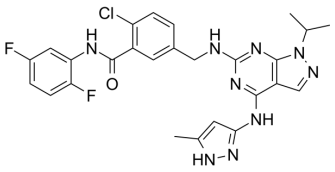
CZS-241

Cat. No.:	HY-149912
CAS No.:	3016297-55-2
Molecular Formula:	$C_{26}H_{24}ClF_2N_9O$
Molecular Weight:	551.98
Target:	Polo-like Kinase (PLK); Apoptosis; Trk Receptor
Pathway:	Cell Cycle/DNA Damage; Apoptosis; Neuronal Signaling; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CZS-241 is an orally active and selective inhibitor of Polo-like Kinase (PLK) 4 (IC_{50}=2.6 nM). CZS-241 inhibits TRKA with an IC_{50} value of 2.74 μM. CZS-241 induces apoptosis and arrests cell cycle at S/G2 phase. CZS-241 shows highly potent antiproliferative activity against leukemia cell lines, and exhibits safety against normal cell lines[1].

IC_{50} & Target

PLK4	TrkA
2.6 nM (IC_{50})	2.74 μM (IC_{50})

In Vitro

CZS-241 inhibits cell proliferation of chronic myeloid leukemia (CML) cell lines K562 and KU-812 with IC_{50}s of 0.096 μM and 0.25 μM, respectively. CZS-241 has little effect on normal cells including HUVECs and L02[1].
CZS-241 (10 μM; 0-120 min) exhibits 31.5 min of half-life $t_{1/2}$ and 41.8 μL/min/kg of CL_{int} in human liver microsomal[1].
CZS-241 (0.3 μM, 1 μM, 3 μM; 48 h) arrests cell cycle at S/G2 phase, induces apoptosis in K562 CML cells[1].
CZS-241 (0.03-0.3 μM) inhibits the phosphorylation of PLK4, increases the FBXW5 expression level but decreases the SAS-6 expression level in K562 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	K562 cells
Concentration:	0.03 μM, 0.1 μM, 0.3 μM, 1 μM, and 3 μM
Incubation Time:	
Result:	Showed insignificant effect on PLK4 relative expression, but decreased the expression of SAS-6 dose-dependently. Increased the expression level of FBXW5.

In Vivo

CZS-241 (30 mg/kg; p.o.; single dose) shows over 4 h of half-life and 70.8% bioavailability in mice[1].
CZS-241 (20 mg/kg/day; p.o.; 21 days) suppresses tumor progression significantly in K562 cells xenograft mouse model[1].
CZS-241 (200 mg/kg; p.o.; single dose) has no obvious signs of toxicity in heart, liver, spleen, lungs, and kidneys of mice, within 7 days of monitoring[1].

Pharmacokinetic Analysis in mice[1]

Route	Dose (mg/kg)	AUC_{last} (ng·h/mL)	AUC_{INF_obs} (ng·h/mL)	$t_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	Cl_{obs} (L·h/kg)	V_{ss_obs} (mL/kg)	MRT $_{INF\_obs}$ (h)	F (%)
i.v.	3	727	739	2.15	/	/	68.7	12615	1.28	70.8
p.o.	30	5177	5231	4.13	0.67	1880	/	/	3.87	/

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

Animal Model:	K562 cells xenograft mouse model[1]
Dosage:	10 mg/kg, 20 mg/kg
Administration:	PO; once daily, for continuous 21 days
Result:	Showed potent antitumor activity with mouse body weight increased normally. Exhibited tumor growth inhibition (TGI) rate of 56.4% at 20 mg/kg/day dosage.

REFERENCES

[1]. Sun Y, et al. Discovery of CZS-241: A Potent, Selective, and Orally Available Polo-Like Kinase 4 Inhibitor for the Treatment of Chronic Myeloid Leukemia. J Med Chem. 2023 Feb 23;66(4):2396-2421.

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