Product Data Sheet

Product Name: AZD-9574
Cat. No.: GC64099

Chemical Properties

Cas. No.	2756333-39-6		
Formula	C21H22F2N6O2	M.Wt	428.44
Solubility	DMSO : 22.22 mg/mL (51.86 mM; ultrasonic and adjust pH to 4 with HCl); DMSO : 8.33 mg/mL (19.44 mM; ultrasonic and warming and heat to 60°C)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	AZD-9574		

Protocol

Cell experiment [1]:

Cell lines	A549 (human lung carcinoma cell line, PARP1+/+/PARP2+/+), A549 PARP1-/- (isogenic knockout), A549 PARP2-/- (isogenic knockout), DLD-1 (human colorectal carcinoma cell line), DLD-1 BRCA2-/- (isogenic knockout), MDA-MB-436 (human breast cancer cell line, BRCA1 mutant), SKOV3 (human ovarian carcinoma cell line), SKOV3 BRCA2-/- (isogenic knockout), UWB1.289 (human ovarian carcinoma cell line, BRCA1 mutant), SJ-G2 (human glioblastoma cell line), GBM39 (human glioblastoma PDX cell line).

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Preparation Method	Cell lines were maintained as per standard conditions. For PARylation assays, cells were treated with AZD-9574 at increasing doses. For colony formation assays, cells were seeded and incubated overnight, then treated with a titration of AZD-9574 (0.1nM to 40μM) for 8 to 13 days. For DNA damage and cell-cycle analysis, cells were treated with AZD9574 for 72 hours, with EdU added 1 hour before fixation.
Reaction Conditions	0.1nM to 40μM; 72 hours to 13 days.
Applications	AZD-9574 demonstrated potent, selective inhibition of PARP1 (over PARP2 and other PARPs) in biochemical and cellular assays. AZD-9574 inhibited PARylation in various cell lines with single-digit nanomolar IC_{50} values. AZD-9574 induced PARP1 trapping on chromatin in a concentration-dependent manner but showed no PARP2 trapping. In HRD cancer cell lines (e.g., MDA-MB-436, DLD-1 BRCA2-/-), AZD-9574 exhibited potent anti-proliferative effects in colony formation assays, induced DNA damage (increased γH2AXSer139 foci), and caused cell-cycle arrest in the G2-M phase. Furthermore, AZD-9574 showed strong synergy with temozolomide (TMZ) in reducing cell viability in MGMT-methylated glioma cell lines (SJ-G2, GBM39).

Animal experiment [2]:

Animal models	C57BL/6 mice harboring syngeneic orthotopic H3K27M-mutant diffuse midline glioma (DMG) brainstem tumors (H3K27MPPcell line), immune competent mice

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Preparation Method	Mice were treated with RT (2Gy, days 0-2 and 4-6) in combination with AZD-9574 (3mg/kg) administered by oral gavage 1 hour before each fraction of radiation and continued for 6 consecutive days.
Dosage form	3mg/kg; oral gavage (p.o.); Once daily for 6 days.
Applications	AZD-9574 in combination with RT significantly prolonged the median survival of mice bearing H3K27M mutant DMG tumors compared to RT alone (75 days vs. 42 days). The treatment enhanced intratumoral NK cell infiltration (frequency of CD3-NK1.1+CD45+cells) and increased NK cell activity, as evidenced by a higher proportion of TNF-α+, CD107a+, and IFN-γ+ NK cells. Furthermore, the combination therapy reduced tumor-associated macrophage numbers within the tumors.

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References:
[1] Staniszewska AD, Pilger D, Gill SJ, et al. Preclinical Characterization of AZD9574, a Blood-Brain Barrier Penetrant Inhibitor of PARP1. Clin Cancer Res. 2024 Apr 1;30(7):1338-1351.
[2] Guo Y, Li Z, Parsels LA, et al. H3K27M diffuse midline glioma is homologous recombination defective and sensitized to radiotherapy and NK cell-mediated antitumor immunity by PARP inhibition. Neuro Oncol. 2025 Sep 17;27(8):2129-2146.

Background

AZD-9574 is a novel, blood-brain barrier permeable PARP1 inhibitor that selectively inhibits PARP1 at single-strand break (SSB) sites[1-2]. AZD-9574 can be used in research related to breast cancer and advanced solid malignancies[3-4].

In vitro, AZD-9574 (0.1nM–40μM) was incubated with homologous recombination repair-

deficient (HRD) cancer cells (such as MDA-MB-436, DLD-1 BRCA2-/-, and SKOV3 BRCA2-/- cells) for 72 hours to 13 days. AZD-9574 significantly inhibited cancer cell colony formation, increased γH2AX signaling, induced G2-M phase cell cycle arrest, and enhanced the synergistic anti-tumor effects of TMZ[5].

In vivo, AZD-9574 (3mg/kg/day) was orally administered to C57BL/6 mice bearing H3K27M diffuse midline glioma (using H3K27MPP cells) in combination with 2Gy radiotherapy (administered 1 hour before each radiation fraction, for 6 consecutive days). AZD-9574 significantly prolonged the overall survival of the mice and enhanced intratumoral NK cell infiltration and activation[6]. AZD-9574 (0.6–3mg/kg) was administered once daily by oral gavage for 7 consecutive days to mouse models bearing patient-derived (H3F3A K27M, TP53R248W, ATRX-deficient) or genetically engineered (H3F3A K27M; Trp53$^{-/-}$) diffuse midline glioma orthotopic xenografts. AZD-9574 significantly extended the survival of these mice and effectively inhibited the growth and recurrence of orthotopic tumors within the mouse brain[7].

References:
[1] Johannes JW, Balazs AYS, Barratt D, et al. Discovery of 6-Fluoro-5-{4-[(5-fluoro-2-methyl-3-oxo-3,4-dihydroquinoxalin-6-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide (AZD9574): A CNS-Penetrant, PARP1-Selective Inhibitor. J Med Chem. 2024 Dec 26;67(24):21717-21728.
[2] Zhou X, Chen K. Discovery of novel radioligand [18F]AZD9574 for selective imaging of PARP1 in the CNS. Acta Pharm Sin B. 2025 Oct;15(10):5489-5490.
[3] Lynce F, Lin NU. From Serendipity to Intention: Development of Brain-Penetrant PARP1-Selective Inhibitors. Clin Cancer Res. 2024 Apr 1;30(7):1217-1219.
[4] Patel JS, Zhou X, Chen J, et al. A novel 18 F-labeled brain penetrant PET ligand for imaging poly(ADP-ribose) polymerase-1. bioRxiv. 2025 Nov 3:2025.11.01.686021.
[5] Guo Y, Li Z, Parsels LA, et al. H3K27M diffuse midline glioma is homologous recombination defective and sensitized to radiotherapy and NK cell-mediated antitumor immunity by PARP inhibition. Neuro Oncol. 2025 Sep 17;27(8):2129-2146.
[6] Staniszewska AD, Pilger D, Gill SJ, et al. Preclinical Characterization of AZD9574, a Blood-Brain Barrier Penetrant Inhibitor of PARP1. Clin Cancer Res. 2024 Apr 1;30(7):1338-1351.
[7] Chen X, Zhang S, Yang L, et al. Zeaxanthin dipalmitate-enriched wolfberry extract improves vision in a mouse model of photoreceptor degeneration. PLoS One. 2024 May

20;19(5):e0302742.

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