

Product Data Sheet

Product Name: Sotorasib

Cat. No.: GC62238

Chemical Properties

Cas. No. 2296729-00-3

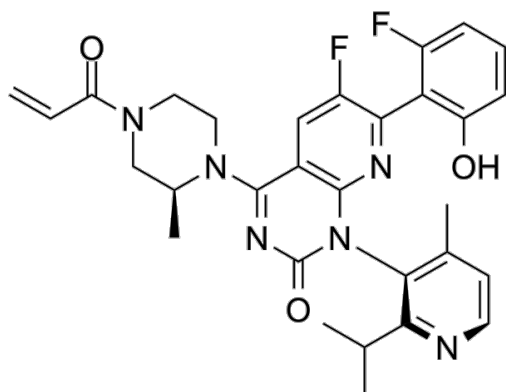
Formula $C_{30}H_{30}F_2N_6O_3$ M.Wt 560.59

Solubility DMSO : 50 mg/mL (89.19 mM; Need ultrasonic) ; Water : 33.33 mg/mL (59.46 mM; ultrasonic and adjust pH to 11 with NaOH) Storage Store at -20°C, protect from light, stored under nitrogen

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 Sotorasib-resistant parental cell line (MIA PaCa-R) and Sotorasib-sensitive parental cell line (MIA PaCa-2)

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

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Preparation Method Cell viability was assayed by MTT assay after incubating different concentrations of Sotorasib with cells for 72 h.

Reaction
Conditions 0-1.6 μ M, 72 h

Applications Sotorasib inhibited MIA PaCa-R and MIA PaCa-2 cell viability with IC₅₀ of 2.789 μ M and 66.17nM, respectively.

Animal experiment [1]:

Animal models MIA PaCa-2 cell-derived tumor xenograft model

Preparation Method Hormonal mice were randomized into 4 groups of 6 mice each to receive either vector or or KPT9274 (100mg/kg every day $\times$ 5 $\times$ 3 weeks), or Sotorasib (25mg/kg every day $\times$ 5 $\times$ 3 weeks), or their combination by oral gavage.

Dosage form 25mg/kg, Five times a week for three weeks, i.g.

Applications Sotorasib significantly reduced tumor volume, tumor weight and tumor size.

References:

[1] Khan H Y, Nagasaka M, Aboukameel A, et al. Anticancer Efficacy of KRASG12C Inhibitors Is Potentiated by PAK4 Inhibitor KPT9274 in Preclinical Models of KRAS G12C-Mutant Pancreatic and Lung Cancers[J]. Molecular Cancer Therapeutics, 2023, 22(12): 1422-1433.

Background

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Sotorasib (AMG510) is a potent covalent inhibitor of *KRAS*^{G12C} (Glycine at position 12 of *KRAS* protein mutated to cysteine) that specifically and irreversibly inhibits *KRAS*^{G12C} by locking *KRAS*^{G12C} in an inactive GDP-bound state. Sotorasib is a chiral compound with potential anti-tumor activity [1].

In NCI-H358 and MIA PaCa-2 cells, Sotorasib almost completely inhibited p-ERK (IC₅₀ is 0.03μM) levels and significantly inhibited cell viability, with IC₅₀ values of 0.006μM and 0.009μM respectively [2]. Using different concentrations of Sotorasib to treat *KRAS* mutant cell line H23 (1μM), wild-type *KRAS* cell line H522 (15μM) and A549 cells (25μM) can inhibit cell viability and induce cell apoptosis [3].

In the *KRAS*^{G12C} tumor model, Sotorasib (30-100mg/kg) inhibited p-ERK in a dose-dependent manner 2 hours after treatment. In mice xenografted with human tumor cells, Sotorasib (3, 10, 30 and 100mg/kg) significantly inhibited the growth of MIA PaCa-2 T2 and NCI-H358 tumors at all doses and at 100mg/kg Tumor regression was observed at the dose [2]. Sotorasib (25mg/kg) significantly reduced the volume, weight, and size of mouse tumors in the MIA PaCa-2 tumor xenograft model without any evidence of organ toxicity or metastatic spread[4].

References:

- [1] Fakih M, O'Neil B, Price T J, et al. Phase 1 study evaluating the safety, tolerability, pharmacokinetics (PK), and efficacy of AMG 510, a novel small molecule *KRAS*^{G12C} inhibitor, in advanced solid tumors[J]. 2019.
- [2] Canon J, Rex K, Saiki A Y, et al. The clinical *KRAS* (G12C) inhibitor AMG 510 drives anti-tumour immunity[J]. *Nature*, 2019, 575(7781): 217-223.
- [3] Barrios-Bernal P, Lucio-Lozada J, Ramos-Ramírez M, et al. A Novel Combination of Sotorasib and Metformin Enhances Cytotoxicity and Apoptosis in *KRAS*-Mutated Non-Small Cell Lung Cancer Cell Lines through MAPK and P70S6K Inhibition[J]. *International Journal of Molecular Sciences*, 2023, 24(5): 4331.
- [4] Khan H Y, Nagasaka M, Aboukameel A, et al. Anticancer Efficacy of *KRAS*^{G12C} Inhibitors Is Potentiated by PAK4 Inhibitor KPT9274 in Preclinical Models of *KRAS* G12C-Mutant Pancreatic and Lung Cancers[J]. *Molecular Cancer Therapeutics*, 2023, 22(12): 1422-1433.

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