Rociletinib

Cat. No.: HY-15729

CAS No.: 1374640-70-6

Molecular Formula: $C_{27}H_{28}F_3N_7O_3$

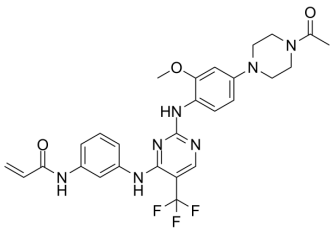
Molecular Weight: 555.55

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 : 125 mg/mL (225.00 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8000 mL	9.0001 mL	18.0002 mL
	5 mM	0.3600 mL	1.8000 mL	3.6000 mL
	10 mM	0.1800 mL	0.9000 mL	1.8000 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 (4.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rociletinib (CO-1686) 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 (CO-1686) (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 (CO-1686) (100 mg/kg/day, p.o.) demonstrates anti-tumor activity in NSCLC EGFR mutant xenograft models. Rociletinib (CO-1686) (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). Briefly, LUM1686 PDX tumor fragments, harvested from donor mice, are inoculated into BALB/c nude mice. Administration of test compounds (Rociletinib (CO-1686)) 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):eaan4368.
- Acta Pharm Sin B. 2020 May;10(5):799-811.
- J Med Chem. 2017 Apr 13;60(7):2944-2962.
- Mol Cancer Ther. 2018 Mar;17(3):603-613.
- Mol Cancer Res. 2021 Jun 28.

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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.

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