Product Data Sheet

Product Name: CFI-400945
Cat. No.: GC13606

Chemical Properties

Cas. No.	1338800-06-8
Chemical Name	(1S,2R)-2-[3-[(1E)-2-[4-[[(2R,6S)-2,6-dimethyl-4-morpholinyl]methyl]phenyl]ethenyl]-1H-indazol-6-yl]-5'-methoxy-spiro[cyclopropane-1,3'-[^{3}H]indol]-2'(1'H)-one
SMILES	C[C@@H]1O[C@H](C)CN(CC2=CC=C(/C=C/C3=NNC4=C3C=CC([C@H]5[C@@]6(C(C=C(OC)C=C7)=C7NC6=O)C5)=C4)C=C2)C1
Formula	$C_{33}H_{34}N_4O_3$
M.Wt	534.7
Solubility	≤12mg/ml in ethanol;10mg/ml in DMSO;20mg/ml in dimethyl formamide
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	CFI-400945

Background

CFI-400945 is an orally active, potent and selective inhibitor of polo-like kinase 4.

Polo-like kinase 4 (PLK4), a unique member of the Polo-like family of kinases, shares little homology with other polo-like kinases. PLK4 plays an essential role in centriole duplication. Overexpression of PLK4 overrides the centriole licensing mechanism and results in centriole amplification with multiple procentrioles forming around each parental centriole. Depletion of PLK4 by RNAi prevents the formation of abnormal centrioles and microtubule-based structures, causing mitotic defects and in some cell lines it can induce apoptosis [2].

In an assay using recombinant human PLK4, CFI-400945 inhibited PLK4 with an IC50 value of 2.8 ± 1.4 nM in an ATP competitive manner with a Ki value of 0.26 ± 0.1 nM. CFI-400945 inhibited autophosphorylation of PLK4 at serine 305 with an EC50 value of 12.3 nM in cells overexpressing PLK4 [1]. CFI-400945 showed no significant inhibitory activity against other PLK family members (PLK1, PLK2, and PLK3 with the IC50s of > 50 μM. In transfected HCT116 cells with TRKA, TRKB, and Tie2/TEK, the EC50 values were 84 nM, 88 nM, and 117 nM, respectively. CFI-400945 inhibited the activity of AURKA and AURKB with the EC50 value of 510 nM and 102 nM. CFI-400945 (≥ 200 nM) decreased the mean centriole number in asynchronous U2OS cells [1]. CFI-400945 inhibited a panel of breast cancer cell growth with the GI50 of 14-165 nM. In mice, the maximum tolerated dose (MTD) of CFI-400945 for once-daily oral administration was estimated to be 7.5-9.5 mg/kg [1].

References:
[1] Mason J M, Lin D C C, Wei X, et al. Functional characterization of CFI-400945, a Polo-like kinase 4 inhibitor, as a potential anticancer agent[J]. Cancer Cell, 2014, 26(2): 163-176.
[2] Sillibourne J E, Bornens M. Polo-like kinase 4: the odd one out of the family[J]. Cell division, 2010, 5(1): 25.

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