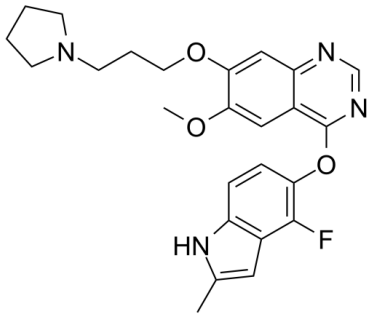
Data Sheet

Product Name:	Cediranib
Cat. No.:	CS-0119
CAS No.:	288383-20-0
Molecular Formula:	C25H27FN4O3
Molecular Weight:	450.51
Target:	Autophagy; PDGFR; VEGFR
Pathway:	Autophagy; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 49 mg/mL (108.77 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

Cediranib (AZD2171) is a highly potent, orally available **VEGFR** tyrosine kinase inhibitor with **IC_{50}**s of <1, <3, 5, 5, 36, 2 nM for Flt1, KDR, Flt4, PDGFRα, PDGFRβ, c-Kit, respectively. IC50 & Target: IC50: <1 nM (Flt1), <3 nM (KDR), 5 nM (Flt4), 5 nM (PDGFRα), 36 nM (PDGFRβ), 2 nM (c-Kit)[1] **In Vitro:** In human umbilical vein endothelial cells, Cediranib inhibits VEGF-stimulated proliferation and KDR phosphorylation with IC_{50} values of 0.4 and 0.5 nM, respectively. In a fibroblast/endothelial cell coculture model of vessel sprouting, Cediranib also reduces vessel area, length, and branching at subnanomolar concentrations[1]. **In Vivo:** Once-daily oral administration of Cediranib ablates experimental (VEGF-induced) angiogenesis and inhibits endochondral ossification in bone or corpora luteal development in ovary; physiologic processes that are highly dependent upon neovascularization. The growth of established human tumor xenografts (colon, lung, prostate, breast, and ovary) in athymic mice is inhibited dose-dependently by Cediranib, with chronic administration of 1.5 mg per kg per day producing statistically significant inhibition in all models. A histologic analysis of Calu-6 lung tumors treated with Cediranib reveals a reduction in microvessel density within 52 hours that becomes progressively greater with the duration of treatment. These changes are indicative of vascular regression within tumors[1].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]The inhibitory activity of Cediranib is determined against a range of recombinant tyrosine kinases [KDR, Flt-1, Flt-4, c-Kit, PDGFR-α, PDGFR-β, CSF-1R, Flt-3, FGFR1, Src, Abl, epidermal growth factor receptor (EGFR), ErbB2, Aur-A, and Aur-B] using ELISA methodology[1]. **Cell Assay:** Cediranib is prepared initially as a 10 mM stock solution in DMSO and diluted in the relevant assay media [1].[1]Proliferation of MG63 osteosarcoma cells is induced by PDGF-AA, which selectively activates PDGFR-α homodimer signaling. Cells are cultured in DMEM without phenol red containing 1% charcoal stripped FCS, 2 mM glutamine, and 1% nonessential amino acids for 24 hours. Cediranib or vehicle is added with PDGF-AA ligand (50 ng/mL) and plates reincubated for 72 hours. Cellular proliferation is determined using a bromodeoxyuridine[1]. **Animal Administration:** [1]For studies in mice, Cediranib is suspended in 1% (w/v) aqueous polysorbate 80 (polyoxyethylene; sorbitan mono-oleate in deionized water) and dosed at 0.1 mL/10 g of body weight. For studies in rats, Cediranib is suspended in a 0.5% (w/v) hydroxypropyl methylcellulose solution containing 0.1% (w/v) aqueous polysorbate 80 and given at 5 mL/kg body weight[1].[1]Rats: Young female Alderley Park rats (6 weeks of age, Wistar derived, n=5) are dosed orally, once daily for 28 days with Cediranib (1.25-5 mg per kg per day) or vehicle. Additional rats (five per group) are treated with Cediranib (5 mg per kg per day) or vehicle for 28 days and maintained for a further 28 days without treatment, to examine the effect of compound withdrawal. Histologic paraffin wax sections of the femorotibial joints and ovaries are stained with H&E. Morphometric image analysis of femorotibial sections is done, with growth plate areas from both the femur and tibia in each joint being combined for an analysis of the effect of compound treatment. The area of corpora lutea in H&E-stained ovary sections is similarly determined by morphometric analysis[1].

Mice: Mice bearing established Calu-6 human lung tumor xenografts (0.2±0.01 cm^3) are selected (day 0) and treated chronically with

Cediranib (6 mg per kg per day, p.o.) or vehicle. Tumors are collected (6-15 per group) 4 hours after the last dose of Cediranib or vehicle, on days 1, 2, 7, 14, and 21. CD31 is then detected in sections using a chromagen end point or fluorescent immunostaining[1].

References:

[1]. Wedge SR, et al. AZD2171: a highly potent, orally bioavailable, vascular endothelial growth factor receptor-2 tyrosine kinase inhibitor for the treatment of cancer. Cancer Res, 2005, 65(10), 4389-4400.

[2]. Zhang L, et al. Pleiotrophin promotes vascular abnormalization in gliomas and correlates with poor survival in patients with astrocytomas. Sci Signal. 2015 Dec 8;8(406):ra125.

CAIndexNames:

Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]-

SMILES:

FC1=C(OC2=C(C(C=C3OCCCN4CCCC4)=NC=N2)C=C3OC)C=CC5=C1C=C(C)N5

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