Batoprotafib

Cat. No.: HY-136173

CAS No.: 1801765-04-7

Molecular Formula: $C_{18}H_{24}ClN_7OS$

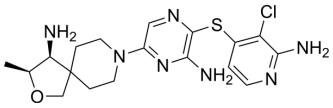
Molecular Weight: 421.95

Target: Phosphatase; SHP2

Pathway: Metabolic Enzyme/Protease; Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (236.99 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3699 mL	11.8497 mL	23.6995 mL
5 mM	0.4740 mL	2.3699 mL	4.7399 mL
10 mM	0.2370 mL	1.1850 mL	2.3699 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 (5.92 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.92 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.92 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Batoprotafib (TNO155) is a potent selective and orally active allosteric inhibitor of wild-type SHP2 (IC_{50}=0.011 μM). Batoprotafib has the potential for the study of RTK-dependent malignancies, especially advanced solid tumors[1].

IC_{50} & Target

IC50: 0.011 μM (SHP2)[1]

In Vitro

Batoprotafib shows an IC_{50} of 0.008 μM in KYSE520 pERK assay and shows an IC_{50} of 0.100 μM in KYSE520 5-day cell proliferation assay. The off-target IC_{50} values are 18 μM, 6.9 μM, and 11 μM for Cav1.2, VMAT, and SST3, respectively[1].
Batoprotafib (0-1000 nM; 6 days) inhibits the viability of NCI-H3255, HCC827, and PC9 cells with IC_{50} values lower than 1.5 μM. Batoprotafib is efficacious in EGFR-mutant NSCLC cell lines[2].
Batoprotafib is efficacious in acquired resistance models of EGFR inhibitors and demonstrates combination benefit with EGFR inhibitors[2].
Batoprotafib enhances the efficacy of $KRAS^{G12C}$ inhibitors against $KRAS^{G12C}$ lung and colorectal cancers[2].
Batoprotafib inhibits immune-suppressive macrophages and synergizes with PD1 blockade[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	PC-9, PC-9 $EGFR^{T790M/C797S}$, HCC827, HCC827-GR (gefinitib-resistant)
Concentration:	0-1000 nM
Incubation Time:	6 days
Result:	Inhibited cell viability with IC_{50}s of 1.56, 1.38, 0.77 and 1.38 μM against PC-9 and PC-9 $EGFR^{T790M/C797S}$, HCC827 and HCC827-GR cells, respectively.

Western Blot Analysis[2]

Cell Line:	PC-14 ($EGFR^{ex19del}$)
Concentration:	3 μM
Incubation Time:	4h and 24 h
Result:	Effectively reduced p-ERK levels at 4 hours but suffered a rebound at 24 hours.

In Vivo

The oral bioavailability in mouse, rat and money are 78%, 86%, and 60%, respectively[1].
Batoprotafib (20 mg/kg; p.o.; twice daily for 40 days) inhibits tumor growth and is more effective when combined with Dabrafenib (HY-14660) plus Trametinib (HY-10999) in nude mice bearing HT-29 xenografts[2].
Batoprotafib (7.5 mg/kg; p.o.; b.i.d. or q.d. for 36 days) plus JDQ-443 (HY-139612) (100 mg/kg; p.o.; q.d.) improves the single-agent activity of JDQ443 in $KRAS^{G12C}$-mutated cell-derived (CDX) models in nude mice[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female athymic nude mice bearing HT-29 xenografts[2]
Dosage:	20 mg/kg alone or 10 mg/kg in combination with Dabrafenib and Trametinib
Administration:	PO, twice daily for 40 days
Result:	Resulted in moderate tumor growth inhibition. Maintained tumor stasis for more than 40 days when combined with Dabrafenib plus Trametinib.

CUSTOMER VALIDATION

- Eur J Cancer. 2021 Oct 26;159:16-23.
- Cancer Res Commun. 2023 Nov 30.

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REFERENCES

[1]. Liu C, et al. Combinations with Allosteric SHP2 Inhibitor TNO155 to Block Receptor Tyrosine Kinase Signaling. Clin Cancer Res. 2021 Jan 1;27(1):342-354.

[2]. Weiss A, et al. Discovery, Preclinical Characterization, and Early Clinical Activity of JDQ443, a Structurally Novel, Potent, and Selective Covalent Oral Inhibitor of KRASG12C. Cancer Discov. 2022 Jun 2;12(6):1500-1517.

[3]. TNO155: SHP2 inhibitor

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