Product Data Sheet

Product Name: Varlitinib (ARRY334543)
Cat. No.: GC12249

Chemical Properties

Cas. No.	845272-21-1		
Chemical Name	4-N-[3-chloro-4-(1,3-thiazol-2-ylmethoxy)phenyl]-6-N-[(4R)-4-methyl-4,5-dihydro-1,3-oxazol-2-yl]quinazoline-4,6-diamine		
SMILES	CC1COC(=N1)NC2=CC3=C(C=C2)N=CN=C3NC4=CC(=C(C=C4)OCC5=NC=CS5)Cl		
Formula	$C_{22}H_{19}ClN_6O_2S$	M.Wt	466.94
Solubility	≥ 23.35mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Varlitinib (ARRY334543)		

Protocol

Animal experiment:

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 mm3. Tumor size measurements are performed twice a week and tumor volumes are calculated[1].

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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

Background

Varlitinib (ARRY-334543; ASLAN001) is a potent, reversible, small molecule pan-EGFR inhibitor with IC50s of 7, 2, 4 nM for HER1, HER2 and HER4, respectively.

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].

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].

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

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[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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