For Research Use Only

Ivacaftor

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Catalog Number: CM03436

产品信息

Catalog Number:
CM03436

CAS号:
873054-44-5

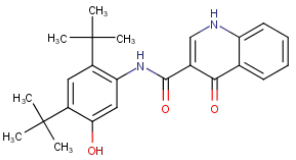
分子式:
$C_{24}H_{28}N_2O_3$

主要靶点:
Autophagy|CFTR

主要通路:
自噬|离子通道

分子量:
392.49

溶解度:
DMSO:72 mg/mL (183.4 mM),H2O: <1 mg/mL,Ethanol:<1 mg/mL



靶点活性

G551D-CFTR:100 nM(EC50, Fisher rat thyroid cells)|F508del-CFTR:25 nM(EC50, Fisher rat thyroid cells)

体外活性

VX-770 increased the forskolin-stimulated IT in temperature-corrected F508del-FRT cells by ~6-fold with an EC50 of 25 ± 5 nM. Before the addition of VX-770, the CFTR channel was exposed to maximally effective concentrations of PKA (75 nM) and ATP (1 mM). Under these conditions, 10 μM VX-770 increased the Po of G551D CFTR by ~6-fold [1]. HEK293 cells transiently expressing ABCB4-wt or the mutants were treated with 10 μmol/L of ivacaftor (VX-770), for 24 hours. Treatment with ivacaftor increased the PC secretion activity by 3-fold for ABCB4-G535D, 13.7-fold for ABCB4-G536R, 6.7-fold for ABCB4-S1076C, 9.4-fold for ABCB4-S1176L and 5.7-fold for ABCB4-G1178S [2].

体内活性

In a rat dose proportionality study, the AUC and Cmax were increased linearly after oral administration of Ivacaftor in a suspension vehicle at doses from 1 to 200 mg/kg (3, 10, 30, and 100 were the intermediate doses). A similar trend was observed in beagle dogs increasing the oral dose from 3 to 80 mg/kg (10, 30, and 60 were the intermediate doses), confirming high levels of oral absorption. The predicted human hepatic clearance of Ivacaftor using allometric scaling from four species was 4.7 mL min?1 kg?1, which is approximately 23% of hepatic blood flow [3].

动物实验

Male mouse,Sprague?Dawley rats,beagle dog,and cynomolgus monkeys (n = 3/group) were administered a single iv dose of compound formulated in dimethyl isosorbide/ethanol/PEG400/5% dextrose in water (D5W) (10%/15%/35%/40%) at the nominal dose indicated in a dose volume of 1 mL/kg.Blood samples (0.3 mL,sodium heparin anticoagulant) were collected from an indwelling carotid cannula at the following nominal time points: at predose,5,15,30,and 45 min and 1,2,4,6,8,12,24,36,and 48 h following iv administration and at predose,0.25,0.50,1,1.5,2,4,8,12,and 24 h following oral administration.The concentration of compound in the plasma samples was determined with a liquid chromatography/tandem mass spectrometry (LC/MS/MS) method,which had a lowest limit of quantitation (LLOQ) of 1 ng/mL and a linearity range between 1 and 2500 ng/mL [3].

细胞实验

HEK293 cells were seeded on poly-lysine precoated six-well plates at a density of 1.3 x 10^6 cells/well. Six hours after seeding, cells were transiently transfected with 1 μg of ABCB4-encoding plasmids using Turbofect, following the manufacturer's instructions. Twenty-four hours post-transfection, cells were washed twice with HBSS, then the medium was replaced by phenol red-free DMEM containing 0.5 mmol/L sodium taurocholate and 0.02% fatty acid–free bovine serum albumin (BSA) in the presence or absence of 10 μmol/L of ivacaftor, 50 μM/L of UDCA, and 10 μmol/L of ivacaftor plus 50 μM/L of UDCA. Media were collected after 24 hours [2].

描述

Ivacaftor (VX-770) is a potentiator of CFTR targeting G551D-CFTR (EC50: 100 nM) and F508del-CFTR (EC50: 25 nM) in Fisher rat thyroid cells, respectively.

储存

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