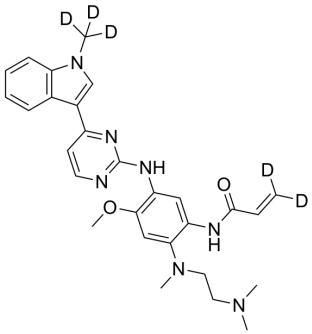
Dosimertinib-d_3

Cat. No.:	HY-142283
CAS No.:	2403760-70-1
Molecular Formula:	$C_{28}H_{28}D_5N_7O_2$
Molecular Weight:	504.64
Target:	EGFR; Isotope-Labeled Compounds
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Dosimertinib-d_3-d_3 is a potent and orally active EGFR inhibitor. Dosimertinib-d_3-d_3 decreases the expression of p-EGFR and p-ERK protein levels. Dosimertinib-d_3-d_3 shows antiproliferative and anti-tumor activity. Dosimertinib-d_3-d_3 has the potential for the research of non-small-cell lung cancer (NSCLC)[1].

In Vitro

Dosimertinib (compound 2h) (1, 10, 100, 100 nM; 2h) decreases the expression of p-EGFR and p-ERK protein levels 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:	A431, H1975, EGFR-L858/T790M BaF3, EGFR-del19/T790M BaF3 Cells
Concentration:	0-10 μM
Incubation Time:	72 h
Result:	Showed antiproliferative activity with IC_{50}s of 243.9, 28.4, 18.0, 3.5 nM for A431, H1975, EGFR-L858/T790M BaF3, EGFR-del19/T790M BaF3 cells, respectively.

Western Blot Analysis[1]

Cell Line:	A431, H1975 cells
Concentration:	1, 10, 100, 100 nM
Incubation Time:	2 h
Result:	Decreased the expression of p-EGFR and p-ERK protein levels in a dose-dependent mannet when co-incubationed with 50 ng/mL EGF.

In Vivo

Dosimertinib (0.75, 1.5, 3 mg/kg; oral gavage, daily for 24 days) shows anti-tumor activity in mouse[1].

Pharmacokinetic Parameters of Dosimertinib in Sprague-Dawley rats[1].

detected compound	dosimertinib

administration route	i.v.	i.g.	i.g.	i.g.
dose (mg/kg)	2	2	6	12
C_0 or C_{max} (nM)	277 ± 105	46.7 ± 10.7	113 ± 19.8	283 ± 137
T_{max} (h)		4.17 ± 2.56	4.67 ± 1.63	5.00 ± 1.67
$t_{1/2}$ (h)	5.40 ± 1.84	3.76 ± 1.08	3.27 ± 0.43	4.04 ± 1.50
AUC_{0-t} (nM·h)	1070 ± 565	459 ± 191	1020 ± 313	2830 ± 1780
CL/F (L/h/kg)	22.3 ± 11.1	32.2 ± 13.6	19.5 ± 5.1	14.9 ± 6.4
bioavailability (%)		41.2	29.6	43.0

Male Sprague-Dawley rats, 2 mg/kg iv; 2, 6, 12 mg/kg for i.g..

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Animal Model:	18-20 g, BALB/c nude mice (H1975 mouse xenograft model)[1]
Dosage:	0.75, 1.5, 3 mg/kg
Administration:	Oral gavage; daily for 24 days
Result:	Significantly reduced tumor size with tumor growth inhibition (TGI) of 72.94% and 97.62% at 1.5, 3 mg/kg, respectively.

REFERENCES

[1]. Chen C, et al. Cyclization strategy leads to highly potent Bromodomain and extra-terminal (BET) Bromodomain inhibitors for the treatment of acute liver injury. Eur J Med Chem. 2022 Dec 16;247:115023.

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