

Product Data Sheet

Product Name: CCR2 antagonist 1

Cat. No.: GC30560

Chemical Properties

Cas. No. 1683534-96-4

SMILES O=C([C@]1(C(C)C)C[C@H](N[C@@H]2CCC3=C2C=CC(Br)=C3)CC1)N4CC5=C(C=C)C(C(F)(F)F)=C5)CC4

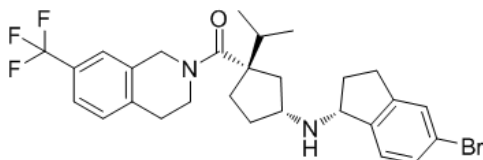
Formula $C_{28}H_{32}BrF_3N_2O$ M.Wt 549.47

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Animal experiment [1]:

Animal models Male apoE^{-/-} mice

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

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Male apoE^{-/-} mice were fed a western-style diet containing 0.25% cholesterol and 15% cocoa butter starting two weeks before the surgery with perivascular collar placement (induce carotid plaque formation). After the surgery, the mice were intraperitoneally injected with CCR2 antagonist 1 (5mg/kg/day) or a vehicle control (n=10 in each group) daily for 4 weeks. During the experiment, the body weight and serum total cholesterol levels of the mice were measured. Carotid artery samples from the mice were collected for histological analysis.

Dosage form 5mg/kg/day for 4 weeks; i.p.

Applications CCR2 antagonist 1 treatment significantly reduced atherosclerotic plaque size in the carotid artery at the site of maximal stenosis in apoE^{-/-} mice.

References:

[1] Bot I, Ortiz Zacarías N V, de Witte W E A, et al. A novel CCR2 antagonist inhibits atherogenesis in apoE deficient mice by achieving high receptor occupancy[J]. Scientific reports, 2017, 7(1): 52.

Background

CCR2 antagonist 1 is a high-affinity and long-residence-time chemokine receptor 2 antagonist with the K_i value of 2.4nM [1]. CCR2 antagonist 1 has been widely used in animal models to target the CCL2-CCR2 axis and prevent the occurrence of atherosclerosis[2]. CCR2 antagonist 1 can be used as a model compound to investigate the relationship between the kinetic stability of the drug target complex and the water-screening hydrogen bonds[3].

In vivo, CCR2 antagonist 1 treatment via intraperitoneal injection at a dose of 5mg/kg/day for 4 weeks significantly reduced atherosclerotic plaque development in the carotid artery at the site of maximal stenosis in apoE^{-/-} mice[4]. Continuous intraperitoneal injection of 30mg/kg dose of CCR2 antagonist 1 for 14 consecutive days could significantly reduce brain metastasis in the E0771-BrM breast cancer mouse model[5].

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- [1] Vilums M, Zweemer A J M, Barmare F, et al. When structure–affinity relationships meet structure–kinetics relationships: 3-((Inden-1-yl) amino)-1-isopropyl-cyclopentane-1-carboxamides as CCR2 antagonists[J]. European journal of medicinal chemistry, 2015, 93: 121-134.
- [2] Bot I, Ortiz Zacarias N V, de Vries H, et al. Longer Receptor Residence Times Improve the Effectiveness of CCR2 Antagonists in the Prevention of Atherosclerosis[J]. Circulation, 2015, 132(suppl_3): A11581-A11581.
- [3] Magarkar A, Schnapp G, Apel A K, et al. Enhancing drug residence time by shielding of intra-protein hydrogen bonds: a case study on CCR2 antagonists[J]. ACS medicinal chemistry letters, 2019, 10(3): 324-328.
- [4] Bot I, Ortiz Zacarías N V, de Witte W E A, et al. A novel CCR2 antagonist inhibits atherogenesis in apoE deficient mice by achieving high receptor occupancy[J]. Scientific reports, 2017, 7(1): 52.
- [5] Ma W, Oliveira-Nunes M C, Xu K, et al. Type I interferon response in astrocytes promotes brain metastasis by enhancing monocytic myeloid cell recruitment[J]. Nature communications, 2023, 14(1): 2632.

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