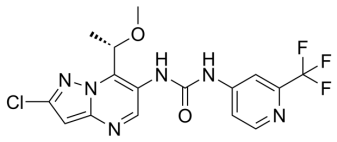
MLT-943

Cat. No.:	HY-134820
CAS No.:	1832576-04-1
Molecular Formula:	$C_{16}H_{14}ClF_3N_6O_2$
Molecular Weight:	414.77
Target:	MALT1
Pathway:	Metabolic Enzyme/Protease; NF-κB
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (602.74 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4110 mL	12.0549 mL	24.1097 mL
	5 mM	0.4822 mL	2.4110 mL	4.8219 mL
	10 mM	0.2411 mL	1.2055 mL	2.4110 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 (5.01 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.01 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MLT-943 is a potent, selective and orally active MALT1 protease inhibitor. MLT-943 inhibits stimulated-IL-2 secretion in PBMC or in whole blood with a similar IC_{50} across species (0.07-0.09 μM in PBMC, 0.6-0.8 μM in whole blood). MLT-943 has anti-inflammatory activities and can be used for FcgR-mediated inflammation research[1].

In Vitro

MLT-943 shows a high potency and selectivity in vitro.?MLT-943 inhibits stimulated IL-2 secretion in PBMC or in whole blood with a similar IC_{50} across species (0.07-0.09 μM in PBMC, 0.6-0.8 μM in whole blood)[1].

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

In Vivo

MLT-943 (oral gavage; 10 mg/kg; QD) prophylactic treatment in the rat collagen-induced arthritis model suppresses anti-collagen antibody production, fully prevents paw swelling, and normalizes joint histology scores?in rat model[1].

MLT-943 (oral gavage; 5 mg/kg; QD; 10 consecutive days) effectively inhibits MALT1 protease activity and results in a

progressive reduction in the frequency of $Foxp^{3+}CD25^{+}$?Treg cells in circulating $CD4^{+}$?T cells, which was maximal after 7 days of treatment. And Discontinuation of MLT-943 treatment after day 10 leads to Treg frequency progressively returning to their original values within 4 days. Suboptimal doses of MLT-943 (0.1 and 0.5 mg/kg QD; p.o.) does not impact the Treg frequency [1].

MLT-943 (oral gavage; 0, 5, 20 or 80 mg/kg/day; 4-13 weeks) causes a reduction in Treg and an increase in total T cell counts, in both 4- and 13-week rat toxicity studies at all dose levels. While a 4-Longer treatment induces severe immune-mediated pathology in multiple organs, with clinical onset starting around week 9 in rat[1].

MLT-943 (p.o. admistration; 3 mg/kg; single dose) exhibits a good PK parameters in vivo. The C_{max} values are 0.7 nM and 0.5 nM, respectively in rat and mice, respectively. And the F% are 86% and 50% in rat and mice, respective[1].

For i.v. admistration the compound is formed in NMP:PEG200 (30/70); For p.o. admistration solution is formed in MC:Tween 80:Water (0.5:0.5:99) solution (Sourced from literature, for reference only)[1].

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

Animal Model:	Naïve rats[1]
Dosage:	5 mg/kg
Administration:	Oral gavage; 5 mg/kg, 10 consecutive days or 0.1 mg/kg MLT-943
Result:	Induced a severe immune-mediated pathology after a prolonged treatment

REFERENCES

[1]. Kea Martin, et al. Pharmacological Inhibition of MALT1 Protease Leads to a Progressive IPEX-Like Pathology. Front Immunol

[2]. Jean Quancard, et al. Optimization of the In Vivo Potency of Pyrazolopyrimidine MALT1 Protease Inhibitors by Reducing Metabolism and Increasing Potency in Whole Blood. J Med Chem. 2020 Dec 10;63(23):14594-14608.

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