For Research Use Only

EAI045

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Catalog Number: CM03906

产品信息

Catalog Number:
CM03906

CAS号:
1942114-09-1

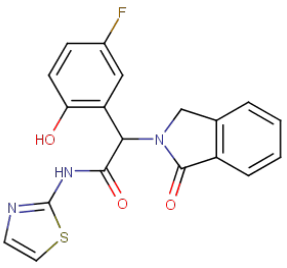
分子式:
$C_{19}H_{14}FN_3O_3S$

主要靶点:
EGFR

主要通路:
JAK/STAT信号通路|蛋白酪氨酸激酶|血管生成

分子量:
383.4

溶解度:
H2O:<1 mg/mL,DMSO:71 mg/mL (185.2 mM),Ethanol:<1 mg/mL



靶点活性

EGFR:1.9 μM|EGFRT790M:0.19 μM|EGFRL858R:0.002 μM|EGFRL858R:0.019 μM

体外活性

EAI045 potently inhibits EGFR Y1173 phosphorylation in H1975 cells (half maximal effective concentration (EC50)=2 nM), but not in HaCaT cells, a keratinocyte cell line with wild-type EGFR. Despite potent inhibition of mutant EGFR, EAI045 shows no anti-proliferative effect in the H1975 and H3255 cell lines with concentrations as high as 10 μM[1]. EAI045 inhibits L858R/T790M mutant with an IC50 of 3 nM. However, EAI045 is not able to completely abolish EGFR autophosphorylation in H1975 NSCLC cell line harboring the L858R/T790M mutant. Dimerization-defective/independent mutants are markedly more sensitive to EAI045. Since EGFR dimerization is required for kinase enzyme activation, EAI045 may be active against one subunit of an EGFR heterodimer/asymmetric dimer[2].

体内活性

Mouse pharmacokinetic studies with EAI045 reveals a maximal plasma concentration of 0.57 μM, a half-life of 2.15 h, and oral bioavailability of 26% after dosing at 20 mg/kg[1]. When combined with cetuximab that blocks EGFR dimerization, EAI045 markedly reduces tumor growth in a mouse model of L858R/T790M-mutant-driven lung cancer. The mice treated alone with EAI045 do not respond. EAI045 in combination with cetuximab also induces marked tumor shrinkage in the mouse model carrying L858R/T790M/C797S, a mutant known to be resistant to all third-generation EGFR TKIs. EAI045 and cetuximab exhibits mechanistic synergy[2].

细胞实验

H1975, H3255 and HaCaT cell lines are plated in solid white 384-well plates at 500 cells per well in 10% FBS RPMI penicillin/streptomycin media. Using a Pin Tool, 50 nl of serial diluted compounds are transferred to the cells. After 3?days, cell viability is measured.(Only for Reference)

描述

EAI045, an allosteric inhibitor, targets towards drug-resistant EGFR mutants but avoids the wild-type receptor.

储存

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