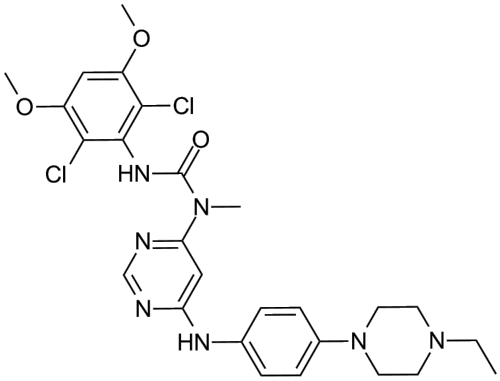
Product Data Sheet

Product Name: BGJ398 (Infigratinib)
Cat. No.: GC10055

Chemical Properties

Cas. No.	872511-34-7		
Chemical Name	3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-[6-[4-(4-ethylpiperazin-1-yl)anilino]pyrimidin-4-yl]-1-methylurea		
SMILES	CCN1CCN(CC1)C2=CC=C(C=C2)NC3=CC(=NC=N3)N(C)C(=O)NC4=C(C(=CC(=C4Cl)OC)OC)Cl		
Formula	$C_{26}H_{31}Cl_2N_7O_3$	M.Wt	560.48
Solubility	≥ 7mg/mL in DMSO with gentle warming	Storage	Store 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	SKOV3ip1 cells
Preparation Method	To measure cell viability of spheroid cultures, SKOV3ip1 cells (5×10^4) were seeded in ultra-low attachment 24-well plates and incubated overnight. BGJ398 were then added, and the cells were incubated for an additional 72 hours. Cells were harvested from each well and transferred to a regular 24-well plate for an additional 12 hours. Attached, live cells were stained with 0.2% crystal violet solution for 20 minutes with gentle agitation. The stained cells were washed with distilled water. For colorimetric analysis, the crystal violet dye was extracted with 1% SDS/PBS, and absorbance was measured at 570nm using an EMax PLUS microplate reader.
Reaction Conditions	0.3125-5μM; 72h
Applications	The survival rate of SKOV3ip1 cells in spheroid culture was significantly reduced after BGJ398 treatment.

Animal experiment [2]:

Animal models	TMK-1 cells xenograft mice model
Preparation Method	Cancer cells (1×10^6) were injected subcutaneously into the right flank of 6- to 8-week-old athymic nude mice. Mice were randomly assigned to either a control or treatment group. When tumors reached approximately $80mm^3$, BGJ398 (10mg/kg, administered by oral gavage) was initiated. Tumor diameters were measured, and volumes were calculated ($width^2 \times length \times 0.5$). Tumors were excised, weighed, and processed for subsequent experiments.
Dosage form	10mg/kg; po; 20d

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Applications Treatment with BGJ398 significantly inhibited tumor growth.

References:
[1]. Cha H J, Choi J H, Park I C, et al. Selective FGFR inhibitor BGJ398 inhibits phosphorylation of AKT and STAT3 and induces cytotoxicity in sphere-cultured ovarian cancer cells[J]. International Journal of Oncology, 2017, 50(4): 1279-1288.
[2]. Schmidt K, Moser C, Hellerbrand C, et al. Targeting fibroblast growth factor receptor (FGFR) with BGJ398 in a gastric cancer model[J]. Anticancer Research, 2015, 35(12): 6655-6665.

Background

BGJ398 (Infigratinib) is an oral, ATP-competitive pan-FGFR tyrosine kinase inhibitor (FGFR1: IC_{50} = 0.9nM; FGFR2: IC_{50} = 1.4nM; FGFR3: IC_{50} = 1nM; FGFR4: IC_{50} = 60nM) [1]. BGJ398 targets the fibroblast growth factor receptors FGFR1, FGFR2, FGFR3, and FGFR4, thereby blocking signal transduction mediated by these receptors and inhibiting FGFR-dependent tumor cell proliferation and angiogenesis [2-3]. BGJ398 is primarily used to treat dwarfism in children [4].

In SKOV3ip1 cells, the survival rate of cell in spheroid culture was significantly reduced after BGJ398 (0.3125-5μM; 72h) treatment [5]. In UMUC-14 cells, the combination of paclitaxel and BGJ398 (0-10μM; 72h) can produce a synergistic effect in promoting cell apoptosis [6].

In TMK-1 cells xenograft mice model, treatment with BGJ398 (10mg/kg; po; 20d) significantly inhibited tumor growth [7]. In Snu16R-derived xenograft mice model, knockdown of BAG3 enhances the anti-tumor effect induced by BGJ398 (30mg/kg; po; 4 weeks) [8].

References:
[1]. Guagnano V, Furet P, Spanka C, et al. Discovery of 3-(2, 6-dichloro-3, 5-dimethoxy-phenyl)-1-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-pyrimidin-4-yl}-1-methyl-urea (NVP-BGJ398), a potent and selective inhibitor of the fibroblast growth factor receptor family of receptor tyrosine kinase[J]. Journal of medicinal chemistry, 2011, 54(20): 7066-7083.
[2]. Szymczyk J, Sluzalska K D, Materla I, et al. FGF/FGFR-dependent molecular mechanisms underlying anti-cancer drug resistance[J]. Cancers, 2021, 13(22): 5796.

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[3]. Agrawal S, Maity S, AlRaawi Z, et al. Targeting drugs against fibroblast growth factor (s)-induced cell signaling[J]. Current drug targets, 2021, 22(2): 214-240.
[4]. Högler W, Ward L M. New developments in the management of achondroplasia[J]. Wiener Medizinische Wochenschrift, 2020, 170(5): 104-111.
[5]. Cha H J, Choi J H, Park I C, et al. Selective FGFR inhibitor BGJ398 inhibits phosphorylation of AKT and STAT3 and induces cytotoxicity in sphere-cultured ovarian cancer cells[J]. International Journal of Oncology, 2017, 50(4): 1279-1288.
[6]. Kim S H, Ryu H, Ock C Y, et al. BGJ398, a pan-FGFR inhibitor, overcomes paclitaxel resistance in urothelial carcinoma with FGFR1 overexpression[J]. International journal of molecular sciences, 2018, 19(10): 3164.
[7]. Schmidt K, Moser C, Hellerbrand C, et al. Targeting fibroblast growth factor receptor (FGFR) with BGJ398 in a gastric cancer model[J]. Anticancer Research, 2015, 35(12): 6655-6665.
[8]. Li K, Deng X, Feng G, et al. Knockdown of Bcl-2-associated athanogene-3 can enhance the efficacy of BGJ398 via suppressing migration and inducing apoptosis in gastric cancer[J]. Digestive Diseases and Sciences, 2021, 66(9): 3036-3044.

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