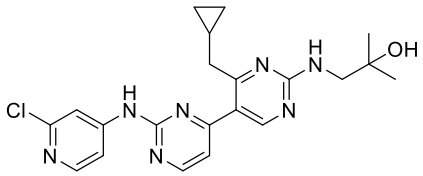
Product data sheet

MedKoo Cat#: 406636 Name: VPS34-IN1 CAS#: 1383716-33-3 Chemical Formula: $C_{21}H_{24}ClN_7O$ Exact Mass: 425.17309 Molecular Weight: 425.91	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

VPS34-IN1 is a potent and selective Vps34 inhibitor with potential anticancer activity. VPS34-IN1 inhibits Vps34 with 25 nM IC50 in vitro, but does not significantly inhibit the activity of 340 protein kinases or 25 lipid kinases tested that include all isoforms of class I as well as class II PI3Ks. Administration of VPS34-IN1 to cells induces a rapid dose-dependent dispersal of a specific PtdIns(3)P-binding probe from endosome membranes, within 1 min, without affecting the ability of class I PI3K to regulate Akt. Combining class I (GDC-0941) and class III (VPS34-IN1) PI3K inhibitors could be used as a strategy to better analyse the roles and regulation of the elusive class II PI3K.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	51.33	120.52
Ethanol	85.0	199.57

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.35 mL	11.74 mL	23.48 mL
5 mM	0.47 mL	2.35 mL	4.70 mL
10 mM	0.23 mL	1.17 mL	2.35 mL
50 mM	0.05 mL	0.23 mL	0.47 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Yuen CK, Wong WM, Mak LF, Wang X, Chu H, Yuen KY, Kok KH. Suppression of SARS-CoV-2 infection in ex-vivo human lung tissues by targeting class III phosphoinositide 3-kinase. J Med Virol. 2021 Apr;93(4):2076-2083. doi: 10.1002/jmv.26583. Epub 2020 Oct 30. PMID: 33026649; PMCID: PMC7675438.
2. Meunier G, Birsen R, Cazelles C, Belhadj M, Cantero-Aguilar L, Kosmider O, Fontenay M, Azar N, Mayeux P, Chapuis N, Tamburini J, Bouscary D. Antileukemic activity of the VPS34-IN1 inhibitor in acute myeloid leukemia. Oncogenesis. 2020 Oct 22;9(10):94. doi: 10.1038/s41389-020-00278-8. PMID: 33093450; PMCID: PMC7581748.

In vivo study

1. Valet C, Levade M, Chicanne G, Bilanges B, Cabou C, Viaud J, Gratacap MP, Gaits-Iacovoni F, Vanhaesebroeck B, Payrastre B, Severin S. A dual role for the class III PI3K, Vps34, in platelet production and thrombus growth. Blood. 2017 Nov 2;130(18):2032-2042. doi: 10.1182/blood-2017-04-781641. Epub 2017 Sep 13. PMID: 28903944; PMCID: PMC5669208.

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7. Bioactivity

Biological target:

Vps34-IN-1 is an inhibitor of Vps34 with an IC50 of 4 nM.

In vitro activity

This study tested the antileukemic activity of the VPS34-IN1 compound in nine AML cell lines. VPS34-IN1 impaired viability and induced dose-dependent cell death in all these tested cell lines (Fig. 1A, B). This study then tested the effects of VPS34-IN1 on the survival of primary leukemic cells from 23 patients with AML. This inhibitor induced a significant death of leukemic cells in this series of AML patients (Fig. (Fig.1C1C and Supplemental Table 1). In contrast, VPS34-IN1 did not induce cell death in normal CD34+ hematopoietic progenitor cells from 6 allogenic BM donors (Fig. 1C).

Reference: Oncogenesis. 2020 Oct; 9(10): 94. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7581748/

In vivo activity

This study first tested the implication of Vps34 in platelet responses in vivo and found a normal tail bleeding time in *Pf4*-Cre-*Pik3c3*$^{lox/lox}$ mice (Figure 5A). The prothrombotic function of platelets tested after ferric chloride–induced mouse carotid injury was significantly decreased, with nearly 50% of *Pf4*-Cre-*Pik3c3*$^{lox/lox}$ mice protected against occlusive arterial thrombus formation (Figure 5B). Ex vivo thrombus formation assay performed under physiological arterial or arteriolar wall shear rates of 500 and 1500 s^{-1}, respectively, using *Pf4*-Cre-*Pik3c3*$^{lox/lox}$ mice blood perfused over a collagen surface showed that Vps34-deficient platelets, despite their ability to normally attach to collagen fibers (supplemental Figure 5A), formed significantly smaller thrombi compared with WT platelets (Figure 5C-D). These data demonstrate that inhibition of Vps34 kinase activity in platelets, independently from its implication in MKs and platelet production, decreases platelet thrombus growth at arterial and arteriolar flows.

Reference: Blood. 2017 Nov 2; 130(18): 2032–2042. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5669208/