

Osimertinib

货号: O3922

储存条件: 粉末-20°C可保存3年; 液体-80°C可保存12月。

产品描述

EGFR (epidermal growth factor receptor) family consists of four members that belong to the ErbB lineage of proteins (ErbB1 - 4) with an external domain that binds activating ligands, such as EGF. EGFR T790M mutation is the most common mechanism of drug resistance. Osimertinib is an irreversible EGFR inhibitor which more potent to mutant-selective EGFR with IC50 values of 12.92 nM, 11.44 nM and 493.8 nM for Exon 19 deletion EGFR, L858R/T790M EGFR and WT EGFR, with a 200-fold selectivity for T790M/L858R over wild type EGFR, in LoVo cells, respectively. Osimertinib potently inhibits EGFR phosphorylation in EGFRm+ (e.g. PC9; <25nM) and EGFRm+/T790M (e.g. H1975; <25nM) cell lines in vitro, whilst demonstrating much less activity against wild-type EGFR lines (e.g. LoVo; >500nM). Consistent with that, AZD9291 showed significantly more potent inhibition of proliferation in mutant EGFR cell lines compared to wild-type in vitro. Oral administration of Osimertinib once daily at dose of 5mg/kg caused profound regression of tumors across EGFRm+ (PC9; 178% growth inhibition) and EGFRm+/T790M (H1975; 119% growth inhibition) tumor models in vivo, after 14 days dosing, and this was associated with profound inhibition of EGFR phosphorylation and key downstream signaling pathways such as AKT and ERK. Chronic long-term treatment of PC9 and H1975 xenograft tumors with Osimertinib led to a complete and sustained macroscopic response, with no visible tumors after 40 days dosing, and being maintained beyond 100 days.

作用机制

Osimertinib may bind to T790M EGFR kinase in the ATP-binding domain (such as T790M and C797S).

产品信息

CAS号	1421373-65-0	
分子式	C28H33N7O2	
分子量	499.61	
溶解度	DMSO	60.0 mg/mL (120.1 mM)
	Water	Insoluble

