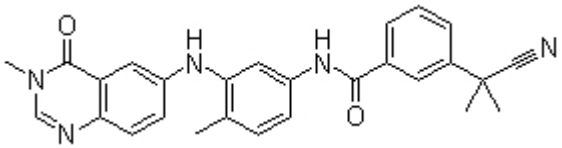
Product Introduction

AZ 628

AZ628 is a new pan-**Raf** inhibitor for BRAF, BRAFV600E, and c-Raf-1 with **IC50** of 105 nM, 34 nM and 29 nM, also inhibits VEGFR2, DDR2, Lyn, Flt1, FMS, etc.

Technical Data:

Molecular Weight (MW):	451.52	
Formula:	$C_{27}H_{25}N_5O_2$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 90 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	878739-06-1	

Biological Activity

AZ628 prevents activation of number of tyrosine protein kinases including VEGFR2, DDR2, Lyn, Flt1, FMS and others. AZ628 suppresses anchorage-dependent and -independent growth, gives rise to cell cycle arrest, and induces apoptosis in colon and melanoma cell lines harboring B-RafV600E mutation. The profile of AZ628 cross-reactivity suggests that similar to sorafenib, AZ628 may be antiangiogenic based on prevention of VEGFR2. [1] AZ628-resistant clones are approximately 100-fold more resistant to AZ628 than the parental cell line, exhibiting IC50 of approximately 10 μM, compared with 0.1 μM for the parental cell

line. Effective suppression of p-ERK1/2 levels is observed in the M14 parental cell line following treatment with increasing concentrations of AZ628. AZ628-resistant clones express elevated CRAF. Elevated CRAF expression is a potential mechanism of acquired resistance to continuous AZ628 exposure, resulting in sustained activation of ERK1/2. p-ERK1/2 activity is not significantly inhibited by exposure to AZ628 in one of these three AZ628-insensitive cell lines (Wm1552C). Unlike in the AZ628-resistant M14 cells in which AZ628 fails to suppress the activation of ERK, AZ628 treatment efficiently attenuates ERK activation in the NRAS mutant melanoma cells.[2]

References

[1] Khazak V, et al. Expert Opin Ther Targets. 2007, 11(12), 1587-1609.
[2] Montagut C, et al. Cancer Res. 2008, 68(12), 4853-4861.

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