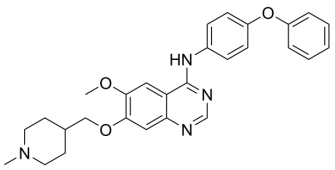
EGFR/C797S-IN-1

Cat. No.:	HY-152019
CAS No.:	2378188-21-5
Molecular Formula:	$C_{28}H_{30}N_4O_3$
Molecular Weight:	470.56
Target:	EGFR
Pathway:	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/C797S-IN-1 is a potent EGFR-C797S inhibitor with an IC_{50} value of 0.128 μM. EGFR/C797S-IN-1 shows anti-proliferative activity and anti-tumor activity. EGFR/C797S-IN-1 inhibits the expression of p-EGFR in a dose-dependent manner[1].

IC_{50} & Target

$EGFR^{L858R/T790M/C797S}$

0.128 μM (IC_{50})

In Vitro

EGFR/C797S-IN-1 (compound 14d) (0-10 μM; 72 h) shows anti-proliferative activities with IC_{50}s of 0.75, 0.09 μM for BaF3-$EGFR^{L858R/T790M/C797S}$, BaF3-$EGFR^{19del/T790M/C797S}$, respectively[1].

EGFR/C797S-IN-1 (1-10000 nM; 24 h) decreases the expression of p-EGFR, p-AKT, p-ERK protein in a dose dependent manner [1].

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

Cell Proliferation Assay[1]

Cell Line:	BaF3 cells with EGFRL858R/T790M/C797S and EGFR19del/T790M/C797S Mutations
Concentration:	0-10 μM
Incubation Time:	72 h
Result:	Showed anti-proliferative activitie with IC_{50}s of 0.75, 0.09 μM for BaF3-$EGFR^{L858R/T790M/C797S}$, BaF3-$EGFR^{19del/T790M/C797S}$, respectively.

Western Blot Analysis[1]

Cell Line:	BaF3-EGFRL858R/T790M/C797S, BaF3-EGFR19del/T790M/C797S cells
Concentration:	1, 10, 100, 1000, 10000 nM
Incubation Time:	24 h
Result:	Decreased the expression of p-EGFR, p-AKT. p-ERK protein in a dose dependent manner.

In Vivo

EGFR/C797S-IN-1 (10, 30 mg/kg; daily for 14 days) significantly decreases tumor growth in a dose-dependent manner in mouse[1].

Pharmacokinetic Parameters of EGFR/C797S-IN-1 in Male Sprague-Dawley rats[1].

Parameter	i.v. (1 mg/kg)	p.o. (10 mg/kg)
T_{max} (h)	0.08±0	3.33±1.15
$T_{1/2}$ (h)	1.97±0.14	3.89±0.42
C_{max} (ng/mL)	69.57±6.78	7.43±1.17
AUC_{0-t} (h*ng/mL)	65.48±5.55	61.12±6.23
$AUC_{0-\infty}$ (h*ng/mL)	67.98±5.56	62.15±6.36
CL-obs (L/h/kg)	14.78±1.19	--
V_{ss}-obs (L/kg)	26.11±2.58	--
F (%)	--	9.33±0.95

Male Sprague-Dawley rats, 1 mg/kg iv ; 10 mg/kg po (dissolved in 5% DMSO, 10% Solutol and 85% Salinet with the concentration of 0.2 mg/mL for i.v. and 1 mg/mL for p.o.)[1].

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

Animal Model:	SD male rats[1]
Dosage:	1 mg/kg for i.v.; 10 mg/kg for p.o.
Administration:	i.v. or p.o.
Result:	Displayed good biochemical activity and promising cellular activity.

Animal Model:	BALB/c nude mice (BaF3-EGFR19del/T790M/C797S xenograft model)[1]
Dosage:	10, 30 mg/kg
Administration:	I.p.; daily for 14 days
Result:	Displayed an obvious suppressive effect of tumor growth, with the TGI at 51.36% and 67.95% at the dosage of 10 mg/kg and 30 mg/kg, respectively.

REFERENCES

[1]. Dou D, et al. Discovery and optimization of 4-anilinoquinazoline derivatives spanning ATP binding site and allosteric site as effective EGFR-C797S inhibitors. Eur J Med Chem. 2022 Dec 15;244:114856.

Caution: Product has not been fully validated for medical applications. For research use only.

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