

Product Data Sheet

Product Name: XAV-939

Cat. No.: GC12781

Chemical Properties

Cas. No. 284028-89-3

Chemical Name 2-[4-(trifluoromethyl)phenyl]-1,5,7,8-tetrahydrothiopyrano[4,3-d]pyrimidin-4-one

SMILES C1CSCC2=C1NC(=NC2=O)C3=CC=C(C=C3)C(F)(F)F

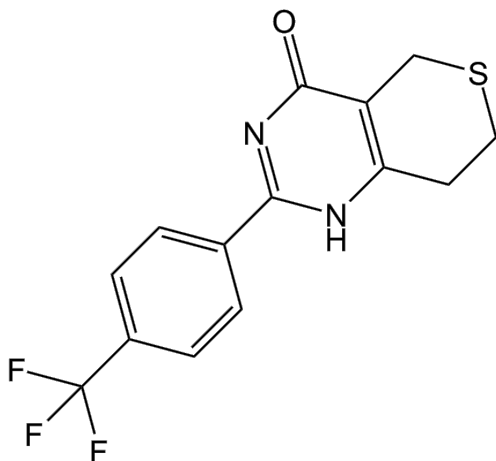
Formula $C_{14}H_{11}F_3N_2OS$ M.Wt 312.31

Solubility $\geq 15.62\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



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

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Protocol

Cell experiment [1]:

Cell lines A549 cells

Preparation Method A549 cells in the logarithmic growth phase were seeded in 96-well plates, at a density of 2×10^4 cells/well, and subsequently treated with various XAV-939 concentrations (0.1, 0.5, 1, 5, 10 $\mu\text{mol/l}$) for 24, 48, 72 and 96 h.

Reaction
Conditions 0.1, 0.5, 1, 5, 10 $\mu\text{mol/l}$ for 24, 48, 72 and 96 h

Applications At all experimental time points, XAV-939 treatment was able to significantly inhibit A549 cell proliferation compared with the control group (F24h=30.382, F48h=52.463, F72h=56.635, F96h=59.274), with the exception of the 5- and 10- $\mu\text{mol/l}$ groups at the 24 h time point.

Animal experiment [2]:

Animal models DBA/2 inbred mice

Preparation Method Mice received an intraperitoneal injection of 100 μl of XAV-939 (2 mg/ml) along with a 10% dimethyl sulfoxide (DMSO; compounded by 0.9% NaCl solution) every day since they received vaccination with the L1210 cells, while according to other experimental groups, mice received intraperitoneal injections along with 100 μl of 10% DMSO solution (compounded by 0.9% NaCl solution) for 21 days continuously.

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Dosage form Intraperitoneal injection, 100 µl of 2 mg/ml for 21 days

Applications In the model, NC, HOTAIR mimics, siRNA HOTAIR, XAV-939, and HOTAIR mimics + XAV-939 groups, the WBC number in PB increased on the 21st day by 341.08, 355.72, 499.85, 196.49, 187.48, and 363.35%. However, the PLT number decreased by 66.37, 69.46, 81.27, 49.24, 50.47, and 72.61%; hemoglobin content decreased by 39.02, 41.05, 60.52, 14.01, 17.20, and 42.36%.

References:

[1]: Li C, Zheng X, Han Y, Lv Y, Lan F, Zhao J. XAV939 inhibits the proliferation and migration of lung adenocarcinoma A549 cells through the WNT pathway. *Oncol Lett.* (2018) 15:8973-82. doi: 10.3892/ol.2018.8491

[2]: Li GJ, Ding H and Miao D: Long-noncoding RNA HOTAIR inhibits immunologic rejection of mouse leukemia cells through activating the Wnt/β-catenin signaling pathway in a mouse model of leukemia. *J Cell Physiol.* 234:10386-10396. 2019.

Background

XAV-939 selectively inhibits β-catenin-mediated transcription. XAV-939 stimulates β-catenin degradation by stabilizing axin, the concentration-limiting component of the destruction complex. XAV939 stabilizes axin by inhibiting the poly-ADP-ribosylating enzymes tankyrase 1 and tankyrase 2 with IC50 values of 5 nM and 2 nM, respectively [1, 2].

XAV-939 inhibited mouse neurofibroma sphere formation with IC50 of 0.1 µM. Western blot confirmed a 50% decrease in total β-catenin with 3 days of XAV-939 exposure (10 nM) [3]. TNKS1 plays a role in cell cycle regulation and that XAV-939 induces an accumulation of NB cell lines at G2/M and S phase of the cell cycle [4].

XAV-939 increases Irradiation (IR) sensitivity of cervical cancer with the PIK3CA-E545K mutation in vivo, XAV-939 and IR inhibited tumor weight by 38% from IR alone in that with PIK3CA-WT [5]. Combinatorial inhibition of transforming growth factor-β (TGF-β) and WNT signaling with SB431542

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and XAV-939 potently enhances the efficiency, quality, and speed of reprogrammed iCMs generated upon delivery of the minimal transcription factor (TF) cocktail, GMT, into postnatal cardiac fibroblasts. SB431542 and XAV-939 significantly improved in vivo reprogramming and cardiac function in mice compared with GMT alone and reduced the number of TFs needed for human reprogramming [6].

References:

- [1]. S.M. Huang, Y.M. Mishina, S. Liu, A. Cheung, F. Stegmeier, G.A. Michaud, O. Charlat, E. Wiellette, Y. Zhang, S. Wiessner, et al. Tankyrase inhibition stabilizes axin and antagonizes Wnt signaling. *Nature*, 461 (2009), pp. 614-620
- [2]. Mohit Narwal, et al. Discovery of tankyrase inhibiting flavones with increased potency and isoenzyme selectivity. *J Med Chem*. 2013 Oct 24;56(20):7880-9.
- [3]. Wu J, Keng VW, Patmore DM, et al. Insertional mutagenesis identifies a STAT3/Arid1b/beta-catenin pathway driving neurofibroma initiation. *Cell Rep*. 2016;14:1979-90.
- [4]. X.H. Tian, W.J. Hou, Y. Fang, J. Fan, H. Tong, S.L. Bai, et al. XAV939, a tankyrase 1 inhibitor, promotes cell apoptosis in neuroblastoma cell lines by inhibiting Wnt/ β -catenin signaling pathway. *J Exp Clin Cancer Res*, 32 (1) (2013 Dec 5), p. 1
- [5]. Jiang W, Wu Y, He T, et al. Targeting of beta-catenin reverses radioresistance of cervical cancer with the PIK3CA E545K mutation. *Mol Cancer Ther* 2020;19(2):337-47.
- [6]. Mohamed, T. M. et al. Chemical enhancement of in vitro and in vivo direct cardiac reprogramming. *Circulation* 135, 978-995 (2017).

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