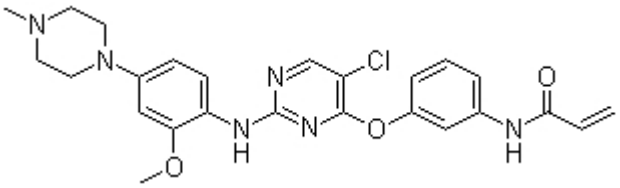
Biochempartner
瀚香生物科技

Product Introduction

WZ4002

WZ4002 is a novel, mutant-selective EGFR inhibitor for **EGFR(L858R)/(T790M)** with **IC50** of 2 nM/8 nM; does not inhibit ERBB2 phosphorylation (T798I).

Technical Data:

Molecular Weight (MW):	494.18	
Formula:	$C_{25}H_{27}ClN_6O_3$	
Solubility (25°C) *** <1 mg/ml means slightly soluble or insoluble:**	DMSO 13 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	1213269-23-8	

Biological Activity

WZ4002 inhibits other EGFR genotypes E746_A750 and E746_A750/T790M with IC50 of 2 and 6 nM. Besides, WZ4002 suppresses widetype ERBB2 with an IC50 of 32 nM. WZ4002 inhibits EGFR, AKT and ERK1/2 phosphorylation in NSCLC cell lines and WZ4002 prevents of EGFR phosphorylation in NIH-3T3 cells expressing different EGFR T790M mutant alleles. For WZ4002, kinases that exhibited greater than 95% inhibition relative to the DMSO control at 10 μM are selected for measurement of their dissociation constants. WZ4002, which possesses an ortho-methoxy group at the C2-aniline substituent, is more selective for EGFR compared to WZ3146. WZ4002 is 100-fold less effective at inhibiting phosphorylation of WT EGFR compared to the quinazoline inhibitors. Similarly, WZ4002 prevents EGFR kinase activity of

recombinant L858R/T790M protein more potently than of WT EGFR, while the opposite is observed with HKI-272 and gefitinib. [1] In addition, the phosphorylated EGFR of Src TKI-resistant H1975 cells, as well as HCC827 cells, is completely suppressed by the third generation EGFR TKI, WZ4002. [2]

In a 2-week efficacy study, WZ4002 treatment results in significant tumor regressions compared to vehicle alone in both T790M containing murine models. [1] Treatment with low-dose WZ4002, and high-dose WZ4002 leads to mean decreases in tracer uptake of 26%, and 36%, respectively. [3]

References

[1] Zhou W, et al. Nature. 2009, 462(7276), 1070-1074.

[2] Sakuma Y, et al. Lab Invest. 2012, 92(3), 371-383.

[3] Zannetti A, et al. J Nucl Med. 2012, 53(3), 443-450.

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