CT-179

Cat. No.: HY-179078

CAS No.: 1996636-69-1

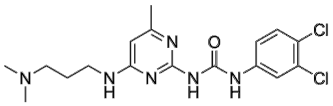
Molecular Formula: $C_{17}H_{22}Cl_2N_6O$

Molecular Weight: 397.30

Target: OLIG2; Apoptosis; Caspase; PARP

Pathway: Neuronal Signaling; Apoptosis; Cell Cycle/DNA Damage; Epigenetics

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (31.46 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5170 mL	12.5849 mL	25.1699 mL
	5 mM	0.5034 mL	2.5170 mL	5.0340 mL
	10 mM	0.2517 mL	1.2585 mL	2.5170 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: ≥ 1.25 mg/mL (3.15 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (3.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CT-179 is a brain-penetrant and orally active OLIG2 inhibitor with a human IC_{50} of 1250 nM. CT-179 disrupts OLIG2 dimerization, phosphorylation, and DNA binding, blocking OLIG2-driven transcription. CT-179 induces G_2/M phase arrest and increases G_0 population. CT-179 induces apoptosis by reducing anti-apoptotic proteins and increasing cleaved caspase-3 and cleaved PARP. CT-179 can be used for the research of subgroup medulloblastoma[1].

IC_{50} & Target		
	Caspase-3	PARP

In Vitro

CT-179 (10 nM-10 μM; 1 hour) dose-dependently disrupts OLIG2 dimerization in live HEK293 cells, with an IC_{50} of 1250 nM[1].
CT-179 (1-10 μM; 1 hour) reduces OLIG2-DNA binding in live HEK293 cells, as shown by increased diffusion of DNA-bound OLIG2 and reduced fractional DNA-bound OLIG2 at concentrations of 1 μM and 10 μM[1].
CT-179 (250 nM; 24 hours) blocks OLIG2-driven transcription in Daoy SHH-medulloblastoma cells, as measured by reduced

activity of an LHX8 promoter luciferase reporter[1].
CT-179 (1 μM) shows minimal relevant off-target kinase inhibition in vitro; while it inhibits FLT3 with an IC_{50} of 20 nM in a cell-free assay, the predicted in vivo cell potency is too low to be biologically meaningful[1].
CT-179 (160 nM-2.5 μM) shows minimal off-target effects in normal human primary cells at biologically relevant concentrations (160 nM, 630 nM), with only limited proliferation reduction observed at the supraphysiological concentration of 2.5 μM[1].
CT-179 (1 nM-10 μM; 7 days) reduces viability in OLIG2-expressing SHH-medulloblastoma cell lines (Daoy, UW228, Med-813) in a manner correlating with OLIG2 expression, with IC_{50} values ranging from 143.6 nM to 965.2 nM, and shows no activity in OLIG2-negative cell lines[1].
CT-179 (1 μM; 17 h-7 days) induces apoptosis, G_2/M phase arrest, and mitotic disruption in Daoy SHH-medulloblastoma cells, and potentiates radiotherapy-induced apoptosis[1].
CT-179 (1 μM; 17-96 hours) induces apoptosis and disrupts mitotic mechanisms in Med-813 SHH-medulloblastoma cells, and potentiates radiotherapy-induced apoptosis[1].
CT-179 (1 μM; 48 hours) induces cell death in patient-derived medulloblastoma explant organoids (including SHH-subgroup R902), and when combined with radiotherapy, further reduces proliferation without increasing stem cell populations[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	Daoy SHH-medulloblastoma
Concentration:	1 μM
Incubation Time:	17 h; 24 h; 48 h; 72 h; 96 h; 7 days;
Result:	Induced apoptosis, shown by dose-dependent increases in cleaved caspase-3 (cC3) and cleaved PARP over time, and reduced levels of anti-apoptotic proteins MCL-1, BCL-2, and BCL-xL. Sensitized Daoy cells to RT-induced apoptosis, with significantly higher apoptotic cell percentages in the combination group compared to single-agent treatments on day 1 and day 3. Induced G_2/M phase arrest, decreased cyclin B1, CDK1, and p-CDK1, and maintained elevated p-HH3, resulting in abnormal nuclear morphology (multinucleation, satellite micronuclei) and disrupted mitotic spindle formation.

