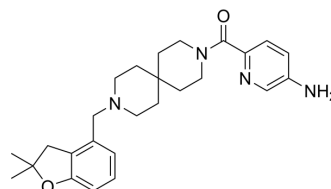


AZ084

Cat. No.:	HY-119217		
CAS No.:	929300-19-6		
Molecular Formula:	C ₂₆ H ₃₄ N ₄ O ₂		
Molecular Weight:	434.57		
Target:	CCR		
Pathway:	GPCR/G Protein; Immunology/Inflammation		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 250 mg/mL (575.28 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
			10 mg	
Preparing Stock Solutions	1 mM	2.3011 mL	11.5056 mL	23.0113 mL
	5 mM	0.4602 mL	2.3011 mL	4.6023 mL
	10 mM	0.2301 mL	1.1506 mL	2.3011 mL
Please refer to the solubility information to select the appropriate solvent.				
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution 			

BIOLOGICAL ACTIVITY

Description	AZ084 is a potent, selective, allosteric and oral active CCR8 allosteric antagonist, with a K _i of 0.9 nM. Has potential to treat asthma ^[1] . AZ084 restrains the formation of the immunologically tolerant pre-metastatic niche (PMN) and tumor cells metastasis in lung by downregulating Treg differentiation. AZ084 can be used in studies of asthma and cancer ^{[1][2]} .
IC₅₀ & Target	CCR8 0.9 nM (K _i)

In Vitro

AZ084 (5 µg/mL; single daily for 4 days) suppresses proportion of Tregs and reduces T cells that expresses CCR8 (co-cultured in vitro with LLC-exo MPF CM)^[1].

?AZ084 (0-10 µM) inhibits AML, DC and T cells with IC₅₀s of 1.3, 4.6 and 5.7 nM, respectively^[2].

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

Cell Viability Assay^[1]

Cell Line:	Splenic T cells
Concentration:	5 µg/mL (single daily)
Incubation Time:	4 days
Result:	Reversed the increased proportion of Tregs among the CD4+ T cells co-cultured in vitro with LLC-exo MPF CM. Reduced T cells that expressed CCR8 (cultured in vitro with by LLC-exo MPF CM).

Cell Viability Assay^[2]

Cell Line:	AML, DC and T cells
Concentration:	0-10 µM
Incubation Time:	
Result:	Showed high potency with pronounced dose-response dependent inhibition of chemotaxis with an IC ₅₀ of 1.3 nM in AML cells.

In Vivo

AZ084 (5 mg/kg; i.p.; every third day for 9 or 21 days) restrains the formation of the immunologically tolerant PMN and tumor cells metastasis in lung by downregulating Treg differentiation^[1].

?AZ084 (434.57-869.14 mg/kg; i.v.; single) shows a bioavailability >70% in rats^[2].

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

Animal Model:	C57BL/6 J mice (subcutaneous LLC tumor model) ^[1] .
Dosage:	5 mg/kg
Administration:	Intraperitoneal injection, every third day for 9 or 21 days.
Result:	Inhibited Treg differentiation and tumor cell colonization of the lungs and reduced the number of CD4+Foxp3+ Tregs in the lungs of LLC-exo pre-injected mice (every third day for 9 days). Inhibited the LLC-exo-induced LLC cell seeding in lung and also significantly reduced Treg accumulation in LLC-exo stimulated mouse lungs(every third day for 21 days).

Animal Model:	Female Balb/C mice, male Wistar rats and female Beagle dogs ^[2] .
Dosage:	434.57-869.14 mg/kg (in 0.9% NaCl)
Administration:	Intravenous injection, single.
Result:	Pharmacokinetic Parameters of AZ084 in Female Balb/C mice, male Wistar rats and female Beagle dogs ^[2] .

IV (434.57-869.14 mg/kg)

Dog plasma protein binding (% free)	45.7
Mu plasma protein binding (% free)	55.6
Hu plasma protein binding (% free)	31.0
Rat plasma protein binding (% free)	47.0
Rat HW plasma PK CL (mL/min/kg)	15.0
Rat HW plasma PK V_{ss} (L/kg)	6.0
Rat HW plasma PK $T_{1/2}$ (h)	5.4
Rat HW plasma PK C_{max} (μ M)	0.5
Rat HW plasma PK bioavailability (%)	68.0

CUSTOMER VALIDATION

- Nat Commun. 2021 Dec 8;12(1):7122.
- Nat Commun. 2020 May 1;11(1):2177.

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REFERENCES

- [1]. Wang M, et al. Tumor-derived exosomes drive pre-metastatic niche formation in lung via modulating CCL1+ fibroblast and CCR8+ Treg cell interactions. Cancer Immunol Immunother. 2022 Apr 15.
- [2]. Connolly S, et al. Orally bioavailable allosteric CCR8 antagonists inhibit dendritic cell, T cell and eosinophil migration. Biochem Pharmacol. 2012 Mar 15;83(6):778-87.

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

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