
Product Data Sheet

Product Name: Tivozanib (hydrate)

Cat. No.: GC15280

Chemical Properties

Cas. No. 682745-40-0

Chemical Name N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-urea, monohydrate

SMILES COC1=C(OC)C=C(C(OC2=CC(Cl)=C(NC(NC3=NOC(C)=C3)=O)C=C2)=CC=N4)C4=C1.O

Formula $C_{22}H_{19}ClN_4O_5 \cdot H_2O$ M.Wt 472.9

Solubility ≤ 25 mg/ml in DMSO; 30mg/ml in dimethyl formamide Storage Store at $-20^{\circ}C$

General For obtaining a higher solubility , please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Evaluation sample solution : ship with blue ice All other available size: ship with RT , or Condition blue ice upon request.

Structure

Background

Tivozanib, also known as AV-951 and KRN-951, is an orally active, ATP-competitive, small-molecule, quinoline-urea derivative. Tivozanib is a pan-VEGFR tyrosine kinase inhibitor.

In vitro: Tivozanib markedly inhibited the ligand-induced phosphorylation of VEGFR1\2 and 3 with the IC50 value of 30 nM\6.5 nM and 15 nM, respectively. Tivozanib also exhibited inhibitory effects on PDGFR and c-Ki with the IC50 value of 1.72 and 1.63 nmol/L, respectively. Tivozanib showed little activity against FGFR-1, Flt3, c-Met, EGFR and IGF-1R [1]. Tivozanib blocked VEGF-dependent activation of mitogen-activated protein kinases and proliferation of endothelial cells. It also inhibited VEGF-mediated migration of human umbilical vein endothelial cells [1].

In vivo: In tumor xenografts athymic rat model, p.o. administration of tivozanib decreased the micro vessel density and suppressed VEGFR2 phosphorylation levels, especially at a concentration of 1mg/kg. Tivozanib almost completely inhibited tumor xenografts growth (TGI > 85%) in athymic rats. Tivozanib displayed antitumor activity against various human tumor xenografts, such as lung, breast, colon, pancreas, ovarian and prostate cancer.[1]. In rat peritoneal disseminated tumor model, tivozanib prolonged the survival of the tumor-bearing rats with the MST of 53.5 days [2].

Clinical trials: Tivozanib has entered phase III clinical trials in patients with advanced renal cell carcinoma. Tivozanib improved progression-free survival (PFS), but not overall survival (OS). The most common adverse events were hypertension and dysphonia [3]. In patients with refractory,

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metastatic colorectal cancer, tivozanib has entered Multicenter phase II study [4].

References:

- [1]. Nakamura K, Taguchi E, Miura T, et al. KRN951, a highly potent inhibitor of vascular endothelial growth factor receptor tyrosine kinases, has antitumor activities and affects functional vascular properties[J]. Cancer research, 2006, 66(18): 9134-9142.
- [2]. Taguchi E, Nakamura K, Miura T, et al. Anti-tumor activity and tumor vessel normalization by the vascular endothelial growth factor receptor tyrosine kinase inhibitor KRN951 in a rat peritoneal disseminated tumor model[J]. Cancer science, 2008, 99(3): 623-630.
- [3]. Motzer R J, Nosov D, Eisen T, et al. Tivozanib versus sorafenib as initial targeted therapy for patients with metastatic renal cell carcinoma: results from a phase III trial[J]. Journal of clinical oncology, 2013, 31(30): 3791-3799.
- [4]. Wolpin B M, Ng K, Zhu A X, et al. Multicenter phase II study of tivozanib (AV-951) and everolimus (RAD001) for patients with refractory, metastatic colorectal cancer[J]. The oncologist, 2013, 18(4): 377-378.

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