Tucatinib

Cat. No.: HY-16069

CAS No.: 937263-43-9

Molecular Formula: $C_{26}H_{24}N_8O_2$

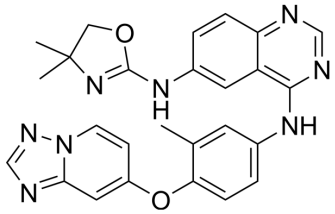
Molecular Weight: 480.52

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (86.72 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0811 mL	10.4054 mL	20.8108 mL
	5 mM	0.4162 mL	2.0811 mL	4.1622 mL
	10 mM	0.2081 mL	1.0405 mL	2.0811 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 30 % SBE-β-CD
   Solubility: 10 mg/mL (20.81 mM); Suspension solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.62 mg/mL (5.45 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.62 mg/mL (5.45 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (4.33 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.33 mM); Suspended solution; Need ultrasonic
6. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tucatinib (Irbinitinib) is a potent, orally active and selective HER2 inhibitor with an IC_{50} of 8 nM.

IC_{50} & Target	HER2
In Vitro	Tucatinib has nanomolar activity against purified HER2 enzyme and is approximately 500-fold selective for HER2 versus EGFR in cell-based assays. Tucatinib selectively inhibits the receptor tyrosine kinase HER2 relative to EGFR[1]. Tucatinib blocks proliferation and the phosphorylation of HER2 and its downstream effector, Akt in HER2 overexpressing cell lines. In the EGFR overexpressing cell lines, it weakly inhibits phosphorylation and proliferation, demonstrating that Tucatinib may have potential to block HER2 signaling without causing the toxicities of EGFR inhibition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tucatinib (ONT-380, 200 mg/kg/d) shows a survival benefit when each drug is dosed at the maximum-tolerated dose[1]. Tucatinib and its active metabolite causes a significant reduction in brain pErbB2 (80%)[2]. Tucatinib (ARRY-380) demonstrates significant dose-related tumor growth inhibition (TGI; 50% at 50 mg/kg/d and 96% at 100 mg/kg/d) with numerous partial regressions (>50% reduction from baseline size) at the higher dose level in 9/12 animals. Tucatinib (50 mg/kg/d) in combination with trastuzumab shows a 98% TGI with complete regressions in 9/12 animals and two partial regressions[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female nude mice[3].
Dosage:	200 mg/kg/d.
Administration:	PO, daily.
Result:	Exhibited anti-tumor activity and benefited survival.

CUSTOMER VALIDATION

- Cancer Discov. 2021 Dec 15;candisc.1265.2020.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Acta Pharmacol Sin. 2022 Feb 28.
- Cell Death Discov. 2023 Nov 2;9(1):406.
- Dis Model Mech. 2023 Mar 13;dmm.049692.

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REFERENCES

[1]. Moulder-Thompson S, et al. Phase 1 Study of ONT-380, a HER2 Inhibitor, in Patients with $HER2^+$ Advanced Solid Tumors, with an Expansion Cohort in HER2+ Metastatic Breast Cancer (MBC). Clin Cancer Res. 2017 Jan 4. pii: clincanres.1496.2016.

[2]. Abstract: In: Proceedings of the 103rd Annual Meeting of the American Association for Cancer Research; 2012 Mar 31-Apr 4; Chicago, IL. Philadelphia (PA): AACR; Cancer Res 2012;72(8 Suppl):Abstract nr 852. doi:1538-7445.AM2012-852

[3]. P. Lee, et al. In Vivo Activity of ARRY-380, a Potent, Small Molecule Inhibitor of ErbB2 in Combination with RP-56976. Cancer Research

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

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