Risovalisib

Cat. No.: HY-123938

CAS No.: 1494684-28-4

Molecular Formula: $C_{24}H_{29}F_3N_8O_5S$

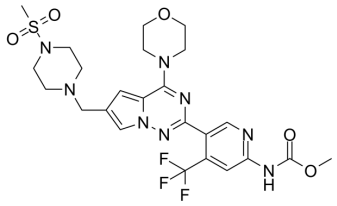
Molecular Weight: 598.6

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 : 50 mg/mL (83.53 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6706 mL	8.3528 mL	16.7056 mL
	5 mM	0.3341 mL	1.6706 mL	3.3411 mL
	10 mM	0.1671 mL	0.8353 mL	1.6706 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Risovalisib (CYH33) is an orally active, highly selective PI3Kα inhibitor with IC_{50}s of 5.9 nM/598 nM/78.7 nM/225 nM against α/β/δ/γ isoform, respectively. Risovalisib inhibits phosphorylation of Akt, ERK and induces significant G1 phase arrest in breast cancer cells and non-small cell lung cancer (NSCLC) cells. Risovalisib has potent activity against solid tumors[1][2][3].

IC_{50} & Target

PI3Kα	PI3Kβ	PI3Kδ	PI3Kγ
5.9 nM (IC_{50})	598 nM (IC_{50})	78.7 nM (IC_{50})	225 nM (IC_{50})

In Vitro

Risovalisib (CYH33) inhibits cell proliferation with IC_{50}s below 1 μM in 56% (18/32) of the breast cancer cell lines[2].

CYH33 (0.012-1 μM; for 24 hours) significantly arrests T47D and MCF7 cells in G1 phase in a concentration-dependent manner [2].

CYH33 (4-1000 nM; 1 hour) concurrently inhibits phosphorylation of ERK and Akt in both T47D and MCF7 cells[2].

CYH33 (0.11-1 μM; 24 hours) fails to induce apoptosis in MCF7 and MDA-MB-231 cells[2].

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

Cell Cycle Analysis[2]

Cell Line:	Sensitive T47D, MCF7 and resistant MDA-MB-231 cells
Concentration:	0.012, 0.037, 0.11, 0.33, 1 μM
Incubation Time:	For 24 hours
Result:	Arrested T47D and MCF7 cells in G1 phase in a concentration-dependent manner, accompanied with concomitant reduced cell population in S phase. Had little effect on cell cycle distribution in resistant MDA-MB-231 cells.

Western Blot Analysis[2]

Cell Line:	Sensitive T47D, MCF7 and resistant MDA-MB-231 cells
Concentration:	4, 12, 37, 111, 333, 1000 nM
Incubation Time:	1 hour
Result:	Concurrently inhibited phosphorylation of ERK and Akt in both T47D and MCF7 cells, whereas it had little effect on phosphorylated ERK (pERK) in MDA-MB-231 cells up to 1 μM.

In Vivo

Risovalisib (CYH33) (2-20 mg/kg; oral; once a day for 21 days) potently restrains tumor growth in mice bearing human breast cancer cell xenografts[2].

Single administration of CYH33 (20 mg/kg; oral) significantly down-regulates the level of phosphorylated Akt in tumor tissues, demonstrating the suppression of PI3K signaling in nude mice[2].

CYH33 (10 mg/kg; oral; once a day for 18-d or 20-d respectively) delays the restoration of blood glucose and area under the curve (AUC) of blood glucose increased upon CYH33 treatment in T47D xenografts and R26-Pik3ca^{H1047R};MMTV-Cre mice[2].

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

Animal Model:	SCID mice aged 4-6 weeks bearing human breast cancer T47D xenografts[2]
Dosage:	2, 5, 10, 20 mg/kg
Administration:	Oral; once a day for 21 days
Result:	Displayed marginal inhibitory effect on the tumor growth at lower doses (2 and 5 mg/kg) and significantly attenuated tumor growth at the dose of 10 or 20 mg/kg, yielding T/C values of 58.36% and 49.42% respectively.

REFERENCES

[1]. Haoyue Xiang, et al. Abstract LB-268: Discovery of clinical candidate methyl (5-(6-((4-(methylsulfonyl)piperazin-1-yl)methyl)-4-morpholinopyrrolo[2,1-f][1,2,4]triazin-2-yl)-4-(trifluoromethyl)pyridin-2-yl)carbamate (CYH33) : A highly potent and selective PI3K alpha inhibitor for the treatment of advanced solid tumors. AACR Annual Meeting 2018; April 14-18, 2018

[2]. Xue-Ling Liu, et al. Decrease in Phosphorylated ERK Indicates the Therapeutic Efficacy of a Clinical PI3Kα-selective Inhibitor CYH33 in Breast Cancer. Cancer Lett. 2018 Oct 1;433:273-282.

[3]. Yuxiang Wang, et al. Simultaneous inhibition of PI3Kα and CDK4/6 synergistically suppresses KRAS-mutated non-small cell lung cancer. Cancer Biol Med. 2019 Feb;16(1):66-83.

Caution: Product has not been fully validated for medical applications. For research use only.

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