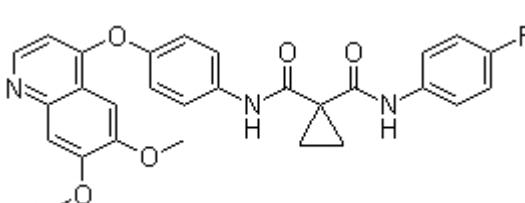


Product Introduction

Cabozantinib (XL184, BMS-907351)

Cabozantinib (XL184, BMS-907351) is a potent VEGFR2 inhibitor with IC₅₀ of 0.035 nM and also inhibits c-Met, Ret, Kit, Flt-1/3/4, Tie2, and AXL with IC₅₀ of 1.3 nM, 4 nM, 4.6 nM, 12 nM/11.3 nM/6 nM, 14.3 nM and 7 nM, respectively.

Technical Data:

Molecular Weight (MW):	501.51	
Formula:	C ₂₈ H ₂₄ FN ₃ O ₅	
Solubility (25°C)	DMSO 100 mg/mL	
* <1 mg/ml means slightly soluble or insoluble:	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20°C Powder	
	6 months-80°C in DMSO	
CAS No.:	849217-68-1	

Biological Activity

XL184 has weak inhibitory activity against RON and PDGFR β with IC₅₀ of 124 nM and 234 nM, respectively, and has low activity against FGFR1 with IC₅₀ of 5.294 μ M. [1] XL184 at low concentration (0.1-0.5 μ M) is sufficient to induce marked inhibition of constitutive and inducible Met phosphorylation and its resultant downstream signaling in MPNST cells, and inhibit HGF-induced MPNST cell migration and invasion. XL184

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also induces marked inhibition of Met and VEGFR2 phosphorylation in cytokine-stimulated human umbilical vein endothelial cells (HUVECs). Although XL-184 has no significant effect on MPNST cell growth at 0.1 μ M, XL184 at 5-10 μ M significantly inhibits the MPNST cell growth. [2]

XL184 treatment at 30 mg/kg in RIP-Tag2 mice with spontaneous pancreatic islet tumors disrupts 83% of the tumor vasculature, reduces pericytes and empty basement membrane sleeves, causes widespread intratumoral hypoxia and extensive tumor cell apoptosis, and slows regrowth of the tumor vasculature after drug withdrawal, more significantly compared with XL999 that blocks VEGFR but not c-Met, leading to only 43% reduction in vascularity, suggesting that concurrent inhibition of VEGFR and other functionally relevant receptor tyrosine kinases (RTK) amplifies angiogenesis inhibition. XL184 also decreases invasiveness of primary tumors and reduces metastasis. [1] XL184 at 30 mg/kg/day significantly abrogates human MPNST xenografts growth and metastasis in SCID mice. [2] Administration of XL184 induces dose-dependent inhibition of tumor growth in breast, lung, and glioma tumor models, in association with decreased tumor and endothelial cell proliferation as well as increased apoptosis. A single oral dose of XL184 is sufficient to induce sustained tumor growth inhibition in MDA-MB-231 tumor-bearing mice and C6 tumor-bearing rats at 100 mg/kg and 10 mg/kg, respectively. [3]

References

- [1] You WK, et al. *Cancer Res*, 2011, 71(14), 4758-4768.
- [2] Torres KE, et al. *Clin Cancer Res*, 2011, 17(12), 3943-3955.
- [3] Yakes FM, et al. *Mol Cancer Ther*, 2011, 10(12), 2298-2308.



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