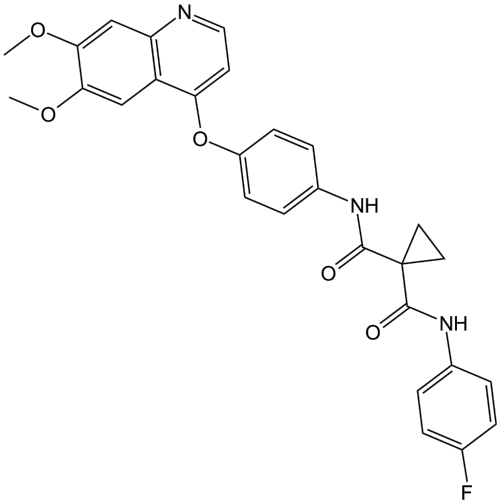
Product Data Sheet

Product Name: Cabozantinib (XL184, BMS-907351)
Cat. No.: GC15779

Chemical Properties

Cas. No.	849217-68-1		
Chemical Name	1-N-[4-(6,7-dimethoxyquinolin-4-yl)oxyphenyl]-1-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide		
SMILES	COC1=CC2=C(C=CN=C2C=C1OC)OC3=CC=C(C=C3)NC(=O)C4(CC4)C(=O)NC5=CC=C(C=C5)F		
Formula	$C_{28}H_{24}FN_3O_5$	M.Wt	501.51
Solubility	≥ 25.1mg/mL in DMSO	Storage	4°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	Huh7 cells
Preparation Method	Huh7 cells were cultured in DMEM medium, supplemented with 10% fetal bovine serum (FBS), and 1% penicillin/streptomycin, at 37°C in an incubator with 5% CO_2. Cells were seeded in a 96-well clear-bottom plate, and 24h later, cells were treated with various concentrations of Cabozantinib (0, 0.001, 0.01, 0.1, 1, 10, and 100μM). After 48h of incubation, cell viability was detected.
Reaction Conditions	0, 0.001, 0.01, 0.1, 1, 10, and 100μM; 48h
Applications	Cabozantinib treatment reduced cell viability of Huh7 cells in a dose-dependent manner.
Animal experiment [2]:	
Animal models	Female BALB/c Nude mice
Preparation Method	Female BALB/c Nude mice (6 weeks old; 18-22g) were housed in specific pathogen-free animal facilities with ad libitum access to food and normal drinking water. Mice were acclimated for approximately 1 week before experiments were initiated. Murine renal carcinoma Renca cells in RPMI media were injected into the right flank of mice. Mice were treated with Cabozantinib at a dose of 10mg/kg in PBS administered by once-daily by oral gavage for 2 weeks. During treatment, tumor length and width were measured using calipers, and tumor volume was calculated using the formula $V=(L\times W\times W)/2$, where V is tumor volume, W is tumor width, and L is tumor length.
Dosage form	10mg/kg/day; 2 weeks; p.o.

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Applications	Cabozantinib treatment attenuated tumor growth in mice with Renca xenografts.

References:

[1] Cai W, Chen Q Y, Dang L H, et al. Apratoxin S10, a dual inhibitor of angiogenesis and cancer cell growth to treat highly vascularized tumors[J]. ACS Medicinal Chemistry Letters, 2017, 8(10): 1007.

[2] Liu H, Sun S, Wang G, et al. Tyrosine kinase inhibitor cabozantinib inhibits murine renal cancer by activating innate and adaptive immunity[J]. Frontiers in Oncology, 2021, 11: 663517.

Background

Cabozantinib (XL184, BMS-907351) is an orally bioavailable and potent inhibitor of MET and VEGFR2 with IC_{50} values of 1.3nM and 0.035nM, respectively[1]. Cabozantinib broadly inhibits various receptor tyrosine kinases to reduce angiogenesis, decrease drug resistance, and metastasis in cancer cells[2]. Cabozantinib has been widely used in cancer research to interrupt tumor growth and progression[3].

In vitro, Cabozantinib treatment for 48 hours significantly inhibited the viability of A498, Huh7, and NCI-H727 cells, with IC_{50} values of 8.456μM, 4.348μM, and 14.01μM, respectively[4]. Treatment with 1μM Cabozantinib for 4 days suppressed the proliferation of K562 cells, increased the expression of CD71 and CD235a, and upregulated the genes involved in heme biosynthesis[5]. Treatment with 5μM Cabozantinib for 72 hours reduced the viability of ST2 cells and blocked the phosphorylation of c-MET, VEGFR2 and AKT[6].

In vivo, Cabozantinib treatment via oral administration at a dose of 10mg/kg/day for 14 days restrained tumor growth, induced extensive tumor necrosis, and promoted neutrophil infiltration in a mouse model of renal cell carcinoma (RCC)[7]. One hour before lipopolysaccharide (LPS) treatment, a single oral administration of Cabozantinib (60mg/kg) alleviated LPS-induced lung injury in mice and mitigated pulmonary fibrosis by inhibiting the TGF-β1/Smad3 pathway[8].

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References:

[1] Yakes F M, Chen J, Tan J, et al. Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth[J]. Molecular cancer therapeutics, 2011, 10(12): 2298-2308.

[2] Srigadha V K, Prabhash K, Noronha V, et al. Cabozantinib: a narrative drug review[J]. Cancer Research, Statistics, and Treatment, 2023, 6(1): 74-87.

[3] El-Khoueiry A B, Hanna D L, Llovet J, et al. Cabozantinib: An evolving therapy for hepatocellular carcinoma[J]. Cancer Treatment Reviews, 2021, 98: 102221.

[4] Cai W, Chen Q Y, Dang L H, et al. Apratoxin S10, a dual inhibitor of angiogenesis and cancer cell growth to treat highly vascularized tumors[J]. ACS Medicinal Chemistry Letters, 2017, 8(10): 1007.

[5] Fu Y H, Ou D L, Yang Y R, et al. Cabozantinib promotes erythroid differentiation in K562 erythroleukemia cells through global changes in gene expression and JNK activation[J]. Cancer Gene Therapy, 2022, 29(6): 784-792.

[6] Dai J, Zhang H, Karatsinides A, et al. Cabozantinib inhibits prostate cancer growth and prevents tumor-induced bone lesions[J]. Clinical Cancer Research, 2014, 20(3): 617-630.

[7] Liu H, Sun S, Wang G, et al. Tyrosine kinase inhibitor cabozantinib inhibits murine renal cancer by activating innate and adaptive immunity[J]. Frontiers in Oncology, 2021, 11: 663517.

[8] Li X, Ma L, Wei Y, et al. Cabozantinib ameliorates lipopolysaccharide-induced lung inflammation and bleomycin--induced early pulmonary fibrosis in mice[J]. International Immunopharmacology, 2021, 101: 108327.

Caution: Product has not been fully validated for medical applications. For research use only.
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