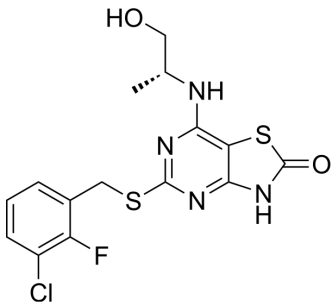
AZ10397767

Cat. No.:	HY-124056
CAS No.:	333742-63-5
Molecular Formula:	$C_{15}H_{14}ClFN_4O_2S_2$
Molecular Weight:	400.88
Target:	CXCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

AZ10397767 is an orally active, selective CXCR2 receptor antagonist with an IC_{50} of 1 nM. AZ10397767 attenuates the Oxaliplatin (HY-17371)-induced NF-κB transcriptional activity and potentiates Oxaliplatin-induced apoptosis in androgen-independent prostate cancer (AIPC) cells. AZ10397767 significantly inhibits neutrophil recruitment into tumors which then adversely affects tumor growth in vitro and in vivo[1][2][3][4].

IC_{50} & Target

CXCR2
1 nM (IC_{50})

In Vitro

AZ10397767 (20 nM; 48 h) abrogates the IL-8-induced (3 nM) increase in proliferation, reducing cell number to below basal levels[2].
AZ10397767 (20 nM; 72 h) increases Oxaliplatin (HY-17371) cytotoxicity, and potentiates Oxaliplatin-induced apoptosis in AIPC cells. AZ10397767 by itself fails to induce apoptosis in either PC3 or DU145 cells[3].
AZ10397767 (20 nM; 24 h) attenuates the Oxaliplatin-induced NF-κB transcriptional activity and the increases in mRNA transcript levels for each of the CXC-chemokines (CXCL8 and CXCL1) and antiapoptotic genes (Bcl-2 and survivin) in the PC3 and DU145 cells[3].

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

Cell Proliferation Assay[2]

Cell Line:	LNCaP cells and 22Rv1 cells
Concentration:	20 nM
Incubation Time:	48 h
Result:	Abrogated the IL-8-induced (3 nM) increase in proliferation, reducing cell number to below basal levels.

Apoptosis Analysis[3]

Cell Line:	PC3 or DU145 cells
Concentration:	20 nM
Incubation Time:	72 h

Result:	Coadministration with 0.1 or 1 μM Oxaliplatin resulted in a marked increase in the sub-G0/G1 cell population in either cell line. Potentiates Oxaliplatin-induced apoptosis in AIPC cells.

RT-PCR[3]

Cell Line:	PC3 or DU145 cells
Concentration:	20 nM
Incubation Time:	24 h
Result:	Attenuated the Oxaliplatin (1 μM)-induced NF-κB transcriptional activity and the increases in mRNA transcript levels for each of the CXC-chemokines (CXCL8 and CXCL1) and antiapoptotic genes (Bcl-2 and survivin) in the PC3 and DU145 cells.

In Vivo

AZ10397767 (100 mg/kg; Orally; twice daily; for 22 days) display reduced neutrophil infiltration accompanied with retardation in tumor growth in A549 xenograft tumors[4].
AZ10397767 (compound 30a) has a CL of 4 ml/min/kg in rat[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SCID mice with A549 cells[4]
Dosage:	100 mg/kg
Administration:	Orally; twice daily; for 22 days
Result:	Tumors were 36% smaller than their control counterparts. Significantly ($p < 0.01$) reduced the number of tumor-infiltrating neutrophils compared to mice receiving vehicle control.

REFERENCES

[1]. Iain Walters, et al. Evaluation of a series of bicyclic CXCR2 antagonists. Bioorg Med Chem Lett. 2008 Jan 15;18(2):798-803.

[2]. Angela Seaton, et al. Interleukin-8 signaling promotes androgen-independent proliferation of prostate cancer cells via induction of androgen receptor expression and activation. Carcinogenesis. 2008 Jun;29(6):1148-56.

[3]. Catherine Wilson, et al. Chemotherapy-induced CXC-chemokine/CXC-chemokine receptor signaling in metastatic prostate cancer cells confers resistance to oxaliplatin through potentiation of nuclear factor-kappaB transcription and evasion of apoptosis. J Pharmacol Exp Ther. 2008 Dec;327(3):746-59.

[4]. Simon Tazzyman, et al. Inhibition of neutrophil infiltration into A549 lung tumors in vitro and in vivo using a CXCR2-specific antagonist is associated with reduced tumor growth. Int J Cancer. 2011 Aug 15;129(4):847-58.

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