

Product Data Sheet

Product Name: ONC206

Cat. No.: GC38935

Chemical Properties

Cas. No. 1638178-87-6

SMILES O=C1N(CC2=CC=C(F)C=C2F)C3=NCCN3C4=C1CN(CC5=CC=CC=C5)CC4

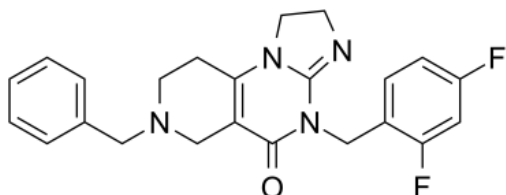
Formula $C_{23}H_{22}F_2N_4O$ M.Wt 408.44

Solubility DMSO: 100 mg/mL (244.83 mM) 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

Cell experiment [1]:

Cell lines ARK1 and SPEC-2

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method Cells were seeded into 96-well culture plates at a density of $3-5 \times 10^3$ cells/well and treated with varying concentrations (0, 0.01, 0.1, 1, 2, 5, 20, 50 μ M) of ONC206 for 72 hours. MTT (5mg/mL) was added at 5 μ L/well at the end of treatment. After 1h of incubation, the MTT reaction was terminated through the addition of DMSO at 100 μ L/well. Absorbance was measured at 575nm using a microplate reader.

Reaction Conditions 0, 0.01, 0.1, 1, 2, 5, 20 and 50 μ M; 1h

Applications ONC206 inhibits the viability of endometrial cancer cells in a dose-dependent manner.

Animal experiment [2]:

Animal models Female athymic mice

Preparation Method At 6 weeks of age, ARK1 cells with a density of 4×10^6 luciferase labeling were intraperitoneally injected into female thymus mice to establish tumors. After 2 weeks, the animals were randomized into three groups for treatment with PBS, ONC201, or ONC206; 100mg/kg ONC201 or ONC206 was administered intraperitoneally twice per week for 6 weeks. The tumor volumes were measured and quantified using the IVIS-Lumina XR in vivo imaging system.

Dosage form 100mg/kg; twice per week for 6 weeks

Applications ONC206 significantly reduces the uterine tumor burden in the mouse model of xenotransplantation.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:

- [1] Zhang Y, Huang Y, Yin Y, et al. ONC206, an Imipridone Derivative, Induces Cell Death Through Activation of the Integrated Stress Response in Serous Endometrial Cancer In Vitro. *Front Oncol* 2020, 10:577141.
- [2] Paraghamian SE, Qiu J, Hawkins GM, et al. A novel dopamine receptor D2 antagonist (ONC206) potentiates the effects of olaparib in endometrial cancer. *Cancer Biol Ther* 2023, 24(1):2202104.

Background

ONC206 is a dopamine D2-like receptor (DRD2/3/4) antagonist belonging to the imipridone class of drugs, with an IC₅₀ of 0.21 μM to 0.32 μM [1]. Dopamine receptors belong to the G-protein coupled receptor family and play an important role in regulating cellular physiological functions. Antagonism of these receptors by ONC206 can interfere with the transmission of growth signals in tumor cells[2]. ONC206 has demonstrated potential in therapeutic research for various solid and hematological malignancies, including endometrial cancer, colorectal cancer, acute myeloid leukemia, etc[3].

In vitro, treatment of ARK1 and SPEC-2 cells with ONC206 (0-50 μM) for 72 hours significantly inhibited cell proliferation in a dose-dependent manner via the DRD2/5 and TRAIL/DR5 pathways[4]. Treatment of U87 GBM cells with ONC206 (0.2 μM) for 72 hours suppressed GBM cell proliferation, induced apoptosis, reduced c-myc protein level, inhibited glycolysis and oxidative phosphorylation, and activated the SOG metabolic pathway[5].

In vivo, intraperitoneal injection of ONC206 (100mg/kg) for 12 days in ARK1-luc cell xenograft mice significantly delayed tumor growth and disrupted the DRD2-mediated p38MAPK/ERK/PGC-1α network, leading to metabolic reprogramming, inhibition of glycolysis and oxidative phosphorylation [6]. Subcutaneous injection of ONC206 (80mg/kg) in Huh7 cells xenograft tumor mice significantly retarded tumor growth[7].

References:

- [1] Staley A, Tucker K, Yin Y, et al. Highly potent dopamine receptor D2 antagonist ONC206 demonstrates anti-tumorigenic activity in endometrial cancer. *Am J Cancer Res* 2021, 11(11):5374-5387.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

- [2] Wang X, Wang ZB, Luo C, et al. The Prospective Value of Dopamine Receptors on Bio-Behavior of Tumor. J Cancer 2019, 10(7):1622-1632.
- [3] Bonner ER, Waszak SM, Grotzer MA, et al. Mechanisms of imipridones in targeting mitochondrial metabolism in cancer cells. Neuro Oncol 2021, 23(4):542-556.
- [4] Zhang Y, Huang Y, Yin Y, et al. ONC206, an Imipridone Derivative, Induces Cell Death Through Activation of the Integrated Stress Response in Serous Endometrial Cancer In Vitro. Front Oncol 2020, 10:577141.
- [5] Ishida CT, Zhang Y, Bianchetti E, et al. Metabolic Reprogramming by Dual AKT/ERK Inhibition through Imipridones Elicits Unique Vulnerabilities in Glioblastoma. Clin Cancer Res 2018, 24(21):5392-5406.
- [6] Paraghamian SE, Qiu J, Hawkins GM, et al. A novel dopamine receptor D2 antagonist (ONC206) potentiates the effects of olaparib in endometrial cancer. Cancer Biol Ther 2023, 24(1):2202104.
- [7] Cao J, Cao F, Wang C, et al. ONC206 targeting ClpP induces mitochondrial dysfunction and protective autophagy in hepatocellular carcinoma cells. Neoplasia 2024, 55:101015.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA