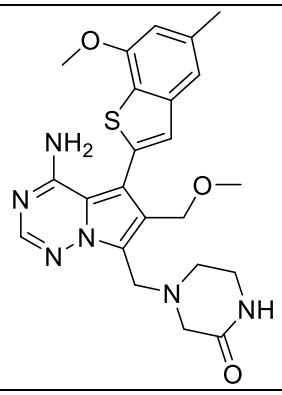
Product data sheet

MedKoo Cat#: 327022 Name: Rogaratinib CAS#: 1443530-05-9 Chemical Formula: $C_{23}H_{26}N_6O_3S$ Exact Mass: 466.1787 Molecular Weight: 466.56	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Rogaratinib, also known as BAY-1163877, is an aberrant fibroblast growth factor receptor (FGFR) inhibitor. Rogaratinib is as an orally available, selective and potent inhibitor of FGFR-1, -2 and -3 kinase activity. FGFRs are a family of receptor tyrosine kinases, which may be upregulated in various tumor cell types and may be involved in tumor cell differentiation and proliferation, tumor angiogenesis, and tumor cell survival.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	5.0	10.72

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.14 mL	10.72 mL	21.43 mL
5 mM	0.43 mL	2.14 mL	4.29 mL
10 mM	0.21 mL	1.07 mL	2.14 mL
50 mM	0.04 mL	0.21 mL	0.43 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Grünewald S, Politz O, Bender S, Héroult M, Lustig K, Thuss U, Kneip C, Kopitz C, Zopf D, Collin MP, Boemer U, Ince S, Ellinghaus P, Mumberg D, Hess-Stumpp H, Ziegelbauer K. Rogaratinib: A potent and selective pan-FGFR inhibitor with broad antitumor activity in FGFR-overexpressing preclinical cancer models. Int J Cancer. 2019 Sep 1;145(5):1346-1357. doi: 10.1002/ijc.32224. Epub 2019 Mar 13. PMID: 30807645; PMCID: PMC6766871.

In vivo study

1. Grünewald S, Politz O, Bender S, Héroult M, Lustig K, Thuss U, Kneip C, Kopitz C, Zopf D, Collin MP, Boemer U, Ince S, Ellinghaus P, Mumberg D, Hess-Stumpp H, Ziegelbauer K. Rogaratinib: A potent and selective pan-FGFR inhibitor with broad antitumor activity in FGFR-overexpressing preclinical cancer models. Int J Cancer. 2019 Sep 1;145(5):1346-1357. doi: 10.1002/ijc.32224. Epub 2019 Mar 13. PMID: 30807645; PMCID: PMC6766871.

7. Bioactivity
Biological target:

Rogaratinib (BAY1163877) is a potent and selective fibroblast growth factor receptor (FGFR) inhibitor.

Product data sheet

In vitro activity

Inhibition of the FGFR pathway by rogaratinib treatment was analyzed by Western blot in rogaratinib-sensitive as well as -insensitive cell lines from various cancer types. In FGFR4-overexpressing MDA-MB-453 breast cancer cells, rogaratinib inhibited auto-phosphorylation of FGFR4 in a concentration-dependent manner and caused inhibition of downstream signaling by preventing ERK1/2 phosphorylation in the same concentration range (Fig.22 a). Similarly, rogaratinib effectively inhibited auto-phosphorylation of FGFR2 as well as phosphorylation of ERK1/2 at 100 nM in NCI-H716 colon cancer cells (Fig.22 b). Furthermore, potent inhibition of ERK1/2 phosphorylation by rogaratinib was observed in the rogaratinib-sensitive RT-112 bladder cancer and NCI-H1581 lung cancer cell lines while UM-UC-3 bladder cancer and NCI-H520 lung cancer cells were less sensitive to rogaratinib-mediated inhibition of downstream phosphorylation, consistent with the differentiated anti-proliferative activity of rogaratinib in these cell lines (Fig.22 c, Supporting Information Table S3). In FGFR1-overexpressing DMS-114 lung cancer and FGFR2-overexpressing MFM-223 breast cancer cells, rogaratinib potently inhibited downstream signaling through ERK1/2 and AKT as determined by MSD-ELISA technology. The IC50 values for inhibition of ERK and AKT phosphorylation for DMS-114 (20 and 26 nM, respectively) and MFM-223 cells (11 and 19 nM, respectively) corresponded well with the IC50 values for proliferation inhibition (42 nM for DMS-114; 27 nM for MFM-223). Rogaratinib also inhibited phosphorylation of ERK1/2 in FGFR1-overexpressing murine C51 colon cancer cells with an IC50 of 280 nM (Fig.22 c). In these cell lines the potency of inhibition of phosphorylation of ERK1/2 correlates directly with the sensitivity of these cell lines to treatment with rogaratinib (Supporting Information Table S4).

Int J Cancer. 2019 Sep 1; 145(5): 1346–1357. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6766871/

In vivo activity

C51 was used in vivo for testing the efficacy of rogaratinib in FGFR-overexpressing cancer models. The maximally tolerated dose for rogaratinib was determined at 75 mg/kg, QD and 50 mg/kg, BID in Balb/cJ mice. In a first experiment, monotherapy of the C51 model in Balb/cJ mice was performed with different doses and schedules of rogaratinib followed by a pharmacokinetic analysis after the last treatment (Fig.33). Rogaratinib demonstrated strong antitumor efficacy in a dose-dependent manner with significant effects at doses reaching functional (pERK) IC50 of C51 cells. Oral treatment at 50 and 75 mg/kg (QD) reduced tumor growth compared to the vehicle group with T/C volume ratios of 0.27 and 0.16, respectively (Figs.33 a–3b, Supporting Information Table S5). In both groups, a 22% partial response (PR) rate (2/9 mice) was observed according to RECIST criteria20 (Fig.33 c). In addition, 1/9 mice (11%) had stable disease (SD) in the 75 mg/kg treatment group. While daily treatment at 25 mg/kg was not efficacious, twice-daily application of 25 mg/kg resulted in a decrease of tumor growth with a T/C volume ratio of 0.47. The efficacy of rogaratinib was further evaluated in the C51 colon cancer model in nude rats to determine efficacy and to support the human dose prediction by extending the analyses to another species. Daily oral treatment with 10 or 50 mg/kg rogaratinib significantly reduced tumor growth with T/C volume ratios of 0.26, and 0.02, respectively (Figs.33 e–3f, Supporting Information Table S5). In the 10 mg/kg group 2/8 (25%) complete responses (CR) and in the 50 mg/kg group 3/8 (37.5%) CR and 1/8 (12.5%) SD were observed (Fig.33 g). Treatment with rogaratinib monotherapy was generally well-tolerated with no body weight losses above 10% or any fatal toxicity in mice or rats (Supporting Information Figs. S2A-B).

Int J Cancer. 2019 Sep 1; 145(5): 1346–1357. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6766871/