Volasertib

Cat. No.: HY-12137

CAS No.: 755038-65-4

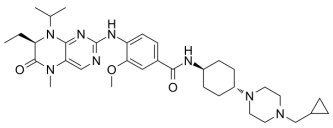
Molecular Formula: $C_{34}H_{50}N_8O_3$

Molecular Weight: 618.81

Target: Polo-like Kinase (PLK); Apoptosis

Pathway: Cell Cycle/DNA Damage; Apoptosis

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (80.80 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	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 >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.36 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Volasertib (BI 6727) is an orally active, highly potent and ATP-competitive Polo-like kinase 1 (PLK1) inhibitor with an IC_{50} of 0.87 nM. Volasertib inhibits PLK2 and PLK3 with IC_{50}s of 5 and 56 nM, respectively. Volasertib induces mitotic arrest and apoptosis. Volasertib, a dihydropteridinone derivative, shows marked antitumor activity in multiple cancer models[1][2].

IC_{50} & Target	PLK1	PLK2	PLK3
	0.87 nM (IC_{50})	5 nM (IC_{50})	56 nM (IC_{50})

In Vitro

Volasertib (BI 6727; 0.01-10000 nM; 72 hours) has EC_{50} values of 11 to 37 nmol/L in multiple cell lines[1].
Volasertib (10-1000 nM; 24 hours) results accumulation of cells with 4N DNA content, indicative of a cell cycle block in G2-M

phase[1].
Volasertib (100 nM; 24-72 hours) induces cell apoptosis at 48 hours[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	Multiple cell lines
Concentration:	0.01-10000 nM
Incubation Time:	72 hours
Result:	Inhibited proliferation of multiple cell lines derived from various cancer tissues, including carcinomas of the colon (HCT 116, EC_{50}=23 nmol/L) and lung (NCI-H460, EC_{50}=21 nmol/L), melanoma (BRO, EC_{50}=11 nmol/L), and hematopoietic cancers (GRANTA-519, EC_{50}=15 nmol/L; HL-60, EC_{50}=32 nmol/L; THP-1, E_{50}=36 nmol/L and Raji, EC_{50}=37 nmol/L) with EC_{50} values of 11 to 37 nmol/L.

Apoptosis Analysis[1]

Cell Line:	NCI-H460 cells
Concentration:	100 nM
Incubation Time:	24, 48, 72 hours
Result:	G2-M arrest at 24 hours was followed by induction of apoptosis at 48 hours.

Cell Cycle Analysis[1]

Cell Line:	NCI-H460 cells
Concentration:	10, 30, 100, 300, 1000 nM
Incubation Time:	24 hours
Result:	Resulted in accumulation of cells with 4N DNA content, indicative of a cell cycle block in G2-M phase.

In Vivo

Volasertib (BI 6727; A total weekly dose of 50 mg/kg; Oral; once a week, twice a week, or daily; for 40 days) shows comparable efficacy in human colon carcinoma xenograft models[1].
Volasertib (15, 20, or 25 mg/kg/day; i.v.; 2 consecutive days per week; for 40 days) leads to significant tumor growth delay and even tumor regression in human colon carcinoma xenograft models [1].
Volasertib (70 mg/kg given once weekly or 10 mg/kg daily; oral) significantly delays tumor growth in a non-small cell lung carcinoma xenograft model derived from NCI-H460 cells[1].
Volasertib (a single dose of 40 mg/kg; iv) causes a significant (13-fold) increase in mitotic cells in HCT 116 tumor-bearing nude mice[1].
Volasertib has high volume of distribution and a long terminal half-life in mice (V_{ss}=7.6 L/kg, $t_{1/2}$=46 h) and rats (V_{ss}=22 L/kg, $t_{1/2}$=54 h)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BomTac:NMRI-Foxn1^{nu} mice (Taconic) were grafted s.c. with HCT 116 human colon carcinoma cells (ATCC CCL-247)[1]
Dosage:	A total weekly dose of 50 mg/kg
Administration:	Oral; once a week, twice a week, or daily; for 40 days

Result:	Showed comparable efficacy and were well tolerated.

Animal Model:	Female BomTac:NMRI-Foxn1^{nu} mice and male Wistar rats of the strain Crl:WI[1]
Dosage:	35 mg/kg (mice) or 10 mg/kg (rat) (Pharmacokinetic Analysis)
Administration:	IV 5-minute infusion; a single dose 5-minute infusion
Result:	Had high volume of distribution and a long terminal half-life in mice (V_{ss}=7.6 L/kg, $t_{1/2}$=46 h) and rats (V_{ss}=22 L/kg, $t_{1/2}$=54 h).

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2020 Aug 13;11(1):4053.
- Mol Cancer Ther. 2018 Apr;17(4):825-837.
- Bioorg Chem. 20 November 2021, 105505.
- Pharmaceutics. 2022 Jun 6;14(6):1209.

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REFERENCES

[1]. Xie FF, et al. Volasertib suppresses tumor growth in cervical cancer. Am J Cancer Res. 2015 Nov 15;5(12):3548-59.

[2]. 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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