

Product Data Sheet

Product Name: Telratolimod (MEDI 9197)

Cat. No.: GC33076

Chemical Properties

Cas. No. 1359993-59-1

SMILES NC1=NC2=CC=CC=C2C3=C1N=C(CCCC)N3OCCCCNC(CCCCCCCCCCCCCCCCCC)=O

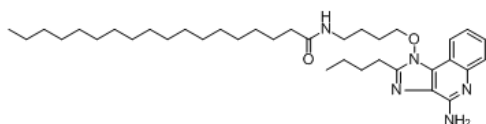
Formula $C_{36}H_{59}N_5O_2$ M.Wt 593.89

Solubility DMSO : 5 mg/mL (8.42 mM); Water : < 0.1 mg/mL (insoluble) 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

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

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Cell experiment [1]:

Cell lines Human PBMCs

Preparation Method 2×10^6 cells/mL human PBMCs were cultured for 24h at 37 °C with 3μM Telratolimod or DMSO. NK cells were then isolated using an EasySep® Human NK Cell Enrichment Kit (Stemcell). K562 target cells (ECACC,) were loaded for 20min with DELFIA BATDA reagent (Perkin Elmer) at 37 °C, washed 5 times in PBS, 0.1% (v/v) BSA, 2.5mM probenecid (ThermoFisher Scientific) and co-cultured with NK cells for 3h at 37 °C in the presence of 2.5mM probenecid. Killing was assessed in supernatants by DELFIA EuTDA readout (Perkin Elmer). Percent specific killing was calculated from the fluorescence values of $((\text{Sample} - (\text{Target cells only} - \text{medium}) - (\text{NK cells only} - \text{medium}) - \text{medium}) \times 100) / (100\% \text{ lysis} - \text{medium})$.

Reaction
Conditions 3μM; 24h

Applications Telratolimod stimulated human PBMC cultures, inducing high levels of Th1 cytokines, IFNγ and IL-12 p70. Telratolimod inhibits the release of IL-5 from human PBMC stimulated by PHA, thereby causing the polyclonal immune response to deviate from the Th 2-like phenotype.

Animal experiment [1]:

Animal models Male Sprague Dawley rats

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Telratolimod and Resiquimod were prepared in sesame oil with 7.5% EtOH (w/w) and citrate buffer, respectively. Telratolimod, Resiquimod, or Vehicle solution were administered via IT or subcutaneous (SC) injection. [14C]-Telratolimod was quantified in rat tissues, whole-blood, and plasma by Quotient Bioresearch Ltd, UK after SC injection. Whole-blood and plasma samples were collected via a tail vein or via cardiac puncture. Plasma samples were taken for direct Quantitative Radiochemical analysis (QRA). Whole-blood samples were taken for oxidation prior to QRA. Distribution of radioactivity in tissues was determined by quantitative whole-body autoradiography (QWBA). Tissue concentrations of radioactivity were determined using calibrated autoradiographic microscopes (GE Healthcare).

Dosage form 0.1、 0.3 and 1mg/kg; single SC injection

Applications Telratolimod induces very low levels of systemic serum TNF α . The radiolabeled Telratolimod can be detected in plasma and whole blood for at least 14 days, and remains at the injection site for at least 28 days.

References:

[1] Mullins S R, Vasilakos J P, Deschler K, et al. Intratumoral immunotherapy with TLR7/8 agonist MEDI9197 modulates the tumor microenvironment leading to enhanced activity when combined with other immunotherapies[J]. Journal for immunotherapy of cancer, 2019, 7: 1-18.

Background

Telratolimod (MEDI 9197) is an effective agonist for toll-like receptor 7 (TLR-7) and toll-like receptor 8 (TLR-8) [1]. TLR is a type of protein that recognizes pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs), and is involved in the regulation of the innate immune system [2]. Telratolimod has anti-tumor activity [3].

In vitro, Telratolimod (3 μ M) stimulated human peripheral blood mononuclear cells (PBMCs) in the culture medium for 24 hours, promoting the production of high levels of Th1-type cytokines, namely IFN γ and IL-12 p70. Telratolimod can inhibit the release of IL-5 by PBMCs stimulated by

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phytohemagglutinin, thereby causing the deviation of the polyclonal immune response from the Th2 phenotype [3].

In vivo, administration of radiolabeled Telratolimod (0.1, 0.3, and 1 mg/kg; single SC injection) in rats showed that Telratolimod induced very low levels of systemic serum TNF- α . Radiolabeled Telratolimod could be detected in plasma and whole blood for at least 14 days and remained at the injection site for at least 28 days. In the mouse melanoma model, a single IT administration of Telratolimod (20 μ g) could increase the percentage of tumor-infiltrating lymphocytes (TIL), enhance T cell activation, and lead to a qualitative transformation from single-cell factor production to double-cell factor production (IFN- γ and tumor necrosis factor α , TNF- α) [3].

References:

- [1] Zhao BG, Vasilakos JP, Tross D, Smirnov D, Klinman DM. Combination therapy targeting toll like receptors 7, 8 and 9 eliminates large established tumors. J Immunother Cancer. 2014 May 13;2:12.
- [2] Federico S, Pozzetti L, Papa A, et al. Modulation of the innate immune response by targeting toll-like receptors: a perspective on their agonists and antagonists[J]. Journal of Medicinal Chemistry, 2020, 63(22): 13466-13513.
- [3] Mullins S R, Vasilakos J P, Deschler K, et al. Intratumoral immunotherapy with TLR7/8 agonist MEDI9197 modulates the tumor microenvironment leading to enhanced activity when combined with other immunotherapies[J]. Journal for immunotherapy of cancer, 2019, 7: 1-18.

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