Apoptosis Analysis[1]

Cell Line:	Med-813 SHH-medulloblastoma
Concentration:	1 μM
Incubation Time:	17 h; 24 h; 48 h; 72 h; 96 h
Result:	Induced apoptosis, with significantly higher apoptotic cell percentages in the CT-179 and combination groups compared to control on day 3. Disrupted mitotic mechanisms, with an initial increase in cyclin B1, CDK1, and p-HH3 over 24 hours (accompanied by decreased p-CDK1), followed by decreases in cyclin B1 and CDK1 and a marked increase in p-CDK1 at later time points.

In Vivo

CT-179 (50 mg/kg; i.p.; twice weekly; two weeks) as a single agent prolongs median event-free survival to 60 days, and combination with radiotherapy further extends median event-free survival to 75.5 days while delaying tumor growth in SHH-subgroup medulloblastoma-bearing NRG mice[1].
CT-179 (75 mg/kg; p.o.; every other day) as a single agent prolongs median event-free survival to 76 days, and combination with radiotherapy further extends median event-free survival to 100.5 days in SHH-subgroup medulloblastoma-bearing NRG mice[1].
CT-179 (80 mg/kg; i.p.; every other day) as a single agent reduces tumor proliferation, induces cell cycle arrest and neuronal

differentiation, slows tumor growth, and improves event-free survival, while combination with radiotherapy further enhances event-free survival in SHH-subgroup medulloblastoma-bearing G-Smo mice[1].
CT-179 (80 mg/kg; i.p.; every other day) combined with POx-Palbo enhances cell cycle arrest, increases apoptosis, and improves event-free survival more effectively than either single agent in SHH-subgroup medulloblastoma-bearing G-Smo mice[1].

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

Animal Model:	NOD-Rag1null IL2rgnull (NRG) (female, 6-7 week-old, orthotopic cerebellar engraftment with Daoy-luci cells)[1]
Dosage:	50 mg/kg
Administration:	i.p.; twice weekly; two weeks
Result:	Increased median event-free survival (EFS) to 60 days (vs. 55 days for vehicle control). Increased median EFS to 75.5 days when combined with radiotherapy, which was statistically significant compared to vehicle, CT-179 alone, and radiotherapy alone. Significantly delayed tumor growth in the brain and spinal cord, with reduced luminescence signal compared to vehicle, CT-179 alone, and radiotherapy alone at day 42.

Animal Model:	NOD-Rag1null IL2rgnull (NRG) (female, 6-7 week-old, orthotopic cerebellar engraftment with Med-813-luci cells)[1]
Dosage:	75 mg/kg
Administration:	p.o.; every other day
Result:	Increased median EFS to 76 days (vs. 71 days for vehicle control). Increased median EFS to 100.5 days when combined with radiotherapy, which was statistically significant compared to vehicle, CT-179 alone, and radiotherapy alone.

Animal Model:	Gfap-Cre/SmoM2 (G-Smo) (genetically engineered SHH-pathway hyperactivation inducing tumor formation by postnatal day 10)[1]
Dosage:	80 mg/kg
Administration:	i.p.; every other day
Result:	Showed a trend toward decreased phosphorylated OLIG2 (p-OLIG2; p=0.057) and significantly reduced phosphorylated RB (p-RB) in tumors after treatment from P10-P16. Increased the G_2/M fraction at 6 hours after a single dose, and by 24 hours, increased G_0 and G_2/M fractions with decreased G_1 and mitotic (p-RB++) fractions. Increased NEUN+ neuronal differentiation and OLIG2+/SOX10− tumor stem cell populations, while reducing tumor cross-sectional area at P17. Significantly improved EFS compared to vehicle controls. Resulted in statistically significant increased EFS when combined with radiotherapy compared to vehicle, CT-179 alone, and radiotherapy alone.

Animal Model:	Gfap-Cre/SmoM2 (G-Smo) (genetically engineered SHH-pathway hyperactivation inducing tumor formation by postnatal day 10)[1]
Dosage:	80 mg/kg plus 25 mg/kg POx-Palbo

Administration:	i.p.; every other day
Result:	Increased G_0 cell fractions, increased G_2/M cell fractions (with reduced mitotic p-RB++ cells, indicating G_2 arrest), and increased cleaved caspase-3-positive apoptotic cells compared to vehicle, CT-179 alone, and POx-Palbo alone. Resulted in improved event-free survival compared to either single agent.

REFERENCES

4.

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