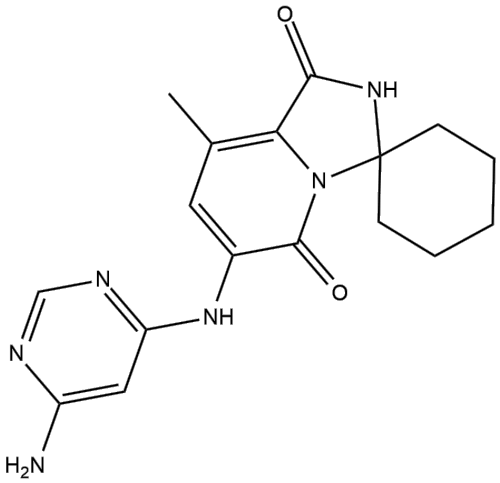
Product Data Sheet

Product Name: Tomivosertib
Cat. No.: GC19131

Chemical Properties

Cas. No.	1849590-01-7		
SMILES	O=C(C1=C(C)C=C(NC2=NC=NC(N)=C2)C(N13)=O)NC43CCCCC4		
Formula	$C_{17}H_{20}N_6O_2$	M.Wt	340.38
Solubility	DMSO : 4.35 mg/mL (12.78 mM);Water : < 0.1 mg/mL (insoluble)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines	U937, MV411, MM6, KG-1, and THP-1 acute myeloid leukemia (AML) cell lines, as well as primary leukemic precursors from AML patients

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Preparation Method	Cells were cultured as previously described. For viability and clonogenic assays, cells were treated with Tomivosertib at indicated doses. For eIF4E phosphorylation assessment, cells were treated with increasing doses of Tomivosertib.
Reaction Conditions	0.1μM to 10μM; 1-4h
Applications	Tomivosertib abrogated phosphorylation of eIF4E on serine 209 at 0.1μM, demonstrating potent inhibition of MNK1/2 activity. Tomivosertib resulted in dose-dependent inhibition of cellular viability in AML cell lines, with greatest suppressive activity against MV411, MM6 and KG-1 cells. Tomivosertib significantly inhibited leukemic progenitor (CFU-L) colony formation in KG-1, MV411, and MM6 cells, and also showed inhibitory effects on primary leukemic precursors from AML patients. Combination of Tomivosertib with Venetoclax resulted in synergistic inhibitory effects on cellular viability and CFU-L growth.

Animal experiment [2]:

Animal models	C57BL/6J wild-type (WT) mice, 4EKI mice (with a mutation at the MNK1/2 phosphorylation site of eIF4E), and MNK1 knockout (KO) mice

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Preparation Method	Mice underwent spared nerve injury (SNI) surgery (ligation and cutting of the tibial and peroneal branches of the left sciatic nerve) or sham surgery. For rule-shifting, marble burying, von Frey, and histology experiments, Tomivosertib was administered orally (p.o.) daily for 7 days, with the last injection 1 hour before behavioral testing. For the conditioned place preference (CPP) experiment, Tomivosertib was administered intraperitoneally (i.p.). Rule-shifting was assessed on day 21 post-SNI. Mice were perfused at 3 weeks post-surgery for immunohistochemistry.
Dosage form	10mg/kg; oral (p.o.); daily for 7 days
Applications	Tomivosertib reversed PNI-induced deficits in an attentional rule-shifting task (a measure of cognitive flexibility), reversed spontaneous pain as assessed by conditioned place preference (CPP), and rescued maladaptive shortening of axon initial segments (AIS) in the medial prefrontal cortex (mPFC) of PNI mice. Tomivosertib had no effect on mechanical withdrawal thresholds (mechanical allodynia).

References:

[1] Suarez M, Blyth GT, Mina AA, et al. Inhibitory effects of Tomivosertib in acute myeloid leukemia. Oncotarget. 2021 May 11;12(10):955-966.
[2] Shiers S, Mwirigi J, Pradhan G, et al. Reversal of peripheral nerve injury-induced neuropathic pain and cognitive dysfunction via genetic and tomivosertib targeting of MNK. Neuropsychopharmacology. 2020 Feb;45(3):524-533.

