# Data Sheet

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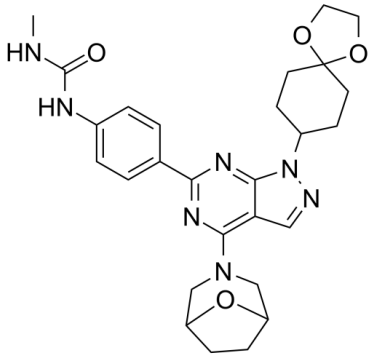
| **Product Name:** | WYE-132 |
| **Cat. No.:** | CS-0066 |
| **CAS No.:** | 1144068-46-1 |
| **Molecular Formula:** | C27H33N7O4 |
| **Molecular Weight:** | 519.60 |
| **Target:** | Apoptosis; mTOR |
| **Pathway:** | Apoptosis; PI3K/Akt/mTOR |
| **Solubility:** | DMSO : 25 mg/mL (48.11 mM; Need ultrasonic) |



## BIOLOGICAL ACTIVITY:

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**. IC50 & Target: IC50: 0.19±0.07 nM (mTOR), 1179 nM (PI3Kα), 2380 nM (PI3Kδ), 1250 nM (hSMG1)[1] **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]. **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].

## PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** WYE-125132 (WYE-132) is dissolved in DMSO as 20 mM stocks and diluted before assays[1].[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].

**Animal Administration:** WYE-125132 (WYE-132) is formulated in 5% ethanol, 2% Tween 80, and 5% polyethylene glycol-400 (Mice)[1].

[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.

## 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.

## CAIndexNames:

Urea, N-[4-[1-(1,4-dioxaspiro[4.5]dec-8-yl)-4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl]phenyl]-N'-methyl-

## SMILES:

O=C(NC1=CC=C(C2=NC(N3CC4CCC(C3)O4)=C5C(N(N=C5)C6CCC7(CC6)OCCO7)=N2)C=C1)NC



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