Mobocertinib succinate

Cat. No.: HY-135815A

CAS No.: 2389149-74-8

Molecular Formula: $C_{36}H_{45}N_7O_8$

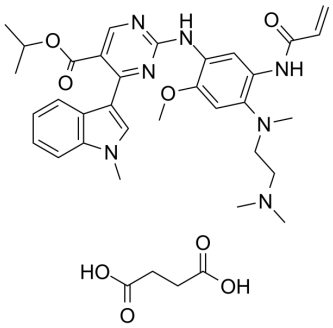
Molecular Weight: 703.78

Target: EGFR

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

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (177.61 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4209 mL	7.1045 mL	14.2090 mL
	5 mM	0.2842 mL	1.4209 mL	2.8418 mL
	10 mM	0.1421 mL	0.7104 mL	1.4209 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (2.96 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (2.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mobocertinib (TAK-788) succinate is an orally active and irreversible EGFR/HER2 inhibitor. Mobocertinib succinate potently inhibits oncogenic variants containing activating EGFRex20ins mutations with selectivity over wild-type EGFR. Mobocertinib succinate can be used in NSCLC research[1][2].

IC_{50} & Target			
	EGFR exon 20 insertion	HER2	EGFR (WT)

In Vitro

Mobocertinib succinate (1.5 nM-10 μM; 7 days) inhibits LU0387 (NPH) cells with IC_{50} of 21 nM[1].
Mobocertinib succinate (2 h) potently inhibits EGFR with common activating mutations (HCC827 (D), HCC4011 (L)) or with a T790M mutation (H1975 (LT)) more potently than WT EGFR (A431 (WT))[1].
Mobocertinib succinate (0.1 nM-1 μM; 6 h) inhibits pEGFR and pERK1/2 in CUTO14 (ASV) cells[1].
Mobocertinib succinate (0.3 nM-1 μM; 6 h) inhibits EGFR and downstream signaling[1].

Mobocertinib succinate (0.01, 0.1 and 1 μM; 6 h) inhibits HER2 signaling in H1781 (HER2 Exon $20^{G776>VC}$), Ba/F3 (HER2 exon 20^{YVMA}) cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	LU0387 (NPH) cells
Concentration:	1.5 nM-10 μM
Incubation Time:	7 days
Result:	Showed good inhibition activity for LU0387 (NPH) cells with IC_{50} of 21 nM.

Cell Viability Assay[1]

Cell Line:	A431 (WT), HCC827 (D), HCC4011 (L), H1975 (LT) cells
Concentration:	
Incubation Time:	2 h
Result:	Inhibited EGFR with common activating mutations of HCC827 (D), HCC4011 (L) cells and T790M mutation of H1975 (LT) with IC_{50}s of 4, 1.3 and 9.8 nM respectively, which more potently than WT EGFR (A431 (WT); IC_{50} of 35 nM).

Western Blot Analysis[1]

Cell Line:	CUTO14 (ASV) cells
Concentration:	0.1 nM-1 μM
Incubation Time:	6 h
Result:	Robustly inhibited EGFR signaling, reaching 80% and 100% inhibition of phosphorylated EGFR (pEGFR) at concentrations of 100 nM and 1 μM, respectively.

Western Blot Analysis[1]

Cell Line:	HCC827 (D), HCC4011 (L), H1975 (LT) cells
Concentration:	0.3 nM-1 μM
Incubation Time:	6 h
Result:	Potently inhibited EGFR and downstream signaling in HCC827 (D), HCC4011 (L) and H1975 (LT) cells.

Western Blot Analysis[2]

Cell Line:	H1781 (HER2 Exon $20^{G776>VC}$), Ba/F3 (HER2 exon 20^{YVMA}) cells
Concentration:	0.01, 0.1 and 1 μM
Incubation Time:	6 h
Result:	Inhibited HER2 signaling in H1781 and Ba/F3-HER2 exon 20^{YVMA} mutant cells at 0.1 μM with significantly decreased phosphorylations of HER2, AKT, and ERK1/2 in a dose-dependent manner.

In Vivo	Mobocertinib succinate (3, 10, 30 mg/kg; p.o.; once daily for 20 days) significantly induces tumor growth inhibition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Athymic Nude-Foxn1^{nu} mice (human NSCLC H1975 LT tumor model)[1].
Dosage:	3, 10, 30 mg/kg
Administration:	Oral; once daily for 20 days.
Result:	Decreased the mean tumor volume by 44% and 92% when at 3 mg/kg and 10 mg/kg, respectively, relative to the tumor size of vehicle group. Induced a 76% tumor regression relative to the pretreatment tumor size at 30 mg/kg.

CUSTOMER VALIDATION

- Cells. 2021, 10(12), 3561.

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REFERENCES

[1]. Gonzalvez F, et al. Mobocertinib (TAK-788): A Targeted Inhibitor of EGFR Exon 20 Insertion Mutants in Non-Small Cell Lung Cancer. Cancer Discov. 2021 Jul;11(7):1672-1687.

[2]. an H, et al. Targeting HER2 Exon 20 Insertion-Mutant Lung Adenocarcinoma with a Novel Tyrosine Kinase Inhibitor Mobocertinib. Cancer Res. 2021 Oct 15;81(20):5311-5324.

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