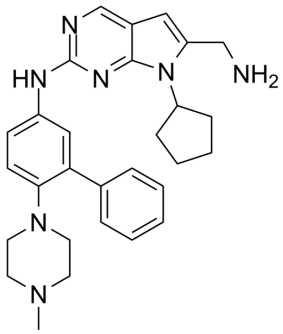
EGFR-IN-47

Cat. No.:	HY-143337
Molecular Formula:	$C_{29}H_{35}N_7$
Molecular Weight:	481.64
Target:	Apoptosis; EGFR
Pathway:	Apoptosis; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

EGFR-IN-47 is a potent and orally active $EGFR^{L858R/T790M/C797S}$ inhibitor with an IC_{50} of 0.01 μM. EGFR-IN-47 induces cell cycle attest and cell apoptosis. EGFR-IN-47 has the potential for the research of NSCLC[1].

IC_{50} & Target

$EGFR^{L858R/T790M/C797S}$

0.07 μM (IC_{50})

In Vitro

EGFR-IN-47 (compound 14aj) (72 h) shows anti-proliferative effects with IC_{50}s of 0.013 μM, 2.972 μM, 1.031 μM for PC-9 ($EGFR^{L858R/T790M/C797S}$), A432, A549 cells, respectively[1].

EGFR-IN-47 (0.01, 0.05, 0.25, 1 μM; 24 h) induces cell cycle attest at the G0/G1-phase[1].

EGFR-IN-47 (0.01, 0.05, 0.25 μM) induces cell deathvia apoptosis in a concentration-dependent manner[1].

EGFR-IN-47 (0.01, 0.05, 0.25, 1 μM) inhibits phosphorylation of the EGFR downstream mediators[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	PC-9 ($EGFR^{L858R/T790M/C797S}$), A432, A549 cells
Concentration:	
Incubation Time:	72 h
Result:	Showed anti-proliferative effects with IC_{50}s of 0.013 μM, 2.972 μM, 1.031 μM for PC-9 ($EGFR^{L858R/T790M/C797S}$), A432, A549 cells, respectively.

Cell Cycle Analysis[1]

Cell Line:	PC-9 $EGFR^{L858R/T790M/C797S}$ cells
Concentration:	0.01, 0.05, 0.25, 1 μM
Incubation Time:	24 h
Result:	Cells were arrest at the G0/G1-phase.

Apoptosis Analysis[1]

Cell Line:	PC-9 $EGFR^{L858R/T790M/C797S}$ cells
Concentration:	0.01, 0.05, 0.25 μM
Incubation Time:	24 h
Result:	Induced cell deathvia apoptosis in a concentration-dependent manner.

Western Blot Analysis[1]

Cell Line:	PC-9 $EGFR^{L858R/T790M/C797S}$ cells
Concentration:	0.01, 0.05, 0.25, 1 μM
Incubation Time:	
Result:	Inhibited phosphorylation of the EGFR downstream mediators.

In Vivo

EGFR-IN-47 (10, 20, 40 mg/kg; i.g.) shows anti-tumor effect with low toxicity[1].
EGFR-IN-47 (20 mg/kg for i.v.; 20 mg/kg for p.o.) shows an ideal oral bioavailability of 66.05%[1].
Pharmacokinetic Parameters of JAK1/TYK2-IN-2 in Male Sprague-Dawley rats[1].

parameter	iv (20 mg/kg)	po (20 mg/kg)
$AUC_{0-\infty}$ (mg/Lh)	15.889	10.494
C_{max} (mg/L)	6.845	0.77
T_{max} (h)	0.083	6
F (%)		66.05
$MRT_{0-\infty}$ (h)	16.439	16.791
V_{ss} (L/kg)	16.015	28.101
CL (L/h/kg)	1.272	2.151
$t_{(1/2)}$ (h)	8.922	11.154

Male Sprague-Dawley rats; 20 mg/kg for i.v.; 20 mg/kg for p.o.[1]
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	6-8 weeks, BALB/c nude mice (PC-9 $EGFR^{L858R/T790M/C797S}$ cells)[1]
Dosage:	10, 20, 40 mg/kg (dissolved in 25% (v/v) PEG400 plus 5% DMSO)
Administration:	I.g.
Result:	Showed anti-tumor effect with low toxicity.

Animal Model:	Male Sprague-Dawley rats[1]
Dosage:	20 mg/kg
Administration:	I.v.; p.o.
Result:	Showed an ideal oral bioavailability of 66.05%.

REFERENCES

[1]. Wang C, et al. Discovery and structural optimization of potent epidermal growth factor receptor (EGFR) inhibitors against L858R/T790M/C797S resistance mutation for lung cancer treatment. Eur J Med Chem. 2022; 237:114381.

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