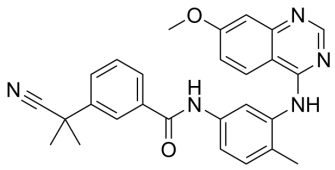
AZ304

Cat. No.:	HY-117273
CAS No.:	942507-42-8
Molecular Formula:	$C_{27}H_{25}N_5O_2$
Molecular Weight:	451.52
Target:	Raf; Autophagy
Pathway:	MAPK/ERK Pathway; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (276.84 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.2147 mL	11.0737 mL	22.1474 mL
5 mM	0.4429 mL	2.2147 mL	4.4295 mL
10 mM	0.2215 mL	1.1074 mL	2.2147 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 (4.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.61 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AZ304 is an ATP-competitive dual BRAF kinase inhibitor, potently inhibits wild type BRAF, V600E mutant BRAF and wild type CRAF, with IC_{50}s of 79 nM, 38 nM and 68 nM, respectively. AZ304 also has significant effect on other kinases, such as p38 (IC_{50}, 6 nM), CSF1R (IC_{50}, 35 nM). Anti-tumor activity[1].

IC_{50} & Target

$BRaf^{V600E}$ 38 nM (IC_{50})	$BRAF^{WT}$ 79 nM (IC_{50})	CRAF 68 nM (IC_{50})	p38 6 nM (IC_{50})
CSF1R	MAP3K7	CSK	

	35 nM (IC_{50})	6400 nM (IC_{50})	7050 nM (IC_{50})

In Vitro

AZ304 (1 nM-100 μM) potently reduces ERK phosphorylation (p-ERK), with a mean EC_{50} of 65 nM in the V600E mutant BRAF containing melanoma cell line A375, and EC_{50}s of 52 nM, 60 nM in the wild type BRAF melanoma cell line SK-MEL-31 with and without EGF[1].AZ304 also potently inhibits p-p38 in both BRAF genetic statuses cell lines[1].

AZ304 (0, 0.1, 1, 10, 100 μM, 48 and 72 hours) dose-dependently inhibits the growth of RKO, HT-29, DiFi, and Caco-2, with GI_{50}s of 4.539 μM, 3.896 μM, 4.987 μM, 1.763 μM (48 hours) and 0.5032 μM, 0.3887 μM, 0.6354 μM, 0.3772 μM (72 hours), respectively[1].

AZ304 (2 μM, 36 and 48 hours) decreases BRAF, p-ERK, p-AKT and p-mTOR levels, increases p-EGFR in both BRAF V600E mutant and BRAF wild type cells. AZ304 down-regulates p-EGFR, inhibits p-ERK, more potently suppresses BRAF, ERK, AKT and mTOR signalling pathways in combination with C225[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	RKO, HT-29, DiFi, Caco-2 cells
Concentration:	0, 0.1, 1, 10, 100 μM
Incubation Time:	48, 72 hours
Result:	Dose-dependently inhibited the growth of V600E mutant BRAF cell lines (RKO, HT-29) and wild-type BRAF cell lines (DiFi, Caco-2).

REFERENCES

[1]. Ma R, et al. AZ304, a novel dual BRAF inhibitor, exerts anti-tumour effects in colorectal cancer independently of BRAF genetic status. Br J Cancer. 2018 May;118(11):1453-1463.

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