limertinib

Cat. No.: HY-138751

CAS No.: 1934259-00-3

Molecular Formula: $C_{29}H_{32}ClN_7O_2$

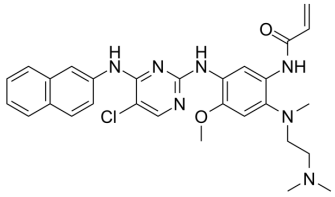
Molecular Weight: 546.06

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 : 41.67 mg/mL (76.31 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8313 mL	9.1565 mL	18.3130 mL
	5 mM	0.3663 mL	1.8313 mL	3.6626 mL
	10 mM	0.1831 mL	0.9157 mL	1.8313 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 (4.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

limertinib (ASK120067) is a potent and orally active inhibitor of $EGFR^{T790M}$ (IC_{50}:0.3 nM) with selectivity over $EGFR^{WT}$ (IC_{50} :6.0 nM). limertinib is a third-generation EGFR-TKI for the research of non-small cell lung cancer (NSCLC)[1].

IC_{50} & Target

$EGFR^{T790M}$	$EGFR^{L858R/T790M}$	EGFR (WT)	$EGFR^{Exon\ 19\ deletion}$
0.5 nM (IC_{50})	0.3 nM (IC_{50})	6 nM (IC_{50})	0.5 nM (IC_{50})

In Vitro

In the in vitro kinase assay limertinib potently inhibits the EGFR L858R/T790M and EGFR T790M resistant mutants with IC_{50} values of 0.3 nM and 0.5 nM, respectively, as well as the $EGFR^{exon19del}$ sensitizing mutant (IC_{50}= 0.5 nM). The $_{50}$ of limertinib against wild-type EGFR ($EGFR^{WT}$) is 6 nM[1].
limertinib selectively inhibits the growth of EGFR-mutant cell lines and exhibits potent antiproliferative activity in the

	mutant EGFR NSCLC cells, with IC_{50} values of 12 nM, 6 nM and 2 nM against NCI-H1975 (T790M mutation), PC-9, and HCC827 cells (sensitizing mutations), respectively. However, it shows moderate or weak anti-growth activities in A431, LoVo and A549 cells ($EGFR^{WT}$), with IC_{50} values ranging from 338 nM to 1541 nM[1]. limertinib (0.1-100 nM) inhibits the phosphorylation of EGFR at Tyrosine residue 1068 and its downstream signaling proteins AKT and ERK in NCI-H1975 cells ($EGFR^{L858R/T790M}$) even at low dosage (0.1-1 nM). Additionally, limertinib inhibits p-EGFR and p-Akt and p-erk in EGFR WT A431 cell until the concentration reaches 10 to 100 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	limertinib (oral gavage; 5-20 mg/kg; once daily; 21 days) results in significantly regressed tumor growth, with a tumor growth inhibition (TGI) rate of 85.7%, and administration of 10 mg/kg limertinib causes dramatic tumor shrinkage with a TGI rate of 99.3%, exhibiting a similar potency with Osimertinib[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	BALB/cA nude mice[1]
Dosage:	5-20 mg/kg
Administration:	Oral gavage; 5-20 mg/kg; once daily; 21 days
Result:	Were well tolerated in animals without observed body weight loss Demonstrated profound and selective antitumor efficacy and decreased TGI rate. Significantly inhibited the phosphorylation of EGFR L858R/T790M and AKT in tumor tissue.

REFERENCES

[1]. Tao Zhang, et al. Discovery of a novel third-generation EGFR inhibitor and identification of a potential combination strategy to overcome resistance. Mol Cancer. 2020 May 13;19(1):90.

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