

Product Data Sheet

Product Name: GSK2636771

Cat. No.: GC17109

Chemical Properties

Cas. No. 1372540-25-4

Chemical Name 2-methyl-1-[[2-methyl-3-(trifluoromethyl)phenyl]methyl]-6-morpholin-4-ylbenzimidazole-4-carboxylic acid

SMILES CC1=C(C=CC=C1C(F)(F)F)CN2C(=NC3=C2C=C(C=C3C(=O)O)N4CCOCC4)C

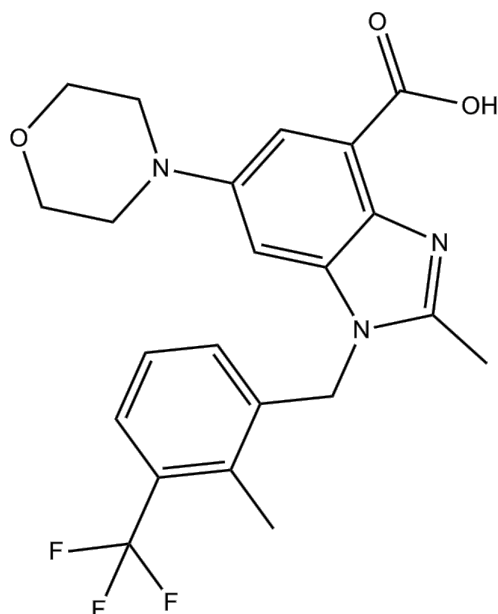
Formula C₂₂H₂₂F₃N₃O₃ M.Wt 433.42

Solubility ≥ 10.825mg/mL 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

Cell experiment [1]:

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Cell lines	DU145 cells (human prostate cancer cell line)
Preparation Method	DU145 cells were maintained in RPMI 1640 medium supplemented with 10% fetal bovine serum, 100U/mL penicillin and 10µg/mL streptomycin at 37°C in a humidified atmosphere containing 5% CO ₂ . DU145 cells were treated with GSK2636771 at 0.038–0.074µM for 18–24h.
Reaction Conditions	0.038–0.074µM; 18–24h
Applications	GSK2636771 significantly blocked the migration and invasion of DU145 cells, with IC ₅₀ of 0.038µM for migration (18h treatment) and 0.074µM for invasion (24h treatment) respectively. GSK2636771 suppressed the phosphorylation of downstream Akt and integrinβ1 in DU145 cells.
Animal experiment [2]:	
Animal models	Tyr:CreER; PTEN ^{flox/lox} ; BRAF ^{V600E/+} (BP) transgenic mice (C57BL/6 background)
Preparation Method	BP mice were treated with 4-hydroxytamoxifen to induce spontaneous Braf-mutant PTEN-null immunotherapy-resistant melanoma formation. Tumor-bearing mice with measurable lesions were randomized into groups to receive GSK2636771 alone or in combination with anti-mouse OX40 agonist antibody. GSK2636771 was suspended in 1%(w/v) methylcellulose and administered to mice daily by oral gavage. Tumor size was monitored every 2 days, and survival was recorded till endpoint.
Dosage form	30mg/kg; oral gavage; daily for 4 weeks

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Applications

GSK2636771 monotherapy mildly delayed tumor growth and marginally extended the survival of BP tumor-bearing mice. The combination of GSK2636771 and anti-OX40 agonist antibody markedly delayed tumor progression, significantly extended the survival of BP tumor-bearing mice, with a synergistic antitumor effect. The combination treatment elevated serum levels of CCL4, CXCL10 and IFN- γ in mice, reduced the proportion of splenic M2 macrophages, promoted Ki-67 expression in tumor-infiltrating CD8⁺ T cells, and no overt adverse effects were observed.

References:

- [1] Zhang Z, Liu J, Wang Y, et al. Phosphatidylinositol 3-kinase β and δ isoforms play key roles in metastasis of prostate cancer DU145 cells. *FASEB J.* 2018 Nov;32(11):5967-5975.
- [2] Peng W, Williams LJ, Xu C, et al. Anti-OX40 Antibody Directly Enhances The Function of Tumor-Reactive CD8⁺ T Cells and Synergizes with PI3K β Inhibition in PTEN Loss Melanoma. *Clin Cancer Res.* 2019 Nov 1;25(21):6406-6416.

