MTI-31

Cat. No.: HY-126077

CAS No.: 1567915-38-1

Molecular Formula: $C_{26}H_{30}N_6O_3$

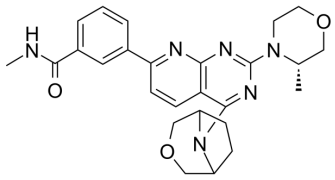
Molecular Weight: 474.55

Target: mTOR

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 : 8.33 mg/mL (17.55 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1073 mL	10.5363 mL	21.0726 mL
	5 mM	0.4215 mL	2.1073 mL	4.2145 mL
	10 mM	0.2107 mL	1.0536 mL	2.1073 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.83 mg/mL (1.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MTI-31 (LXI-15029) is a potent, orally active and highly selective inhibitor of mTORC1 and mTORC2. MTI-31 is selective for mTOR (K_d: 0.20 nM) versus PIK3CA, PIK3CB and PIK3G with >5,000 fold selectivity in mTOR binding assays. MTI-31 shows an IC_{50} of 39 nM for mTOR in LANCE assay of mTOR substrate phosphorylation with 100 μM ATP. MTI-31 can be used for the research of breast cancer[1].

IC_{50} & Target			
mTOR	mTOR	mTORC1	mTORC2
0.2 nM (Ki)	39 nM (IC_{50}, 100 μM ATP)		

In Vitro

MTI-31 acts as a potent and selective inhibitor of mTOR enzymatic activity capable of targeting both mTORC1 and mTORC2 functions in cancer cells[1].

MTI-31 (0.01-100 μM) elicits a potent and more substantial inhibition of cell growth than that of Rapamycin[1].

Treatment with MTI-31 for 6 h demonstrates a dose-dependent inhibition of both the mTORC1 substrates P-S6K1(T389), P-

S6(S235/6), P-4EBP1(T70) and mTORC2 substrate P-AKT(S473), achieving 50% inhibition at ≤0.12 μM in three representative tumor cell lines harboring mTOR pathway dysregulation (786-O renal, U87MG glioma and MDA-MB-453 breast)[1].
MTI-31-induced apoptosis requires mTORC2-regulated Bim- and GSK3 activity[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	MDA-MB-453 cells
Concentration:	0.01, 0.1, 1, 10, 100 μM
Incubation Time:	3 days
Result:	Significantly inhibited cellular proliferation after treatment for 3 days.

Western Blot Analysis[1]

Cell Line:	786-O renal, U87MG glioma and MDA-MB-453 breast cells
Concentration:	0.12, 0.37, 1.11, 3.33, 10 μM
Incubation Time:	6 hours
Result:	Demonstrated a dose-dependent inhibition of both the mTORC1 substrates P-S6K1(T389), P-S6(S235/6), P-4EBP1(T70) and mTORC2 substrate P-AKT(S473).

In Vivo

MTI-31 is a potent mTOR inhibitor in vivo and elicits strong antitumor efficacy. MTI-31(5-40 mg/kg; orally) is efficacious in several tumor models harboring HER2+/PIK3CAmut and/or PTEN-deficiency exemplified by MDA-MB-453 and 786-O[1].
Treatment of tumor bearing nude mice with orally administered MTI-31 inhibits growth of H1975 tumors (25 mg/kg/d; orally) or U87MG tumors (30 mg/kg/d; orally)[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female nude mice bearing tumors of MDA-MB-453, 786-O or HCC1806[1]
Dosage:	2.5, 5, 10, 20, 40 mg/kg for MDA-MB-453 and 786-O; 20 and 40 mg/kg for HCC1806
Administration:	Treated orally via a once daily (qd) regimen
Result:	Was efficacious in several tumor models harboring HER2+/PIK3CAmut and/or PTEN-deficiency exemplified by MDA-MB-453 and 786-O. Demonstrated a dose proportional tumor growth inhibition (TGI) with a minimum efficacious dose (MED) of 5 mg/kg (>50% TGI, $p<0.01$) and a maximum tolerated dose (MTD) of 40 mg/kg (7-15% body weight loss without mortality). In contrast, had limited efficacy in the HER2-/PIK3CAwt HCC1806 breast tumor model even at the highest 40 mg/kg.

REFERENCES

[1]. Zhang Q, et, al. A Novel mTORC1/2 Inhibitor (MTI-31) Inhibits Tumor Growth, Epithelial-Mesenchymal Transition, Metastases, and Improves Antitumor Immunity in Preclinical Models of Lung Cancer. Clin Cancer Res. 2019 Jun 15;25(12):3630-3642.

[2]. Qian J, et, al. Molecular regulation of apoptotic machinery and lipid metabolism by mTORC1/mTORC2 dual inhibitors in preclinical models of HER2+/PIK3CAmut breast cancer. Oncotarget. 2016 Oct 11;7(41):67071-67086.

[3]. Wang X, et, al. Non-immunogenic, low-toxicity and effective glioma targeting MTI-31 liposomes . J Control Release. 2019 Dec 28;316:381-392.

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

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