Alpelisib

Cat. No.: HY-15244

CAS No.: 1217486-61-7

Molecular Formula: $C_{19}H_{22}F_3N_5O_2S$

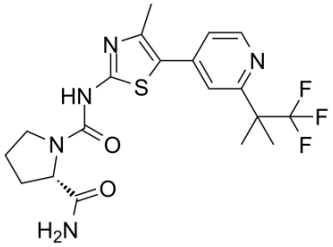
Molecular Weight: 441.47

Target: PI3K

Pathway: PI3K/Akt/mTOR

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 : 83.33 mg/mL (188.76 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2652 mL	11.3258 mL	22.6516 mL
5 mM	0.4530 mL	2.2652 mL	4.5303 mL
10 mM	0.2265 mL	1.1326 mL	2.2652 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 (4.71 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.71 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.71 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 5 mg/mL (11.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Alpelisib (BYL-719) is a potent, selective, and orally active PI3Kα inhibitor. Alpelisib (BYL-719) shows efficacy in targeting PIK3CA-mutated cancer. Alpelisib (BYL-719) also inhibits p110α/p110γ/p110δ/p110β with IC_{50}s of 5/250/290/1200 nM, respectively. Antineoplastic activity[1][2][3].

IC_{50} & Target	p110α	p110γ	p110δ	p110β

	5 nM (IC_{50})	250 nM (IC_{50})	290 nM (IC_{50})	1200 nM (IC_{50})
	p110α-H1047R 4 nM (IC_{50})	p110α-E545K 4 nM (IC_{50})		

In Vitro

Alpelisib (BYL-719) potently inhibits the 2 most common PIK3CA somatic mutations (H1047R, E545K; IC_{50}s~4 nM). Alpelisib potently inhibits Akt phosphorylation in cells transformed with PI3Kα (IC_{50}=74±15 nM) and shows significant reduced inhibitory activity in PI3Kβ or PI3Kδ isoforms transformed cells (≥15-fold compared with PI3Kα)[2].
Alpelisib (BYL-719, 0-50 μM; 72 hours) inhibits the cell growth of osteosarcoma cell lines MG63, HOS, POS-1 and MOS-J in a dose-dependent manner[3].
Alpelisib (BYL-719) significantly alters the distribution of cell cycle phases. Alpelisib (BYL-719, 25 μM; 18 hours) induces a cell cycle arrest in the G0/G1 phase of human and murine osteosarcoma cell lines[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[3]

Cell Line:	MG63, HOS, POS-1, MOS-J
Concentration:	10, 20, 30, 40, 50 μM
Incubation Time:	72 hours
Result:	Inhibited the cell growth of all osteosarcoma cell lines tested in a dose-dependent manner with IC_{50}s of 6-15 μM and with IC_{90}s of 24-42 μM.

Cell Cycle Analysis[3]

Cell Line:	MG63, HOS, POS-1, MOS-J
Concentration:	25 μM
Incubation Time:	18 hours
Result:	Induced a cell cycle arrest in the G0/G1 phase of human and murine osteosarcoma cell .

In Vivo

Alpelisib (BYL-719) (12.5 mg/kg and 50 mg/kg for C57Bl/6J mice; 50 mg/kg for female Rj:NMRI-nude mice; oral administration; daily) significantly reduces tumor volumes and deposition of ectopic bone matrix[3].
Alpelisib has moderate terminal elimination half-life ($t_{1/2}$=2.9±0.2 h) for rat (1 mg/kg, iv) [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	A 5-week-old female Rj:NMRI-nude mice with human HOS-MNNG osteosarcoma cells; A 5-week-old male C57Bl/6J mice with mouse MOS-J osteosarcoma cells[3]
Dosage:	12.5 mg/kg and 50 mg/kg for C57Bl/6J mice; 50 mg/kg for female Rj:NMRI-nude mice
Administration:	Oral administration; daily
Result:	Significantly reduced tumor volumes and simultaneously reduced tumor growth.

Animal Model:	Female Sprague Dawley rats [1]
Dosage:	1 mg/kg (Pharmacokinetic Analysis)
Administration:	I.V.
Result:	$t_{1/2}$=2.9±0.2 hours.

CUSTOMER VALIDATION

- Nature. 2018 Jun;558(7711):540-546.
- Science. 2017 Dec 1;358(6367). pii: eaan4368.
- Cancer Discov. 2020 Aug;10(8):1226-1239.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Blood. 2019 Jan 3;133(1):70-80.

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REFERENCES

[1]. Furet P, et al. Discovery of NVP-BYL719 a potent and selective phosphatidylinositol-3 kinase alpha inhibitor selected for clinical evaluation. Bioorg Med Chem Lett. 2013 Jul 1;23(13):3741-8.

[2]. Fritsch C, et al. Characterization of the novel and specific PI3Kα inhibitor NVP-BYL719 and development of the patient stratification strategy for clinical trials. Mol Cancer Ther. 2014 May;13(5):1117-29.

[3]. Gobin B, et al. BYL719, a new α-specific PI3K inhibitor: single administration and in combination with conventional chemotherapy for the treatment of osteosarcoma. Int J Cancer. 2015 Feb 15;136(4):784-96.

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