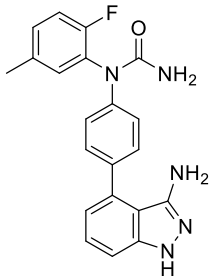
Product data sheet

MedKoo Cat#: 200060 Name: Linifanib (ABT-869) CAS#: 796967-16-3 Chemical Formula: $C_{21}H_{18}FN_5O$ Exact Mass: 375.14954 Molecular Weight: 375.4	
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:

Linifanib, also known as ABT-869, is an orally bioavailable, small-molecule receptor tyrosine kinase (RTK) inhibitor with potential antineoplastic activity. Linifanib inhibits members of the vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) receptor families; it exhibits much less activity against unrelated RTKs, soluble tyrosine kinases, or serine/threonine kinases. This agent does not have a general antiproliferative effect due to its high dose requirement. However, linifanib may exhibit potent antiproliferative and apoptotic effects on tumor cells whose proliferation is dependent on mutant kinases, such as fms-related tyrosine kinase receptor-3 (FLT3).

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	19.08	50.83
DMSO:PBS (pH 7.2) (1:5)	0.2	0.53
DMF	20.0	53.28

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.66 mL	13.32 mL	26.64 mL
5 mM	0.53 mL	2.66 mL	5.33 mL
10 mM	0.27 mL	1.33 mL	2.66 mL
50 mM	0.05 mL	0.27 mL	0.53 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. Hernandez-Davies JE, Zape JP, Landaw EM, Tan X, Presnell A, Griffith D, Heinrich MC, Glaser KB, Sakamoto KM. The multitargeted receptor tyrosine kinase inhibitor linifanib (ABT-869) induces apoptosis through an Akt and glycogen synthase kinase 3β-dependent pathway. Mol Cancer Ther. 2011 Jun;10(6):949-59. doi: 10.1158/1535-7163.MCT-10-0904. Epub 2011 Apr 6. PMID: 21471285; PMCID: PMC3112478.

2. Shankar DB, Li J, Tapang P, Owen McCall J, Pease LJ, Dai Y, Wei RQ, Albert DH, Bouska JJ, Osterling DJ, Guo J, Marcotte PA, Johnson EF, Soni N, Hartandi K, Michaelides MR, Davidsen SK, Priceman SJ, Chang JC, Rhodes K, Shah N, Moore TB, Sakamoto KM, Glaser KB. ABT-869, a multitargeted receptor tyrosine kinase inhibitor: inhibition of FLT3 phosphorylation and signaling in acute myeloid leukemia. Blood. 2007 Apr 15;109(8):3400-8. doi: 10.1182/blood-2006-06-029579. Epub 2007 Jan 5. PMID: 17209055; PMCID: PMC1852258.

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In vivo study

1. Chen J, Guo J, Chen Z, Wang J, Liu M, Pang X. Linifanib (ABT-869) Potentiates the Efficacy of Chemotherapeutic Agents through the Suppression of Receptor Tyrosine Kinase-Mediated AKT/mTOR Signaling Pathways in Gastric Cancer. Sci Rep. 2016 Jul 8;6:29382. doi: 10.1038/srep29382. PMID: 27387652; PMCID: PMC4937412.
2. Ikeda AK, Judelson DR, Federman N, Glaser KB, Landaw EM, Denny CT, Sakamoto KM. ABT-869 inhibits the proliferation of Ewing Sarcoma cells and suppresses platelet-derived growth factor receptor beta and c-KIT signaling pathways. Mol Cancer Ther. 2010 Mar;9(3):653-60. doi: 10.1158/1535-7163.MCT-09-0812. Epub 2010 Mar 2. PMID: 20197394; PMCID: PMC2837519.

7. Bioactivity

Biological target:

Linifanib (ABT-869) is a multi-target inhibitor of VEGFR and PDGFR family with IC50s of 4, 3, 66, and 4 nM for KDR, FLT1, PDGFRβ, and FLT3, respectively.

In vitro activity

Linifanib is effective at inhibiting phosphorylation of FLT3 in Ba/F3 FLT3 ITD cell lines at a concentration of 10nM (Fig. 4a). In addition, Linifanib reduced phosphorylation of AKT at Ser473 after treatment with 10nM of Linifanib (Fig. 4b). To test whether GSK3β phosphorylation was affected after treatment with Linifanib, the ITD mutant cells were treated with 10nM Linifanib phosphorylation of GSK 3β at Ser9 (Fig. 4c) or GSK 3α at Ser21 (data not shown) was examined. Treatment with 10nM Linifanib resulted in decreased phosphorylation of GSK3β Ser 9 as early as 60 minutes (Fig. 4c).

Reference: Mol Cancer Ther. 2011 Jun; 10(6): 949–959. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3112478/

In vivo activity

To analyze the potential effects of ABT-869 on a metastatic model of Ewing sarcoma, GFP/Luciferase-expressing A4573 and TC71 cells (A4573-GFP/LUC, TC71-GFP/LUC) were generated through lentiviral transduction followed by sorting for GFP. The sorted cells were cultured and injected through the tail vein into female NOD/SCID mice. Six mice were analyzed per treatment group. Engraftment and disease progression were monitored by acquiring in vivo bioluminescent images at least once per week. The mice began treatment the day after injection. Kaplan-Meier analysis demonstrated a survival benefit in the treatment group compared to the vehicle control group with both the A4573 GFP/LUC cell lines (p=0.015) (Figure 6A) and TC71-GFP/LUC (p=0.002) (Figure 6B). Furthermore, the tagged cells showed evidence of more aggressive disease in mice treated with ABT-869 compared to untreated mice (Figure 6C). As previously observed, the mice tolerated the ABT-869 well, maintained their normal activity levels and weight (16). These results suggest that survival is prolonged and disease progression is suppressed in mice treated with ABT-869.

Reference: Mol Cancer Ther. 2010 Mar; 9(3): 653–660. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2837519/

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.