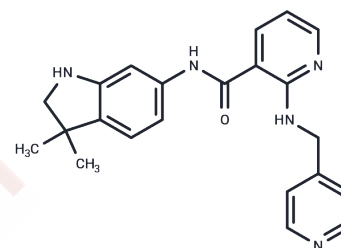


Motesanib

Chemical Properties

CAS No. :	453562-69-1
Formula:	C ₂₂ H ₂₃ N ₅ O
Molecular Weight:	373.45
Appearance:	no data available
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year



Biological Description

Description	Motesanib (AMG 706) is an orally bioavailable receptor tyrosine kinase inhibitor with potential antineoplastic activity. AMG 706 selectively targets and inhibits vascular endothelial growth factor (VEGFR), platelet-derived growth factor (PDGFR), Kit, and Ret receptors, thereby inhibiting angiogenesis and cellular proliferation.
Targets(IC50)	c-Kit, VEGFR
In vitro	Motesanib exhibits extensive efficacy against the VEGFR family in humans, with more than 1000-fold selectivity over EGFR, Src, and p38 kinase. It notably reduces VEGF-triggered proliferation in HUVECs, achieving an IC ₅₀ of 10 nM, but demonstrates minimal influence on bFGF-driven proliferation, with an IC ₅₀ exceeding 3,000 nM. Furthermore, Motesanib effectively hinders PDGF-stimulated proliferation and SCF-induced c-kit phosphorylation, presenting IC ₅₀ values of 207 nM and 37 nM, respectively. However, it lacks efficacy against EGF-induced EGFR phosphorylation and the viability of A431 cells. While having limited antiproliferative effects on HUVECs growth on its own, Motesanib markedly enhances the sensitivity of these cells to fractionated radiation.
In vivo	Motesanib, at a dose of 100 mg/kg, significantly reduces VEGF-induced vascular permeability in a time-dependent manner. When administered orally once or twice daily, it effectively suppresses VEGF-induced angiogenesis in the rat corneal model, with ED ₅₀ values of 4.9 mg/kg and 2.1 mg/kg, respectively. Furthermore, Motesanib promotes dose-dependent regression of established A431 xenografts by targeting tumor cell neovascularization. In combination with radiation, it demonstrates pronounced anti-tumor efficacy in head and neck squamous cell carcinoma (HNSCC) xenograft models. Additionally, Motesanib alone, or when combined with docetaxel or tamoxifen, significantly curtails tumor growth and blood vessel density in MCF-7, MDA-MB-231, or Cal-51 xenografts in a dose-dependent manner.
Kinase Assay	Optimal enzyme, ATP, and substrate (gastrin peptide) concentrations are established for each enzyme using homogeneous time-resolved fluorescence (HTRF) assays. Motesanib is tested in a 10-point dose-response curve for each enzyme using an ATP concentration of two-thirds K _m for each. Most assays consist of enzyme mixed with kinase reaction buffer [20 mM Tris-HCl (pH 7.5), 10 mM MgCl ₂ , 5 mM MnCl ₂ , 100 mM NaCl, 1.5 mM EGTA]. A final concentration of 1 mM DTT, 0.2 mM NaVO ₄ , and 20 µg/mL BSA is added before each assay. For all assays, 5.75 mg/mL streptavidin-allophycocyanin and 0.1125 nM Eu-PT66 are added immediately before the HTRF reaction. Plates are incubated for 30 minutes at room temperature and read on a Discovery instrument. IC ₅₀ values are

calculated using the Levenberg-Marquardt algorithm into a four-parameter logistic equation.

Cell Research

Cells are preincubated for 2 hours with different concentrations of Motesanib, and exposed with 50 ng/mL VEGF or 20 ng/mL bFGF for an additional 72 hours. Cells are washed twice with DPBS, and plates are frozen at -70°C for 24 hours. Proliferation is assessed by the addition of CyQuant dye, and plates are read on a Victor 1420 workstation. IC50 data are calculated using the Levenberg-Marquardt algorithm into a four-parameter logistic equation.

Solubility Information

Solubility

DMSO: 50 mg/mL (133.89 mM), Sonication is recommended.
(< 1 mg/mL refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6777 mL	13.3887 mL	26.7773 mL
5 mM	0.5355 mL	2.6777 mL	5.3555 mL
10 mM	0.2678 mL	1.3389 mL	2.6777 mL
50 mM	0.0536 mL	0.2678 mL	0.5355 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.

Reference

- Polverino A, et al. AMG 706, an oral, multikinase inhibitor that selectively targets vascular endothelial growth factor, platelet-derived growth factor, and kit receptors, potently inhibits angiogenesis and induces regression in tumor xenografts. *Cancer Res*
- Kruser TJ, et al. Augmentation of radiation response by motesanib, a multikinase inhibitor that targets vascular endothelial growth factor receptors. *Clin Cancer Res*, 2010, 16(14), 3639-3647.
- Coxon A, et al. Broad antitumor activity in breast cancer xenografts by motesanib, a highly selective, oral inhibitor of vascular endothelial growth factor, platelet-derived growth factor, and Kit receptors. *Clin Cancer Res*, 2009, 15 (1), 110-118.

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