CHK1-IN-9

Cat. No.: HY-161383

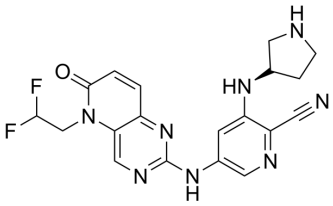
Molecular Formula: $C_{19}H_{18}F_2N_8O$

Molecular Weight: 412.4

Target: Checkpoint Kinase (Chk)

Pathway: Cell Cycle/DNA Damage

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CHK1-IN-9 (compound 11) is an orally active CHK1 inhibitor with an IC_{50} value of 0.55 nM. CHK1-IN-9 can enhance the effect of DNA-damaging drugs on tumor cells. CHK1-IN-9 has synergistic anticancer effects with Gemcitabine (HY-17026)[1].

IC_{50} & Target

Chk1
0.55 nM (IC_{50})

In Vitro

CHK1-IN-9 (compound 11) (11.11, 33.33, 100, and 300 nM, 16 h) can inhibit the proliferation of tumor cells, with the IC_{50} value of 202 nM for MV-4-11 cells[1].

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

Cell Proliferation Assay [1]

Cell Line:	OVCAR3, HT-29, A549, HL-60, HCT116, A2780 and MDAMB-468 cells
Concentration:	11.11, 33.33, 100, and 300 nM
Incubation Time:	16 h
Result:	Alone had an IC_{50} value of 1166.5 nM for HT-29, and 63.53 nM when combined with Gemcitabine (HY-17026).

In Vivo

CHK1-IN-9 (compound 11) (30 mg/kg/day for 21 days□iv or po) demonstrates a tumor growth inhibition (TGI) value of 20.6% in the HT-29 xenograft mouse model when used alone, and shows greater antitumor activity (TGI = 42.8%) when combined with Gemcitabine (HY-17026)[1].

Pharmacokinetic Analysis in the HT-29 xenograft mouse model Model[1]

Route	Dose (mg/kg)	C_0 (ng/mL)	C_{max} (ng/mL)	$T_{1/2}$ (h)	T_{max} (h)	AUC_{0-t} (ng·h/mL)	$AUC_{0-\infty}$ (ng·h/mL)	MRT_{0-t} (h)	MRT_{0-t} (h)	Cl (mL/kg/min)	V_{ss} (L/kg)	F (%)
i.v.	2	860	526	5.70	0.08	327	341	2.67	3.91	98.4	23.3	/

p.o.	10	/	81.1	1.51	0.08	40.7	47.3	1.00	1.65	/	/	2.77

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

REFERENCES

[1]. Hu S, et al. Discovery of pyrido[3,2-d]pyrimidin-6(5H)-one derivatives as checkpoint kinase 1 (CHK1) inhibitors with potent antitumor efficacy. Eur J Med Chem. 2024 Apr 5;269:116351.

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