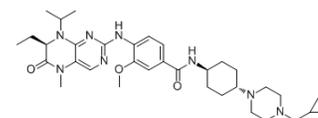


Volasertib

Cat. No.:	HY-12137		
CAS No.:	755038-65-4		
Molecular Formula:	C ₃₄ H ₅₀ N ₈ O ₃		
Molecular Weight:	618.81		
Target:	Polo-like Kinase (PLK)		
Pathway:	Cell Cycle/DNA Damage		
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 : 50 mg/mL (80.80 mM; Need ultrasonic)					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
		1 mM		1.6160 mL	8.0800 mL	16.1600 mL
		5 mM		0.3232 mL	1.6160 mL	3.2320 mL
		10 mM		0.1616 mL	0.8080 mL	1.6160 mL
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.04 mM); Clear solution					
	2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (4.04 mM); Clear solution					
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.04 mM); Clear solution					

BIOLOGICAL ACTIVITY

Description	Volasertib is a highly potent Polo-like kinase 1 (PLK1) inhibitor with an IC₅₀ of 0.87 nM, as well as the two closely related kinases PLK2 and PLK3 with IC₅₀ s of 5 and 56 nM, respectively.
IC ₅₀ & Target	IC ₅₀ : 0.87 nM (PLK1), 5 nM (PLK2), 56 nM (PLK3) ^[3]
In Vitro	Volasertib is potent against HeLa and Caski cells with IC ₅₀ values of 0.02 μM and 2.02 μM, respectively. Volasertib

	(0.03 μ M) induces cell cycle arrest at G2/M Phase in cervical cancer cells. Volasertib (0.003-0.03 μ M) induces apoptosis in HeLa cells, and Volasertib (0.3-3 μ M) results in Caski cell apoptosis. Volasertib (1, 3 μ M or 0.01,0.03 μ M) augments the fluorescent intensity of DHE in Caski and HeLa cells in a dose-dependent manner ^[1] . Volasertib shows inhibitory activities against the proliferation of all 40 cell lines tested, with a mean half-maximal growth inhibitory concentration of 313 nM (range: 4-5000 nM) ^[2] . Volasertib inhibits proliferation of multiple cell lines derived from various cancer tissues, including carcinomas of the colon (HCT 116, EC ₅₀ =23 nM) and lung (NCI-H460, EC ₅₀ =21 nM), melanoma (BRO, EC ₅₀ =11 nM), and hematopoietic cancers (GRANTA-519, EC ₅₀ =15 nM; HL-60, EC ₅₀ =32 nM; THP-1, EC ₅₀ =36 nM and Raji, EC ₅₀ =37 nM) with EC ₅₀ values of 11 to 37 nM. Volasertib (100 nM) causes G2-M arrest and induces apoptosis in NCI-H460 cells ^[3] .
In Vivo	Volasertib (15 mg/kg, i.p.) potentiates the activity of cisplatin to inhibit xenograft tumor growth of cervical cancer cells in nude mice ^[1] . Volasertib (70 mg/kg, p.o. once a week or 10 mg/kg, p.o. daily) significantly delays tumor growth in a non-small cell lung carcinoma xenograft model. In addition, Volasertib (15 mg/kg, i.v.) markedly suppresses tumor growth and is well tolerated ^[3] .

PROTOCOL

Kinase Assay ^[3]	Enzyme activity assays for Plk1, Plk2, and Plk3 are done in the presence of serially diluted inhibitor using 20 ng of recombinant kinase and 10 μ g casein from bovine milk as substrate. Kinase reactions are done in a final volume of 60 μ L for 45 min at 30°C [15 mM MgCl ₂ , 25 mM MOPS (pH 7.0), 1 mM DTT, 1% DMSO, 7.5 μ M ATP, 0.3 μ Ci γ - ³² P-ATP]. Reactions are terminated by the addition of 125 μ L of ice-cold 5% TCA. After transferring the precipitates to MultiScreen mixed ester cellulose filter plates, plates are washed with 1% TCA and quantified radiometrically. Dose-response curves are used for calculating IC ₅₀ values. To establish a kinase selectivity profile, additional kinase assays are done by contract research organizations or reagents are purchased from commercial sources and assays are done according to the supplier's instructions. Appropriate positive and negative controls are included in the assay design. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay ^[1]	Cells are firstly seeded into a 96-well plate at a density of 5000 cells per well, and incubated with drugs in three parallel wells for 72 hr. Then MTT is added to each well at a final concentration of 0.5 mg/mL. After incubation for 4 hr, formazan crystals are dissolved in 100 μ L of DMSO, and absorbance at 570 nm is measured by plate reader. The concentrations required to inhibit growth by 50% (IC ₅₀) are calculated from survival curves ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration ^[3]	Female BomTac: NMRI-Foxn1nu mice are grafted s.c. with 2 \times 10 ⁶ HCT 116 human colon carcinoma cells (ATCC CCL-247), 1 \times 10 ⁶ NCI-H460 non-small cell lung cancer cells (ATCC HTB-177), or CXB1 human colon carcinoma tumor pieces derived from patient material by serial transplantation in nude mice. When tumors have reached a volume of appr 50 to 100 mm ³ , animals are randomized into treatment and control groups of 10 mice each. Volasertib is formulated in hydrochloric acid (0.1 N), diluted with 0.9% NaCl, and injected i.v. into the tail vein at the indicated dose and schedule. For oral treatment, Volasertib is resuspended in 0.5% Natrosol 250 hydroxyethyl-cellulose and given intragastrally via gavage needle. An administration volume of 10 mL per kilogram of body weight is used for both administration routes. Tumor volumes are determined thrice a week using a caliper. The results are converted to tumor volume (mm ³) by the formula length \times width ² \times π /6. The weight of the mice is determined as an indicator of tolerability on the same days. Median tumor volumes on the last day of the experiment are used to calculate treated versus control values (= tumor volumetreated mice \times 100/tumor volumecontrol mice). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- *Mol Cancer Ther.* 2018 Apr;17(4):825-837.
- *Biochim Biophys Acta.* 2018 May;1862(5):1134-1147.
- *Cell Physiol Biochem.* 2017 Oct 16;43(4):1.
- *Sci Rep.* 2017 Sep 8;7(1):11026.
- *PLoS Negl Trop Dis.* 2016 Jan 11;10(1):e0004356.

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REFERENCES

- [1]. Xie FF, et al. Volasertib suppresses tumor growth and potentiates the activity of cisplatin in cervical cancer. *Am J Cancer Res.* 2015 Nov 15;5(12):3548-59.
- [2]. Abbou S, et al. Polo-like Kinase Inhibitor Volasertib Exhibits Antitumor Activity and Synergy with Vincristine in Pediatric Malignancies. *Anticancer Res.* 2016 Feb;36(2):599-609.
- [3]. Rudolph D, et al. BI 6727, a Polo-like kinase inhibitor with improved pharmacokinetic profile and broad antitumor activity. *Clin Cancer Res.* 2009 May 1;15(9):3094-102. Epub
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Caution: Product has not been fully validated for medical applications. For research use only.

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