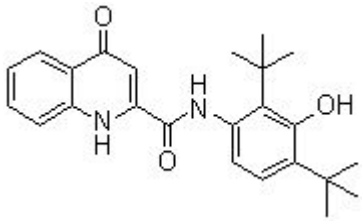
Product Introduction

Ivacaftor (VX-770)

Ivacaftor (VX-770) is a potentiator of CFTR targeting **G551D-CFTR** and **F508del-CFTR** with **EC50** of 100 nM and 25 nM, respectively.

Technical Data:

Molecular Weight (MW):	392.49	
Formula:	$C_{24}H_{28}N_2O_3$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 78 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	873054-44-5	

Biological Activity

Ivacaftor (10 μM) significantly increases the forskolin-stimulated Cl^- secretion (I_T) by ~4-fold with an EC50 of 100 nM in the recombinant Fisher rat thyroid (FRT) cells expressing G551D gating mutation of CFTR, and by ~6-fold with an EC50 of 25 nM in the recombinant cells expressing temperature-corrected F508del processing mutation of CFTR. Consistent with the increases in the forskolin-stimulated I_T, Ivacaftor (10 μM) increases the open probability (P_o) of G551D-, F508del-, and wild-type CFTR by ~6-fold, ~5-fold and ~2-fold, respectively, indicating that Ivacaftor acts directly on CFTR to increase its gating activity. In

primary cultured human CF bronchial epithelia (HBE) carrying the G551D and F508del CFTR mutations, Ivacaftor (10 μM) potently increases the forskolin-stimulated I_T by ~10-fold from 5% to a maximum level of 48% of that measured in non-CF HBE, with an EC50 of 236 nM displaying ~70-fold more potency compared with the commonly used CFTR potentiator genistein, which has an EC50 of 16 μM. In HBE with F508del homozygous CFTR, Ivacaftor causes a significant increase in the forskolin-stimulated I_T with an EC50 of 22 nM, to a less extent from 4% to 16% of non-CF HBE compared with the effect in G551D/F508del HBE. Due to CFTR potentiation, Ivacaftor inhibits excessive ENaC-mediated Na^+ and fluid absorption with an IC50 of 43 nM, and decreases the amiloride response, resulting in an increase in the surface fluid and cilia beat frequency (CBF) in G551D/F508del HBE. [1]

The first potent and orally available CFTR potentiator to enter human clinical trials.

References

[1] Van Goor F, et al. Proc Natl Acad Sci U S A, 2009, 106(44), 18825-18830.

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