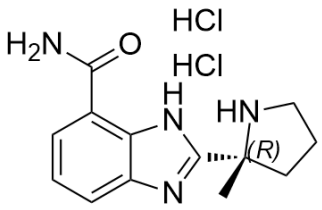
Veliparib dihydrochloride

Cat. No.:	HY-10130
CAS No.:	912445-05-7
Molecular Formula:	$C_{13}H_{18}Cl_2N_4O$
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

H_2O : ≥ 50 mg/mL (157.62 mM)
DMSO : ≥ 3.2 mg/mL (10.09 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1525 mL	15.7624 mL	31.5249 mL
	5 mM	0.6305 mL	3.1525 mL	6.3050 mL
	10 mM	0.3152 mL	1.5762 mL	3.1525 mL

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 K_is of 5.2 nM and 2.9 nM in cell-free assays, respectively.

IC_{50} & 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 EC_{50} 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 slDNA, 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.
- Clin Cancer Res. 2017 Feb 15;23(4):1001-1011.
- Theranostics. 2020 Jul 25;10(21):9477-9494.
- Neoplasia. 2019 Apr 24;21(6):533-544.
- Neoplasia. 2018 Mar 28;20(5):478-488.

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REFERENCES

[1]. Donawho CK, et al. ABT-888, an orally active poly(ADP-ribose) polymerase inhibitor that potentiates DNA-damaging agents in preclinical tumor models. Clin Cancer Res. 2007 May 1;13(9):2728-37.

[2]. Penning TD, et al. Discovery of the Poly(ADP-ribose) polymerase (PARP) inhibitor 2-[(R)-2-methylpyrrolidin-2-yl]-1H-benzimidazole-4-carboxamide (ABT-888) for the treatment of cancer. J Med Chem. 2009 Jan 22;52(2):514-23.

[3]. Albert JM, et al. Inhibition of poly(ADP-ribose) polymerase enhances cell death and improves tumor growth delay in irradiated lung cancer models. Clin Cancer Res. 2007 May 15;13(10):3033-42.

[4]. Robert J. Kinders, et al. Preclinical Modeling of a Phase 0 Clinical Trial: Qualification of a Pharmacodynamic Assay of Poly (ADP-Ribose) Polymerase in Tumor Biopsies of Mouse Xenografts. Clin Cancer Res. Author manuscript; available in PMC 2009 Nov 1.

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