Mubritinib

Cat. No.: HY-13501

CAS No.: 366017-09-6

Molecular Formula: $C_{25}H_{23}F_3N_4O_2$

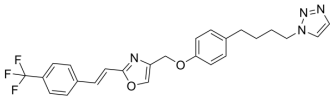
Molecular Weight: 468.47

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 : 50 mg/mL (106.73 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1346 mL	10.6730 mL	21.3461 mL
	5 mM	0.4269 mL	2.1346 mL	4.2692 mL
	10 mM	0.2135 mL	1.0673 mL	2.1346 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.34 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mubritinib (TAK-165) is a potent and selective EGFR2/HER2 inhibitor with an IC_{50} of 6 nM.

IC_{50} & Target

HER2
6 nM (IC_{50})

In Vitro

Mubritinib (TAK-165) specifically inhibits HER2 tyrosine kinase with an IC_{50} 6 nM and does not inhibit other types tyrosine kinase up to 25 000 nM. Mubritinib inhibits HER2 phosphorylation and its down-stream Akt and MAPK in HER2 strongly expressing cells (BT474 breast cancer cell line). Mubritinib sensitivity depends on HER2 levels of each cell line. Especially, BT474 cells which over-express HER2 strongly is highly sensitive (IC_{50}=0.005 μM) and PC-3 cells which express HER2 very weakly is less sensitive (IC_{50}=4.62 μM). But, HT1376 and ACHN cells that over-expressed EGFR showed high IC_{50} (IC_{50}>25 μM)

	[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In the xenograft model, treatment with Mubritinib (TAK-165) significantly inhibits growth of UMUC-3, ACHN, and LN-REC4. The antitumor effect after 14 days treatment are 22.9%, 26.0%, and 26.5% in UMUC3, ACHN and LN-REC4, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells are treated with Mubritinib at various concentrations (5 nM-25 μM) for 72 h. After the incubation period, the cells are counted. The IC_{50} value is calculated from a dose-response curve generated by least-squares linear regression of the response[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: UMUC-3 and LN-REC4 cells are implanted with 50% Matrigel solution. After the tumor volume reaches 200–300 mm^3 in LN-REC4 and UMUC-3 cells and to 100–200 mm^3 in ACHN, the mice are treated orally twice daily for 14 days with vehicle (control) or 10 or 20 mg/kg per day of Mubritinib[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Death Dis. 2021 Apr 14;12(4):397.
- Microbiol Spectr. 2023 Jun 6;e0474522.
- bioRxiv. 2023 Apr 19.
- Oncotarget. 2020 Nov 3;11(44):3921-3932.

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REFERENCES

[1]. Nagasawa J, et al. Novel HER2 selective tyrosine kinase inhibitor, TAK-165, inhibits bladder, kidney and androgen-independent prostate cancer in vitro and in vivo. Int J Urol. 2006 May;13(5):587-92.

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