Pyrotinib dimaleate

Cat. No.: HY-104065B

CAS No.: 1397922-61-0

Molecular Formula: $C_{40}H_{39}ClN_6O_{11}$

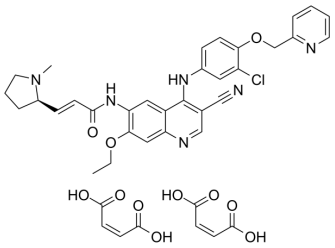
Molecular Weight: 815.22

Target: EGFR

Pathway: JAK/STAT Signaling; 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 : ≥ 106 mg/mL (130.03 mM)

DMSO : 100 mg/mL (122.67 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.2267 mL	6.1333 mL	12.2666 mL
5 mM	0.2453 mL	1.2267 mL	2.4533 mL
10 mM	0.1227 mL	0.6133 mL	1.2267 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: 2.5 mg/mL (3.07 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.07 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Pyrotinib dimaleate (SHR-1258 dimaleate) is a potent and selective EGFR/HER2 dual inhibitor with IC_{50}s of 13 and 38 nM, respectively[1].

IC_{50} & Target

HER2	EGFR
38 nM (IC_{50})	13 nM (IC_{50})

In Vitro

Pyrotinib dimaleate has high potency in HER2-dependent cell lines (BT474, SK-OV-3), while showing much weaker inhibition in the HER2 negative cell line (MDA-MB-231). Pyrotinib dimaleate inhibits BT474 and SK-OV-3 cells with IC_{50}s of 5.1 and 43 nM, respectively. Pyrotinib dimaleate displays high selectivity as HKI-272 when tested in a panel of different kinases such as

	KDR, c-Kit, PDGFRβ, c-Src and C-Met (c-Src with an IC_{50} of 790 nM, and others >3000 nM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pyrotinib dimaleate has acceptable bioavailability of 20.6%, 43.5% and 13.5% in nude mice, rats and dogs, respectively. Pyrotinib dimaleate has favorable drug-like physicochemical properties and shows relatively higher oral exposure in human subjects (oral; $t_{1/2}$=15 h) with a much longer half life than that of preclinical animal species such as mouse (i.v.; $t_{1/2}$=1.56 h; i.g.; $t_{1/2}$=2.52 h) and rat (i.v.; $t_{1/2}$=4.42 h; i.g.; $t_{1/2}$=3.38 h)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cancer cells (A431, SK-BR-3 and NCI-N87) are treated at a suitable concentration of Pyrotinib for 72 hours. Cell proliferation is determined by a sulforhodamine B (SRB) method. The IC_{50} values are calculated by the data of inhibition rates of serial concentrations of Pyrotinib dimaleate[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] Sprague Dawley (SD) rats (200-250g, 3 males and 3 females) are used .Test compounds (include Pyrotinib dimaleate) are administrated in both intravenous (i.v. ; 3 mg/kg) and intragastric (i.g. ;3 mg/kg) for rats to obtain their bioavailability. Plasma samples of nude mice is collected at pre-dose and 0.083, 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24 h after the IV administration [1]. Mice[1]: In vivo efficacy studies are performed on BALB/Ca-nude mice (6 to 7 weeks, female) from SLAC. Nude mice are hypodermic inoculated BT-474 human breast cancer cell or SK-OV-3 ovarian cancer cell. After tumor grows to 150-250 mm^3, mice are randomly divided into groups and dosed with Pyrotinib (2.5, 5, 10, 20 mg/kg) once daily. The volume of tumors and the weight of the mice are measured and recorded for 2-3 times per weeks[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Thorac Oncol. 2023 Sep 5;S1556-0864(23)00802-X.
- Cell Rep Med. 2023 Jan 10;100911.
- Int J Biol Macromol. 2023 May 19;242(Pt 2):124870.
- J Med Chem. 2019 May 9;62(9):4772-4778.
- Lung Cancer. 2018 Dec;126:72-79.

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REFERENCES

[1]. Li X, et al. Discovery and development of Pyrotinib: A novel irreversible EGFR/HER2 dual tyrosine kinase inhibitor with favorable safety profiles for the treatment of breast cancer. Eur J Pharm Sci. 2017 Jan 21. pii: S0928-0987(17)30043-X.

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