For Research Use Only

Refametinib

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Catalog Number: CM05069

产品信息

Catalog Number:
CM05069

CAS号:
923032-37-5

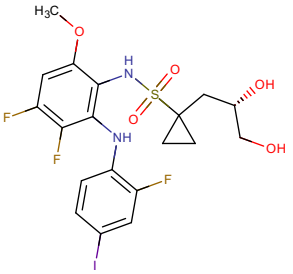
分子式:
$C_{19}H_{20}F_3IN_2O_5S$

主要靶点:
MEK

主要通路:
MAPK信号通路

分子量:
572.34

溶解度:
H2O:<1 mg/mL,Ethanol:93 mg/mL (162.5 mM),DMSO:93 mg/mL (162.5 mM)



靶点活性

MEK1:19 nM|MEK2:47 nM

体外活性

RDEA119 is selectively bound directly to an allosteric pocket in the MEK1/2 enzymes, and highly efficacious at inhibiting cell proliferation in several tumor cell lines, including A375, SK-MEI-28, Colo205, HT-29 and BxPC3. RDEA119 inhibits anchorage-dependent growth of human cancer cell lines harboring the gain-of-function V600E BRAF mutant with GI50 values ranging from 67 to 89 nM. Under anchorage-independent conditions, GI50 values for all cell lines tested are similar (40-84 nM). RDEA119 shows a tissue selectivity that reduces its potential for central nervous system–related side effects. [1] RDEA119 potently inhibits the proliferation of the 4 cell lines that harbored BRAF mutation but has no or modest effects on the other 4 cells that harbored wild-type BRAF (IC50 of 0.034-0.217 μM vs. 1.413-34.120 μM). This inhibitory effect of RDEA119 in selected cell lines OCUT1 (BRAF V600E(+), PIK3CA H1047R(+)) and SW1376 (BRAF V600E(+)) is enhanced by combination with the mTOR inhibitor, temsirolimus. RDEA119 and temsirolimus also show synergistic effects on autophagic death of OCUT1 and KAT18 cells selectively tested. [2]

体内活性

Oral administration of RDEA119 at 50 mg/kg on a once daily x 14 schedule leads to a 68% tumor growth inhibition (TGI) in human melanoma A375 tumor model. Oral administration of RDEA119 at 25 mg/kg on a once a once daily x 14 schedule leads to a 123% TGI in human colon carcinoma Colo205 tumor model (TGI > 100% occurs when the tumor shrinks below its starting volume). A dose of 25 mg/kg once daily x 14 produces 56% and 67% TGI for HT-29 and A431 tumors, respectively. [1]

细胞实验

For anchorage-dependent growth inhibition experiments, cells are plated in white 384-well plates at 1,000/20 μL/well or white 96-well microplates at 4,000/100 μL/well. After 24-h incubation at 37 °C, 5% CO2, and 100% humidity, RDEA119 is incubated for 48 hours at 37 °C and assayed using CellTiter-Glo. For the 96-well anchorage-independent growth assay, wells of an "ultralow binding" plate (Corning) are filled with 60 μL of a 0.15% agarose solution in complete RPMI 1640. Then, 60 μL of complete RPMI 1640 containing 9,000 cells in 0.15% agarose are added per well. After 24 hour, 60 μL of a 3 × drug solution in agarose-free complete RPMI 1640 are added. After 7 d, 36 μL of 6 × 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)- 2H-tetrazolium, inner salt reagent are added per well. After 2 hours at 37 °C, absorbance at 490 nm is determined on the M5 plate reader. (Only for Reference)

描述

Refametinib (RDEA119, Bay 86-9766) is an effective, ATP non-competitive and specific inhibitor of MEK1/2 (IC50: 19/47 nM).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years