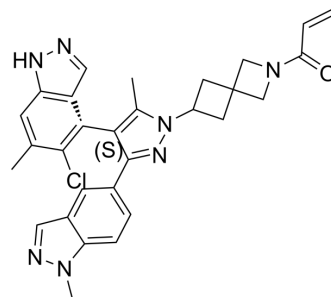


(S)-JDQ-443

Cat. No.:	HY-139612A		
CAS No.:	2653994-10-4		
Molecular Formula:	C ₂₉ H ₂₈ ClN ₇ O		
Molecular Weight:	526.03		
Target:	Ras; PERK		
Pathway:	GPCR/G Protein; Cell Cycle/DNA Damage		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



BIOLOGICAL ACTIVITY

Description	(S)-JDQ-443 is an isomer of JDQ-443 (HY-139612). JDQ-443 is an orally active, potent, selective, and covalent KRAS G12C inhibitor (extracted from patent WO2021120890A1). JDQ-443 shows antitumor activity ^{[1][2]} .
In Vitro	JDQ-443 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] . JDQ443 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.
In Vivo	JDQ443 (10-100 mg/kg, Orally, daily for 14 days) shows antitumor activity and inhibits the growth of tumor in a dose-dependent manner in KRAS G12C-mutated CDX models ^[2] . JDQ443 (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] . JDQ443 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.

REFERENCES

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

[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.

Caution: Product has not been fully validated for medical applications. For research use only.

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