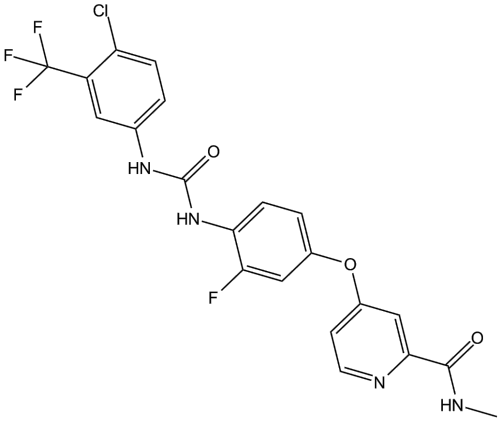
Product Data Sheet

Product Name: Regorafenib
Cat. No.: GC10111

Chemical Properties

Cas. No.	755037-03-7		
Chemical Name	4-(4-(3-(4-chloro-3-(trifluoromethyl)phenyl)ureido)-3-fluorophenoxy)-N-methylpicolinamide		
SMILES	CNC(=O)C1=NC=CC(=C1)OC2=CC(=C(C=C2)NC(=O)NC3=CC(=C(C=C3)Cl)C(F)(F)F)F		
Formula	$C_{21}H_{15}ClF_4N_4O_3$	M.Wt	482.82
Solubility	≥100mg/mL in DMSO	Storage	Desiccate at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	NCI-H1703, NCI-H2170, SK-MES-1 cells
Preparation Method	Lung squamous cell carcinoma (LSCC) cell lines were exposed to different concentrations of Regorafenib for 24, 48, and 72h, 0-5μM for NCI-H1703 and 0-20μM for NCI-H2170 and SK-MES-1. Cell proliferation was measured by SRB assay.
Reaction Conditions	0-20μM; 24, 48, 72h
Applications	Regorafenib decreased the survival fractions of LSCC cells in a dose- and time-dependent manner.

Animal experiment [2]:

Animal models	Female athymic nu/nu mice
Preparation Method	Mice with orthotopic adrenal SK-N-SH neuroblastoma xenograft tumours were treated with vehicle or Regorafenib. Mice in group 1 were gavage-fed once daily with vehicle alone, while the other group of mice was fed once daily with Regorafenib at 30mg/kg. Both groups of mice were treated for 14 days and then euthanised by CO_2 followed by cervical dislocation. Tumours were harvested, weighed and photographed.
Dosage form	30mg/kg; 14 days; p.o.

Caution: Product has not been fully validated for medical applications. For research use only.
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Applications	Regorafenib reduces xenograft tumour growth. The average final weight of the tumors in the control group was 2.16g, while the average final weight of the tumors in the Regorafenib-treated group was only 0.35g.

References:
[1] Hu X, Wu L, Zhang Z, et al. The anti-tumor effect of regorafenib in lung squamous cell carcinoma in vitro[J]. Biochemical and Biophysical Research Communications, 2018, 503(2): 1123-1129.
[2]Subramonian D, Phanhthilath N, Rinehardt H, et al. Regorafenib is effective against neuroblastoma in vitro and in vivo and inhibits the RAS/MAPK, PI3K/Akt/mTOR and Fos/Jun pathways[J]. British journal of cancer, 2020, 123(4): 568-579.

Background

Regorafenib is an orally active multi-kinase inhibitor with IC_{50} values of 13/4.2/46, 22, 7, 1.5 and 2.5nM for VEGFR1/2/3, PDGFRβ, Kit, RET and Raf-1, respectively[1]. Regorafenib has good anti-tumor and anti-angiogenic activities[2, 3].

In vitro, Regorafenib (0-20μM) treatment of lung squamous cell carcinoma (LSCC) cell lines (NCI-H1703, NCI-H2170, SK-MES-1 cells) for 24-72h, inhibited cell proliferation in a dose- and time-dependent manner and induced cell G0/G1 phase arrest[4]. Regorafenib (2.5-10μM) treatment of HepG2 cells for 24-96h, inhibited cell growth in a dose- and time-dependent manner, induced cell apoptosis, and increased the level of phosphorylated c-Jun[5].

In vivo, oral treatment of mice with adrenal SK-N-SH neuroblastoma orthotopically implanted with Regorafenib (30mg/kg) for 14 days, significantly inhibited tumor growth in the mice, with the average final weight of the tumor in the control group being 2.16g and the average final weight of the tumor in the Regorafenib-treated group being only 0.35g[6]. Oral treatment of mice with metastatic colon cancer model with Regorafenib (30mg/kg) for 14 days, inhibited tumor growth and metastasis in the mice, significantly reduced tumor angiogenesis, and significantly reduced the number of infiltrating macrophages[7].

References:

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[1] Wilhelm S M, Dumas J, Adnane L, et al. Regorafenib (BAY 73-4506): a new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity[J]. International journal of cancer, 2011, 129(1): 245-255.
[2] Chen C H, Hsu F T, Chen W L, et al. Induction of apoptosis, inhibition of MCL-1, and VEGF-A expression are associated with the anti-cancer efficacy of magnolol combined with regorafenib in hepatocellular carcinoma[J]. Cancers, 2021, 13(9): 2066.
[3] Lim Y, Han S W, Yoon J H, et al. Clinical implication of anti-angiogenic effect of regorafenib in metastatic colorectal cancer[J]. PLoS One, 2015, 10(12): e0145004.
[4] Hu X, Wu L, Zhang Z, et al. The anti-tumor effect of regorafenib in lung squamous cell carcinoma in vitro[J]. Biochemical and Biophysical Research Communications, 2018, 503(2): 1123-1129.
[5] Carr B I, Cavallini A, Lippolis C, et al. Fluoro-Sorafenib (Regorafenib) effects on hepatoma cells: growth inhibition, quiescence, and recovery[J]. Journal of cellular physiology, 2013, 228(2): 292-297.
[6] Subramonian D, Phanhthilath N, Rinehardt H, et al. Regorafenib is effective against neuroblastoma in vitro and in vivo and inhibits the RAS/MAPK, PI3K/Akt/mTOR and Fos/Jun pathways[J]. British journal of cancer, 2020, 123(4): 568-579.
[7] Abou-Elkacem L, Arns S, Brix G, et al. Regorafenib inhibits growth, angiogenesis, and metastasis in a highly aggressive, orthotopic colon cancer model[J]. Molecular cancer therapeutics, 2013, 12(7): 1322-1331.

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