Background

GSK2636771 is an orally active selective PI3K β inhibitor ($K_i=0.89\text{nM}$; $IC_{50}=5.2\text{nM}$). GSK2636771 binds to the ATP-binding pocket of the p110 β catalytic subunit, blocking the phosphorylation of PIP₂ to PIP₃, thereby inhibiting the downstream AKT-S6 pathway, suppressing proliferation of PTEN-deficient tumor cells, and inducing G1 phase cell cycle arrest. GSK2636771 can be used in research related to PTEN-deficient solid tumors and castration-resistant prostate cancer^[1-4].

In vitro, GSK2636771 (0.038–0.074 μM) treatment of DU145 human prostate cancer cells for 18–24h. GSK2636771 significantly inhibited DU145 cell migration and invasion, and reduced the phosphorylation levels of Akt and integrin β ^[5]. GSK2636771 (1 μM , 10 μM) treatment of 24 human endometrioid endometrial carcinoma cell lines (including PTEN mutant and PTEN wild-type), PTEN-deficient p110 β -dependent PC3 prostate cancer cells, BT549 breast cancer cells, and HCC70 breast cancer cells for 4h or 72h. GSK2636771 reduced the activity of cancer cells. GSK2636771 significantly reduced the phosphorylation levels of AKT(Ser473) and AKT(Thr308) in PC3, BT549, and HCC70 cells^[6].

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In vivo, GSK2636771 (30mg/kg) was administered by oral gavage to C57BL/6 mice bearing spontaneously formed Braf-mutant PTEN-null immunotherapy-resistant melanoma for 21 days. GSK2636771 delayed tumor growth and extended survival in tumor-bearing mice. When combined with an anti-OX40 agonist antibody, GSK2636771 elevated serum levels of CCL4, CXCL10, and IFN- γ in mice, reduced the proportion of splenic M2 macrophages, and promoted Ki-67 expression in T cells, dendritic cells, and M1 macrophages^[7]. GSK2636771 (30mg/kg; oral) combined with fulvestrant (5mg/week; subcutaneous) was administered to female athymic nude mice bearing xenografts of anti-fulvestrant-resistant PTEN-deficient ER-positive ZR75-1 cells, with or without triple combination with BYL719 (25mg/kg; oral) for 11 weeks. GSK2636771 combined with fulvestrant induced rapid tumor regression. The triple combination of GSK2636771, BYL719, and fulvestrant prevented tumor regrowth and maintained tumor regression^[8].

References:

- [1] Hosford SR, Dillon LM, Bouley SJ, et al. Combined Inhibition of Both p110 α and p110 β Isoforms of Phosphatidylinositol 3-Kinase Is Required for Sustained Therapeutic Effect in PTEN-Deficient, ER⁺ Breast Cancer. Clin Cancer Res. 2017 Jun 1;23(11):2795-2805.
- [2] Sato S, Huang XP, Kroeze WK, et al. Discovery and Characterization of Novel GPR39 Agonists Allosterically Modulated by Zinc. Mol Pharmacol. 2016 Dec;90(6):726-737.
- [3] Janku F, Jegede OA, Puhalla SL, et al. PIK3CB Inhibitor GSK2636771 in Cancers With *PTEN* Mutation/Deletion or Loss of PTEN Protein Expression: Results From the NCI-MATCH ECOG-ACRIN Trial (EAY131) Subprotocols N and P. JCO Precis Oncol. 2025 Aug;9:e2500265.
- [4] He C, Duan S, Dong L, et al. Characterization of a novel p110 β -specific inhibitor BL140 that overcomes MDV3100-resistance in castration-resistant prostate cancer cells. Prostate. 2017 Aug;77(11):1187-1198.
- [5] Zhang Z, Liu J, Wang Y, et al. Phosphatidylinositol 3-kinase β and δ isoforms play key roles in metastasis of prostate cancer DU145 cells. FASEB J. 2018 Nov;32(11):5967-5975.
- [6] Weigelt B, Warne PH, Lambros MB, et al. PI3K pathway dependencies in endometrioid endometrial cancer cell lines. Clin Cancer Res. 2013 Jul 1;19(13):3533-44.
- [7] Peng W, Williams LJ, Xu C, et al. Anti-OX40 Antibody Directly Enhances The Function of Tumor-Reactive CD8⁺ T Cells and Synergizes with PI3K β Inhibition in PTEN Loss Melanoma. Clin Cancer Res. 2019 Nov 1;25(21):6406-6416.
- [8] Hosford SR, Dillon LM, Bouley SJ, et al. Combined Inhibition of Both p110 α and p110 β Isoforms of Phosphatidylinositol 3-Kinase Is Required for Sustained Therapeutic Effect in PTEN-Deficient,

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