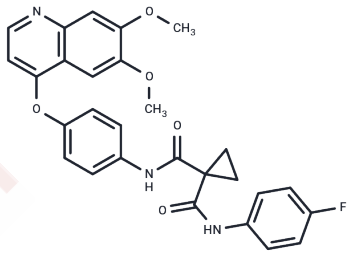
Data Sheet (Cat.No.T2586)

TargetMol

Cabozantinib

Chemical Properties



CAS No. : 849217-68-1

Formula: C28H24FN3O5

Molecular Weight: 501.51

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Cabozantinib (XL184) is a multi-targeted tyrosine kinase receptor inhibitor that inhibits VEGFR2, c-Met, Kit, Axl, and Flt3 (IC50=0.035/1.3/4.6/7/11.3 nM). Cabozantinib exhibits both antitumor and antiangiogenic activity.
Targets(IC50)	Apoptosis,FLT,c-RET,c-Kit,c-Met/HGFR,TAM Receptor,VEGFR
In vitro	**METHODS**: Prostate cancer cells LNCaP, C4-2B and PC-3 were treated with Cabozantinib (0.01-5 μM) for 72 h. Cell viability was measured by WST-1 Assay. **RESULTS**: Cabozantinib inhibited cell viability of LNCaP, C4-2B and PC-3 cell lines in a dose-dependent manner. [1] **METHODS**: Human renal cancer cells 786-O and A498 were treated with Cabozantinib (10-100 nM) for 1 h, followed by stimulation with HGF (1 nM) for 20 min, and the expression levels of target proteins were detected by Western Blot. **RESULTS**: 10 nM Cabozantinib treatment inhibited HGF activation of pMET, pAKT, pERK and p-mTOR.[2]
In vivo	**METHODS**: To detect anti-tumor activity in vivo, Cabozantinib (60 mg/kg) was administered orally to SCID mice injected intra-tibially with prostate cancer cells Ace-1 once daily for five weeks. **RESULTS**: Cabozantinib inhibited the progression of Ace-1 cells in vivo. [1] **METHODS**: To assay antitumor activity in vivo, Cabozantinib (1-60 mg/kg) was orally administered to nu/nu mice bearing tumors MDA-MB-231, H441, or C6 once daily for 12-14 days. **RESULTS**: Cabozantinib inhibited tumor growth in a dose-dependent manner. [3]
Kinase Assay	The inhibition profile of cabozantinib against a broad panel of 270 human kinases was determined using luciferase-coupled chemiluminescence, 33P-phosphoryl transfer, or AlphaScreen technology. Recombinant human full-length, glutathione S-transferase tag or histidine tag fusion proteins were used, and half maximal inhibitory concentration (IC50) values were determined by measuring phosphorylation of peptide substrate poly (Glu, Tyr) at ATP concentrations at or below the Km for each respective kinase. The mechanism of kinase inhibition was evaluated using the AlphaScreen Assay by determining the IC50 values over a range of ATP concentrations [1].
Cell Research	Receptor phosphorylation of MET, VEGFR2, AXL, FLT3, and KIT were, respectively, assessed in PC3, HUVEC, MDA-MB-231, FLT3-transfected BaF3, and KIT-transfected MDA-MB-231 cells. Cells were serum starved for 3 to 24 hours, then incubated for 1 to 3 hours

Cell Research	in serum-free medium with serially diluted cabozantinib before 10-minute stimulation with ligand: HGF (100 ng/mL), VEGF (20 ng/mL), SCF (100 ng/mL), or ANG1 (300 ng/mL). Receptor phosphorylation was determined either by ELISA using specific capture antibodies and quantitation of total phosphotyrosine or immunoprecipitation and Western blotting with specific antibodies and quantitation of total phosphotyrosine. Total protein served as loading controls [1].
Animal Research	Female nu/nu mice were housed according to the Exelixis Institutional Animal Care and Use Committee guidelines. H441 cells (3 × 10^6) were implanted intradermally into the hind flank and when tumors reached approximately 150 mg, tumor weight was calculated using the formula: (tumor volume = length (mm) × width^2 (mm^2)]/2, mice were randomized (n = 5 per group) and orally administered a single 100 mg/kg dose of cabozantinib or vehicle. Tumors were collected at the indicated time points. Pooled tumor lysates were subjected to immunoprecipitation with anti-MET and Western blotting with anti-phosphotyrosine MET. After blot stripping, total MET was quantitated as a loading control. In a separate experiment, naive mice (n = 5 per group) were administered a single 100 mg/kg dose of cabozantinib or vehicle, followed by intravenous administration of HGF (10 μg per mouse) 10 minutes before liver collection. Analysis of MET phosphorylation in liver lysates was as described above. In a separate experiment, naive mice (n = 5 per group) were administered a single 100 mg/kg dose of cabozantinib or vehicle, followed by intravenous administration of VEGF (10 μg per mouse) 30 minutes before lung collection. Pooled lung lysates were subjected to immunoprecipitation with FLK1 and Western blotting with anti-phosphotyrosine. After blot stripping, total FLK1 was quantitated as a loading control [1].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 63.1 mg/mL (125.82 mM),Sonication and heating are recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 9.3 mg/mL (18.54 mM),Suspension. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.994 mL	9.9699 mL	19.9398 mL
5 mM	0.3988 mL	1.994 mL	3.988 mL
10 mM	0.1994 mL	0.997 mL	1.994 mL
50 mM	0.0399 mL	0.1994 mL	0.3988 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Dai J, et al. Cabozantinib inhibits prostate cancer growth and prevents tumor-induced bone lesions. Clin Cancer Res. 2014 Feb 1;20(3):617-30.
Chu T H, Ko C Y, Tai P H, et al. Leukocyte cell-derived chemotaxin 2 regulates epithelial-mesenchymal transition and cancer stemness in hepatocellular carcinoma. Journal of Biological Chemistry. 2022: 102442.
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Xie Z, et al. MET Inhibition in Clear Cell Renal Cell Carcinoma. J Cancer. 2016 Jun 18;7(10):1205-14.
Yakes FM, et al. Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth. Mol Cancer Ther. 2011 Dec;10(12):2298-308.
Zaccagnino A, Vynnytska-Myronovska B, Stöckle M, et al.An In Vitro Analysis of TKI-Based Sequence Therapy in Renal Cell Carcinoma Cell Lines.International Journal of Molecular Sciences.2023, 24(6): 5648.
Di T, Luo Q, Song J, et al.APG-1252 combined with Cabozantinib inhibits hepatocellular carcinoma by suppressing MEK/ERK and CREB/Bcl-xl pathways.International Immunopharmacology.2024, 139: 112615.
Haga Y, Ray R, Ray R B.Silmitasertib in Combination With Cabozantinib Impairs Liver Cancer Cell Cycle Progression, Induces Apoptosis, and Delays Tumor Growth in a Preclinical Model.Molecular Carcinogenesis.2024
Breitenecker K, Hedrich V, Pupp F, et al.Synergism of the receptor tyrosine kinase Axl with ErbB receptors mediates resistance to regorafenib in hepatocellular carcinoma.Frontiers in Oncology.2023, 13: 1238883.