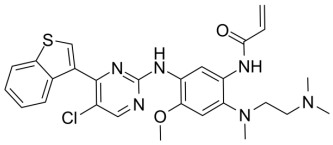
EGFR-IN-44

Cat. No.:	HY-145844
Molecular Formula:	$C_{27}H_{29}ClN_6O_2S$
Molecular Weight:	537.08
Target:	EGFR; Apoptosis
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

EGFR-IN-44 (Compound 6a) is a potent, orally active EGFR tyrosine kinase inhibitor with an IC_{50} of 4.11 nM. EGFR-IN-44 induces cell apoptosis and shows an oral bioavailability value of 33.57%. EGFR-IN-44 can be studied for non-small-cell lung cancers[1].

IC_{50} & Target

IC_{50}: 0.26 nM (EGFR T790M/L858R), 1.33 nM (EGFR L858R), 4.11 nM (EGFR)[1]

In Vitro

EGFR-IN-44 (Compound 6a) (0-10 μM, 72 h) shows anti-proliferative activities against tumor cell lines[1].
EGFR-IN-44 binds to the ATP binding site of EGFR[1].
EGFR-IN-44 (0-10 nM, 48 h) induces H1975 cell apoptosis via the mitochondrial pathway, arrests cell cycle in G0/G1 phase, and suppresses cell migration[1].
EGFR-IN-44 (0-10 nM, 48 and 72h) shows hypotoxicity against normal cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	H1975 ($EGFR^{T790M/L858R}$), PC9 ($EGFR^{del19}$), and H292 ($EGFR^{WT}$)
Concentration:	0-10 μM
Incubation Time:	72 h
Result:	Showed anti-proliferative activities with IC_{50} values of 0.0022 ± 0.001, 0.0048 ± 0.001, and 4.499 ± 0.057 μM against H1975, PC9, and H292 cells, respectively.

Apoptosis Analysis[1]

Cell Line:	H1975
Concentration:	1, 5, and 10 nM
Incubation Time:	48 h
Result:	Effectively induced cell apoptosis in a dose-dependent manner. Resulted in 33.7%, 52.4%, and 56.2% apoptosis at 1, 5, and 10 μM, respectively, compared to 5.81% apoptosis in the control group.

Western Blot Analysis[1]

Cell Line:	H1975
Concentration:	5, 10, and 25 nM
Incubation Time:	48 h and 72 h
Result:	Dose-dependently upregulated the expression levels of the proapoptotic proteins Bad and Bax and downregulated the expression level of the antiapoptotic protein Bcl-2. Sufficiently reduced the phosphorylation of EGFR and AKT.

Cell Cycle Analysis[1]

Cell Line:	H1975
Concentration:	5 nM
Incubation Time:	0, 12, 24, or 48 h
Result:	Exhibited a significant increase in the G0/G1 cell population and a dramatic decrease in G2/M phase.

Cell Cytotoxicity Assay[1]

Cell Line:	LO2, HK2, HLF, and 293A
Concentration:	0.1, 1, 5, and 10 μM
Incubation Time:	48 h and 72 h
Result:	Showed hypotoxicity with IC_{50} values of 7.247, 4.586, 3.787, and 2.925 μM against LO2, HK2, HLF, and 293A cells, respectively. The cell morphology was changed compared to the control.

In Vivo

EGFR-IN-44 (Compound 6a) (25 mg/kg; i.g.; daily, 7days) shows strong antitumor activity without obvious toxicity[1].

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

Animal Model:	Male BALB/c nude mice (5 weeks old, 18 - 20 g), H1975 xenograft model[1]
Dosage:	25 mg/kg
Administration:	Intragastric administration, daily, 7 days
Result:	Showed strong tumor inhibition (TGI = 90.24%) without obvious toxicity.

Animal Model:	Male Sprague–Dawley (SD) rats[1]
Dosage:	1 mg/kg and 5 mg/kg
Administration:	Intravenous injection and oral administration (Pharmacokinetic Analysis)
Result:	In Vivo PK parameters of EGFR-IN-44 [1]

Parameters	EGFR-IN-44	

Dose(mg/kg)	5 (po)	1 (iv)
$t_{1/2}$ (h)	8.60 ± 1.8	1.42 ± 0.1
T_{max} (h)	4.00 ± 0.002	/
C_{max} (ng/mL)	80.40 ± 2.7	/
Vz_{F_pred} (L/kg)	220.80 ± 41.2	6.83 ± 08
AUC_{0-t} (H.ng/mL)	490.41 ± 29.9	291.91 ± 38.2
$AUC_{0-\infty}$ (H.ng/mL)	491.02 ± 44.2	295.76 ± 38.8
MRT_{0-last} (h)	7.93 ± 0.8	1.35 ± 01
CL (mL/h/kg)	17.79 ± 3.9	3.12 ± 0.4
F(%)	33.57 ± 5.9	/

$F = (AUC_{0-inf-PO} \times DOSE_{IV})/(AUC_{0-inf-IV} \times DOSE_{PO})*100\%$.

REFERENCES

[1]. Baijiao An, et al. Novel third-generation pyrimidines-based EGFR tyrosine kinase inhibitors targeting EGFR T790M mutation in advanced non-small cell lung cancer. Bioorg Chem. 2022 May;122:105743.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA