Umbralisib

Cat. No.: HY-12279

CAS No.: 1532533-67-7

Molecular Formula: $C_{31}H_{24}F_3N_5O_3$

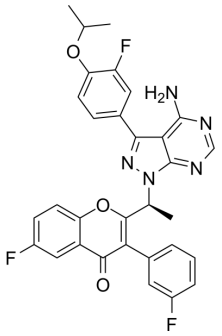
Molecular Weight: 571.55

Target: PI3K; Casein Kinase

Pathway: PI3K/Akt/mTOR; Cell Cycle/DNA Damage; Stem Cell/Wnt

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (43.74 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7496 mL	8.7481 mL	17.4963 mL
	5 mM	0.3499 mL	1.7496 mL	3.4993 mL
	10 mM	0.1750 mL	0.8748 mL	1.7496 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (3.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Umbralisib (TGR-1202) is an orally active, potent and selective dual PI3Kδ and casein kinase-1-ε (CK1ε) inhibitor, with EC_{50} of 22.2 nM and 6.0 μM, respectively. Umbralisib exhibits unique immunomodulatory effects on chronic lymphocytic leukemia (CLL) T cells. Umbralisib can be used for haematological malignancies reseach[1][2][3][4].

IC_{50} & Target

PI3Kδ 22.2 nM (EC50)	PI3Kδ 6.2 nM (Kd)	PI3Kγ 1400 nM (Kd)	PI3Kβ >10000 nM (Kd)
PI3Kα >10000 nM (Kd)			

In Vitro

Umbralisib causes a half-maximal inhibition of human whole blood CD19 cell proliferation between 100-300 nM[3]. Umbralisib (10 nM-100 μM) inhibits phosphorylated AKT at Ser473 in a concentration-dependent manner in human

	lymphoma and leukemia cell lines[4]. Umbralisib (15-50 μM) potently represses the expression of c-Myc in the DLBCL cell line LY7, and is uniquely characterized with structural features suitable for targeting CK1ε in lymphoma cells[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Umbralisib (150 mg/kg, daily p.o.) significantly shrinks the tumors by day 25 in a subcutaneous xenograft model of T-cell acute lymphoblastic leukemia (T-ALL) in NOD/SCID mice using the MOLT-4 cell line[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2023 Jun 12;41(6):1103-1117.e12.
- J Med Chem. 2020 Nov 25;63(22):13973-13993.
- Mol Pharm. 2022 Oct 21.

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REFERENCES

[1]. Maharaj K, et al. The dual PI3Kδ/CK1ε inhibitor umbralisib exhibits unique immunomodulatory effects on CLL T cells. Blood Adv. 2020 Jul 14;4(13):3072-3084.

[2]. Burris HA 3rd, et al. Umbralisib, a novel PI3Kδ and casein kinase-1ε inhibitor, in relapsed or refractory chronic lymphocytic leukaemia and lymphoma: an open-label, phase 1, dose-escalation, first-in-human study. Lancet Oncol. 2018 Apr;19(4):486-496.

[3]. Swaroop Vakkalankaa, et al. Inhibition of PI3Kδ kinase by a selective, small molecule inhibitor suppresses B-cell proliferation and leukemic cell growth.

[4]. Deng C, et al. Silencing c-Myc translation as a therapeutic strategy through targeting PI3Kδ and CK1ε in hematological malignancies. Blood. 2017 Jan 5;129(1):88-99

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