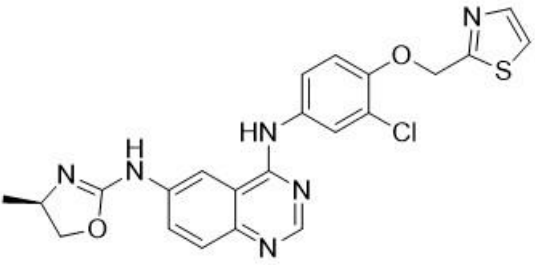


Product data sheet



MedKoo Cat#: 205660 Name: Varlitinib CAS#: 845272-21-1 Chemical Formula: C ₂₂ H ₁₉ ClN ₆ O ₂ S Exact Mass: 466.09787 Molecular Weight: 466.94	
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:

Varlitinib, also known as ARRY-543 and ASLAN001, is an orally bioavailable inhibitor of the epidermal growth factor receptor family with potential antineoplastic activity. Varlitinib selectively and reversibly binds to both EGFR (ErbB-1) and Her-2/neu (ErbB-2) and prevents their phosphorylation and activation, which may result in inhibition of the associated signal transduction pathways, inhibition of cellular proliferation and cell death. EGFR and Her-2 play important roles in cell proliferation and differentiation and are upregulated in various human tumor cell types.

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	20.0	43.55

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.14	10.71	21.42
5 mM	0.43	2.14	4.28
10 mM	0.21	1.07	2.14
50 mM	0.04	0.21	0.43

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. Liu CY, Chu PY, Huang CT, Chen JL, Yang HP, Wang WL, Lau KY, Lee CH, Lan TY, Huang TT, Lin PH, Dai MS, Tseng LM. Varlitinib Downregulates HER/ERK Signaling and Induces Apoptosis in Triple Negative Breast Cancer Cells. *Cancers (Basel)*. 2019 Jan 17;11(1):105. doi: 10.3390/cancers11010105. PMID: 30658422; PMCID: PMC6356324.
2. Dokduang H, Jamnongkarn W, Promraksa B, Suksawat M, Padthaisong S, Thanee M, Phetcharaburanin J, Namwat N, Sangkhamanon S, Titapun A, Khuntikeo N, Klanrit P, Loilome W. In vitro and in vivo Anti-Tumor Effects of Pan-HER Inhibitor Varlitinib on Cholangiocarcinoma Cell Lines. *Drug Des Devel Ther*. 2020 Jun 11;14:2319-2334. doi: 10.2147/DDDT.S250061. PMID: 32606601; PMCID: PMC7296552.

In vivo study

1. Liu CY, Chu PY, Huang CT, Chen JL, Yang HP, Wang WL, Lau KY, Lee CH, Lan TY, Huang TT, Lin PH, Dai MS, Tseng LM. Varlitinib Downregulates HER/ERK Signaling and Induces Apoptosis in Triple Negative Breast Cancer Cells. *Cancers (Basel)*. 2019 Jan 17;11(1):105. doi: 10.3390/cancers11010105. PMID: 30658422; PMCID: PMC6356324.
2. Dokduang H, Jamnongkarn W, Promraksa B, Suksawat M, Padthaisong S, Thanee M, Phetcharaburanin J, Namwat N, Sangkhamanon S, Titapun A, Khuntikeo N, Klanrit P, Loilome W. In vitro and in vivo Anti-Tumor Effects of Pan-HER Inhibitor

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Varlitinib on Cholangiocarcinoma Cell Lines. Drug Des Devel Ther. 2020 Jun 11;14:2319-2334. doi: 10.2147/DDDT.S250061. PMID: 32606601; PMCID: PMC7296552.

7. Bioactivity

Biological target:

Varlitinib (ASLAN001) is a potent, reversible, small molecule pan-EGFR inhibitor with IC50s of 7, 2, 4 nM for HER1, HER2 and HER4, respectively

In vitro activity

In this study, the efficacy of varlitinib, a reversible small molecule pan-HER inhibitor in TNBC was evaluated. To explore varlitinib's anti-tumor activity, cells were treated with varlitinib at various concentrations. Compared with MCF 10A cell lines, most of the cell lines exhibited lower IC50 except MDA-MB-231 cells (Figure 1B and Figure S1). Moreover, varlitinib significantly induced cell apoptosis in MDA-MB-453 and MDA-MB-468 cells but not in MDA-MB-231 cells (Figure 1B,C). Data showed varlitinib reduced pEGFR, pHER3 and pHER4 in MDA-MB-468 cells as well as reduced pHER2 in SK-BR-3 cells (Figure 2A,B). Activation of HER receptors leads to the activation of downstream pathways including RAS/RAF/MEK/ERK and PI3K/Akt signaling. The western blot results demonstrated that varlitinib treatment inhibited EGFR, AKT, MEK and ERK activation in MDA-MB-453 and MDA-MB-468 cells. In addition, varlitinib treatment also resulted in increased levels of cleaved PARP and cleaved Caspase-3 in these TNBC cell lines. Conversely, varlitinib did not inhibit MEK/ERK signaling in MDA-MB-231 cells (Figure 2C). Our results showed that varlitinib treatment inhibited cell migration, invasion and mammosphere formation of MDA-MB-231 and MDA-MB-468 cells (Figure 4A-C).

Cancers (Basel). 2019 Jan; 11(1): 105. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6356324/>

In vivo activity

Nude mice were subcutaneously implanted with MDA-MB-468 cells to evaluate anti-tumor activity of varlitinib. Once xenograft tumor sizes reached 200 mm³ varlitinib were orally administered. Varlitinib suppressed tumor growth in MDA-MB-468 xenograft mice with no effect on body weight (Figure 5A-C). In comparison to the control group, varlitinib treatment significantly suppressed EGFR and ERK activation with increased PARP cleavage (Figure 5D). Immunohistochemical staining was performed to further examine protein expression and localization within the xenograft tumors. The results showed that varlitinib treatment reduced EGFR and ERK phosphorylation and elicited cell apoptosis with M30 staining (Figure 5D,E). These results demonstrated varlitinib exerting anti-tumor activity in TNBC via the inhibition of HER receptor and downstream signaling.

Cancers (Basel). 2019 Jan; 11(1): 105. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6356324/>

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.