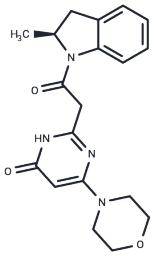
Data Sheet (Cat.No.T16841)

TargetMol

SAR-260301

Chemical Properties



CAS No. : 1260612-13-2

Formula: C19H22N4O3

Molecular Weight: 354.4

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	SAR-260301, an orally available and selective inhibitor of PI3Kβ [IC50: 23 nM].
Targets(IC50)	PI3K
In vitro	SAR-260301 inhibits pAktS473 (a measured IC50: 0.06 μM and an estimated IC90: 2 μM), in the UACC-62 tumor cell line assay. SAR260301 inhibits PI3Kβ-dependent proliferation/viability in low serum conditions (IC50: 196 nM), in the MEF-3T3-myr-p110β mechanistic model. SAR260301 inhibits LNCaP cell proliferation in low and high serum conditions (IC50: 2.9 and 5.0 μM, respectively), after 4-day treatment, whereas it is inactive in these conditions in PC3 cells at concentrations up to 10 μM, despite target engagement). SAR260301 also leads to antitumor activities in PTEN-deficient/BRAF-mutant human melanoma cells, inhibiting cell proliferation (IC40: 6.5 and 3.3 μM for UACC-62 and WM-266.4, respectively, after 4-day treatment). After prolonged treatment, SAR260301 at 3 or 10 μM inhibits PC3 cell proliferation in low serum conditions, with a cytostatic effect achieved for 14 days, despite some cell death induction observed at 10 μM [2].
In vivo	SAR-260301 is well tolerated at the active dose, with no sign of toxicity and no bodyweight loss. SAR-260301 displays antitumor efficacy in human PTEN-deficient melanoma models in mice as a single agent. SAR-260301 treatment leads to a statistically significant tumor growth inhibition as measured by a ΔT/ΔC of 39% (p = 0.054 versus control mice) on day 15 post-tumor implantation. SAR-260301(p.o.) reveals sustained target inhibition (≥50%) of pAkt-S473 for at least 7 h. SAR-260301 has moderate terminal elimination half-life (t1/2=0.87 h, 1.4 h, 2.5 h, 0.87h, 6.9 h and 4.5 h for female SCID mice (3 mg/kg, iv), mice (10 mg/kg, p.o.), mice (100 mg/kg, p.o.), female nude rats (3 mg/kg, iv), rat (10 mg/kg, p.o.), male beagle dogs (10 mg/kg, p.o.)) [1].

Solubility Information

Solubility	DMSO: 125 mg/mL (352.71 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (11.29 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.8217 mL	14.1084 mL	28.2167 mL
5 mM	0.5643 mL	2.8217 mL	5.6433 mL
10 mM	0.2822 mL	1.4108 mL	2.8217 mL
50 mM	0.0564 mL	0.2822 mL	0.5643 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Certal V, et al. Discovery and optimization of pyrimidone indoline amide PI3Kβ inhibitors for the treatment of phosphatase and tensin homologue (PTEN)-deficient cancers. J Med Chem. 2014 Feb 13;57(3):903-20.
Bonnevaux H, et al. Concomitant Inhibition of PI3Kβ and BRAF or MEK in PTEN-Deficient/BRAF-Mutant Melanoma Treatment: Preclinical Assessment of SAR260301 Oral PI3Kβ-Selective Inhibitor. Mol Cancer Ther. 2016 Jul;15(7):1460-71.

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