EGFR T790M/L858R-IN-2

Cat. No.: HY-149824

Molecular Formula: $C_{28}H_{28}FN_7O$

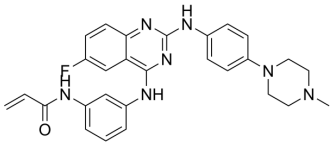
Molecular Weight: 497.57

Target: EGFR; Apoptosis

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

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (200.98 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0098 mL	10.0488 mL	20.0977 mL
	5 mM	0.4020 mL	2.0098 mL	4.0195 mL
	10 mM	0.2010 mL	1.0049 mL	2.0098 mL

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

BIOLOGICAL ACTIVITY

Description

EGFRT790M/L858R-IN-2 is a potent and selective EGFRT790M/L858R inhibitor with IC_{50} values of 3.5, 1290 nM for EGFRT790M/L858R, EGFR WT, respectively. EGFRT790M/L858R-IN-2 decreases the expression of p-EGFR, P-AKT, P-ERK1/2. EGFRT790M/L858R-IN-2 induces Apoptosis and cell cycle arrest in the G1 phase. EGFRT790M/L858R-IN-2 shows anti-cancer activity[1].

IC_{50} & Target

$EGFR^{L858R/T790M}$	EGFR (WT)	$EGFR^{T790M}$	$EGFR^{L858R}$
3.5 nM (IC_{50})	1290 nM (IC_{50})	6.7 nM (IC_{50})	2.1 nM (IC_{50})

In Vitro

EGFRT790M/L858R-IN-2 (compound 28f) (0.1, 1, 10 μM; 4 h) decreases the expression of p-EGFR, P-AKT, P-ERK1/2 in a dose-dependent manner in H1975, HCC827 cells[1].

EGFRT790M/L858R-IN-2 (0.1, 1, 10 μM; 48 h) induces apoptosis and cell cycle arrest in the G1 phase in H1975, HCC827 cells[1].

EGFRT790M/L858R-IN-2 (0.1, 1, 10 μM; 14 days) inhibits colony formation and cell migration in a dose-dependent manner[1].

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

Western Blot Analysis[1]

Cell Line:	H1975, HCC827, A549, A431cells

Concentration:	0.1, 1, 10 μM
Incubation Time:	4 h
Result:	Decreased the expression of p-EGFR, P-AKT, P-ERK1/2 in a dose-dependent manner in H1975, HCC827 cells, showed a weak inhibitory effect on EGF-induced EGFR and AKT and ERK1/2 phosphorylation in A549 and A431 cells.

Apoptosis Analysis[1]

Cell Line:	H1975, HCC827, A549, A431cells
Concentration:	0.1, 1, 10 μM
Incubation Time:	48 h
Result:	Significantly induced apoptosis of H1975 and HCC827 cells in a dose-dependent manner, exhibited weaker apoptosis-inducing ability than osimertinib in A549 and A431 cells, inducing only 14.80 and 17.93% apoptosis, respectively, at 10 μM.

Cell Cycle Analysis[1]

Cell Line:	H1975, HCC827, A549, A431cells
Concentration:	0.1, 1, 10 μM
Incubation Time:	48 h
Result:	Induced cell cycle arrest in the G1 phase with the G0/G1 phase ratios approximately 80.5% for H1975 and approximately 81.1% for HCC827，approximately 63.8% for A549 and approximately 64.5% for A431 cells.

In Vivo

EGFRT790M/L858R-IN-2 (5, 10, 20 mg/kg; i.p.; daily) inhibits tumor growth in a dose-dependent manner[1].

Pharmacokinetic Parameters of EGFRT790M/L858R-IN-2 in Male Sprague-Dawley rats[1].

parameter	i.v. (1 mg/kg)
$T_{1/2}$ (h)	1.76 ± 0.65
C_{max} (ng/mL)	649.90 ± 54.71
AUC_{0-t} (h*ng/ml)	1036.86 ± 137.03
$AUC_{0-\infty}$ (h ng/ml)	1048.74 ± 134.39
V_z (mL/kg)	2515.40 ± 1184.92
CL(mL/min/kg)	16.07 ± 2.06

Male Sprague-Dawley rats, 1 mg/kg iv[1]

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

Animal Model:	6-8 weeks, BALB/c female nude mice(H1975 cell xenografts)[1]
Dosage:	5, 10, 20 mg/kg
Administration:	I.p.; once per day
Result:	Inhibited tumor growth, both in volume and weight in a dose-dependent manner.

REFERENCES

[1]. Pei J, et al. Design, Synthesis, and Antitumor Activity of Potent and Selective EGFR L858R/T790M Inhibitors and Identification of a Combination Therapy to Overcome Acquired Resistance in Models of Non-small-cell Lung Cancer. J Med Chem. 2023 Apr 27;66(8):5719-5752.

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