ATM Inhibitor-8

Cat. No.: HY-155090

CAS No.: 2956666-60-5

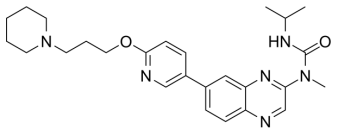
Molecular Formula: $C_{26}H_{34}N_6O_2$

Molecular Weight: 462.59

Target: ATM/ATR

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR

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



BIOLOGICAL ACTIVITY

Description

ATM Inhibitor-8 (Compound 10r) is a highly potent, selective and orally active ATM inhibitor,with an IC_{50} of 1.15 nM. ATM Inhibitor-8 exhibits anti-tumor activity[1].

IC_{50} & Target

IC50:1.15 nM (ATM)[1]

In Vitro

ATM Inhibitor-8 inhibits the proliferation of colorectal cancer cells (HCT116, SW620) and breast cancer cells (MCF-7) [1].
ATM Inhibitor-8(200 nM) inhibits the viability of MCF-7 cell combined with 4.22 μM Etposide (HY-13629) and 0.036 μM Irinotecan (HY-16562)[1].
ATM Inhibitor-8 (200 nM) inhibits the viability of SW620 cell with 0.22 μM Irinotecan (HY-16562) and inhibits cell colony with 0.02 μM[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis

Cell Line:	HCT116 cell[1]
Concentration:	200 nM
Incubation Time:	4 h
Result:	:Inhibted ATM pathway obviously combined with 25 μM Irinotecan.

Cell Cycle Analysis

Cell Line:	HCT116 cell[1]
Concentration:	200 nM
Incubation Time:	48 h
Result:	Decreased G0/G1 phase cells and increased G0/G1 phase cells with the concentration increase.

In Vivo

ATM Inhibitor-8 inhibits the growth of tumor combined with 40 mg/kg Irinotecan in SW620 mice model [1].
ATM Inhibitor-8(10 mg/kg, i.v.) has a good value of PK in Balb/c mice which means a lower plasma clearance , higher plasma exposure as well as excellent oral bioavailability. [1].

ATM Inhibitor-8 Pharmacokinetic Analysis in Balb/c Mice[1]

□□□□□□□□[1]

Route	Dose (mg/kg)	C_{max} (ng/mL)	T_{max} (h)	$t_{1/2}$ (h)	Cl_{obs} (L·h/kg)	V_{ss_obs} (L/kg)	AUC_{INF_obs} (ng·h/mL)	F (%)
i.v.	10	6793.55	0.88	5.29	0.78	5.93	13027.01	/
p.o.	10	10216.65	0.33	3.37	0.73	3.52	13952.23	107.10

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Animal Model:	Mouse xenograft model of human colon cancer[1].
Dosage:	40 mg/kg combined with Irinotecan(40 mg/kg)
Administration:	ATM Inhibitor-8, 20 or 40 mg/kg, p.o. once daily for 3 days every week starting 24 h post-irinotecan dosing (40 mg/kg, i.p. once weekly).
Result:	Inhibited tumor growth significantly.

REFERENCES

[1]. D Deng, et al. Discovery and Evaluation of 3-Quinoxalin Urea Derivatives as Potent, Selective, and Orally Available ATM Inhibitors Combined with Chemotherapy for the Treatment of Cancer via Goal-Oriented Molecule Generation and Virtual Screening. J Med Chem. 2023 Jul 27□

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