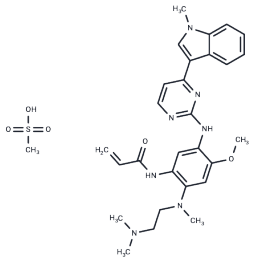
Data Sheet (Cat.No.T3634)

TargetMol

Osimertinib mesylate

Chemical Properties



CAS No. : 1421373-66-1

Formula: C29H37N7O5S

Molecular Weight: 595.71

Appearance: no data available

Storage: store at low temperature,store under nitrogen
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Osimertinib mesylate (AZD-9291 mesylate) is an EGFR third-generation inhibitor that inhibits the T790M resistance mutation produced by second-generation EGFR inhibitors with irreversible and oral activity. Osimertinib mesylate has antitumor activity for the treatment of EGFR-mutated non-small-cell lung cancer.
Targets(IC50)	EGFR
In vitro	**METHODS**: Human non-small cell lung cancer cells PC-9 (exon 19del), H3255 (L858R), PC-9ER (exon 19del+T790M) and H1975 (L858R+T790M) were treated with Osimertinib mesylate (0.0001-10 μmol/L) for 72 h, and the growth inhibition of the cells was detected by using MTS method. growth inhibition was detected using the MTS. **RESULTS**: Osimertinib dose-dependently induced the growth of PC-9, H3255, PC-9ER, and H1975 cells with IC50s of 41, 26, 41, and 31 nM, respectively. [1] **METHODS**: EGFR-mutated human non-small cell lung cancer cells PC-9, H1975, H1650 and H3255 were treated with Osimertinib mesylate (0.1-1000 nM) for 6 h, and the expression levels of the target proteins were detected by Western Blot. **RESULTS**: Osimertinib inhibited pEGFR (Y1068), pERK (P-p44/42), and pAKT (S473) in EGFR mutant tumor cells. [2] **METHODS**: Human non-small cell lung cancer cells NCI-H1975 were treated with Osimertinib mesylate (10-100 nM) for 24 h, then irradiated with 2-20 Gy, and the cell cycle was analyzed by Flow Cytometry. **RESULTS**: The proportion of G2/M and S-phase cells was dose-dependently reduced in the combination treatment group, and the G2/M-phase cell cycle was arrested after reduced irradiation with Osimertinib. [3]
In vivo	**METHODS**: To detect anti-tumor activity in vivo, Osimertinib mesylate (5-10 mg/kg) was orally administered once daily for seven days to SCID mice bearing human lung cancer tumors H1975, PC9 and A431. **RESULTS**: Osimertinib treatment significantly inhibited the growth of H1975, PC9 and A431 tumors, indicating antitumor activity in vivo. [4] **METHODS**: To detect the anti-tumor activity in vivo, Osimertinib mesylate (6 mg/kg) was administered orally to SHO-SCID mice constructed with PC-9/ffluc cells as a model of leptomeningeal carcinomatosis (LMC) once daily for fifty days. **RESULTS**: Osimertinib treatment significantly delayed the progression of LMC. Osimertinib, a third-generation EGFR-TKI, may be an effective treatment for first- or second-generation EGFR-TKI-resistant LMC caused by EGFR-mutant tumors. [5]

Kinase Assay	Kinase assays were performed as per the EMD Millipore profiling service protocol using peptide or protein substrates in a filter-binding radioactive ATP transferase assay for protein [1].
Cell Research	PC-9 cells were seeded into T75 flasks (5 × 10^5 cells/flask) in RPMI growth media and incubated at 37°C, 5% CO2. The following day the media was replaced with media supplemented with a concentration of EGFR inhibitor equal to the EC50 concentration predetermined in PC-9 cells. Media changes were carried out every 2-3 days and resistant clones allowed to grow to 80% confluency prior to the cells being trypsinised and reseeded at the original seeding density in media containing twice the concentration of EGFR inhibitor. Dose escalations were continued until a final concentration of 1.5μM gefitinib, 1.5μM afatinib, 1.5μM WZ4002 or 160nM AZD9291 were achieved [1].
Animal Research	The generation of EGFRL858R and EGFRL858R+T790M mice (male and female) was previously described Doxycycline was administered by feeding mice (aprox 3 week old) with doxycycline-impregnated food pellets (625 ppm) and treated for about 3 months during which time tumors developed. Afatinib and AZD9291 were suspended in 1% Polysorbate 80 and administered via oral gavage once daily at the doses of 7.5 mg/kg and 5 mg/kg, respectively. Mice were imaged weekly at the Vanderbilt University Institute of Imaging Science. For immunoblot analysis, mice were treated for eight hours with drug as described before dissection and flash freezing of the lungs. Lungs were pulverized in liquid nitrogen before lysis as described above [1].

Solubility Information

Solubility	DMSO: 5.96 mg/mL (10 mM),Sonication is recommended. H2O: 20 mg/mL (33.57 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6787 mL	8.3933 mL	16.7867 mL
5 mM	0.3357 mL	1.6787 mL	3.3573 mL
10 mM	0.1679 mL	0.8393 mL	1.6787 mL
50 mM	0.0336 mL	0.1679 mL	0.3357 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

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.
Liu N N, Zhou J, Jiang T, et al. A dual action small molecule enhances azoles and overcomes resistance through co-targeting Pdr5 and Vma1: Osimertinib targets Pdr5 and Vma1. Translational Research. 2022
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.
Wang N, et al. Osimertinib (AZD9291) increases radio-sensitivity in EGFR T790M non-small cell lung cancer. Oncol Rep. 2019 Jan;41(1):77-86.
Finlay MR, et al. Discovery of a potent and selective EGFR inhibitor (AZD9291) of both sensitizing and T790M resistance mutations that spares the wild type form of the receptor. J Med Chem. 2014 Oct 23;57(20):8249-67.
Nanjo S, et al. High efficacy of third generation EGFR inhibitor AZD9291 in a leptomeningeal carcinomatosis model with EGFR-mutant lung cancer cells. Oncotarget. 2016 Jan 26;7(4):3847-56.

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