Data Sheet (Cat.No.T7134)

TargetMol

Mavacamten

Chemical Properties

CAS No. : 1642288-47-8

Formula: C15H19N3O2

Molecular Weight: 273.33

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Mavacamten (MYK-461) is an orally bioavailable inhibitor of cardiac myosin ATPase,(IC50s of 490, 711 nM for bovine cardiac and human cardiac, respectively)
Targets(IC50)	Myosin
In vitro	MYK-461 is found to have an IC50 value of 490 nM in the bovine system, 711 nM in the human system, and 2140 nM in the rabbit system, indicating selectivity of >4-fold for cardiac myosin[1]
In vivo	MYK-461 reduces cardiac contractility, prevents left ventricular hypertrophy, and reverses pathologic remodeling. In cats, it relieves left ventricular outflow tract obstruction[2]
Animal Research	Five?cats received a combination of alfaxalone and midazolam for anesthetic induction, followed by inhaled isoflurane and oxygen maintenance.?Blood pressure was measured via an automated blood pressure cuff at five-minute intervals with supplementary continuous monitoring by arterial line when arterial access could be obtained.? Following induction of anesthesia, a complete baseline echocardiogram was performed (timepoint #1).?Cats were then treated with atropine 0.04 mg/kg IV, followed by an infusion of isoproterenol 0.04 μg/kg/min IV to elevate heart rate back to pre-anesthetized values and induce the previously observed LVOT obstruction.?After five to seven minutes, a stable heart rate of 200–220 bpm was reached and a complete echocardiogram was performed (timepoint #2).?At the completion of imaging, a ten-minute intravenous infusion of MYK-461 (n = 5) at 0.3 mg/kg/hr IV was started.?Focused echocardiography was performed after five minutes (timepoint #3).?After ten minutes, the MYK-461 infusion rate was lowered to 0.12 mg/kg/hr IV, a blood sample was drawn and an echocardiogram performed (timepoint #4).?If ventricular function remained hypercontractile or within normal limits by visual inspection, another blood sample was obtained and the MYK-461infusion rate was increased to 0.36 mg/kg/hr IV for ten minutes.?Focused echocardiography was performed after five minutes (timepoint #5).? After ten minutes, the MYK-461 infusion rate was lowered to 0.15 mg/kg/hr IV, a blood sample was drawn and an echocardiogram performed (timepoint #6).?Following imaging, the isoproterenol infusion was discontinued.?When heart rate returned to baseline levels (five to seven minutes), a complete echocardiogram was performed on MYK-461 alone (timepoint #7).?Study drug was then discontinued, and animals were awakened, extubated and moved to recovery.?Three of five cats were available to return

Animal Research	for a control arm of this experiment after a 6-week washout period.The experiment was completed with identical methodology with the exception that MYK-461 was substituted for vehicle (control) at matched volumes/infusion rates[2].

Solubility Information

Solubility	DMSO: 62.5 mg/mL (228.66 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (7.32 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.6586 mL	18.2929 mL	36.5858 mL
5 mM	0.7317 mL	3.6586 mL	7.3172 mL
10 mM	0.3659 mL	1.8293 mL	3.6586 mL
50 mM	0.0732 mL	0.3659 mL	0.7317 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Kawas R F , Anderson R L , Ingle S R B , et al. A small molecule modulator of cardiac myosin acts on multiple stages of the myosin chemomechanical cycle[J]. Journal of Biological Chemistry, 2017, 292(40):jbc.M117.776815.
Stern J A , Markova S , Ueda Y , et al. A Small Molecule Inhibitor of Sarcomere Contractility Acutely Relieves Left Ventricular Outflow Tract Obstruction in Feline Hypertrophic Cardiomyopathy[J]. Plos One, 2016, 11(12):e0168407.

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