Luminespib

Cat. No.: HY-10215

CAS No.: 747412-49-3

Molecular Formula: $C_{26}H_{31}N_3O_5$

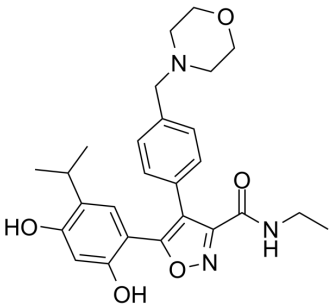
Molecular Weight: 465.54

Target: HSP; Autophagy; Apoptosis

Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 62 mg/mL (133.18 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1480 mL	10.7402 mL	21.4804 mL
	5 mM	0.4296 mL	2.1480 mL	4.2961 mL
	10 mM	0.2148 mL	1.0740 mL	2.1480 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: ≥ 2.5 mg/mL (5.37 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.37 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.37 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.37 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Luminespib (VER-52296) is a potent HSP90 inhibitor with IC_{50}s of 7.8 and 21 nM for HSP90α and HSP90β, respectively[1].

IC_{50} & Target	HSP90α	HSP90β	GRP94	TRAP-1
	7.8 nM (IC_{50})	21 nM (IC_{50})	535 nM (IC_{50})	85 nM (IC_{50})

In Vitro

Luminespib is a potent and selective HSP90 inhibitor, with IC_{50}s and K_is of 21 ± 16, 8.2 ± 0.7 nM against HSP90β and of 7.8 ± 1.8, 9.0 ± 5.0 nM for HSP90α. Luminespib shows weak activity against GRP94 and TRAP-1 wich IC_{50}s of 535 ± 51 nM (K_i, 108 nM) and 85 ± 8 nM (K_i, 53 nM), respectively. Luminespib exhibits inhibitory effect on proliferation of various human tumor cell lines (2.3-49.6 nM), induces cell cycle arrest and apoptosis and depletes client proteins in human cancer cells (80 nM)[1]. Luminespib (100 nM) significantly reduces CD40L fibroblast-induced changes in immunophenotype and STAT3 signaling but with no effect on the viability of chronic lymphocytic leukemia (CLL) cells. Luminespib (500 nM) in combination with NSC 118218 more effectively induces apoptosis in cells in co-culture than either drug alone, and overcomes fibroblast-derived resistance to Hsp90 inhibitor[2]. Luminespib shows great inhibition of pancreatic cancer cells with IC_{50} of at 10 nM. Luminespib (10 nM) reduces the expression and the epidermal growth factor (EGF)-mediated activation of EGFR and substantially disrupts EGF signaling in terms of diminishing downstream phosphorylation of $ERK^{Thr202/Tyr204}$. Luminespib (10 nM) significantly blocks pancreatic cancer cell migration and invasion both in the absence and presence of EGF[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Luminespib (50, 75 mg/kg, i.p.) significantly inhibits tumor growth rate, reducing the mean weights of tumors on day 11 in human tumor xenografts[2]. Luminespib (50 mg/kg/week, 3×25 mg/kg/week) significantly reduces tumor growth rates and lowers tumor weights in the L3.6pl pancreatic cancer cell-bearing mice model[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]

Cell lines are grown in DMEM/10% FCS, 2 mM glutamine, and nonessential amino acids in a humidified atmosphere of 5% CO_2 in air. All lines are free of Mycoplasma. Cell proliferation is determined using the SRB assay for tumor cells and prostate epithelial cells, the WST-1 assay for MCF10A and HB119, or an alkaline phosphatase assay for HUVEC and HDMEC. GI_{50} is the compound concentration inhibiting cell proliferation by 50% compared with vehicle controls. Active caspase-3/7 is measured using a homogenous caspase assay kit[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1]

Mice[1]

For efficacy studies, human tumor xenografts are established s.c. in athymic mice. WM266.4 cells are also injected i.v. to generate experimental lung metastases and PC3LN3 prostate carcinoma cells are implanted into the prostates of male mice. Dosing by i.p. with Luminespib commences when tumors are well established. Tumor growth is monitored and at study end samples are harvested for analysis[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Blood. 2018 Jul 19;132(3):307-320.
- Nat Commun. 2017 Sep 4;8(1):422.
- Clin Cancer Res. 2018 Feb 15;24(4):794-806.
- Leukemia. 2019 Jun;33(6):1373-1386.
- J Biomed Sci. 2021 Jul 23;28(1):55.

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REFERENCES

[1]. Eccles, Suzanne A., et al. NVP-AUY922: A Novel Heat Shock Protein 90 Inhibitor Active against Xenograft Tumor Growth, Angiogenesis, and Metastasis. Cancer Research (2008), 68(8), 2850-2860.

[2]. Best OG, et al. Heat shock protein-90 inhibitor, NVP-AUY922, is effective in combination with NSC 118218 against chronic lymphocytic leukemia cells cultured on CD40L-stromal layer and inhibits their activated/proliferative phenotype. Leuk Lymphoma. 2012 J

[3]. Moser C, et al. Stoeltzing O.Targeting HSP90 by the novel inhibitor NVP-AUY922 reduces growth and angiogenesis of pancreatic cancer. Anticancer Res. 2012 Jul;32(7):2551-61.

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