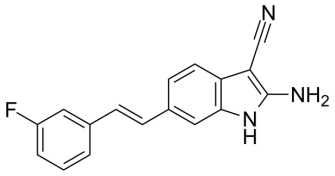
GSK2643943A

Cat. No.:	HY-111458
CAS No.:	2449301-27-1
Molecular Formula:	$C_{17}H_{12}FN_3$
Molecular Weight:	277
Target:	Deubiquitinase
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 125 mg/mL (451.26 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.6101 mL	18.0505 mL	36.1011 mL
	5 mM	0.7220 mL	3.6101 mL	7.2202 mL
	10 mM	0.3610 mL	1.8051 mL	3.6101 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: ≥ 2.08 mg/mL (7.51 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (7.51 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GSK2643943A is a deubiquitinating enzyme (DUB) inhibitor targeting USP20. GSK2643943A has affinity with an IC_{50} of 160 nM for USP20/Ub-Rho. GSK2643943A has anti-tumor efficacy and can be used for the research of oral squamous cell carcinoma (OSCC) [1][2].

IC_{50} & Target

IC50: 160 nM (USP20/Ub-Rho)[1]

In Vitro

GSK2643943A blocks the USP20-mediated cleavage of protein-ubiquitin bonds[2].
GSK2643943A (1 μM, 5 μM; overnight) renders SCC9 cells more susceptible to oHSV-1 induced oncolysis[2].
GSK2643943A (1μM) leds to a notable increase of virus yields in SCC9 with 0.01 MOI T1012G infection[2].

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

Cell Viability Assay[2]

Cell Line:	SCC9 cells
Concentration:	1 μM, 5 μM (GSK+0.01 MOI T1012) 1 μM (GSK+0.01 MOI/ 1 MOI T1012)
Incubation Time:	overnight
Result:	Displayed a significant drop in viability (R50%) (5 μM GSK+0.01 MOI T1012 infection) and 50% loss of SCC9 viability (1 μM GSK+0.01 MOI T1012 infection) . Remarkably reduced the viability of SCC9 upon exposure to 1 MOI T1012G infection.

Western Blot Analysis[2]

Cell Line:	SCC9 cells
Concentration:	1 μM
Incubation Time:	3h, 9 h and 20 h
Result:	Generally up-regulated the expression of viral proteins at various phases.

RT-PCR[2]

Cell Line:	SCC9 cells
Concentration:	1 μM
Incubation Time:	9 h
Result:	Significantly increased the accumulation of viral ICP8 and VP16 Mrna in SCC9 cells.

In Vivo

GSK2643943A (5 mg/kg, i.p., daily, for 6 days) potentiates oHSV-1-induced oncolysis in SCC9 tumors[2].

GSK2643943A (2.5 mg/kg, i.p., daily, for 9 days) plays a regulatory role in oHSV-1 T1012G replication and oncolysis in SCC7 cells[2].

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

Animal Model:	The subcutaneous xenograft model[2]. (SCC9 or SCC7 cells (8×10^6 cells or 1×10^6 cells), 5-week-old, female, BALB/c nude mice or C3H/HeN mice, four groups, n = 6-7, per group)[2]
Dosage:	5 mg/kg
Administration:	GSK2643943A (alone): intraperitoneal administration, daily, for 6 days. GSK2643943A (combination): intraperitoneal administration, daily for 6 days + intratumoral injection with 50 mL of 1×10^6 PFU T1012G in PBS on day 1, day 4, and day 7.
Result:	Caused a visible drop of tumor volumes and significantly reduced the tumor volumes in mice with combined treatment of GSK2643943A and oHSV-1 T1012G. Increased slightly viral ICP0 and gD mRNA accumulation in SCC9 tumors.

Animal Model:	The SCC7 mouse model[2].

Dosage:	2.5 mg/kg
Administration:	GSK2643943A (alone): intraperitoneal administration, daily, for 9 days. GSK2643943A (combination): intraperitoneal administration, daily, for 9 days + intratumoral injection, with 50 mL of 1×10^7 PFU T1012G in PBS on days 1, 4, 7, and 10.
Result:	Caused a visible drop of tumor volumes, significantly reduced in mice with combined treatment of GSK and oHSV-1 T1012G. Increased slightly viral ICP0 and gD mRNA accumulation in SCC7 tumors.

CUSTOMER VALIDATION

- Mol Ther Oncolytics. 11 November 2021.
- Arch Pharm (Weinheim). 2023 May 17;e2200661.
- bioRxiv. 2023 Jul 28.

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REFERENCES

[1]. Nishi Kumari, et al. Targeting the Ubiquitin Proteasome System in Cancer. Shahzad, Hafiz Naveed (2018). Neoplasm Targeting the Ubiquitin Proteasome System in Cancer. , 10.5772/intechopen.69560(Chapter 8).

[2]. Ruitao Lu, et al. USP18 and USP20 restrict oHSV-1 replication in resistant human oral squamous carcinoma cell line SCC9 and affect the viability of SCC9 cells. Mol Ther Oncolytics. 2021 Nov 11;23:477-487.

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