No.: 912445-05-7
Molecular Formula: C₁₃H₁₈Cl₂N₄O
Molecular Weight: 317.21
Target: PARP; Autophagy
Pathway: Cell Cycle/DNA Damage; Epigenetics; 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
H₂O : ≥ 50 mg/mL (157.62 mM)
DMSO : ≥ 3.2 mg/mL (10.09 mM)
* “≥” means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.1525 mL</td>
<td>15.7624 mL</td>
<td>31.5249 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.6305 mL</td>
<td>3.1525 mL</td>
<td>6.3050 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3152 mL</td>
<td>1.5762 mL</td>
<td>3.1525 mL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description
Veliparib (dihydrochloride) is a potent inhibitor of PARP1 and PARP2 with Kᵢs of 5.2 nM and 2.9 nM in cell-free assays, respectively.

IC₅₀ & Target
Ki: 5.2 nM [PARP1], 2.9 nM [PARP2][¹]

In Vitro
Veliparib is inactive to SIRT2 (>5 μM)[¹]. Veliparib inhibits the PARP activity with EC₅₀ of 2 nM in C41 cells[²]. Veliparib can decrease the PAR levels in both irradiated and nonirradiated H460 cells. Veliparib reduces clonogenic survival and inhibits DNA repair by PARP-1 inhibition in H460 cells. Veliparib increases apoptosis and autophagy in H460 cells when combination with radiation[³]. Veliparib inhibits PARP activity in H1299, DU145 and 22RV1 cells and the inhibition is independent of p53 function. Veliparib (10 μM) suppresses the surviving fraction (SF) by 43% in the clonogenic H1299 cells. Veliparib shows effective radiosensitivity in oxic H1299 cells. Veliparib can attenuate the SF of hypoxic-irradiated cells including H1299, DU145 and 22RV1[⁴].

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

The oral bioavailability of Veliparib is 56%-92% in mice, SD rats, beagle dogs, and cynomolgus monkeys after oral administration\(^1\). Veliparib (25 mg/kg, i.p.) can improve tumor growth delay in a NCI-H460 xenograft model. Combination with radiation, veliparib decreases the tumor vessel formation\(^3\). Veliparib reduces intratumor PAR levels by more than 95% at a dose of 3 and 12.5 mg/kg in A375 and Colo829 xenograft models and the suppression can be maintained over time\(^4\).

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

PROTOCOL

**Kinase Assay** \(^1\)

PARP assays are conducted in a buffer containing 50 mM Tris (pH 8.0), 1 mM DTT, 1.5 μM \(^3\)H NAD\(^+\) (1.6 μCi/mmol), 200 nM biotinylated histone H1, 200 nM siDNA, and 1 nM PARP-1 or 4 nM PARP-2 enzyme. Reactions are terminated with 1.5 mM benzamide, transferred to streptavidin Flash plates, and counted using a TopCount microplate scintillation counter.

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

**Animal Administration** \(^1\)

For B16F10 syngeneic studies, 6×10\(^4\) cells are mixed with 50% Matrigel and inoculated by s.c. injection into the flank of 6- to 8-week-old female C57BL/6 mice (20 g). For cisplatin efficacy studies, female nude mice are implanted s.c. by trocar with fragments (20-30 mm\(^3\)) of human tumors harvested from s.c. grown tumors in nude mice hosts. For the carboplatin and MX-1 cyclophosphamide studies, female scid mice are inoculated with 200 μL of a 1:10 dilution of tumor brei in 45% Matrigel and 45% Spinner MEM. For these established tumor studies, tumors are allowed to grow to the indicated size and then randomized to therapy groups. For DOHH-2 xenograft studies, 1×10\(^6\) cells are mixed with 50% Matrigel and inoculated by s.c. injection into the flank of male scid mice. Veliparib is delivered by either oral route or continuous infusion using s.c. placement of 14-day Alzet OMP model 2002 in a vehicle containing 0.9% NaCl adjusted to pH 4.0. The OMP delivers at a rate of 12 μL daily and Veliparib doses are calculated accordingly. Temozolomide, cisplatin, carboplatin, and cyclophosphamide are formulated according to the manufacturers’ recommendations.

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

CUSTOMER VALIDATION

- Cancer Discov. 2017 Sep;7(9):984-998.

See more customer validations on [www.MedChemExpress.com](http://www.MedChemExpress.com)

REFERENCES


Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898       Fax: 609-228-5909       E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA