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- Trockeneiszuschlag
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- Expressversand

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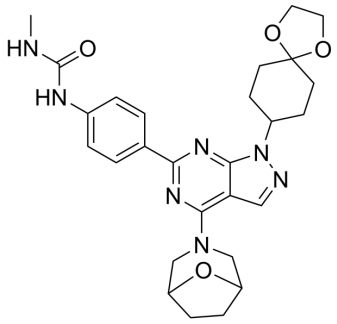
WYE-132

Cat. No.:	HY-10044
CAS No.:	1144068-46-1
Molecular Formula:	$C_{27}H_{33}N_7O_4$
Molecular Weight:	519.6
Target:	mTOR; Apoptosis
Pathway:	PI3K/Akt/mTOR; Apoptosis
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 : 25 mg/mL (48.11 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9246 mL	9.6228 mL	19.2456 mL
5 mM	0.3849 mL	1.9246 mL	3.8491 mL
10 mM	0.1925 mL	0.9623 mL	1.9246 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 (4.81 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

WYE-132 (WYE-125132) is a highly potent, ATP-competitive, and specific mTOR kinase inhibitor (IC_{50}: 0.19±0.07 nM; >5,000-fold selective versus PI3Ks). WYE-132 (WYE-125132) inhibits mTORC1 and mTORC2.

IC_{50} & Target

mTOR 0.19 nM (IC_{50})	mTORC1	mTORC2	PI3Kα 1.179 μM (IC_{50})
PI3Kδ 2.38 μM (IC_{50})	hSMG1 1.25 μM (IC_{50})		

In Vitro

WYE-132 (WYE-125132) potently inhibits recombinant mTOR via an ATP-competitive mechanism. WYE-132 is a potent antiproliferative agent against a panel of cancer cell lines with IC_{50} values generally in the nanomolar range. In the typical 3-day dose-response studies, WYE-132 exhibits a more profound antiproliferative activity than CCI-779 in MDA361 and other

	cells, as shown by the sharper inhibition at doses up to 10 μM. Fluorescence-activated cell sorting (FACS) analysis of inhibitor-treated (1 μM, 24 hours) MDA468, PC3MM2, U87MG, A549, and HCT116 cells indicates that WYE-132 elicits a more profound increase in G_1-phase and a reduction in S-phase cells than CCI-779. The WYE-132-induced cell death is evident at 10 and 30 nM (6.2% and 13%, respectively) and is dose dependent, reaching 47% at 1 μM and 59% at 3 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	A single i.v. administration of 50 mg/kg WYE-132 (WYE-125132) into tumor-bearing mice leads to suppression of P-S6K(T389) and P-AKT(S473) for at least 8 hours in PC3MM2, MDA361, HCT116, and HT29 tumors, whereas the steady-state level of P-AKT(T308) is not significantly reduced, indicating that the antitumor efficacy of WYE-132 under such dosing regimens reflects the suppression of mTOR rather than PI3K. Oral administration of WYE-132 causes dose-dependent tumor growth delay in the PI3K/mTOR- and HER2-hyperactive MDA361 tumors with significant antitumor activity at 5 mg/kg, which correlates with a suppression P-S6 and P-AKT(S473) but not P-AKT(T308). An optimal dose of 50 mg/kg WYE-132 induces a substantial regression of large MDA361 tumors. WYE-132 also causes a potent and substantial tumor growth delay in the PTEN-null U87MG glioma[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cell lines of MDA-MB-361, MDA-MB-231, MDA-MB-468, BT549, LNCap, A549, H1975, H157, H460, U87MG, A498, 786-O, HCT116, MG63, Rat1, HEK293, HeLa and PC3MM2 are used. MDA361 cells are treated for 3 d with CCI-779 and WYE-132 (0.1 nM, 1 nM, 10 nM,100 nM, 1000 nM 10μM and 100μM). Cell growth assays and IC_{50} determination are performed. For immunoblotting, cultured cells are treated as indicated. Total cell lysates are prepared using NuPAGE lithium dodecyl sulfate sample buffer and immunoblotted with various antibodies[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] For mTOR biomarker studies, various tumors (400 mm^3) grown s.c. in female nude mice are dosed by a single i.v. or oral injection with vehicle or WYE-125132 formulated in 5% ethanol, 2% Tween 80, and 5% polyethylene glycol-400. Tumor lysates are prepared and immunoblotted. For efficacy studies, nude mice bearing U87MG, MDA361, H1975, A549, A498, or 786-O tumors are staged and randomized into treatment groups (n=10). Mice are dosed orally with vehicle or WYE-125132 following qd x5 cycle regimen (5 d on, 2 d off) for up to four cycles. Temsirolimus/CCI-779 is formulated as WYE-132 and dosed i.v. once weekly. Bevacizumab is formulated in PBS and dosed i.p. via its clinical regimen (200 μg/mouse; once weekly). Tumor growth is monitored and analyzed. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Cell Rep. 2021 Apr 6;35(1):108959.
- Front Pharmacol. 2020 Nov 11;11:580407.
- Molecules. 2020 Apr 23;25(8):1980.

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REFERENCES

[1]. Yu K, et al. Beyond rapalog therapy: preclinical pharmacology and antitumor activity of WYE-125132, an ATP-competitive and specific inhibitor of mTORC1 and mTORC2.Cancer Res. 2010 Jan 15;70(2):621-631.

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