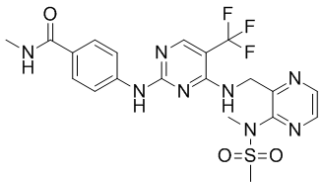
Data Sheet

Product Name:	Defactinib
Cat. No.:	HY-12289
CAS No.:	1073154-85-4
Molecular Formula:	C20H21F3N8O3S
Molecular Weight:	510.49
Target:	FAK
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO: ≥ 39 mg/mL



BIOLOGICAL ACTIVITY:

Defactinib is a novel **FAK** inhibitor, which inhibits FAK phosphorylation at the Tyr397 site in a time– and dose–dependent manner. IC50 & Target: FAK[1]

In Vitro: VS–6063 inhibits FAK phosphorylation at the Tyr397 site in a time– and dose–dependent manner. The combination of VS–6063 and Paclitaxel markedly decreases proliferation and increases apoptosis, which results in 92.7% to 97.9% reductions in tumor weight. RPPA data shows that VS–6063 reduces levels of AKT and YB–1 in taxane–resistant cell lines. The expression of pFAK (Tyr397) is statistically significantly inhibited by VS–6063 in a dose–dependent manner in all cell lines. VS–6063 inhibits pFAK (Tyr397) expression within 3 hours, with a gradual return of expression by 48 hours[1].

In Vivo: VS–6063 doses of 25 mg/kg twice a day or greater statistically significantly inhibits pFAK (Tyr397) at 3 hours, with return of expression noted by 24 hours. Therefore, administration of VS–6063 at 25 mg/kg twice a day is selected as the dosing schedule for subsequent therapy experiments. For therapy experiments, female nude mice bearing HeyA8 tumors in the peritoneal cavity are randomly divided into 4 groups (n=10 per group): 1) vehicle orally twice daily and phosphate–buffered saline intraperitoneally weekly (control); 2) VS–6063 25 mg/kg orally twice daily; 3) PTX intraperitoneally weekly; and 4) both VS–6063 25 mg/kg orally twice daily and PTX intraperitoneally weekly. There is an 87.4% reduction in tumor weight by PTX monotherapy in the HeyA8 model, and combination therapy resulted in the greatest tumor weight reduction, with a 97.9% reduction (P=0.05 compared with PTX). In the SKOV3ip1 model, a 92.7% tumor weight reduction is observed in the combination group compared with PTX (P<0.001)[1].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: Defactinib is prepared in phosphate–buffered saline[1].[1]Mice[1]

To determine the antitumor effects of VS–6063, SKOV3ip1, SKOV3–TR, HeyA8, and HeyA8–MDR cells are injected intraperitoneally. One week after tumor cell injection, mice are randomly assigned to 4 groups of 10 mice (control, PTX alone, VS–6063 alone, and PTX with VS–6063); treatment is initiated at 3–4 weeks following injection. PTX at 2 mg/kg (SKOV3ip1 and SKOV3–TR) or 2.5 mg/kg (HeyA8 and HeyA8–MDR) is given intraperitoneally weekly; VS–6063 at 25 mg/kg is given orally twice every day. Control mice received HBSS intraperitoneally once a week and vehicle orally twice every day. Mice are monitored daily for adverse effects of therapy and are killed on day 35 (SKOV3ip1 or SKOV3–TR), day 28 (HeyA8 or HeyA8–MDR), or when any of the mice seemed moribund. Total body weight, tumor incidence and mass, and the number of tumor nodules are recorded. Tumors are either fixed in formalin or embedded in paraffin or snap frozen in optimal cutting temperature (OCT) compound in liquid nitrogen.

References:

[1]. Kang Y, et al. Role of focal adhesion kinase in regulating YB–1–mediated paclitaxel resistance in ovarian cancer. J Natl Cancer Inst. 2013 Oct 2;

105(19):1485–95.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA