Volasertib trihydrochloride

Cat. No.: HY-12137A

CAS No.: 946161-17-7

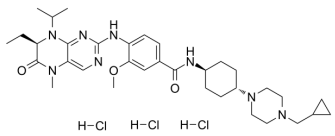
Molecular Formula: $C_{34}H_{53}Cl_3N_8O_3$

Molecular Weight: 728.2

Target: Polo-like Kinase (PLK); Apoptosis

Pathway: Cell Cycle/DNA Damage; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Volasertib (BI 6727) trihydrochloride is an orally active, highly potent and ATP-competitive Polo-like kinase 1 (PLK1) inhibitor with an IC_{50} of 0.87 nM. Volasertib trihydrochloride inhibits PLK2 and PLK3 with IC_{50}s of 5 and 56 nM, respectively. Volasertib trihydrochloride induces mitotic arrest and apoptosis. Volasertib trihydrochloride, 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 trihydrochloride (BI 6727 trihydrochloride; 0.01-10000 nM; 72 hours) has EC_{50} values of 11 to 37 nmol/L in multiple cell lines[1].

Volasertib trihydrochloride (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 trihydrochloride (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 trihydrochloride (BI 6727 trihydrochloride; 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 trihydrochloride (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 trihydrochloride (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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