Product Datasheet

PF-04691502

Catalog No. **BP-02295** · CAS **1013101-36-4** · Form **free base** · Physical state **solid** · Color **off-white to gray** · Version **1.0** · Revision **2026-09-10**

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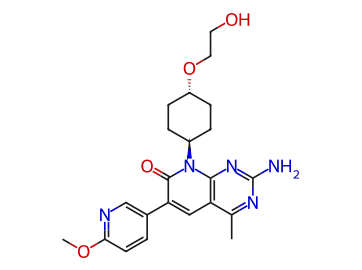
Target	Research area
PI3K; mTOR; Autophagy	**Cancer**

Molecular formula	$C_{22}H_{27}N_5O_4$
Molecular weight	**425.4809**

STRUCTURE



DESCRIPTION

PF-04691502 is a potent and selective inhibitor of PI3K and mTOR. PF-04691502 binds to human PI3Kα, β, δ, γ and mTOR with Kis of 1.8, 2.1, 1.6, 1.9 and 16 nM, respectively.

BIOLOGICAL ACTIVITY

In Vitro

PF-04691502 inhibits recombinant mouse PI3Kα in an ATP-competitive inhibitor. PF-04691502 potently inhibits AKT phosphorylation on S473 and T308 in all the 3 cancer cell lines with IC50 values of 3.8 to 20 nM and 7.5 to 47 nM, respectively. Using a 96-well plate-based P-S6RP(S235/236) ELISA assay, PF-04691502 potently inhibits mTORC1 activity with an IC50 of 32 nM. PF-04691502 inhibits cell proliferation of BT20, SKOV3, and U87MG with IC50 values of 313, 188, and 179 nM, respectively. In PIK3CA-mutant and PTEN-deleted cancer cell lines, PF-04691502 reduces phosphorylation of AKT T308 and AKT S473 (IC50 of 7.5-47 nM and 3.8-20 nM, respectively) and inhibits cell proliferation (IC50 of 179-313 nM). PF-04691502 inhibits mTORC1 activity in cells as measured by PI3K-independent nutrient stimulated assay, with an IC50 of 32 nM and inhibits the activation of PI3K and mTOR downstream effectors including AKT, FKHRL1, PRAS40, p70S6K, 4EBP1, and S6RP.

In Vivo

Nude mice bearing U87MG tumors are administered orally once a day with PF-04691502 at 0.5, 1, 5, and 10 mg/kg (maximum tolerated dose, MTD). Treatment with 10 mg/kg results in a significant reduction of P-AKT(S473) levels at 1 hour postdosing, and persistent inhibition is observed for 8 hours. P-AKT(S473) recovers to above baseline 24 hours after 10 mg/kg treatment. For P-S6RP(S235/236), a similar inhibition time course is observed, but after 24 hours of treatment, P-S6RP levels remain lower than vehicle tumors. Modulation of the AKT downstream effector, P-PRAS40(T246), and mTOR downstream effector, P-4EBP1(T37/46), is observed. The PF-04691502-treated tumors are also evaluated by immunohistochemistry for levels of P-AKT(S473), total AKT, P-S6RP, and total S6RP. Phosphorylation of AKT and S6RP are significantly reduced at 4 hours after a single dose of PF-04691502 at 10 mg/kg. Dose-dependent tumor growth inhibition (TGI) is obtained in the U87MG xenograft model and approximately

73% TGI is observed at the MTD dose of 10 mg/kg.

SOLUBILITY

Soluble in DMSO

REFERENCES

[1]. Yuan J, et al. PF-04691502, a potent and selective oral inhibitor of PI3K and mTOR kinases with antitumor activity. Mol Cancer Ther. 2011 Nov;10(11):2189-99.

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