Varlitinib

Cat. No.: HY-10530

CAS No.: 845272-21-1

Molecular Formula: $C_{22}H_{19}ClN_6O_2S$

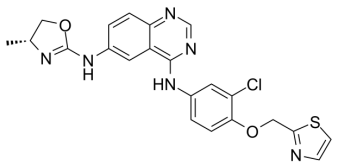
Molecular Weight: 466.94

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (71.38 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1416 mL	10.7080 mL	21.4160 mL
	5 mM	0.4283 mL	2.1416 mL	4.2832 mL
	10 mM	0.2142 mL	1.0708 mL	2.1416 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.45 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.45 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Varlitinib (ASLAN001) is a potent, reversible, small molecule pan-EGFR inhibitor with IC_{50}s of 7, 2, 4 nM for HER1, HER2 and HER4, respectively[1].

IC_{50} & Target

HER1	HER2	HER4
7 nM (IC_{50})	2 nM (IC_{50})	4 nM (IC_{50})

In Vitro

In cell-based assays using tumor cells that over-express EGFR (A431) or ErbB-2 (BT474), Varlitinib (ARRY-334543) potently

	inhibits substrate phosphorylation. Varlitinib is shown to be highly selective for EGFR/ErbB-2, and does not show any significant activity when screened against a panel of 104 kinases[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Varlitinib treatment potently inhibits tumor growth with complete tumor regression observed at dosing of 100 mg/kg twice a day. After five days of Varlitinib treatment, phosphorylation of HER1-3, RAS/RAF/MEK/MAPK, p70S6K, S6 ribosomal, 4EBP1, Cdk-2, Cdc-2 and retinoblastoma are strongly inhibited. Varlitinib treatment results in a significant reduction in survivin and a concomittant increase in Caspase 3 cleavage products[1]. In murine xenograft models, Varlitinib (ARRY-334543) demonstrates significant dose-related (25, 50, 100 mg/kg) tumor growth inhibition in A431-derived tumors when administered orally, twice a day, for 21 days[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: The effects of Varlitinib is tested in patient-derived HCC xenograft in SCID mice (HCC29-0909A) with co-expression of HER1, HER2 and HER3 recepors. Mice are treated with Varlitinib when the tumors reach the size of approximately 100-150 mm^3. Tumor size measurements are performed twice a week and tumor volumes are calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.

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REFERENCES

[1]. Hsieh C, et al. Varlitinib to demonstrate anti-tumour efficacy in patient-derived hepatocellular carcinoma xenograft models. Journal of Clinical Oncology 34, no. 15_suppl

[2]. Miknis G, et al. ARRY-334543, A potent, orally active small molecule inhibitor of EGFR and ErbB-2.Proc Amer Assoc Cancer Res, Volume 46, 2005

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