

Product Data Sheet

Product Name: Linifanib (ABT-869)

Cat. No.: GC17958

Chemical Properties

Cas. No. 796967-16-3

Chemical Name 1-[4-(3-amino-1H-indazol-4-yl)phenyl]-3-(2-fluoro-5-methylphenyl)urea

SMILES CC1=CC(=C(C=C1)F)NC(=O)NC2=CC=C(C=C2)C3=C4C(=CC=C3)NN=C4N

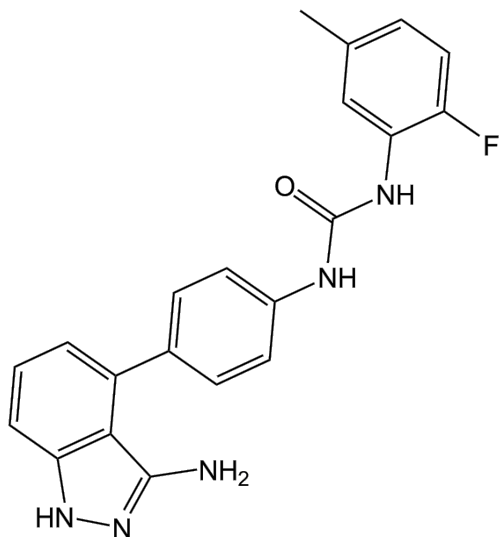
Formula $C_{21}H_{18}FN_5O$ M.Wt 375.41

Solubility $\geq 18.75\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment [1]:

Cell lines Ba/F3 FLT3 ITD mutant and WT cells

Preparation method The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

Reacting condition 0.1 nM ~ 10 µM; 24 hrs

Applications Linifanib was more effective at inhibiting cell growth in ITD mutant cells with the IC50 value of 0.55 nM. In addition, treatment with 10 nM of Linifanib induced apoptosis in ITD mutant cells, but showed no observable effect on WT cells.

Animal experiment [1]:

Animal models NOD/SCID mice with ITD mutant cells

Dosage form 0.2 mL/20 g; p.o.; q.d.

Applications In NOD/SCID mice with ITD mutant cells, Linifanib decreased leukemia progression. On day 7, untreated mice exhibited rapid progression of ITD mutant cells, whilst mice treated with Linifanib showed no detectable disease. In addition, Linifanib significantly prolonged survival duration of Ba/F3 FLT3 ITD-injected mice.

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Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Jenny E. Hernandez-Davies, Joan P. Zape, Elliot M. Landaw, et al. The Multitargeted Receptor Tyrosine Kinase Inhibitor Linifanib (ABT-869) Induces Apoptosis through an Akt and Glycogen Synthase Kinase 3 β -Dependent Pathway. Mol. Cancer Ther., 2011, 10(6):949-59.

Background

Linifanib (ABT-869) is an effective ATP-competitive tyrosine kinase inhibitor against the platelet-derived growth factor (PDGF) receptor and the vascular endothelial growth factor receptor (VEGFR) families, including constitutively active FMS-like receptor tyrosine kinase 3 (FLT3) [1][2]. It is of IC₅₀ values of 0.55 nmol/L and 6 μ mol/L to the cell growth in Ba/F3 FLT3 ITD mutant cells and in Ba/F3 FLT3 WT cells, respectively [1].

FLT3 is important in controlling the proliferation and differentiation of hematopoietic cells. Patients with acute myeloid leukemia (AML) showed activating mutations in FLT3. These mutations caused abnormal cell proliferation [1].

Linifanib at a concentration of 10 nmol/L induced apoptosis in internal tandem duplication (ITD) mutant cells, but showed no effect in WT cells. Treatment with linifanib did not differentiate WT cells from FLT3 mutant cells with mutation at D835V, in inhibiting proliferation or reducing cell viability. In Ba/F3 FLT3 ITD cell lines, linifanib at a concentration of 10 nmol/L, effectively inhibited the phosphorylation of FLT3. 10 nmol/L linifanib reduced the phosphorylation of Akt at Ser473 [1].

Daily orally treatment with linifanib by gavage in NOD/SCID mice with ITD mutant cell decreased the leukemia progression rate compared with the control. On day 7, ITD mutant cells showed rapid progression in control mice, whereas linifanib-treated mice showed no detectable disease. In addition, daily linifanib-treated mice with ITD mutant cells showed significantly longer ($P < 0.01$) survival duration than control mice with ITD mutant cells only [1].

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- [2]. Joyce E. Ohm, Michael R. Shurin, Clemens Esche, et al. Effect of Vascular Endothelial Growth Factor and FLT3 Ligand on Dendritic Cell Generation In Vivo. *Journal of Immunology*, 1999, 163:3260-3268.

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