Tinodasertib

Cat. No.: HY-112424

CAS No.: 1464151-33-4

Molecular Formula: $C_{25}H_{20}N_4O_2$

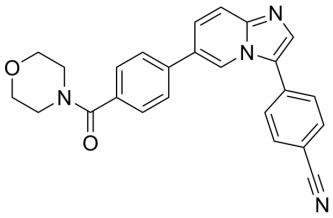
Molecular Weight: 408.45

Target: MNK

Pathway: MAPK/ERK Pathway

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (122.41 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4483 mL	12.2414 mL	24.4828 mL
5 mM	0.4897 mL	2.4483 mL	4.8966 mL
10 mM	0.2448 mL	1.2241 mL	2.4483 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: ≥ 5 mg/mL (12.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (12.24 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (12.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tinodasertib (ETC-206) is a selective MNK1 and MNK2 inhibitor with IC_{50}s of 64 nM and 86 nM, respectively.

IC_{50} & Target

MNK1	MNK2
64 nM (IC_{50})	86 nM (IC_{50})

In Vitro

Tinodasertib (ETC-206) inhibits eIF4E phosphorylation in HeLa cell line with an IC_{50} of 321 nM. The anti-proliferative effects

	of ETC-206 are assessed in vitro, using CellTiter-Glo viability assay against 25 hematological cancer cell lines including the K562 cell line that overexpresses eIF4E (K562 o/e eIF4E). The IC_{50}s are 1.71 μM, 3.36 μM, 3.70 μM, 4.81 μM, 5.13 μM, 5.05 μM, 6.70 μM, 9.76 μM, and 48.8 μM for SU-DHL-6, GK-5, MC 116, P3HR-1, DOHH2, MPC-11, Ramos.2G6.4C10, AHH-1, and K562 o/e eIF4E cells, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The antitumor effect of ETC-206 is then assessed in a K562 e/o eIF4E mouse xenograft model after oral administration at 25, 50, or 100 mg/kg alone or in combination with a 2.5 mg/kg fixed dose of Dasatinib throughout the study. Dasatinib at 2.5 mg/kg elicits a tumor growth inhibition (TGI) of 88% with one tumor-free animal. In contrast, ETC-206 alone only yields a maximum TGI of 23% at the highest administered dose of 100 mg/kg, which does not impede tumor growth, and is similar to the nontreated animals. ETC-206 with 2.5 mg/kg of Dasatinib not only increases tumor growth inhibition in a dose-dependent manner but, more importantly leads to 2, 5, and 8 out of 8 tumor-free animals at 25, 50, and 100 mg/kg, respectively. The combination of ETC-206 and Dasatinib inhibits tumor growth at all tested doses, and no weight loss is recorded. Both the combination of ETC-206 and Dasatinib and, on the other hand, the dual MNK1/2 and BCR-ABL1 inhibitors prevent tumor growth in the same mouse xenograft model. ETC-206 has moderate terminal elimination half-life ($t_{1/2}$=1.7 h, and 1.77 h for mouse (1 mg/kg, i.v.), mouse (5 mg/kg, p.o.))[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The anti-proliferative effects of ETC-206 are assessed in vitro, using CellTiter-Glo viability assay against 25 hematological cancer cell lines including the K562 cell line that overexpresses eIF4E (K562 o/e eIF4E). The IC_{50}s are in general in the micromolar range[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] CD-1 female mice (6-8 weeks old) are weighed, and those selected for dosing are 24±2 g. Three mice are randomly grouped per time point. Mice are administered a single dose of 1 mg/kg of ETC-206 via tail vein injection or a single dose of 5 mg/kg of ETC-206 via oral gavage. The volume of injection for intravenous (i.v.) and oral (p.o.) administration is 4 mL/kg and 8 mL/kg, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Yang H, et al. Optimization of Selective Mitogen-Activated Protein Kinase Interacting Kinases 1 and 2 Inhibitors for the Treatment of Blast Crisis Leukemia. J Med Chem. 2018 May 24;61(10):4348-4369.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA