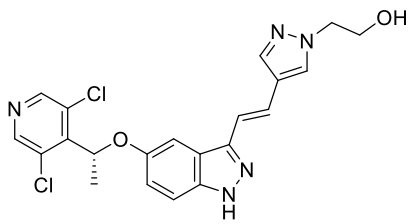
Product data sheet

MedKoo Cat#: 205527 Name: LY2874455 CAS#: 1254473-64-7 Chemical Formula: $C_{21}H_{19}Cl_2N_5O_2$ Exact Mass: 443.09158 Molecular Weight: 444.31	
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:

LY2874455 is a novel and potent FGF/FGFR Inhibitor. It exhibits a potent activity against FGF/FGFR-mediated signaling in several cancer cell lines and shows an excellent broad spectrum of antitumor activity in several tumor xenograft models representing the major FGF/FGFR relevant tumor histologies including lung, gastric, and bladder cancers and multiple myeloma, and with a well-defined pharmacokinetic/pharmacodynamic relationship.

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	69.0	155.30
Ethanol	88.0	198.06

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.25 mL	11.25 mL	22.51 mL
5 mM	0.45 mL	2.25 mL	4.50 mL
10 mM	0.23 mL	1.13 mL	2.25 mL
50 mM	0.05 mL	0.23 mL	0.45 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. Kabashima A, Hirsova P, Bronk SF, Hernandez MC, Truty MJ, Rizvi S, Kaufmann SH, Gores GJ. Fibroblast growth factor receptor inhibition induces loss of matrix MCL1 and necrosis in cholangiocarcinoma. J Hepatol. 2018 Jun;68(6):1228-1238. doi: 10.1016/j.jhep.2018.01.026. Epub 2018 Mar 9. PMID: 29408314; PMCID: PMC5960421.
2. Wu D, Guo M, Philips MA, Qu L, Jiang L, Li J, Chen X, Chen Z, Chen L, Chen Y. Crystal Structure of the FGFR4/LY2874455 Complex Reveals Insights into the Pan-FGFR Selectivity of LY2874455. PLoS One. 2016 Sep 12;11(9):e0162491. doi: 10.1371/journal.pone.0162491. PMID: 27618313; PMCID: PMC5019380.

In vivo study

1. Hanes R, Munthe E, Grad I, Han J, Karlsen I, McCormack E, Meza-Zepeda LA, Stratford EW, Myklebost O. Preclinical Evaluation of the Pan-FGFR Inhibitor LY2874455 in FRS2-Amplified Liposarcoma. Cells. 2019 Feb 21;8(2):189. doi: 10.3390/cells8020189. PMID: 30795553; PMCID: PMC6406403.
2. Zhao G, Li WY, Chen D, Henry JR, Li HY, Chen Z, Zia-Ebrahimi M, Bloem L, Zhai Y, Huss K, Peng SB, McCann DJ. A novel, selective inhibitor of fibroblast growth factor receptors that shows a potent broad spectrum of antitumor activity in several tumor

xenograft models. Mol Cancer Ther. 2011 Nov;10(11):2200-10. doi: 10.1158/1535-7163.MCT-11-0306. Epub 2011 Sep 7. PMID: 21900693.

7. Bioactivity

Biological target:

LY2874455 is a pan-FGFR inhibitor with IC50s of 2.8, 2.6, 6.4, 6 nM for FGFR1, FGFR2, FGFR3, FGFR4, respectively.

In vitro activity

To confirm that LY (LY2874455) inhibits FGFR signaling, this study examined phosphorylation of the common FGFR receptor substrate, FRS2 (fibroblast growth factor receptor substrate 2), in KMCH and KMBC cells. As indicated in Fig. 1A, FRS2, was phosphorylated in both CCA cell lines at baseline; and incubation with LY blocked this phosphorylation, indicating inhibition of FGFR signaling cascades. Further studies demonstrated that LY also induces cell death in both the KMCH and KMBC cell lines (Fig. 1B).

Reference: J Hepatol. 2018 Jun; 68(6): 1228–1238. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960421/

In vivo activity

Already from day 4 of treatment this study observed significant inhibition of tumor growth compared to control-treated mice (Figure 5A). To confirm that LY2874455 reduced FGFR signaling in vivo, this study performed a kinetic study of FGFR signaling proteins. Tumors were harvested at 3, 24 and 48 h after last treatment (end of study) and protein lysates were subjected to Western blotting to analyze the phosphorylation levels of FRS2 and ERK. The endogenous level of phosphorylated FRS2 in the LS70x tumors was, as in the cell lines, below detection (data not shown). However, ERK phosphorylation was clearly reduced 3 h after treatment and remained reduced for at least 24 h (Figure 5B, quantified in Figure S4C).

Reference: Cells. 2019 Feb; 8(2): 189. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6406403/