Ensartinib dihydrochloride

Cat. No.: HY-103714A

CAS No.: 2137030-98-7

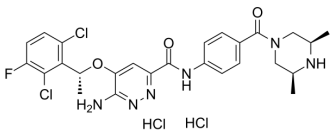
Molecular Formula: $C_{26}H_{29}Cl_4FN_6O_3$

Molecular Weight: 634.36

Target: Anaplastic lymphoma kinase (ALK); c-Met/HGFR

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

DMSO : 35.71 mg/mL (56.29 mM; Need ultrasonic)
H_2O : 33.33 mg/mL (52.54 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5764 mL	7.8820 mL	15.7639 mL
5 mM	0.3153 mL	1.5764 mL	3.1528 mL
10 mM	0.1576 mL	0.7882 mL	1.5764 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 14.29 mg/mL (22.53 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.28 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.28 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ensartinib dihydrochloride (X-396 dihydrochloride) is a potent and dual ALK/MET inhibitor with IC_{50}s of <0.4 nM and 0.74 nM, respectively.

IC_{50} & Target

IC50: <0.4 nM (ALK), 0.74 nM (MET)[1]

In Vitro

Ensartinib (X-396) dihydrochloride is a potent and dual ALK/MET inhibitor with IC_{50}s of <0.4 nM and 0.74 nM, respectively.

	Ensartinib dihydrochloride is potent in H3122 lung cancer cells harboring EML4-ALK E13;A20 (IC_{50}: 15 nM). Ensartinib dihydrochloride is also potent in H2228 lung cancer cells harboring EML4-ALK E6a/b; A20 (IC_{50}: 45 nM). Furthermore, X-376 is potent in SUDHL-1 lymphoma cells harboring NPM-ALK (IC_{50}: 9 nM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ensartinib (X-396) dihydrochloride shows substantial bioavailability and moderate half-lives in vivo. Nude mice harboring H3122 xenografts are treated with Ensartinib dihydrochloride at 25 mg/kg bid. Ensartinib dihydrochloride significantly delays the growth of tumors compared to vehicle alone. In the xenograft experiments, Ensartinib dihydrochloride appears well-tolerated in vivo. Mouse weight is unaffected by Ensartinib dihydrochloride treatment. Drug-treated mice appear healthy and do not display any signs of compound related toxicity. To further assess potential side effects of Ensartinib dihydrochloride, additional systemic toxicity and toxico-kinetic studies are performed in Sprague Dawley (SD) rats. Following 10 days of repeated oral administration of Ensartinib dihydrochloride at 20, 40, 80 mg/kg in SD rats, all animals survive to study termination. The no significant toxicity (NST) levels are determined to be 80 mg/kg for Ensartinib dihydrochloride. At NST levels, Ensartinib dihydrochloride achieves an AUC of 66 μM×hr and a C_{max} of 7.19 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For viability experiments, cells are seeded in 96-well plates at 25%-33% confluency and exposed to drugs. The human lung adenocarcinoma cell lines H3122 and H2228 are treated with Ensartinib (10, 30, 100, 300 and 1000 nM). SUDHL-1 lymphoma cells are treated with Ensartinib (5, 10, 30, 100 and 300 nM). SY5Y neuroblastoma cells are treated with Ensartinib (30, 100, 300 and 1000 nM). At 72 hours post Ensartinib addition, Cell Titer Blue Reagent is added and fluorescence is measured on a Spectramax spectrophotometer. All experimental points are set up in hextuplicate replicates and are performed at least two independent times. IC_{50}s are calculated using GraphPad Prism version 5 for Windows. The curves are fit using a nonlinear regression model with a log (inhibitor) vs. response formula[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Nude mice (***nu/nu***) are injected with H3122 cells. Once tumors reach an average volume of 450 mm^3, a total of 27 athymic mice harboring H3122 tumors are randomized and dosed via oral gavage with 25 mg/kg Ensartinib or the control vehicle. Two, five, and fifteen hours after the single treatment (3 tumors/timepoint/group), mice are sacrificed and serum is collected for assessment of drug concentration using an LC-MS based bioanalytical method[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancers. 2020 Mar 28;12(4):813.
- Drug Des Dev Ther. 2020 Nov 30;14:5259-5273.

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REFERENCES

[1]. Lovly CM, et al. Insights into ALK-driven cancers revealed through development of novel ALK tyrosine kinaseinhibitors. Cancer Res. 2011 Jul 15;71(14):4920-31.

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

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