Opnurasib

Cat. No.: HY-139612

CAS No.: 2653994-08-0

Molecular Formula: $C_{29}H_{28}ClN_7O$

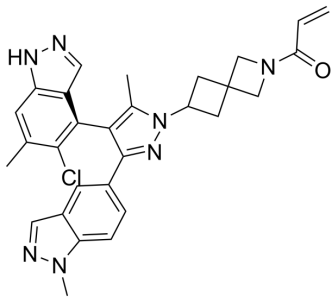
Molecular Weight: 526.03

Target: Ras; PERK

Pathway: GPCR/G Protein; MAPK/ERK Pathway; Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 80 mg/mL (152.08 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9010 mL	9.5052 mL	19.0103 mL
	5 mM	0.3802 mL	1.9010 mL	3.8021 mL
	10 mM	0.1901 mL	0.9505 mL	1.9010 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.95 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.95 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Opnurasib (JDQ-443) (NVP-JDQ443) is an orally active, potent, selective, and covalent KRAS G12C inhibitor (extracted from patent WO2021120890A1). Opnurasib shows antitumor activity[1][2].

IC_{50} & Target

KRas G12C

In Vitro

Opnurasib (NVP-JDQ443) traps the GDP-bound inactive conformation of KRAS[1].
?Opnurasib promotes dose-dependent reductions of phosphorylated ERK (pERK) levels and the proliferation of the KRASG12C-mutated cell lines NCI-H358 and NCI-H2122, with IC_{50} values of 0.018 and 0.063 μM, respectively[2].
?Opnurasib covalently and selectively binds and inhibits GDP-bound KRASG12C with low reversible binding affinity to the RAS switch II pocket, and also inhibits proliferation of KRASG12C-mutated and KRAS G12C/H95, G12C/R68S, and G12C/Y96

double-mutant cell lines[2].

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

Western Blot Analysis

Cell Line:	Ba/F3 cells[2]
Concentration:	0, 0.3, 1 μM
Incubation Time:	30 min, 4 h
Result:	Inhibited signaling (pERK) and proliferation of the KRAS G12C/H95 double mutants G12C/H95R and G12C/H95Q.

In Vivo

Opnurasib (10-100 mg/kg, Orally, daily for 14 days) shows antitumor activity in KRAS G12C-mutated CDX models[2].

?Opnurasib (Orally, 100 mg/kg, daily (JDQ443) + 7.5 mg/kg, twice daily (TNO155), for 36 days) shows greater cell growth inhibition or cell killing compared with single-agent JDQ443 when combined with TNO155[2].

?Opnurasib generates categorical antitumor responses in PDX models of NSCLC and colorectal tumors that are improved by combination treatment with other agents[2].

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

Animal Model:	KRAS G12C tumor-bearing nude mice (MIA PaCa-2 (PDAC); NCIH2122, LU99, HCC44, NCI-H2030 (NSCLC); and KYSE410 (esophageal cancer))[2]
Dosage:	10, 30, 100 mg/kg
Administration:	Orally, daily for 14 days
Result:	Inhibited the growth of all models in a dose-dependent manner.

Animal Model:	Three KRAS G12C-mutated CDX models (LU99, NCI-H2030, and KYSE410)[2]
Dosage:	100 mg/kg (JDQ443) + 7.5 mg/kg (TNO155)
Administration:	Orally, daily (JDQ443) or twice daily (TNO155), for 36 days
Result:	Combined with TNO155, showed either greater tumor efficacy compared with each agent alone (H2030, KYSE410) or a delayed time to tumor progression (LU99).

REFERENCES

[1]. [2] Weiss A, Lorthiois E, Barys L, et al. Discovery, Preclinical Characterization, and Early Clinical Activity of JDQ443, a Structurally Novel, Potent and Selective, Covalent Oral Inhibitor of KRASG12C. Cancer Discov. 2022;candisc.0158.2022.

[2]. LIU BO, et al. PYRAZOLYL DERIVATIVES USEFUL AS ANTI-CANCER AGENTS. Patent WO2021120890A1.

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