Rociletinib hydrobromide

Cat. No.: HY-15729A

CAS No.: 1446700-26-0

Molecular Formula: $C_{27}H_{29}BrF_3N_7O_3$

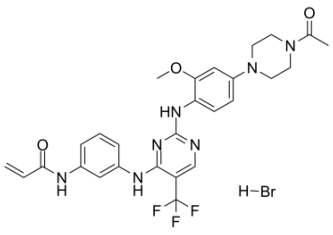
Molecular Weight: 636.46

Target: EGFR

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

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 59 mg/mL (92.70 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.5712 mL	7.8560 mL	15.7119 mL
5 mM	0.3142 mL	1.5712 mL	3.1424 mL
10 mM	0.1571 mL	0.7856 mL	1.5712 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 (3.93 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.93 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Rociletinib hydrobromide (CO-1686 hydrobromide) is an orally delivered kinase inhibitor that specifically targets the mutant forms of EGFR including T790M, and the K_i values for EGFRL858R/T790M and EGFRWT are 21.5 nM and 303.3 nM, respectively.

IC_{50} & Target

$EGFR^{L858R/T790M}$	$EGFR^{T790M}$
21.5 nM (Ki)	303.3 nM (Ki)

In Vitro

Rociletinib (0.1 μM) inhibits EGFR potently and irreversibly, and inhibits more than 50% of 23 targets. Rociletinib potently

	and selectively inhibits growth of NSCLC cells expressing mutant EGFR and induces apoptosis. Rociletinib resistant NSCLC cell lines are sensitive to AKT inhibition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Rociletinib (100 mg/kg/day, p.o.) demonstrates anti-tumor activity in NSCLC EGFR mutant xenograft models. Rociletinib (50 mg/kg bid, p.o.) demonstrates anti-tumor activity in human EGFR-L858R and EGFR-L858R-T790M expressing transgenic mice [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells are seeded at 3,000 cells/well in growth media supplemented with 5% FBS, 2 mM L-glutamine, and 1 % P/S, allowed to adhere overnight, and treated with a dilution series of test compound (Rociletinib) for 72 hr. Cell viability is determined by CellTiter Glo and results are represented as background-subtracted relative light units normalized to a DMSO-treated control. Growth inhibition (GI_{50}) values are determined by GraphPad Prism 5.04. Combination index (CI) data is generated using CalcuSyn. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Briefly, NCr nu/nu mice are sub-cutaneously implanted with 1×10^7 tumor cells in 50% Matrigel (injection volume of 0.2 mL/mouse). Once tumors reached 100-200 mm^3, Animals are dosed with compounds (Rociletinib) as outlined (N=10 animals/gp). The LUM1686 PDX xenograft study is performed by CrownBio. Briefly, LUM1686 PDX tumor fragments, harvested from donor mice, are inoculated into BALB/c nude mice. Administration of test compounds (Rociletinib) is initiated at a mean tumor size of approximately 160 mm^3. Tumor growth is monitored over time to determine tumor growth inhibition of the experimental agent vs. vehicle. The endpoint of the experiment is a mean tumor volume (MTV) in control group of 2000 mm^3. Percent TGI is defined as the difference between the MTV of the designated control group and the MTV of the drug-treated group, expressed as a percentage of the MTV of the designated control group. Data is presented as mean±standard error of the mean (SEM). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367). pii: eaan4368.
- Acta Pharm Sin B. 2020 Jan.
- J Med Chem. 2017 Apr 13;60(7):2944-2962.
- Mol Cancer Ther. 2018 Mar;17(3):603-613.
- ChemMedChem. 2017 Nov 22;12(22):1857-1865.

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REFERENCES

[1]. Walter AO, et al. Discovery of a mutant-selective covalent inhibitor of EGFR that overcomes T790M-mediated resistance in NSCLC. Cancer Discov. 2013 Sep 25.

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

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