Sotorasib

Cat. No.: HY-114277

CAS No.: 2296729-00-3

Molecular Formula: $C_{30}H_{30}F_2N_6O_3$

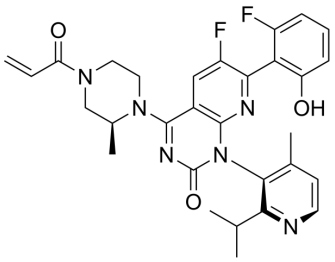
Molecular Weight: 560.59

Target: Ras

Pathway: GPCR/G Protein; MAPK/ERK Pathway

Storage: -20°C, stored under nitrogen

* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (89.19 mM; Need ultrasonic)

H_2O : 33.33 mg/mL (59.46 mM; ultrasonic and adjust pH to 11 with NaOH)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7838 mL	8.9192 mL	17.8383 mL
5 mM	0.3568 mL	1.7838 mL	3.5677 mL
10 mM	0.1784 mL	0.8919 mL	1.7838 mL

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

In Vivo

1. Add each solvent one by one: 20% HP-β-CD in saline
   Solubility: 10 mg/mL (17.84 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sotorasib (AMG-510) is a first-in-class, orally bioavailable, and selective KRAS G12C covalent inhibitor. Sotorasib irreversibly inhibits KRAS G12C by locking it in an inactive GDP-bound state. Sotorasib is the first KRAS G12C inhibitor in clinical development and leads to the regression of KRAS G12C tumors[1][2].

IC_{50} & Target

KRAS(G12C)

In Vitro

In cellular assays, Sotorasib (AMG-510) covalently modifies KRAS G12C and inhibits KRAS G12C signaling as measured by phosphorylation of ERK1/2 (p-ERK) in all KRAS p.G12C-mutant cell lines[2].
?Sotorasib (AMG-510; 1-10 μM; 72 hours) also potently impairs cellular viability in both NCI-H358 and MIA PaCa-2 with IC_{50} ≈0.006 μM and 0.009 μM, respectively. Non-KRASG12C lines are insensitive to Sotorasib (IC_{50}>7.5 μM)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay [3]

Cell Line:	NCI-H358 and MIA PaCa-2 cells
Concentration:	1-10 μM
Incubation Time:	72 hours
Result:	Potently impaired cellular viability in both NCI-H358 and MIA PaCa-2 (IC_{50}≈0.006 μM and 0.009 μM respectively).

In Vivo

In preclinical tumor models, Sotorasib (AMG-510) rapidly and irreversibly binds to KRAS G12C, providing durable suppression of the mitogen-activated protein kinase (MAPK) signaling pathway. Sotorasib (orally; once daily) is capable of inducing tumor regression in mouse models of KRAS G12C cancer[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Cancer. 2023 May 20;22(1):86.
- Nat Genet. 2022 Dec;54(12):1983-1993.
- Cancer Discov. 2024 Jan 18.
- Cancer Discov. 2022 Jun 30;cd.22.0044.
- Nat Cell Biol. 2021 Apr;23(4):377-390.

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REFERENCES

[1]. Marwan Fakih, et al, Phase 1 study evaluating the safety, tolerability, pharmacokinetics (PK), and efficacy of AMG 510, a novel small molecule KRASG12Cinhibitor, in advanced solid tumors. Journal of Clinical Oncology.

[2]. Karen Rex, et al. Abstract 3090: In vivo characterization of AMG 510 - a potent and selective KRASG12Ccovalent small molecule inhibitor in preclinical KRASG12Ccancer models. Experimental and Molecular Therapeutics.

[3]. Brian A. Lanman, et al.Abstract 4455: Discovery of AMG 510, a first-in-human covalent inhibitor of KRASG12C for the treatment of solid tumors. Cancer Chemistry.

[4]. Canon J, et al. The clinical KRAS(G12C) inhibitor AMG 510 drives anti-tumour immunity. Nature. 2019 Nov;575(7781):217-223.

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