Product Data Sheet

Product Name: Simmiparib
Cat. No.: GC67962

Chemical Properties

Cas. No.	1551355-46-4		
Formula	$C_{23}H_{18}F_4N_6O_2$	M.Wt	486.42
Solubility	DMSO : 100 mg/mL (205.58 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	Simmiparib		

Background

Simmiparib is a highly potent and orally active **PARP1** and **PARP2** inhibitor with **IC_{50}** values of 1.75 nM and 0.22 nM, respectively. Simmiparib has more potent PARP1/2 inhibition than its parent Olaparib . Simmiparib induces DNA double-strand breaks (DSB) accumulation and G2/M arrest in homologous recombination repair (HR)-deficient cells, thereby inducing **apoptosis**. Simmiparib exhibits remarkable anticancer activities in cells and nude mice bearing xenografts[1].

Simmiparib (0-10 μM; 3 days) exhibits anti-proliferative activity against various cancer cells[1].

Simmiparib (0-10 μM; 48 h) induces typical G2/M arrest in Capan-1 cells[1].

Simmiparib (0.1-2 μM; 24 h) induces apoptosis in MDA-MB-436 and V-C8 ($BRCA2^{-/-}$) cells, and increases dose-dependently the levels of γH2AX[1].

Simmiparib (1-10 μM; 48 h or 72 h) increases the phosphorylation levels of Chk1 and Chk2 and the protein levels of p-Cyclin B1 (S147), Cyclin B1, p-CDK1 (Y15) and CDK1[1].

Cell Proliferation Assay[1]

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Product Data Sheet

Cell Line:	Various cancer cells harboring deficient BRCA1, BRCA2, PTEN and EWS-FLI1
Concentration:	0-10 μM
Incubation Time:	3 days
Result:	Exhibited anti-proliferative activity against MDA-MB-436 ($BRCA1^{-/-}$), RD-ES (EWS-FLI1), DoTc2-4510 ($BRCA2^{-/-}$), Capan-1 ($BRCA2^{-/-}$) and U251 ($PTEN^{-/-}$) with IC_{50}s of 0.2 nM, 4.6 nM, 20 nM, 21 nM and 36 nM, respectively.

Cell Cycle Analysis[1]

Cell Line:	Capan-1 cells
Concentration:	0, 1, 3 and 10 μM
Incubation Time:	48 h
Result:	Induced typical G2/M arrest in a concentration-dependent manner.

Apoptosis Analysis[1]

Cell Line:	MDA-MB-436
Concentration:	0.1 and 1 μM
Incubation Time:	24 h
Result:	Led to 39.64% and 42.98% apoptosis at 0.1 and 1 μM, respectively.Increased dose-dependently the levels of γH2AX.

Apoptosis Analysis[1]

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Cell Line:	V-C8 (BRCA2$^{-/-}$)
Concentration:	0.5 and 2 μM
Incubation Time:	24 h
Result:	Caused more than 57% apoptosis.

Western Blot Analysis[1]

Cell Line:	Capan-1
Concentration:	1 and 10 μM
Incubation Time:	48 h or 72 h
Result:	Increased the phosphorylation levels of Chk1 and Chk2 but did not change the levels of the corresponding total proteins.Increased the protein levels of p-Cyclin B1 (S147), Cyclin B1, p-CDK1 (Y15) and CDK1.

Simmiparib (2, 4 and 8 mg/kg; p.o.; qd, for 14 days) inhibits the growth of tumor in V-C8 (BRCA2$^{-/-}$) and MDA-MB-436 (BRCA2$^{-/-}$) xenograft mice models[1].
Simmiparib (10 and 50 mg/kg; p.o.; qd, for 42 days) inhibits the growth of BRCA1-mutated breast cancer in xenograft mice model[1].

Animal Model:	Female BALB/cA nude mice (Subcutaneously injected with BRCA2$^{-/-}$ V-C8 cells and BRCA2$^{-/-}$ MDA-MB-436 cells)[1]
Dosage:	2, 4 and 8 mg/kg
Administration:	p.o.; qd, for 14 days

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Result:	Apparently inhibited the growth of the V-C8 tumor with an inhibition rate of 74.53% at 8 mg/kg.Suppressed the growth of the BRCA1-deficient MDA-MB-436 xenografts in a dose-dependent manner with its average inhibition rates of 64.93, 82.98 and 85.79% at 2, 4 and 8 mg/kg.Did not cause significant loss of body weight.
Animal Model:	Female BALB/cA nude mice (Subcutaneously injected with cancer cells derived from BRCA1-mutated BR-05-0028 breast cancer tissue)[1]
Dosage:	10 and 50 mg/kg
Administration:	p.o.; qd, for 42 days
Result:	Elicited dose-dependent growth inhibition with the inhibition rate of 76.73% and 93.82% at 10 mg/kg and 50 mg/kg, respectively.

[1]. Yuan B, et al. Poly(ADP-ribose)polymerase (PARP) inhibition and anticancer activity of simmiparib, a new inhibitor undergoing clinical trials. Cancer Lett. 2017 Feb 1;386:47-56.

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