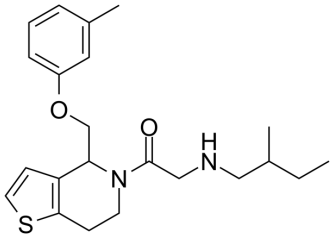
RU-SKI 43

Cat. No.:	HY-18366
CAS No.:	1043797-53-0
Molecular Formula:	$C_{22}H_{30}N_2O_2S$
Molecular Weight:	386.55
Target:	Hedgehog
Pathway:	Stem Cell/Wnt
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	RU-SKI 43 is a potent and selective Hedgehog acyltransferase (Hhat) inhibitor with an IC_{50} of 850 nM. RU-SKI 43 reduces Gli-1 activation through Smoothened-independent non-canonical signaling and decreases Akt and mTOR pathway activity. RU-SKI 43 has anti-cancer activity[1].
IC_{50} & Target	IC50: 850 nM (Hhat)[1]
In Vitro	RU-SKI 43 (10 μM; for 6 days) strongly decreases cell proliferation (83% in AsPC-1 cells) in AsPC-1 and Panc-1 cells[2]. RU-SKI 43 (10 or 20 μM; 5 hours) causes dose-dependent inhibition of Shh palmitoylation following only 5 hours[1]. RU-SKI 43 (10 μM; for 72 hours) causes a 40% decrease in Gli-1 levels in AsPC-1 cells[2]. RU-SKI 43 (10μM; 48 hours) results in decreased phosphorylation (47-67%) of four proteins in the Akt pathway, including Akt (phosphorylation at both Thr307 and Ser473), PRAS40, Bad and GSK-3β. RU-SKI 43 treatment also decreases phosphorylation of mTOR and S6, members of the mTOR signaling pathway[2]. RU-SKI 43 behaves as an uncompetitive inhibitor (K_i=7.4 μM) with respect to Shh, and as a noncompetitive inhibitor (K_i=6.9 μM) with respect to ^{125}I-iodo-palmitoylCoA[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	AsPC-1 and Panc-1 pancreatic cancer cells
Concentration:	10 μM
Incubation Time:	For 6 days (drugs were replenished every 48 hours)
Result:	Strongly decreased cell proliferation (83% in AsPC-1 cells).

Western Blot Analysis[1]

Cell Line:	COS-1 cells expressing HA-Hhat and Shh
Concentration:	10 or 20 μM
Incubation Time:	5 hours
Result:	Caused dose-dependent inhibition of Shh palmitoylation following only 5 hours.

In Vivo	RU-SKI 43 has a $t_{1/2}$ of 17 min in mouse plasma after IV administration[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Petrova E, et al. Hedgehog acyltransferase as a target in pancreatic ductal adenocarcinoma. Oncogene. 2014 Jan 27. doi: 10.1038/onc.2013.575.

[2]. Petrova E, et al. Inhibitors of Hedgehog acyltransferase block Sonic Hedgehog signaling.Nat Chem Biol. 2013 Apr;9(4):247-9.

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

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