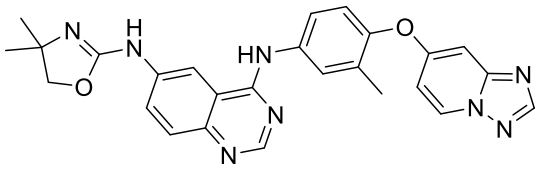
Product data sheet

MedKoo Cat#: 200291 Name: Tucatinib CAS#: 937263-43-9 Chemical Formula: $C_{26}H_{24}N_8O_2$ Exact Mass: 480.2022 Molecular Weight: 480.53	
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:
Tucatinib, also known as Irbinitinib, ARRY-380 and ONT-380, is a n orally bioavailable inhibitor of the human epidermal growth factor receptor tyrosine kinase ErbB-2 (also called HER2) with potential antineoplastic activity. ErbB-2 inhibitor ARRY-380 selectively binds to and inhibits the phosphorylation of ErbB-2, which may prevent the activation of ErbB-2 signal transduction pathways, resulting in growth inhibition and death of ErbB-2-expressing tumor cells. ErbB-2 is overexpressed in a variety of cancers and plays an important role in cellular proliferation and differentiation.

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
DMF	1.0	2.08
DMSO	49.0	101.97
DMSO:PBS (pH 7.2) (1:2)	0.33	0.69

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.08 mL	10.41 mL	20.81 mL
5 mM	0.42 mL	2.08 mL	4.16 mL
10 mM	0.21 mL	1.04 mL	2.08 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Jing W, Zhou M, Chen R, Ye X, Li W, Su X, Luo J, Wang Z, Peng S. In vitro and ex vivo anti-tumor effect and mechanism of Tucatinib in leukemia stem cells and ABCG2-overexpressing leukemia cells. Oncol Rep. 2021 Mar;45(3):1142-1152. doi: 10.3892/or.2020.7915. Epub 2020 Dec 30. PMID: 33650639; PMCID: PMC7859976.

In vivo study

1. Kulukian A, Lee P, Taylor J, Rosler R, de Vries P, Watson D, Forero-Torres A, Peterson S. Preclinical Activity of HER2-Selective Tyrosine Kinase Inhibitor Tucatinib as a Single Agent or in Combination with Trastuzumab or Docetaxel in Solid Tumor Models. Mol Cancer Ther. 2020 Apr;19(4):976-987. doi: 10.1158/1535-7163.MCT-19-0873. PMID: 32241871.

7. Bioactivity
Biological target:

HER2 inhibitor with an IC50 of 8 nM

Product data sheet

In vitro activity

To investigate the effects of tucatinib on leukemia cells, MTT assays were subsequently performed to determine the cytotoxicity of tucatinib on 2 leukemia cell lines. As shown in Fig. 1B and C, >80% of the HL60/ABCG2 and K562/ABCG2 ABCG2-overexpressing cell lines, and their parental cell lines, HL60 and K562, survived 0.4 µM tucatinib treatment. Therefore, 0.4 µM tucatinib was selected as the maximum working concentration for further experiments. Subsequently, whether tucatinib, at various concentrations, could increase the sensitivity of ABCG2-overexpressing leukemia drug resistant cells to mitoxantrone and topotecan was investigated. As shown in Tables I and andII,II, the ABCG2-overexpressing HL60/ABCG2 and K562/ABCG2 cell lines showed higher IC50 values to the ABCG2 substrates, mitoxantrone and topotecan compared with that in their parental cell lines, respectively. In the presence of 0.1 and 0.2 µM tucatinib, there was a significant increase in sensitivity of the cell lines to the two drugs. Tucatinib (0.4 µM) further increased the sensitivity of leukemia cells to the two drugs in both the ABCG2-overexpressing HL60/ABCG2 and K562/ABCG2 cell lines, and its efficacy was comparable to that of the known ABCG2 inhibitor, FTC (2.5 µM). Conversely, tucatinib did not significantly alter the IC50 value of cisplatin in all the leukemia cell lines, which is a non-ABCG2 substrate. Taken together, these results suggested that tucatinib may significantly sensitize ABCG2-overexpressing leukemia cells to become anti-neoplastic.

Reference: Oncol Rep. 2021 Mar; 45(3): 1142–1152. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7859976/

In vivo activity

The ability of tucatinib to prevent tumor cell growth in vivo was investigated in HER2+ breast and gastric cancer CDX xenograft models. Female immunocompromised mice implanted with BT-474 cells were treated with tucatinib and evaluated for response. Mice treated with tucatinib exhibited tumor growth delay at doses of 25 or 50 mg/kg tucatinib administered orally every day. This effect was similar to mice treated with trastuzumab monotherapy (Fig. 4A). In contrast, mean tumor volume (MTV) increased > 4-fold in mice treated with vehicle (Fig. 4A).

Reference: Mol Cancer Ther. 2020 Apr;19(4):976-987. https://mct.aacrjournals.org/content/19/4/976.long