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产品名称：5-(2-氯苯基)-7-氟-1,2-二氢-8-甲氧基-3-甲基吡唑并[3,4-b][1,4]苯并二氮杂卓

产品别名：R1530

生物活性：

Description

R1530 is the multikinase inhibitor with potential antiangiogenesis and antineoplastic activities. IC50 Value: Target: VEGFR; PDGFR R1530 is also a mitosis-angiogenesis inhibitor (MAI) that inhibits multiple receptor tyrosine kinases involved in angiogenesis, such as vascular endothelial growth factor receptor (VEGFR)-1, -2, -3, platelet-derived growth factor receptor (PDGFR),Flt-3, and fibroblast growth factor receptor (FGFR) -1, -2. In addition, this agents exhibits anti-proliferative activity by initiating mitotic arrest and inducing apoptosis. in vitro: In the presence of R1530, polyploid cancer cells underwent apoptosis or became senescent which translated into potent in vitro and in vivo efficacy. Normal proliferating cells were resistant to R1530-induced polyploidy thus supporting the rationale for cancer therapy by induced polyploidy. Mitotic checkpoint kinase BubR1 was found downregulated during R1530-induced exit from mitosis, a likely consequence of PLK4 inhibition [1]. R1530 strongly inhibited human tumor cell proliferation. Growth factor-driven proliferation of endothelial and fibroblast cells was also inhibited [2]. in vivo: Significant tumor growth inhibition was demonstrated in a lung cancer xenograft model with a range of once daily, weekly and twice-weekly doses of R1530 (3.125-50 mg/kg qd, 100 mg/kg qw, 100 mg/kg biw). Daily doses were most effective in the lung cancer model and also had significant growth inhibitory effects in models of colorectal, prostate, and breast tumors. Tumor regression occurred in all models treated with the maximum tolerated daily dose (50 mg/kg). The doses of 25 and 50 mg/kg qd resulted in biologically significant increased survival in all tested models. After oral administration in nude mice, R1530 showed good tissue penetration. Exposure was dose dependent up to 100 mg/kg with oral administration [2]. Toxicity: N/A Clinical trial: A Multiple Ascending Dose Study of R-1530 in Patients With Advanced Solid Tumors. Phase 1

Solvent&Solubility

In Vitro:

DMSO : ≥ 53 mg/mL (148.55 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8028 mL	14.0142 mL	28.0285 mL
5 mM	0.5606 mL	2.8028 mL	5.6057 mL
10 mM	0.2803 mL	1.4014 mL	2.8028 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References

[1]. Tovar C, et al. Small-molecule inducer of cancer cell polyploidy promotes apoptosis or senescence: Implications for therapy. Cell Cycle. 2010 Aug 15;9(16):3364-75.

[2]. Kolinsky K, et al. Preclinical evaluation of the novel multi-targeted agent R1530. Cancer Chemother Pharmacol. 2011 Dec;68(6):1585-94.