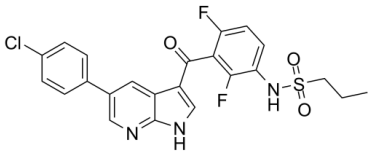
Data Sheet

Product Name:	Vemurafenib
Cat. No.:	CS-0216
CAS No.:	918504-65-1
Molecular Formula:	C23H18ClF2N3O3S
Molecular Weight:	489.92
Target:	Autophagy; Raf
Pathway:	Autophagy; MAPK/ERK Pathway
Solubility:	DMSO : ≥ 100 mg/mL (204.11 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

Vemurafenib (PLX4032; RG7204) is a first-in-class, selective, potent inhibitor of **B-RAF** kinase, with **IC_{50}**s of 31 and 48 nM for RAF^{V600E} and c-RAF-1, respectively. IC50 & Target: IC50: 31 nM ($BRAF^{V600E}$), 48 nM (c-RAF-1) **In Vitro:** Vemurafenib (PLX4032) selectively blocks the RAF/MEK/ERK pathway in BRAF mutant cells[1]. RG7204 is a potent inhibitor of proliferation in those expressing RAF^{V600E} but not $BRAF^{WT}$ in 17 melanoma cell lines. Vemurafenib (RG7204) induces MEK and ERK phosphorylation at high concentrations in CHL-1 cells [2]. Ectopic expression of EGFR in melanoma cells is sufficient to cause resistance to PLX4032[3]. **In Vivo:** Vemurafenib (PLX4032, 20, 25, 75 mg/kg, p.o.) causes dose-dependent inhibition of tumor growth, with higher exposures resulting in tumor regression of BRAF mutant xenografts[1]. RG7204 (12.5, 25, and 75 mg/kg, p.o.) significantly inhibits tumor growth and induced tumor regression in mice bearing LOX tumor xenografts[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Vemurafenib (RG7204) is prepared at 10 times the final assay concentration in media containing 1% DMSO.[2]Briefly, cells are plated in 96-well microtiter plates at a density of 1,000 to 5,000 cells per well in a volume of 180 µL. For the assay, Vemurafenib (RG7204) is prepared at 10 times the final assay concentration in media containing 1% DMSO. Twenty-four hours after cell plating, 20 µL of the appropriate dilution are added to plates in duplicate. The plates are assayed for proliferation 6 days after the cells are plated according to the procedure. **Animal Administration:** Vemurafenib is dissolved in an aqueous vehicle containing 2% Klucel LF.[2] Athymic nude mice, are with ages 13 to 14 weeks, and weighing approximately 23 to 25 g. For the LOX xenografts, 2×10^6 cells in 0.2 mL of PBS are injected s.c. into the right lateral flank. Vemurafenib (RG7204), formulated as MBP, is suspended at the desired concentration as needed for each dose group in an aqueous vehicle containing 2% Klucel LF and adjusted to pH 4 with dilute HCl. NSC 362856 is of 250-mg capsules. Capsules are opened and combined into one bulk supply. To prepare the stock dosing material, NSC 362856 is first dissolved in 100% DMSO followed by dilution with saline to form a final milky white suspension in 10% DMSO/90% saline (pH 3.4).

References:

[1]. Bollag G, et al. Clinical efficacy of a RAF inhibitor needs broad target blockade in BRAF-mutant melanoma. Nature, 2010, 467(7315), 596-599.

[2]. Yang H, et al. RG7204 (PLX4032), a selective BRAFV600E inhibitor, displays potent antitumor activity in preclinical melanoma models. Cancer Res, 2010, 70(13), 5518-5527.

[3]. Prahallad A, et al. Unresponsiveness of colon cancer to BRAF(V600E) inhibition through feedback activation of EGFR. Nature, 2012, 483(7387), 100-103.

[4]. Shelledy L, et al. Vemurafenib: First-in-Class BRAF-Mutated Inhibitor for the Treatment of Unresectable or MetastaticMelanoma. J Adv Pract Oncol. 2015 Jul-Aug;6(4):361-5.

CAIndexNames:

1-Propanesulfonamide, N-[3-[[5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl]carbonyl]-2,4-difluorophenyl]-

SMILES:

FC1=CC=C(C(F)=C1C(C2=CNC3=NC=C(C=C32)C4=CC=C(C=C4)Cl)=O)NS(CCC)(=O)=O

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