Palupiprant

Cat. No.: HY-103088

CAS No.: 1369489-71-3

Molecular Formula: $C_{22}H_{18}F_5N_3O_4$

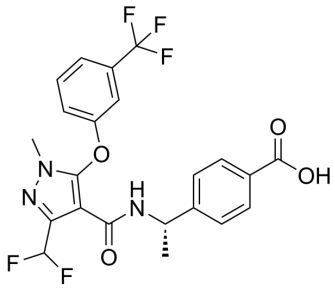
Molecular Weight: 483

Target: Prostaglandin Receptor

Pathway: GPCR/G Protein

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 : ≥ 100 mg/mL (207.04 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0704 mL	10.3520 mL	20.7039 mL
	5 mM	0.4141 mL	2.0704 mL	4.1408 mL
	10 mM	0.2070 mL	1.0352 mL	2.0704 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.31 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.31 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.31 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Palupiprant (E7046) is an orally bioavailable and specific EP4 antagonist, with IC_{50} of 13.5 nM and K_i of 23.14 nM. Palupiprant exhibits anti-tumor activities[1][2].

IC_{50} & Target

IC50: 13.5 nM (EP4)[2]
Ki: 23.14 nM (EP4)[2]

In Vitro	Palupiprant (E7046) reverses the immunosuppressive effects of PGE2 on activation and differentiation of human myeloid cells through selective EP4 antagonism[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In the CT-26 tumor model, the Palupiprant/RT combination causes the anti-tumor memory response of 9 animals. In the 4T1 model, the combination of Palupiprant and RT also produces significant better tumor growth inhibition activity compared with each treatment alone. The combination significantly improves survival by inhibiting the subsequent spontaneous lung metastasis of 4T1 tumors[1]. Palupiprant (150 mg/kg) inhibits the growth of multiple syngeneic tumor models. Blockade of EP4 signaling promotes anti-tumor DC differentiation and slows tumor growth in mice. Palupiprant treatment reduces the growth or even rejected established tumors in vivo in a manner dependent on both myeloid and CD8C T cells. Furthermore, co-administration of Palupiprant and E7777, an IL-2-diphtheria toxin fusion protein that preferentially kills Tregs, synergistically disrupts the myeloid and Treg immunosuppressive networks, resulting in effective and durable anti-tumor immune responses in mouse tumor models[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Bone marrow (BM) cells are flushed from femurs of BALB/c mice using sterile CM. Freshly harvested (BM) cells (0.5×10^6) are differentiated in the presence of 20 ng/mL recombinant mouse GM-CSF, ±PGE2 (10 nM), at 37°C, for 8 d. CM C fresh GM-CSF ± PGE2 is changed on days 3 and 6. After in vitro differentiation, cells are analyzed by flow cytometry. For certain experiments, CT26, 4T1 cell supernatants, and/or EP1 (SC-57089), EP2 (ER-880696), EP3 (L-798106), or EP4 (E7046) antagonists at 1 mM, are added to the BM cells. To assess the effect of differentiated BM cells on T cell proliferation, mouse BM cells differentiated are co-cultured for 72 hours with anti-CD3/CD28 Dynabeadsstimulated and CFSE (1 mM)-stained T cells. T cell proliferation is assessed by CFSE dilution using flow cytometry. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	For the tumor isograft efficacy studies, 6-week old female BALB/c mice are implanted with cancer cells: 1×10^5 CT26 or 4T1 cells or 8×10^5 H22 cells per mouse s.c., or 1×10^5 EMT6 cells in the mammary fat pad. C57BL/6 mice are implanted s.c. with 1×10^6 Pan02 cells per mouse, and A/J mice are implanted s.c. with 2-3 mm^3 SAI/N tumor fragments. To investigate the role of T cells in the anti-tumor response, 6 week old female nude mice (which lack T cells) are injected s.c. with 1×10^5 CT26 cells. When tumors reach approximately 50-100 mm^3, tumor-bearing mice are randomly assigned to vehicle or treatment groups, and treatment regimens begin. E7046 is administered per oral (p.o.) as a 100 or 150 mg/kg suspension in 0.5% MC, daily for 21 d (QDx21). For the combination studies, E7777 is administered intravenously (i.v.) at 2.5 mg/mouse in saline, as 2 to 3 doses injected one week apart (Q7Dx2-3). Tumor volumes and body weights are recorded 2-3 times a week. For comparison with current immunotherapies, in addition to vehicle control and E7046 C E7777 groups, mice are assigned to anti-PD1 antibodies or anti-mouse PD-1 C antimouse CTLA4 antibodies treatment groups. Anti-PD-1 and anti-CTLA-4 antibodies (1 mg/mL), are administered i.p. in 100 mL, 3 times 4 d apart (Q4Dx3) for a total of 300 mg each. Isotype controls are administered i.p. at 1 mg/mL to the control group. For the CD4CT and CD8CT lymphocyte depletion, antimouse CD4 or anti-mouse CD8 antibodies or their isotype controls are administered in 100 mL, i.p. at 2.5 mg/mL every 4 days, for a total of 4 injections per mouse (1 mg). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Res Commun. 2023 Jul 13.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. X. Bao, et al. Combination of a Novel EP4 Antagonist E7046 and Radiation Therapy Promotes Anti-tumor Immune Response and Tumor Rejection in Preclinical Tumor Models. International Journal of Radiation Oncology Biology Physics

[2]. Diana I. Albu, et al. EP4 Antagonism by E7046 diminishes Myeloid immunosuppression and synergizes with Treg-reducing IL-2-Diphtheria toxin fusion protein in restoring anti-tumor immunity. OncoImmunology.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA