Pyrotinib

Cat. No.: HY-104065

CAS No.: 1269662-73-8

Molecular Formula: $C_{32}H_{31}ClN_6O_3$

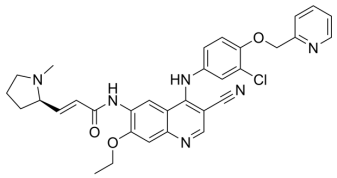
Molecular Weight: 583.08

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

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 : 10 mg/mL (17.15 mM; ultrasonic and adjust pH to 6 with HCl)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7150 mL	8.5752 mL	17.1503 mL
	5 mM	0.3430 mL	1.7150 mL	3.4301 mL
	10 mM	0.1715 mL	0.8575 mL	1.7150 mL

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

BIOLOGICAL ACTIVITY

Description

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

IC_{50} & Target

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

In Vitro

Pyrotinib 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). It inhibits BT474 and SK-OV-3Pyrotinib cells with IC_{50}s of 5.1 and 43 nM, respectively [1].

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

In Vivo

Pyrotinib has acceptable bioavailability of 20.6%, 43.5% and 13.5% in nude mice, rats and dogs, respectively. The TGI % (tumor growth inhibition) of Pyrotinib on day 21 is 109%, 157%, 159% at the doses of 5 mg/kg, 10 mg/kg, 20 mg/kg respectively. Pyrotinib in SK-OV-3 ovarian xenograft model shows TGI% on day 21 of 2%, 12%, 83% at the doses of 2.5 mg/kg, 5 mg/kg, 10 mg/kg respectively), which further confirms its robust in vivo antitumor efficacy at 10 mg/kg[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 with a series of concentrations 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 test compounds[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats: Test compounds (include Pyrotinib) are administrated in both intravenous (i.v.) and intragastric (i.g.) for mice 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: 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 week[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.
- Mol Syst Biol. 2023 Dec 18.
- Int J Biol Macromol. 2023 May 19;242(Pt 2):124870.
- J Med Chem. 2019 May 9;62(9):4772-4778.

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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.

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