Background

Tomivosertib is an orally active MNK1/2 inhibitor (IC_{50} = 1–2nM). Tomivosertib specifically downregulates the translation of key oncogenic factors (Cyclin D1 and c-Myc) and immune checkpoint proteins (PD-L1) by inhibiting the phosphorylation of eIF4E at serine 209. Tomivosertib

can be used in research related to acute myeloid leukemia, breast cancer, lymphoma, non-small cell lung cancer, and prostate cancer[1-4].

In vitro, Tomivosertib (0–100nM) treated breast cancer cell lines (MDA-MB-231, MDA-MB-468, MCF7, T47D, SUM149) for 24 hours. Tomivosertib significantly inhibited the expression of PD-L1 and PD-L2, suppressed eIF4E phosphorylation, inhibited global translation, and increased chemosensitivity[5]. Tomivosertib (0.1–10μM) treated acute myeloid leukemia cell lines such as U937, MV411, and MM6 for 1–4 hours. Tomivosertib significantly inhibited phosphorylation of eIF4E at serine 209, reduced cell viability, and impaired clonogenic capacity[6].

In vivo, Tomivosertib (10mg/kg; five days per week) was administered orally to pancreatic cancer mouse models, combined with a ketogenic diet, for two weeks. Tomivosertib significantly suppressed pancreatic tumor growth, lowered blood β-hydroxybutyrate levels, and inhibited the translation of PPARα and Hmgcs2 in the liver[7]. Tomivosertib (10mg/kg; daily oral administration) was given to C57BL/6J wild-type (WT) mice, 4EKI mice, or MNK1 knockout (KO) mice that had undergone spared nerve injury (SNI) surgery, for 7 days. Tomivosertib reversed the deficits in rule-shifting tasks, spontaneous pain in SNI mice, and rescued the shortening of the axon initial segment (AIS) in the medial prefrontal cortex (mPFC)[8].

References:
[1] Kevin R. Webster, Vikas K Goel, et al. eFT508, a Potent and Selective Mitogen-Activated Protein Kinase Interacting Kinase (MNK) 1 and 2 Inhibitor, Is Efficacious in Preclinical Models of Diffuse Large B-Cell Lymphoma (DLBCL). Blood 2015; 126 (23): 1554.
[2] Xu Y, Poggio M, Jin HY, et al. Translation control of the immune checkpoint in cancer and its therapeutic targeting. Nat Med. 2019 Feb;25(2):301-311.
[3] Li Y, Uhelski ML, North RY, et al. Tomivosertib reduces ectopic activity in dorsal root ganglion neurons from patients with radiculopathy. Brain. 2024 Sep 3;147(9):2991-2997.
[4] Yang X, Liu Z, Yin X, et al. Inhibition MNK-eIF4E-β-catenin preferentially sensitizes gastric cancer to chemotherapy. Fundam Clin Pharmacol. 2022 Aug;36(4):712-720.
[5] Yang ZY, Jiang CW, Zhang WL, et al. Treatment with eFT-508 increases chemosensitivity in breast cancer cells by modulating the tumor microenvironment. J Transl Med. 2022 Jun 18;20(1):276.
[6] Suarez M, Blyth GT, Mina AA, et al. Inhibitory effects of Tomivosertib in acute myeloid leukemia. Oncotarget. 2021 May 11;12(10):955-966.

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[7] Yang H, Zingaro VA, Lincoff J, et al. Remodelling of the translatome controls diet and its impact on tumorigenesis. Nature. 2024 Sep;633(8028):189-197.
[8] Shiers S, Mwirigi J, Pradhan G, et al. Reversal of peripheral nerve injury-induced neuropathic pain and cognitive dysfunction via genetic and tomivosertib targeting of MNK. Neuropsychopharmacology. 2020 Feb;45(3):524-533.

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