UNC2025 hydrochloride

Cat. No.: HY-12344A

CAS No.: 2070015-17-5

Molecular Formula: $C_{28}H_{41}ClN_6O$

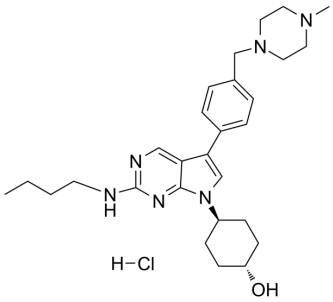
Molecular Weight: 513.12

Target: FLT3

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 55 mg/mL (107.19 mM; Need ultrasonic)

DMSO : 10 mg/mL (19.49 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9489 mL	9.7443 mL	19.4886 mL
5 mM	0.3898 mL	1.9489 mL	3.8977 mL
10 mM	0.1949 mL	0.9744 mL	1.9489 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (194.89 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1 mg/mL (1.95 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (1.95 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UNC2025 hydrochloride is a potent, ATP-competitive, and highly orally active Mer/Flt3 inhibitor with IC_{50} values of 0.74 nM and 0.8 nM, respectively. UNC2025 hydrochloride is >45-fold selectivity for MERTK relative to Axl (IC_{50}= 122 nM; K_i = 13.3 nM). UNC2025 hydrochloride exhibits an excellent PK properties, and can be used for the investigation of acute leukemia[1].

IC_{50} & Target

IC50: 0.74 nM (Mer); 0.8 nM (Flt3)[1]

In Vitro

UNC2025 is against FLT3, MER, AXL, TRKA, TRKC, QIK, TYRO3, SLK, NuaK1, KIT and Met with IC_{50} values of 0.35 nM, 0.46 nM, 1.65 nM, 1.67 nM, 4.38 nM, 5.75 nM, 5.83 nM, 6.14 nM, 7.97 nM , 8.18 nM and 364 nM, respectively[1].

UNC2025 (0-60 nM; 1 hour) mediates potent inhibition of Mer phosphorylation with an IC_{50} of 2.7 nM in 697 B-ALL cells[1].
UNC2025 (0-60 nM; 1 hour) results in decreased phosphorylation of Flt3 with an IC_{50} of 14 nM in Flt3-ITD positive Molm-14 acute myeloid leukemia cells[1].
UNC2025 (3 nM-3 μM; 1 hour) decreases p-MEK, p-AXL, p-TYRO3 expression as a concentration manner in 32D Cells[1].
UNC2025 (14 nM–10 μM; 48 hours) inhibits MERTK signaling and colony-forming potential in a MERTK-expressing patient sample with a 20-fold difference in sensitivity of MERTK-expressing leukemia blasts relative to normal cord or marrow blood mononuclear cells[2].
UNC2025 (25-300 nM; 1 hour) mediates potent and dose-dependent decreases in MERTK phosphorylation/activation in both cell lines and inhibition of MERTK correlated with decreased phosphorylation of previously reported MERTK-dependent signaling components STAT6, AKT, and ERK1/2[2].

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

Western Blot Analysis[1]

Cell Line:	32D Cells
Concentration:	0 nM, 3 nM, 10 nM, 20 nM, 30 nM, 100 nM, 1000 nM, 3000 nM
Incubation Time:	1 hour
Result:	Inhibited p-MEK, p-AXL, p-TYRO3 expression.

Cell Proliferation Assay[1]

Cell Line:	Mononuclear cells
Concentration:	14 nM–10 μM
Incubation Time:	48 hours
Result:	Showed IC_{50} values ranged from 9.0 nM to >10 μM with a median IC_{50} of 2.38 μM.

Western Blot Analysis[2]

Cell Line:	Kasumi-1 AML and 697 B-ALL cells
Concentration:	25-300 nM
Incubation Time:	48 hours
Result:	Decresed p-MERTK, p-STAT6, p- AKT and p-ERK1/2 expression as a dose-dependent manner.

In Vivo

UNC2025 (intravenous injection or oral adminstration; 3 mg/kg) exhibits an excellent PK properties: low clearance (9.2 mL/min kg), longer half-life (3.8 h), and high oral exposure (100%), it shows T_{max}, C_{max}, and AUClast 0.50 hour, 1.6 μM, and 9.2 h μM, respectively[2].
UNC2025 (orally adminstration; 50 or 75 mg/kg; 34 and 70 days) mediates a statistically significant dose-dependent reduction in tumor burden relative to vehicle. mediates dose-dependent increases in median survival from 26 days after initiation of treatment in vehicle-treated mice, to 34 and 70 days in mice treated with 50 or 75 mg/kg UNC2025, respectively [2].

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

Animal Model:	NSG mice injected with 697 B-ALL cells[2]
Dosage:	50 or 75 mg/kg
Administration:	Oral adminstration

Result:	Delayed the disease progression.

CUSTOMER VALIDATION

- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Oncol Rep. 2020 Oct;44(4):1322-1332.

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REFERENCES

[1]. Zhang W, et al. UNC2025, a Potent and Orally Bioavailable MER/FLT3 Dual Inhibitor. J Med Chem. 2014 Aug 28;57(16):7031-41.

[2]. DeRyckere D, et al. UNC2025, a MERTK Small-Molecule Inhibitor, Is Therapeutically Effective Alone and in Combination with CL14377 in Leukemia Models.Clin Cancer Res. 2017 Mar 15;23(6):1481-1492.

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