Oritinib mesylate

Cat. No.: HY-139920A

CAS No.: 2180164-79-6

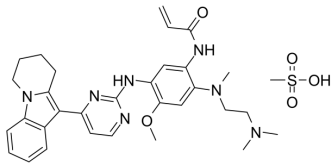
Molecular Formula: $C_{32}H_{41}N_7O_5S$

Molecular Weight: 635.78

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

Oritinib (SH-1028) mesylate is a selective, orally active, and pyrimidine-based irreversible inhibitor of EGFR with an IC_{50} of 18 nM. Oritinib (SH-1028) mesylate exhibits potent activity against EGFR sensitive and resistant (T790 M) mutations. Oritinib (SH-1028) mesylate significantly inhibits proliferation of tumor cells with EGFR sensitive and resistant mutation[1].

IC_{50} & Target

EGFR (WT) 18 nM (IC_{50})	$EGFR^{L858R}$ 0.7 nM (IC_{50})	$EGFR^{L861Q}$ 4 nM (IC_{50})	$EGFR^{L858R/T790M}$ 0.1 nM (IC_{50})
$EGFR^{d746-750}$ 1.4 nM (IC_{50})	$EGFR^{d746-750/T790M}$ 0.89 nM (IC_{50})		

In Vitro

Oritinib (SH-1028) (72 hours; 10 μmol/L and the 3-fold dilution; nine times) mesylate selectively inhibits EGFR-mutated NCI-H1975, H3255 and PC-9 cells, with IC_{50} values of 3.93, 9.39 and 7.63 nM, respectively, which is more sensitive than the inhibition of wild-type EGFR in A431 cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	A431 ($EGFR^{WT}$), H3255 ($EGFR^{L858R}$), PC-9 ($EGFR^{d746-750}$) and NCI-H1975 ($EGFR^{L858R/T790M}$) cells
Concentration:	0.001, 0.01, 0.1, 1, and 10 μM
Incubation Time:	72 hours
Result:	Selectively inhibited EGFR-mutated NCI-H1975, H3255 and PC-9 cells, with IC_{50}s of 3.93±1.12, 9.39±0.88 and 7.63±0.18 nmol/L, respectively, which were about 198-, 83- and 102-fold more sensitive than the inhibition of wild-type EGFR in A431 cells (IC_{50} =778.89±134.74 nM).

In Vivo

Oritinib (SH-1028) (p.o.; once daily for consecutive 14 days; 2.5-15 mg/kg) mesylate inhibits EGFR-mutant tumor progression but not wild-type EGFR in vivo[1].

Oritinib (SH-1028) (p.o.; once daily for consecutive 14 days; 2.5-15 mg/kg) mesylate only induces a moderate tumor growth inhibition in A431 (wild-type EGFR) tumor xenografts, while causes profound and sustained tumor shrinkage in both NCI-H1975 and PC-9 xenograft models with EGFR mutations with 5 mg/kg/day[1].

Oritinib (SH-1028) (p.o.; once daily for consecutive 14 days; 2.5-15 mg/kg) mesylate shows good bioavailability, and is distributed extensively from the plasma to the tissues with T_{max} of 1.5-2 h, and AUC_{0-t} values of SH-1028 in plasma are 118, 300 and 931 ng × h/ml on Day 1, while 272, 308 and 993 ng × h/ml on Day 14[1].

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

Animal Model:	Nu/Nu female nude mice (6-8 weeks) bearing human lung cancer cell lines[1]
Dosage:	2.5, 5, and 15 mg/kg (SH-1028) and control group (osimertinib, 5 mg/kg)
Administration:	p.o.; once daily for consecutive 14 days
Result:	Only induced a moderate tumor growth inhibition in A431 (wild-type EGFR) tumor xenografts, while caused profound and sustained tumor shrinkage in both NCI-H1975 and PC-9 xenograft models with EGFR mutations with 5 mg/kg/day.

REFERENCES

[1]. Han L, et al. SH-1028, An Irreversible Third-Generation EGFR TKI, Overcomes T790M-Mediated Resistance in Non-Small Cell Lung Cancer. Front Pharmacol. 2021;12:665253.

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