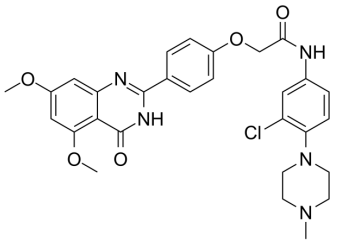
BRD4/CK2-IN-1

Cat. No.:	HY-145260
CAS No.:	2756851-99-5
Molecular Formula:	$C_{29}H_{30}ClN_5O_5$
Molecular Weight:	564.03
Target:	Epigenetic Reader Domain; Casein Kinase; Apoptosis; Autophagy
Pathway:	Epigenetics; Cell Cycle/DNA Damage; Stem Cell/Wnt; Apoptosis; Autophagy
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BRD4/CK2-IN-1 is the first highly effective and oral active dual-target inhibitor of BRD4/CK2 (bromodomain-containing protein 4/casein kinase 2), with IC_{50}s of 180 nM and 230 nM for BRD4 and CK2, respectively. BRD4/CK2-IN-1 has strong anticancer activity without obvious toxicities. BRD4/CK2-IN-1 induces apoptosis and autophagy-associated cell death in triple-negative breast cancer (TNBC)[1]

IC_{50} & Target	BRD4	CK2
	180 nM (IC_{50})	230 nM (IC_{50})

In Vitro

BRD4/CK2-IN-1 (compound 44e) (0-25 μM; 24 hours) has anti-proliferation effect with IC_{50}s of 2.66 and 3.52 μM in MDA-MB-231 and MDA-MB-468 cells, respectively[1].

BRD4/CK2-IN-1 (0-10 μM; 24 hours) dose-dependently induces apoptosis of MDA-MB-231 and MDA-MB-468 cells[1].

BRD4/CK2-IN-1 (0-10 μM; 24 hours) dose-dependently downregulates Bcl-2 but upregulates Bax and cleaved caspase-3[1].

BRD4/CK2-IN-1 (0-10 μM; 24 hours) significantly downregulates the autophagy substrate p62 and up-regulated beclin-1 and LC3II in MDA-MB-231 and MDA-MB[1].

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

Cell Viability Assay[1]

Cell Line:	MDA-MB-231, MDA-MB-468 cells
Concentration:	0, 0.19, 0.39, 0.78, 1.56, 3.13, 6.25, 12.5, 25 μM
Incubation Time:	24 hours
Result:	Showed anti-proliferative rates in MDA-MB-231 and MDA-MB-468 cells (IC_{50} = 2.66 and 3.52 μM, respectively).

Apoptosis Analysis[1]

Cell Line:	MDA-MB-231, MDA-MB-468 cells
Concentration:	0, 2.5, 5, 10 μM
Incubation Time:	24 hours
Result:	Dose-dependently induced apoptosis of MDA-MB-231 and MDA-MB-468 cells.

Western Blot Analysis[1]

Cell Line:	MDA-MB-231, MDA-MB-468 cells
Concentration:	0, 2.5, 5, 10 μM
Incubation Time:	24 hours
Result:	Dose-dependently downregulated Bcl-2 but upregulated Bax and cleaved caspase-3.

Cell Line:	
Concentration:	
Incubation Time:	
Result:	

In Vivo

BRD4/CK2-IN-1 (25 and 50 mg/kg; intragastric administration; daily for 19 days) inhibits tumor growth in TNBC xenograft models[1].

BRD4/CK2-IN-1 (25 and 50mg/kg; intragastric administration; daily for 19 days) shows weak toxicity measured by body weight loss in the MDA-MB-231 and MDA-MB-468 xenograft models[1].

Preliminary Assessment of Pharmacokinetics (PK) profile of BRD4/CK2-IN-1[1].

Parameter	iv (1 mg/kg)	po (10 mg/kg)
$T_{1/2}$ (h)	4.21±0.57	5.14±0.71
C_{max} (ng/mL)	237±11	206±6
AUC_{0-t} (ng·h/mL)	579±49	2079±130
$AUC_{0-\infty}$ (ng·h/mL)	588±36	2090±146
V_Z (L/kg)	21.1±2.6	
CL ((mL/min)/kg)	57.4±1.3	
F (%)		32.5

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Animal Model:	Female nude mice (BALB/c, 6-8 weeks, 20-22 g) bearing MDA-MB-231 cells[1]
Dosage:	25 and 50 mg/kg
Administration:	Intragastric administration; daily for 19 days
Result:	Had the most pronounced tumor growth inhibition (TGI) (63.8%) in the MDA-MB-231 xenograft tumor model at 50 mg/kg.

REFERENCES

[1]. Zhang J, et al. Discovery of Novel Dual-Target Inhibitor of Bromodomain-Containing Protein 4/Casein Kinase 2 Inducing Apoptosis and Autophagy-Associated Cell Death for Triple-Negative Breast Cancer Therapy. J Med Chem. 2021;64(24):18025-18053.

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