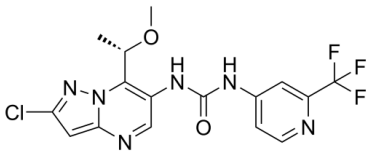
Data Sheet

Product Name:	MLT-943
Cat. No.:	CS-0159257
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
Solubility:	DMSO : 250 mg/mL (602.74 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

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].

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].

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.

CAIndexNames:

Urea, N-[2-chloro-7-[(1S)-1-methoxyethyl]pyrazolo[1,5-a]pyrimidin-6-yl]-N′-[2-(trifluoromethyl)-4-pyridinyl]-

SMILES:

CO[C@H](C1=C(NC(NC2=CC=NC(C(F)(F)F)=C2)=O)C=NC3=CC(Cl)=NN13)C

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

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA