CCR4-351 hydrochloride

Cat. No.: HY-131349A

CAS No.: 2174938-71-5

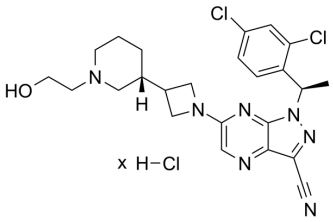
Molecular Formula: $C_{24}H_{28}Cl_3N_7O$

Target: CCR

Pathway: GPCR/G Protein; Immunology/Inflammation

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro	DMSO : 170 mg/mL (Need ultrasonic)
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 4.25 mg/mL (Infinity mM); Clear solution 2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 4.25 mg/mL (Infinity mM); Clear solution

BIOLOGICAL ACTIVITY

Description	CCR4-351 hydrochloride is an orally active, potent and selective CCR4 antagonist. CCR4-351 hydrochloride, featuring a novel piperidinyl-azetidine motif, has IC_{50}s of 22 nM and 50 nM in the calcium flux and CTX assay. CCR4-351 hydrochloride has antitumor activity[1].
IC_{50} & Target	CCR4
In Vitro	CCR4-351 (compound 38) hydrochloride shows no activity in a CYP450 induction assay[1]. CCR4-351 hydrochloride inhibits the migration of mouse iT_{reg} cells with an IC_{50} of 39 nM, while the IC_{50} in human iT_{reg} cells is 33 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CCR4-351 (compound 38; 50 mg/kg; PO; daily; for 40 days) hydrochloride significantly reduces the tumor growth[1]. CCR4-351 (0.5 mg/kg; IV) hydrochloride has low clearance (CL=10.2 mL/min/kg), medium volume of distribution (V_{ss}=5.2 L/kg), a $T_{1/2}$ of 6.9 h, and good bioavailability (%F = 29) of oral dosing in mouse[1]. CCR4-351 hydrochloride has low clearance (CL=7.3 mL/min/kg), a half-life of 12.7 hr, and is 44% bioavailable in dog. CCR4-351 hydrochloride has low clearance (CL=3.7 mL/min/kg), a long terminal half-life (10.7 hr), and good bioavailability (%F = 41) in cynomolgus monkey[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. Animal Model: Six-to eight-week-old, female C57BL/6 mice with Pan02-OVA tumor[1]

Dosage:	50 mg/kg
Administration:	PO; daily; for 40 days
Result:	Significantly reduced the tumor growth.

Animal Model:	Rat and mouse[1]
Dosage:	0.5 mg/kg of IV; 2 mg/kg of PO
Administration:	IV or PO
Result:	Possessed medium clearance (CL=47.6 mL/min/kg) and was 49% bioavailable upon oral dosing in rat. Had low clearance (CL=10.2 mL/min/kg), medium volume of distribution (V_{ss}=5.2 L/kg), a $T_{1/2}$ of 6.9 h, and good bioavailability (%F = 29) of oral dosing in mouse.

REFERENCES

[1]. Omar Robles, et al. Novel Piperidinyl-Azetidines as Potent and Selective CCR4 Antagonists Elicit Antitumor Response as Single Agent and in Combination with Checkpoint Inhibitors. J Med Chem. 2020 Jul 15.

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