Osimertinib

Cat. No.: HY-15772

CAS No.: 1421373-65-0

Molecular Formula: $C_{28}H_{33}N_7O_2$

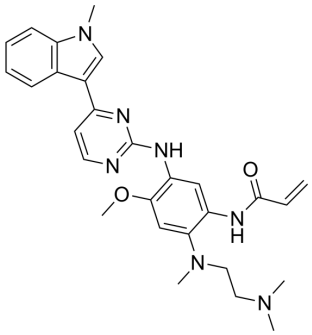
Molecular Weight: 499.61

Target: EGFR

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

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (200.16 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0016 mL	10.0078 mL	20.0156 mL
5 mM	0.4003 mL	2.0016 mL	4.0031 mL
10 mM	0.2002 mL	1.0008 mL	2.0016 mL

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

In Vivo

1. Add each solvent one by one: 0.5%HPMC >> 1%Tween80
   Solubility: 5 mg/mL (10.01 mM); Suspened solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.00 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.00 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Osimertinib (AZD9291) is a covalent, orally active, irreversible, and mutant-selective EGFR inhibitor with an apparent IC_{50} of 12 nM against L858R and 1 nM against L858R/T790M, respectively. Osimertinib overcomes T790M-mediated resistance to EGFR inhibitors in lung cancer[1].

IC_{50} & Target	$EGFR^{L858R}$	$EGFR^{L858R/T790M}$

	12 nM (IC_{50}, Enzyme assays)	1 nM (IC_{50}, Enzyme assays)

In Vitro

Osimertinib (AZD9291) (0-10 μM; 72 hours) dramatically inhibits cell proliferation with IC_{50}s of 41, 26, 41, and 31 nM, respectively[2].

?Osimertinib (0-10 μM; 72 hours) inhibits cell proliferation (Ba/F3 cells harboring a T790M mutation, exon 19del+T790M, or L858R+T790M) with IC_{50}s of 6, 7, and 74 nM, respectively[2].

?Osimertinib (0-10 μM; 72 hours) inhibits Ba/F3 cells harboring EGFR exon 20 insertion mutations (IC_{50} ranging from 16 to 701 nM for A763_Y764insFQEA (FQEA), Y764_V765insHH (HH), A767_V769dupASV (ASV), and D770_N771insNPG (NPG) cells)[2].

?Osimertinib shows high levels of phenotype potency in both sensitizing-mutant (mean IC_{50} of 8 nM in PC-9) and T790M (mean IC_{50}s of 11 and 40 nM in H1975 and PC-9VanR respectively) EGFR cell lines. Osimertinib has much less activity towards wild-type EGFR (mean IC_{50}s of 650 and 461 nM in Calu3 and H2073 respectively)[1].

?Osimertinib (0.1 μM; 48 hours) induces apoptosis in Ba/F3 cells (apoptosis rates of 40.9% and 90% in EGFR exon 19del+T790M, EGFR L858R+T790M respectively) [2].

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

Cell Proliferation Assay[2]

Cell Line:	Ba/F3 cells (harboring a T790M mutation, exon 19del+T790M, or L858R+T790M)
Concentration:	0.0001, 0.001, 0.01, 0.1, 1, 10 μM
Incubation Time:	72 hours
Result:	Inhibited cell proliferation (IC_{50}s=6, 7, 74 nM, respectively)

Cell Proliferation Assay[2]

Cell Line:	PC-9, H3255, PC-9ER, and H1975 cells
Concentration:	0.0001, 0.001, 0.01, 0.1, 1, 10 μM
Incubation Time:	72 hours
Result:	Dramatically inhibited cell proliferation (IC_{50}s=41, 26, 41, 31 nM, respectively)

Cell Proliferation Assay[2]

Cell Line:	Ba/F3 cells (harboring EGFR exon 20 insertion mutations: FQEA, HH, ASV, NPG)
Concentration:	0.0001, 0.001, 0.01, 0.1, 1, 10 μM
Incubation Time:	72 hours
Result:	Inhibited cell proliferation (IC_{50}s=16, 701, 230, 38 nM, respectively)

Apoptosis Analysis[2]

Cell Line:	Ba/F3 cells (harboring EGFR exon 19del+T790M or EGFR L858R+T790M)
Concentration:	0.1 μM
Incubation Time:	48 hours
Result:	Induced apoptosis with the rates of 40.9% and 90% in EGFR T790M positive mutations cells, respectively.

In Vivo

Osimertinib (0.1-25 mg/kg; p.o.; daily for 14 days) induces significant dose-dependent regression in both PC-9 (ex19del) and

H1975 (L858R/T790M) tumor xenograft models[1].

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

Animal Model:	PC-9 (ex19del) and H1975 (L858R/T790M) tumor xenograft models[1]
Dosage:	0.1-10 mg/kg (PC-9 xenograft models); 0.5- 25 mg/kg (H1975 xenograft models)
Administration:	p.o.; daily for 14 days
Result:	Induced significant dose-dependent regression in both PC-9 (ex19del) and H1975 (L858R/T790M) tumor xenograft models.

CUSTOMER VALIDATION

- Cancer Cell. 2020 Jan 13;37(1):104-122.e12.
- Cancer Discov. 2019 Jul;9(7):926-943.
- Nat Cancer. 2023 Jun;4(6):829-843.
- Nat Cancer. 2022 Apr;3(4):402-417.
- ACS Nano. 2022 Jul 21.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Cross DA, et al. AZD9291, an irreversible EGFR TKI, overcomes T790M-mediated resistance to EGFR inhibitors in lung cancer. Cancer Discov. 2014 Sep;4(9):1046-61.

[2]. Hirano T, et al. Pharmacological and Structural Characterizations of Naquotinib, a Novel Third-Generation EGFR Tyrosine Kinase Inhibitor, in EGFR-Mutated Non-Small Cell Lung Cancer. Mol Cancer Ther. 2018 Apr;17(4):740-750.

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