

Product Data Sheet

Product Name: BAY 87-2243

Cat. No.: GC12698

Chemical Properties

Cas. No. 1227158-85-1

Chemical Name 5-(1-((2-(4-cyclopropylpiperazin-1-yl)pyridin-4-yl)methyl)-5-methyl-1H-pyrazol-3-yl)-3-(4-(trifluoromethoxy)phenyl)-1,2,4-oxadiazole

SMILES CC1=CC(C2=NC(C3=CC=C(OC(F)(F)F)C=C3)=NO2)=NN1CC4=CC=NC(N5CCN(C6CC6)CC5)=C4

Formula $C_{26}H_{26}F_3N_7O_2$

M.Wt 525.53

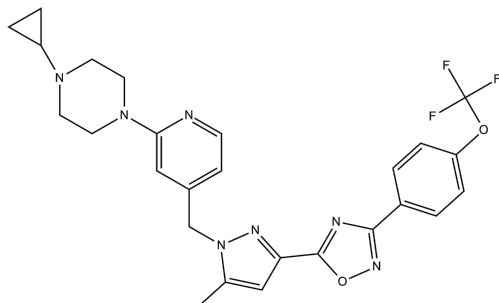
Solubility $\geq 8.76\text{mg/mL}$ in DMSO

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]:

Cell lines H460 (human large cell lung cancer cell line)

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

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H460 cells were cultured for 16h under normoxia or hypoxia (1% pO_2) in the presence of various concentrations of BAY 87-2243 (10, 100, and 1000nM), mRNA expression levels of the HIF target genes CA9, ADM, ANGPTL4 and the negative control gene EGLN2 were quantified by RT-PCR.

Reaction Conditions 10, 100, and 1000nM; 16h

Applications BAY 87-2243 suppressed HIF-1 target gene expression dose dependently under hypoxia. And the expression of EGLN2 was not affected by BAY 87-2243 treatment neither under normoxia nor under hypoxia.

Animal experiment [1]:

Animal models Nude mice carrying H460 xenograft tumors

Preparation Method Nude mice bearing established H460 human tumor xenografts were treated orally, once daily with BAY 87-2243 (0.5, 1, 2, and 4mg/kg for 21 days and tumor weight was analyzed. Total RNA from H460 xenograft tumors was isolated 16h after last oral dosage of BAY 87-2243 at day 22 and the mRNA expression levels of HIF-1 target genes CA9, ANGPTL4, EGLN3 were quantified by real-time PCR.

Dosage form 0.5, 1, 2, 4mg/kg; once daily; 21 days; p.o.

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Applications BAY 87-2243 reduced tumor weight dose dependently in line with a dose-dependent reduction of the mRNA expression levels of the HIF-1 target genes CA9, ANGPTL4, and EGLN3.

References:

[1] ELLINGHAUS P, HEISLER I, UNTERSCHENMANN K, et al. BAY 87-2243, a highly potent and selective inhibitor of hypoxia-induced gene activation has antitumor activities by inhibition of mitochondrial complex I[J]. Cancer Medicine, 2013, 2(5): 611-624.

Background

BAY 87-2243 is a highly potent and selective inhibitor of hypoxia-inducible factor-1 (HIF-1) [1]. HIF-1 is a transcription factor that regulates cellular responses to low oxygen environments and participates in biological processes such as angiogenesis, cell survival, glucose metabolism, and invasion through the activation of genes related to hypoxia adaptation[2, 3]. BAY 87-2243 is often used in combination with radiotherapy or targeted agents in the treatment and research of melanoma, hepatocellular carcinoma, and head and neck squamous cell carcinoma[4, 5, 6].

In vitro, treatment of H460 cells with BAY 87-2243 (10, 100, 1000nM) for 16h significantly inhibited the mRNA expression of hypoxia-induced HIF target genes (CA9, Adrenomedullin (ADM), and Angiopoietin-like 4 (ANGPTL4)), while having no effect on the non-hypoxia-responsive gene EGLN2[1]. Co-culture of CD4⁺T cells purified from rats with an experimental autoimmune myasthenia gravis (EAMG) inflammation model with BAY 87-2243 (1μM) for 48h reduced the proportions of Th1, Th17, and Th1/17 cells, increased the proportion of Treg cells, and decreased the concentrations of IFN-γ, IL-17, and IL-6 in the culture supernatant[7].

In vivo, oral administration of BAY 87-2243 (9 mg/kg; once daily) for just 3 days to nude mice bearing UT-SCC-5 xenografts significantly reduced the pimonidazole hypoxia fraction (pHF) and the necrosis fraction (NF) in the tumors. Treatment for 5 and 7 days also significantly decreased the relative vascular area (RVA)[6]. Alternate-day oral treatment with BAY 87-2243 (4mg/kg) for 28 days in mice bearing PMP xenografts significantly reduced MUC2 mRNA and protein expression levels in tumor

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tissue and inhibited the growth of mucinous tumors^[8].

References:

- [1] ELLINGHAUS P, HEISLER I, UNTERSCHMANN K, et al. BAY 87-2243, a highly potent and selective inhibitor of hypoxia-induced gene activation has antitumor activities by inhibition of mitochondrial complex I[J]. Cancer Medicine, 2013, 2(5): 611-624.
- [2] SEMENZA G L. Targeting HIF-1 for cancer therapy[J]. Nature Reviews Cancer, 2003, 3(10): 721-732.
- [3] ADAMS J, DIFAZIO L, ROLANDELLI R, et al. HIF-1: a key mediator in hypoxia[J]. Acta Physiologica Hungarica, 2009, 96(1): 19-28.
- [4] SCHÖCKEL L, GLASAUER A, BASIT F, et al. Targeting mitochondrial complex I using BAY 87-2243 reduces melanoma tumor growth[J]. Cancer & Metabolism, 2015, 3(1): 11.
- [5] LI Y L, RAO M J, ZHANG N Y, et al. BAY 87-2243 sensitizes hepatocellular carcinoma Hep3B cells to histone deacetylase inhibitors treatment via GSK-3 β activation[J]. Experimental and Therapeutic Medicine, 2019, 17(6): 4547-4553.
- [6] HELBIG L, KOI L, BRÜCHNER K, et al. BAY 87-2243, a novel inhibitor of hypoxia-induced gene activation, improves local tumor control after fractionated irradiation in a schedule-dependent manner in head and neck human xenografts[J]. Radiation Oncology, 2014, 9(1): 207.
- [7] YU L, RAN H, LU Y, et al. Targeting HIF-1 α alleviates the inflammatory responses and rebuilds the CD4⁺ T cell subsets balance in the experimental autoimmune myasthenia gravis inflammation model via regulating cellular and humoral immunity[J]. Life Sciences, 2024, 336: 122287.
- [8] DILLY A K, LEE Y J, ZEH H J, et al. Targeting hypoxia-mediated mucin 2 production as a therapeutic strategy for mucinous tumors[J]. Translational Research, 2016, 169: 19-30.

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