

MRTX849

货号: M5249

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

KRAS is one of the most frequently mutated oncogenes in cancer. KRAS^{G12C} mutations are present in lung and colon adenocarcinoma as well as smaller fractions of other cancers. MRTX849 is a potent, selective, and covalent KRAS^{G12C} inhibitor. MRTX849 demonstrated much greater modification of KRAS^{G12C} when preloaded with GDP compared with GTP supporting that MRTX849 binds to and stabilizes the inactive GDP-bound form of KRAS^{G12C}. In the KRAS^{G12C}-mutant H358 lung and MIA PaCa-2 pancreatic cancer cell lines, MRTX849 demonstrated an upward electrophoretic mobility shift of KRAS^{G12C} protein band migration by immunoblot, indicative of covalent modification of KRAS^{G12C}. MRTX849 potently inhibited cell growth in the vast majority of KRAS^{G12C}-mutant cell lines with IC₅₀ values ranging between 10 and 973 nM in the 2D format and between 0.2 and 1042 nM in the 3D format. *In vivo*, the modified fraction of KRAS^{G12C} was 74% at 6 hours post-dose and gradually decreased to 47% by 72 hours after a single oral dose of MRTX849 at 30 mg/kg to H358 xenograft-bearing mice. To evaluate the effect of MRTX849 on KRAS-dependent signal transduction *in vivo*, a single dose of MRTX849 at 10, 30 or 100 mg/kg was administered to H358 tumor-bearing mice. Dose-dependent inhibition of ERK1/2 and pS6^{S235/36} phosphorylation was observed at 6 hours post-dose. Finally, significant, dose-dependent, anti-tumor activity was observed at the 3, 10, 30 and 100 mg/kg dose levels of MRTX849 in the MIA PaCa-2 model.

产品信息

CAS号	2326521-71-3	
分子式	C32H35ClFN7O2	
分子量	604.12	
溶解度	DMSO	100.0 mg/mL (165.5 mM)
	Water	Insoluble
	Ethanol	50.0 mg/mL(82.8 mM)

