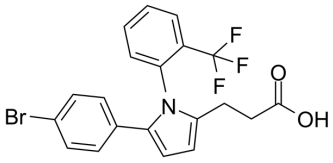
Poloppin

Cat. No.:	HY-124761
CAS No.:	683808-78-8
Molecular Formula:	$C_{20}H_{15}BrF_3NO_2$
Molecular Weight:	438.24
Target:	Polo-like Kinase (PLK); Autophagy
Pathway:	Cell Cycle/DNA Damage; Autophagy
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Poloppin is a potent, cell penetrant inhibitor of the mitotic Polo-like kinase (PLK) (IC_{50}=26.9 μM) and prevents the protein-protein interaction via the Polo-box domain (PBD) (K_d= 29.5 μM). Poloppin selectively kills cells expressing mutant KRAS, enhancing death in mitosis. Poloppin is used for the study of KRAS-mutant cancers as single agents, or in combination with c-MET inhibitors[1].

IC_{50} & Target

IC50: 26.9 μM (mitotic Polo-like kinase (PLK))
Kd: 26.9 μM (protein-protein interaction via the Polo-box domain (PBD))[1]

In Vitro

Poloppin (0-200 μM) competitively inhibits the binding of a TAMRA-labeled substrate peptide to the PLK1 PBD, exhibiting an IC_{50} value of 26.9 μM in an FP assay; the isothermal titration calorimetry of Poloppin binding to the PBD domain of PLK1 with a K_d of 29.5 μM[1].

Poloppin (0-100 μM) triggers a dose-dependent mitotic arrest and induces multiple anomalies in mitosis in cells, the EC_{50} value is 29.9 μM. In representative images of U2OS cells with 12.5 μM Poloppin, <5% of cells exhibit normal metaphase chromosome alignment, and shows bipolar or disordered spindles and non-congressed chromosomes in cells[1].

Poloppin (0-200 μM; 24 hours) inhibits SW48 isogenic parental or KRAS G12D cells growth with GI_{50} values of 13.7 μM and 5.3 μM, respectively. It inhibits KRAS wild-type p53 and KRAS MUT p53 MEFs cells with GI_{50} values of 51.1 and 49.5 μM, respectively. When the medium is added 500nM 4-OH Tamoxifen to the culture media overnight, Poloppin inhibits KRAS wild-type p53 and KRAS MUT p53 MEFs cells with GI_{50} values of 43.7 μM and 17.6 μM, respectively[1].

Poloppin (0-10 μM; 72 hours) sensitizes mutant KRAS-expressing cells to inhibitors of the c-MET tyrosine kinase. SW48 cell bearing mutant KRAS are sensitized to Poloppin after inhibition of c-MET, the GI_{50} values of Poloppin combination with Crizotinb (HY-50878) are 0.23 uM and 0.08 uM, respectively in SW48 KRAS WT and KRAS G12D cells. In the contrast, the GI_{50} values are 0.56 uM and 0.63 uM in SW48 KRAS WT or KRAS MUT cells when treated with Crizotinib alone[1].

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

Cell Viability Assay[1]

Cell Line:	SW48 isogenic parental or KRAS G12D cells
Concentration:	0-200 μM
Incubation Time:	24 hours
Result:	Inhibited cell growth expressing mutant KRAS in two-dimensional and organoid Cultures.

Cell Cytotoxicity Assay[1]

Cell Line:	SW48 isogenic parental or KRAS G12D cells
Concentration:	0-200 μM
Incubation Time:	24 hours
Result:	Selectively increased sensitization of mutant KRAS-expressing cells to inhibitors of the c-MET tyrosine kinase.

REFERENCES

[1]. Ana J Narvaez, et al. Modulating Protein-Protein Interactions of the Mitotic Polo-like Kinases to Target Mutant KRAS. Cell Chem Biol. 2017 Aug 17;24(8):1017-1028.e7.

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