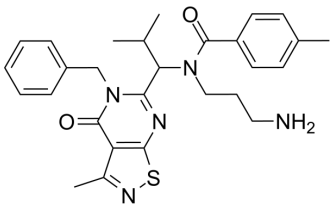
AZD4877

Cat. No.:	HY-13224
CAS No.:	758722-49-5
Molecular Formula:	$C_{28}H_{33}N_5O_2S$
Molecular Weight:	503.66
Target:	Kinesin; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AZD4877 is another isostere to Ispinesib (HY-50759)and also a kinesin spindle protein (Eg5) inhibitor with IC_{50} of 2 nM.AZD4877 arrests cell mitosis, leads to the formation of the monopolar spindle phenotype and induces apoptosis. AZD4877 inhibits circulating peripheral blood mononuclear cells (PBMCs) and has anti-cancer activity[1][2][3][4][5].
IC_{50} & Target	IC50: 2 nM (Eg5)[5]
In Vitro	AZD4877 (10 nM, 24 or 48 hours) induces apoptosis in human bladder cancer cells and AZD4877-sensitive cells generally expressed high levels of p63[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. Apoptosis Analysis[2]

Cell Line:	UC1, UC3, UC6, UC12, UC15, RT4,JB,BV, T24 cell line
Concentration:	10 nM
Incubation Time:	24 or 48 hours
Result:	Induced apoptosis in human bladder cancer cells

In Vivo	AZD4877 (i.v., 6 mg/kg, 12 mg/kg; single dose) has a significant reduction in cell viability and increase in cleaved caspase 3 levels by 48 h post dose in a rat hollow fiber model[1]. AZD4877 (i.v., 6 mg/kg; single dose) shows a $T_{1/2}$ of 3.5 h, and CL of 36 mL/min/kg in Hans Wistar rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Theoclitou ME, et.al. Discovery of (+)-N-(3-aminopropyl)-N-[1-(5-benzyl-3-methyl-4-oxo-[1,2]thiazolo[5,4-d]pyrimidin-6-yl)-2-methylpropyl]-4-methylbenzamide (AZD4877), a kinesin spindle protein inhibitor and potential anticancer agent. J Med Chem. 2011 Oct 13;54(19):6734-50.

[2]. Marquis L, et.al. p63 expression correlates with sensitivity to the Eg5 inhibitor ZD4877 in bladder cancer cells. Cancer Biol Ther. 2012 May;13(7):477-86.

[3]. Gerecitano JF, et.al. A Phase I trial of the kinesin spindle protein (Eg5) inhibitor AZD4877 in patients with solid and lymphoid malignancies. Invest New Drugs. 2013 Apr;31(2):355-62.

[4]. Shahin R, et.al. Kinesin spindle protein inhibitors in cancer: from high throughput screening to novel therapeutic strategies. Future Sci OA. 2022 Feb 21;8(3):FSO778.

[5]. Myers SM, et.al. Recent findings and future directions for interpolar mitotic kinesin inhibitors in cancer therapy. Future Med Chem. 2016;8(4):463-89.

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