Product Datasheet

OSI-027

Catalog No. **BP-02110** · CAS **936890-98-1** · Form **free base** · Physical state **solid** · Color **light yellow to yellow** · Version **1.0** · Revision **2026-09-14**

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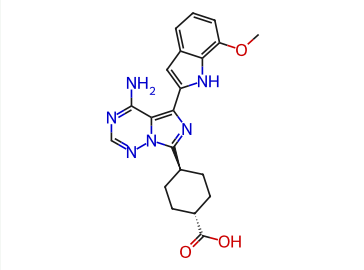
Target	Research area
mTOR; Autophagy	**Cancer**

Molecular formula	$C_{21}H_{22}N_6O_3$
Molecular weight	**406.4378**

STRUCTURE



DESCRIPTION

OSI-027 (ASP7486) is a potent, selective, orally active and ATP-competitive mTOR kinase activity inhibitor with an IC50 of 4 nM. OSI-027 targets both mTORC1 and mTORC2 with IC50s of 22 nM and 65 nM, respectively.

BIOLOGICAL ACTIVITY

In Vitro

OSI-027 is an ATP-competitive inhibitor, which targets both mTORC1 and mTORC2 with IC50s of 22 nM and 65 nM. OSI-027 also inhibits PI3K-α, PI3K-γ and DNA-PK with IC50s of 1.3 μM, 0.42 μM and 1.0 μM. OSI-027 inhibits mTOR signaling of phospho-4E-BP1 with an IC50 of 1 μM.

In Vivo

Effects on GEO colorectal xenograft growth treated with Rapamycin or OSI-027 for 12 days are consistent with our in vitro experiments. Treatment with Rapamycin (20 mg/kg) inhibits phospho-S6 and phospho-4E-BP1, while Akt phosphorylation is increased by 29%. In contrast, OSI-027 (65 mg/kg) inhibits both mTORC1 and mTORC2 effectors. After 2 hours, decreased 4E-BP1, Akt, and S6 phosphorylation is observed and inhibition of S6 and Akt is sustained for 24 hours. The plasma drug concentration of OSI-027 inversely correlated with these effects on mTORC1 and mTORC2 signaling. The median plasma drug concentration with OSI-027 is 21.3 μM at 2 hours and 14.9 μM at 8 hours. The in vivo efficacy of OSI-027 plus Sunitinib is tested in H292 human lung and Ovcar-5 human ovarian xenograft tumors. H292 tumors, treated with OSI-027 (50 mg/kg) for 21 days have 61% median tumor growth inhibition for the duration of treatment (TGI). Sunitinib (40 mg/kg) for 21 days had 47% median TGI. Combining OSI-027 with Sunitinib, however, has a median TGI of 100% with 59% maximal tumor regression, a statistically significant improvement over either agent alone. Ovcar-5 xenograft tumors treated with OSI-027 or Sunitinib have a 55% and 68% median TGI, respectively. OSI-027 administered with Sunitinib has a significantly better median TGI of 100% with 38% maximal tumor regression.

In the Rapamycin (RAPA) group, three rats exhibit symptoms typical of LTx-aGVHD and die 27 to 35 days after liver

transplantation (LT); the remaining five rats do not develop LTx-aGVHD symptoms and survive for more than 100 days. In contrast, seven rats in the OSI-027 group survive for more than 100 days without symptoms of LTx-aGVHD, and only one rat exhibits LTx-aGVHD symptoms and dies on day 33 after LT.

SOLUBILITY

Soluble in DMSO

REFERENCES

[1]. Falcon BL, et al. Reduced VEGF production, angiogenesis, and vascular regrowth contribute to the antitumor properties of dual mTORC1/mTORC2 inhibitors. Cancer Res. 2011 Mar 1;71(5):1573-83.

[2]. Mateo J, et al. A first in man, dose-finding study of the mTORC1/mTORC2 inhibitor OSI-027 in patients with advanced solid malignancies. Br J Cancer. 2016;114(8):889-896.

[3]. Zhang Y, et al. PP2AC Level Determines Differential Programming of p38-TSC-mTOR Signaling and Therapeutic Response to p38-Targeted Therapy in Colorectal Cancer. EBioMedicine. 2015 Nov 19;2(12):1944-56.

[4]. Zhi X, et al. OSI-027 modulates acute graft-versus-host disease after liver transplantation in a rat model. Liver Transpl. 2017 Sep;23(9):1186-1198.