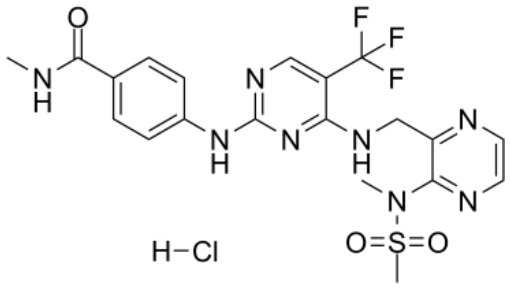
Product Data Sheet

Product Name: Defactinib hydrochloride
Cat. No.: GC35827

Chemical Properties

Cas. No.	1073160-26-5		
SMILES	O=C(NC)C1=CC=C(NC2=NC=C(C(F)(F)F)C(NCC3=NC=CN=C3N(C)S(=O)(C)=O)=N2)C=C1.[H]Cl		
Formula	$C_{20}H_{22}ClF_3N_8O_3S$	M.Wt	546.95
Solubility	DMSO: 30 mg/mL (54.85 mM); Water: < 0.1 mg/mL (insoluble)	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]:

Cell lines Esophageal squamous cell carcinoma (ESCC)

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Preparation Method	The antiproliferative effect of Defactinib hydrochloride on ESCC cells was evaluated using 3-(4, 5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2- (4-sulfophenyl)-2H-tetrazolium, inner salt (MTS) method. Briefly, 3×10^3 indicated cells in 100μL of RPMI 1640 medium were seeded in 96-well plates. Twenty-four hours later, cells were attached and treated with different doses of Defactinib hydrochloride (0-25μM) for 72h. Then, the medium was discarded, and cells were incubated with MTS solution for 1h. Plates were scanned spectrophotometrically at 490nm, and the number of viable cells was positively correlated with the formazan product.
Reaction Conditions	0-25μM; 72h
Applications	Defactinib hydrochloride significantly inhibited the growth of tumor cells.

Animal experiment [2]:

Animal models	NCI-H358 cells xenograft tumor mice model
Preparation Method	A suspension of NCI-H358 cells (4×10^6 cells) was subcutaneously injected into the right flank of 6-week-old female BALB/c nu/nu mice and maintained under pathogen-free conditions. When tumors reached approximately 70-120mm in size, mice were randomly divided into four groups (n = 6 per group): 1) vehicle, 2) Defactinib hydrochloride (10mg/kg), 3) avutometinib (0.3mg/kg), and 4) avutometinib plus Defactinib hydrochloride. Avutometinib and Defactinib hydrochloride were dissolved in 20% hydroxypropyl-β-cyclodextrin/normal saline. Dosing was continued once daily by oral gavage until day 28, and the body weight and general condition of the mice were monitored daily.
Dosage form	10mg/kg; ig; 28d

Caution: Product has not been fully validated for medical applications. For research use only.
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Product Data Sheet

Applications Defactinib hydrochloride monotherapy inhibits tumor growth.

References:
[1]. Zhang L, Zhao D, Wang Y, et al. Focal adhesion kinase (FAK) inhibitor?defactinib suppresses the malignant progression of human esophageal squamous cell carcinoma (ESCC) cells via effective blockade of PI3K/AKT axis and downstream molecular network[J]. Molecular carcinogenesis, 2021, 60(2): 113-124.
[2]. Yoshimura A, Horinaka M, Yaoi T, et al. Epithelial-mesenchymal transition status is a remarkable biomarker for the combination treatment with avutometinib and defactinib in KRAS-mutated non-small cell lung cancer[J]. British Journal of Cancer, 2024, 131(2): 361-371.

Background

Defactinib hydrochloride is a small molecule kinase inhibitor that selectively inhibits FAK and Pyk2 [1]. Defactinib hydrochloride inhibits FAK autophosphorylation (e.g., at Tyr397) and blocks integrin-mediated downstream RAS/MEK/ERK and PI3K/Akt signaling pathways, thereby inhibiting tumor cell proliferation, migration, survival, and angiogenesis [2-3]. Defactinib hydrochloride is commonly used to treat recurrent KRAS-mutant low-grade serous ovarian cancer [4].

In esophageal squamous cell carcinoma, Defactinib hydrochloride (0-25μM; 72h) significantly inhibited the growth of tumor cells [5]. In A549 cells, Defactinib hydrochloride (1μM; 48h) partially abolished G9a-enhanced invasion in cells [6].

In NCI-H358 cells xenograft tumor mice model, Defactinib hydrochloride (10mg/kg; ig; 28d) monotherapy inhibits tumor growth [7]. In A427 cells xenograft tumor mice model, Defactinib hydrochloride (10mg/kg; ip; 21d) inhibits tumor growth [8].

References:
[1]. Moore K, Walter A. Defactinib hydrochloride. Dual FAK1/PYK2 inhibitor, Treatment of non-small cell lung cancer, treatment of malignant mesothelioma, treatment of ovarian cancer[J]. Drugs of the Future, 2014, 39(11).
[2]. Ryzhakov G, Almuttaqi H, Corbin A L, et al. Defactinib inhibits PYK2 phosphorylation of IRF5 and

reduces intestinal inflammation[J]. Nature Communications, 2021, 12(1): 6702.
[3]. Riordan J D, Nathanson T A, Varzavand A, et al. A critical role of FAK signaling in Rac1-driven melanoma cell resistance to MAPK pathway inhibition[J]. bioRxiv, 2024: 2024.12. 22.629990.
[4]. Banerjee S N. Avutometinib/Defactinib May be a New SOC in Low-Grade Serous Ovarian Cancer[J]. Cancer Network, 2023: NA-NA.
[5]. Zhang L, Zhao D, Wang Y, et al. Focal adhesion kinase (FAK) inhibitor-defactinib suppresses the malignant progression of human esophageal squamous cell carcinoma (ESCC) cells via effective blockade of PI3K/AKT axis and downstream molecular network[J]. Molecular carcinogenesis, 2021, 60(2): 113-124.
[6]. Sun T, Zhang K, Pangeni R P, et al. G9a promotes invasion and metastasis of non–small cell lung cancer through enhancing focal adhesion kinase activation via NF-κB signaling pathway[J]. Molecular Cancer Research, 2021, 19(3): 429-440.
[7]. Yoshimura A, Horinaka M, Yaoi T, et al. Epithelial-mesenchymal transition status is a remarkable biomarker for the combination treatment with avutometinib and defactinib in KRAS-mutated non-small cell lung cancer[J]. British Journal of Cancer, 2024, 131(2): 361-371.
[8]. Liu J, Xue L, Xu X, et al. FAK-targeting PROTAC demonstrates enhanced antitumor activity against KRAS mutant non-small cell lung cancer[J]. Experimental Cell Research, 2021, 408(2): 112868.

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