AS-99 TFA

Cat. No.: HY-141429A

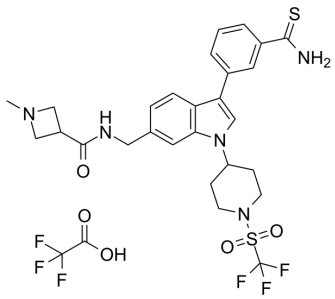
Molecular Formula: $C_{29}H_{31}F_6N_5O_5S_2$

Molecular Weight: 707.71

Target: Histone Methyltransferase; Apoptosis

Pathway: Epigenetics; Apoptosis

Storage: -20°C, protect from light, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (141.30 mM; Need ultrasonic)
H_2O : 12.5 mg/mL (17.66 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.4130 mL	7.0650 mL	14.1301 mL
5 mM	0.2826 mL	1.4130 mL	2.8260 mL
10 mM	0.1413 mL	0.7065 mL	1.4130 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.53 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AS-99 TFA is a first-in-class, potent and selective ASH1L histone methyltransferase inhibitor (IC_{50}= 0.79 μM, K_d= 0.89 μM) with anti-leukemic activity. AS-99 TFA blocks cell proliferation, induces apoptosis and differentiation, downregulates MLL fusion target genes, and reduces the leukemia burden in vivo[1].

IC_{50} & Target

0.79 μM (ASH1L histone methyltransferase)[1]

In Vitro

AS-99 TFA is tested against a panel of 20 histone methyltransferases, including NSD1, NSD2, NSD3, and SETD2. NO significant inhibition is observed at 50 μM of AS-99 TFA on any of the tested histone methyltransferases, indicating over 100-fold selectivity towards ASH1L[1].
AS-99 shows a several fold weaker effect on the proliferation of leukemia cells without MLL1 translocations, such as SET2

and K562, with no or limited effects at 10 μM or higher concentrations[1].
AS-99 (1-8 μM; 7 days) TFA also induces apoptosis in the MLL leukemia cells, but not in the K562 cells, as assessed by the quantification of the Annexin V positive cells[1].
AS-99 TFA suppresses MLL fusion driven transcriptional programs[1].
AS-99 results in a reduced number of H3K36me2 peaks when compared to the DMSO-treated cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[1]

Cell Line:	MOLM13 cells
Concentration:	2-6 μM
Incubation Time:	7 days
Result:	Led to a dose-dependent downregulation of canonical MLL fusion target genes required for leukemogenesis including MEF2C, DLX2, FLT3, and HOXA9.

In Vivo

AS-99 (30 mg/kg; i.p.; q.d., treated for 14 consecutive days) TFA reduces leukemia burden in mice[1].
AS-99 TFA is used for in vivo studies in mice, which reveals favorable exposure in plasma upon i.v. and i.p. administration (AUC = 9701 hr* ng/mL and 10,699 hr* ng/mL, respectively), suitable half-life (~5–6 h) and Cmax >10 μM[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	8- to 10-week old female NSG mice (bearing MV4;11 cells)[1]
Dosage:	30 mg/kg
Administration:	I.p.; q.d., treated for 14 consecutive days
Result:	Reduced the leukemia burden in the xenotransplantation mouse model of MLL leukemia without affecting blood counts in normal mice.

REFERENCES

[1]. David S. Rogawski, Jing Deng, Hao Li, Tomasz Cierpicki, Jolanta Grembecka, et al. Discovery of first-in-class inhibitors of ASH1L histone methyltransferase with anti-leukemic activity. Nat Commun. 2021 May 14;12(1):2792.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA