Product Data Sheet

Chemical Properties

Product Name: CHIR-124  
Cas No.: 405168-58-3  
M.Wt: 419.91  
Formula: C23H22ClN5O

Chemical Name: 4-[[3S]-1-azabicyclo[2.2.2]octan-3-yl]amino]-6-chloro-3-(1,3-dihydr obenzimidazol-2-ylidene)quinolin-2-one

Canonical SMILES: C1CN2CCC1C(C2)NC3=C4C=C(CC4=NC(=O)C3=C5NC6=CC=CC=C6N 5)Cl

Solubility: Soluble in DMSO > 10 mM

Storage: Store at -20°C

General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shopping Condition: Evaluation sample solution: ship with blue ice  
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Chk
Pathways: Cell Cycle/Checkpoint >> Chk
Description: CHIR-124, a selective inhibitor, inhibits Chk1 with IC50 value of 0.3nM 2,000-fold more potently
than Chk2 with IC50 value of 0.7μM. CHIR-124 also potently targets other kinases such as PDGFR with IC50 value of 6.6nM and FLT3 with IC50 value of 5.8nM [1]. CHIR-124 abrogates the S and G2-M checkpoints induced by topoisomerase I poisons and selectively sensitizes tumors lacking p53 function to undergo mitotic death. In addition, CHIR-124 enhances the antitumor effect of irinotecan in tumor xenografts by inhibiting the G2-M checkpoint and inducing apoptosis.

In vitro, the effect of a matrix of camptothecin and CHIR-124 combinations in a number of human cancer cell lines, including breast carcinoma (MDA-MB-231 and MDA-MB-435) and colon carcinoma (SW-620 and Colo205), all of which are mutant for p53. When cells were simultaneously exposed to a matrix of different concentration combinations of CHIR-124 and SN-38 for 48 h, significant synergy or >10% deviation from additivity was observed in the concentration ranges of $\geq 4.2 \times 10^8$ mol/L for SN-38 and $\geq 6.0 \times 10^8$ mol/L for CHIR-124. Compared to IR alone, the number of mitotic cells increased dramatically in p53-/− HCT116 cells after concomitant Chir-124 exposure, while no such effect was observed in p53-sufficient WT HCT116 cells. Chir-124 was able to radiosensitize HCT116 cells that lack checkpoint kinase-2 (CHK2) or that were deficient for the spindle checkpoint protein Mad2. Additionally, Chir-124 could radiosensitize tetraploid cell lines, which were resistant to DNA damaging agents. Radiosensitization mediated by Chir-124 is greatly influenced by the p53 and cell cycle checkpoint system [1, 2].

In vivo, severe combined immunodeficient mice harboring MDA-MD-435 tumor xenografts were randomized into the treatment of 10 mg/kg CHIR-124, 20 mg/kg CHIR-124, 10 mg/kg CHIR-124 with 5 mg/kg CPT-11, or 20 mg/kg CHIR-124 with 5 mg/kg CPT-11. CPT-11 was given i.p. four times daily ×5 on days 1 to 5, while CHIR-124 was given orally four times daily ×6 on days 2 to 7 in captisol. Tumors harvested from mice sacrificed on day 4 of treatment were examined for apoptosis by terminal deoxynucleotidyl transferase-mediated nick-end labeling staining and for mitotic index by immunofluorescence labeling with phospho-histone H3 antibody in a similar study [1].

Reference:

Caution
FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will
maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.