USP25/28 inhibitor AZ1

Cat. No.: HY-117370

CAS No.: 2165322-94-9

Molecular Formula: $C_{17}H_{16}BrF_4NO_2$

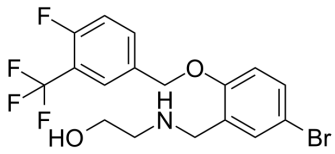
Molecular Weight: 422.21

Target: Deubiquitinase

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 250 mg/mL (592.12 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3685 mL	11.8424 mL	23.6849 mL
5 mM	0.4737 mL	2.3685 mL	4.7370 mL
10 mM	0.2368 mL	1.1842 mL	2.3685 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 (4.93 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.93 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

USP25/28 inhibitor AZ1 (AZ1) is an orally active, selective, noncompetitive, dual ubiquitin specific protease (USP) 25/28 inhibitor with IC_{50}s of 0.7 μM and 0.6 μM, respectively. USP25/28 inhibitor AZ1 attenuates colitis and tumorigenesis in the mice model[1][2].

IC_{50} & Target

IC50: 0.7 μM (USP25) and 0.6 μM (USP28)[1]

In Vivo

USP25/28 inhibitor AZ1 (AZ1; 40 mg/kg; gavage; daily; for 7 days) protects from dextran sulfate sodium (DSS)-induced weight loss and diarrhea and impaired colon shortening[1].

USP25/28 inhibitor AZ1 (20 mg/kg/day; gavage; 6 times a week in the 1, 3, 6 weeks) treatment significantly reduces tumor numbers in colons. Expression of Wnt-related genes and levels of pSTAT3 are decreased and levels of SOCS3 are increased in tumors. AZ1 gavage does not alleviate DSS-induced colitis in $Usp25^{-/-}$ mice or the spontaneous colitis of $Il10^{-/-}$ mice[1].

USP25/28 inhibitor AZ1 (20 mg/kg/day; gavage; every 3 days from 13-20 weeks) significantly inhibits tumorigenesis in the colon and prolonged the survival of AOM/Vil-Cre;$Trp53^{fl/fl}$ (VP) mice. AZ1 treatment has minimal effect on tumorigenesis in the USP25-deficient background[1].

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

Animal Model:	12-week old male $Usp25^{+/+}$ and $Usp25^{-/-}$ mice[1]
Dosage:	40 mg/kg
Administration:	Gavage; daily; for 7 days
Result:	Protected from dextran sulfate sodium (DSS)-induced weight loss and diarrhea and impaired colon shortening and potentiated the expression of proinflammatory cytokines and antibacterial peptides in colons of $Usp25^{-/-}$ mice compared to control counterparts.

REFERENCES

[1]. Wrigley JD, et al. Identification and Characterization of Dual Inhibitors of the USP25/28 Deubiquitinating EnzymeSubfamily. ACS Chem Biol. 2017 Dec 15;12(12):3113-3125.

[2]. Xiao-Meng Wang, et al. The deubiquitinase USP25 supports colonic inflammation and bacterial infection and promotes colorectal cancer. Nature Cancer volume 1, pages811–825(2020).

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