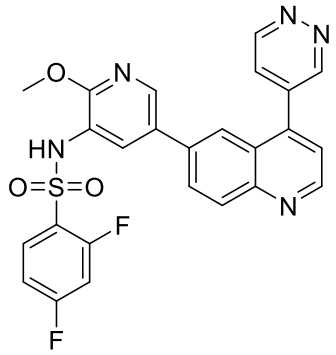
Product data sheet

MedKoo Cat#: 205480 Name: Omipalisib CAS#: 1086062-66-9 Chemical Formula: $C_{25}H_{17}F_2N_5O_3S$ Exact Mass: 505.10202 Molecular Weight: 505.5	
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:

Omipalisib, also known as GSK2126458, is a small-molecule pyridylsulfonamide inhibitor of phosphatidylinositol 3-kinase (PI3K) with potential antineoplastic activity. PI3K inhibitor GSK2126458 binds to and inhibits PI3K in the PI3K/mTOR signaling pathway, which may trigger the translocation of cytosolic Bax to the mitochondrial outer membrane, increasing mitochondrial membrane permeability and inducing apoptotic cell death. Bax is a member of the proapoptotic Bcl2 family of proteins. PI3K, often overexpressed in cancer cells, plays a crucial role in tumor cell regulation and survival.

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	10.0	19.8

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.98 mL	9.89 mL	19.78 mL
5 mM	0.40 mL	1.98 mL	3.96 mL
10 mM	0.20 mL	0.99 mL	1.98 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Rønnow SR, Dabbagh RQ, Genovese F, Nanthakumar CB, Barrett VJ, Good RB, Brockbank S, Cruwys S, Jessen H, Sorensen GL, Karsdal MA, Leeming DJ, Sand JMB. Prolonged Scar-in-a-Jar: an in vitro screening tool for anti-fibrotic therapies using biomarkers of extracellular matrix synthesis. Respir Res. 2020 May 7;21(1):108. doi: 10.1186/s12931-020-01369-1. PMID: 32381012; PMCID: PMC7203825.
2. Evans JF, Rue RW, Mukhitov AR, Obraztsova K, Smith CJ, Krymskaya VP. Inhibition of Growth of TSC2-Null Cells by a PI3K/mTOR Inhibitor but Not by a Selective MNK1/2 Inhibitor. Biomolecules. 2019 Dec 24;10(1):28. doi: 10.3390/biom10010028. PMID: 31878201; PMCID: PMC7022412.

In vivo study

1. Zhu DS, Dong JY, Xu YY, Zhang XT, Fu SB, Liu W. Omipalisib Inhibits Esophageal Squamous Cell Carcinoma Growth Through Inactivation of Phosphoinositide 3-Kinase (PI3K)/AKT/Mammalian Target of Rapamycin (mTOR) and ERK Signaling. Med Sci Monit. 2020 Aug 17;26:e927106. doi: 10.12659/MSM.927106. PMID: 32804918; PMCID: PMC7450785.
2. Wong K, Di Cristofano F, Ranieri M, De Martino D, Di Cristofano A. PI3K/mTOR inhibition potentiates and extends palbociclib activity in anaplastic thyroid cancer. Endocr Relat Cancer. 2019 Apr 1;26(4):425-436. doi: 10.1530/ERC-19-0011. Epub 2019 Jan 1. PMID: 30699064; PMCID: PMC6602869.

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7. Bioactivity

Biological target:

Omipalisib (GSK2126458) is an inhibitor of PI3K and has K_is of 0.019 nM/0.13 nM/0.024 nM/0.06 nM and 0.18 nM/0.3 nM for p110α/β/δ/γ, mTORC1/2, respectively.

In vitro activity

Many dual catalytic mTOR inhibitors do not have tolerable clinical profiles, so this study investigated a clinically acceptable dual PI3K/mTOR inhibitor omipalisib (GSK2126458) that has completed a Phase 1 clinical trial in patients with advanced solid tumors and another Phase 1 trial in patients with idiopathic pulmonary fibrosis. The PI3K/mTOR inhibitor effectively reduced phosphorylation of S6, 4E-BP1, Akt and, in an additive manner with rapamycin, inhibited cell growth. This study demonstrated that omipalisib dose-dependently inhibits pAkt and both mTORC1 protein synthetic pathways and, in an additive manner with rapamycin, inhibited the growth of TSC2-null cells. Omipalisib, or another inhibitor of both major mTORC1 growth pathways and pAkt, might provide therapeutic options for TSC2-deficient cancers including, but not limited to, LAM. It is suggested that a clinically tolerable PI3K/mTOR inhibitor might be beneficial in LAM, as monotherapy or in combination with rapamycin, and in other mTORC1-driven neoplastic diseases.

Biomolecules. 2020 Jan; 10(1): 28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7022412/

In vivo activity

This study aimed to investigate the antineoplastic effects of omipalisib and its underlying molecular mechanisms in ESCC using a high throughput screen. MTT assay and clone formation were used to determine cell viability and proliferation. Flow cytometry was conducted to detect cell cycle distribution and apoptosis. Global gene expression and mRNA expression levels were determined by RNA sequencing and real-time PCR, respectively. Protein expression was evaluated in the 4 ESCC cell lines by Western blot analysis. Finally, a xenograft nude mouse model was used to evaluate the effect of omipalisib on tumor growth in vivo. In the pilot screening of a 1404-compound library, we demonstrated that omipalisib markedly inhibited cell proliferation in a panel of ESCC cell lines. Mechanistically, omipalisib induced G0/G1 cell cycle arrest and apoptosis. RNA-seq, KEGG, and GSEA analyses revealed that the PI3K/AKT/mTOR pathway is the prominent target of omipalisib in ESCC cells. Treatment with omipalisib decreased expression of p-AKT, p-4EBP1, p-p70S6K, p-S6, and p-ERK, therefore disrupting the activation of PI3K/AKT/mTOR and ERK signaling. In the nude mouse xenograft model, omipalisib significantly suppressed the tumor growth in ESCC tumor-bearing mice without obvious adverse effects.

Med Sci Monit. 2020; 26: e927106-1–e927106-13. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7450785/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.