Tizaterkib

Cat. No.: HY-111483

CAS No.: 2097416-76-5

Molecular Formula: $C_{24}H_{24}F_2N_8O_2$

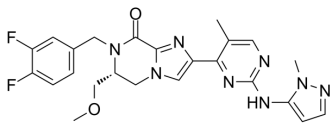
Molecular Weight: 494.5

Target: ERK

Pathway: MAPK/ERK Pathway; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (202.22 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0222 mL	10.1112 mL	20.2224 mL
5 mM	0.4044 mL	2.0222 mL	4.0445 mL
10 mM	0.2022 mL	1.0111 mL	2.0222 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.21 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tizaterkib (AZD0364) is a potent and selective ERK2 inhibitor extracted from patent WO2017080979A1, compound example 18, has an IC_{50} of 0.6 nM.

IC_{50} & Target

ERK2

0.6 nM (IC_{50})

In Vitro	Tizaterkib is measured in the ERK2 mass spectrometry and A375 phospho-p90RSK assays with IC_{50}s of 0.6 nM and 5.7 nM, respectively. Tizaterkib can inhibit the growth of a panel of cancer cell lines (A549, H2122, H2009, and Calu6 cell lines) with KRAS mutations as a monotherapy and this effect is synergistically enhanced by treatment with Selumetinib[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tumor growth inhibition by Tizaterkib ethanesulfonic acid (Example 18a) in combination with MEK inhibitor Selumetinib is measured. Studies are performed in the A549 xenograft model. Selumetinib is dosed twice daily (BiD) 8 hours apart and Tizaterkib ethanesulfonic acid is dosed once daily (QD) 4 hours after the first Selumetinib dose. Both compounds are dosed continuously for 3 weeks. Both vehicles are dosed in the vehicle group. Both Selumetinib and Tizaterkib ethanesulfonic acid reduce tumor growth relative to vehicle only control. The combination of Selumetinib and Tizaterkib ethanesulfonic acid results in a reduction in tumor growth[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	KRAS-mutant Non-Small Cell Lung Cancer (NSCLC) A549, H2122, H2009, and Calu6 cell lines are seeded in 384-well black, clear bottomed plates, cultured for 18-24 hours and treated with increasing concentrations of AZD-0364 (7.143 nM, 61 nM, 357 nM, 2.143 μM and 10 μM) and Selumetinib (0-10 μM) in a 6×6 dosing matrix. Cells are seeded at a concentration such that cells in untreated wells are approximately 80% confluent at the end of the assay. After 3 days of treatment, live cell number is determined using a Sytox Green endpoint[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] A549 is a human non small cell lung cancer line carrying an oncogenic mutation in the KRAS gene (G12S). Female nude mice are implanted subcutaneously (s.c.) on the left flank, with 5×10^6 A549 cells (ATCC) per mouse.Tumor growth is monitored by twice weekly calliper measurement and volumes are calculated. Once tumors have reached a volume of ~200-300mm^3 animals are randomised into groups of 7-11 and are treated with a continuous combination schedule of Selumetinib (ARRY-142886) 25 mg/kg BiD and AZD-0364 ethanesulfonic acid 25 mg/kg QD (four hours after first Selumetinib dose), both are dosed by peroral route. Tumor volumes are measured twice weekly after dosing commenced[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Vet Microbiol. 2021, 109061.

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REFERENCES

[1]. WARD, Richard, Andrew, et al. DIHYDROIMIDAZOPYRAZINONE DERIVATIVES USEFUL IN THE TREATMENT OF CANCER. WO2017080979A1.

Caution: Product has not been fully validated for medical applications. For research use only.

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