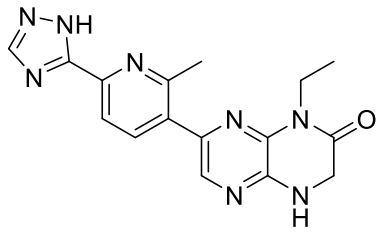
Product data sheet

MedKoo Cat#: 205829 Name: CC-115 CAS#: 1228013-15-7 (free base) Chemical Formula: $C_{16}H_{16}N_8O$ Exact Mass: 336.14471 Molecular Weight: 336.14	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

CC-115 is a dual inhibitor of DNA-dependent protein kinase (DNA-PK) and mammalian target of rapamycin (mTOR), with potential antineoplastic activity. CC-115 binds to and inhibits the activity of DNA-PK and both raptor-mTOR (TOR complex 1 or TORC1) and rictor-mTOR (TOR complex 2 or TORC2), which may lead to a reduction in cellular proliferation of cancer cells expressing DNA-PK and TOR. DNA-PK, a serine/threonine kinase and a member of the PI3K-related kinase subfamily of protein kinases, is activated upon DNA damage and plays a key role in repairing double-stranded DNA breaks via the DNA nonhomologous end joining (NHEJ) pathway.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	43.5	129.41

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.97 mL	14.87 mL	29.75 mL
5 mM	0.59 mL	2.97 mL	5.95 mL
10 mM	0.30 mL	1.49 mL	2.97 mL
50 mM	0.06 mL	0.30 mL	0.59 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Tsuji T, Sapinoso LM, Tran T, Gaffney B, Wong L, Sankar S, Raymon HK, Mortensen DS, Xu S. CC-115, a dual inhibitor of mTOR kinase and DNA-PK, blocks DNA damage repair pathways and selectively inhibits ATM-deficient cell growth in vitro. Oncotarget. 2017 Aug 18;8(43):74688-74702. doi: 10.18632/oncotarget.20342. PMID: 29088817; PMCID: PMC5650372.
2. Zheng B, Sun X, Chen XF, Chen Z, Zhu WL, Zhu H, Gu DH. Dual inhibition of DNA-PKcs and mTOR by CC-115 potently inhibits human renal cell carcinoma cell growth. Aging (Albany NY). 2020 Oct 27;12(20):20445-20456. doi: 10.18632/aging.103847. Epub 2020 Oct 27. PMID: 33109772; PMCID: PMC7655216.

In vivo study

1. Zheng B, Sun X, Chen XF, Chen Z, Zhu WL, Zhu H, Gu DH. Dual inhibition of DNA-PKcs and mTOR by CC-115 potently inhibits human renal cell carcinoma cell growth. Aging (Albany NY). 2020 Oct 27;12(20):20445-20456. doi: 10.18632/aging.103847. Epub 2020 Oct 27. PMID: 33109772; PMCID: PMC7655216.

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7. Bioactivity

Biological target:

CC-115 is a potent and dual DNA-PK and mTOR kinase inhibitor with IC50s of 13 nM and 21 nM, respectively, that blocks both mTORC1 and mTORC2 signaling.

In vitro activity

To evaluate the impact of CC-115 inhibition of mTOR kinase and DNA-PK, CC-115 was tested in vitro across a panel of 123 cancer cell lines composed of 40 lymphoma and leukemia, 22 breast cancer, 11 hepatocellular carcinoma, 11 head and neck cancer, and 39 lung cancer cell lines. CC-115 has potent growth inhibitory activity against the majority of the cancer cell lines with GI50 values ranging from 0.015 μM to 1.77 μM (Figure2A2A and Supplementary Table 2). While selective inhibitors of mTOR kinase have been reported to primarily result in cell cycle arrest without significant induction of apoptosis in solid tumor lines, in a subset of both hematological and solid tumor cell lines, CC-115 induced strong apoptosis. CC-115 also inhibited NHEJ activity in a concentration-dependent manner. Partial inhibition was observed with 0.5 μM CC-115 treatment (lane 3) and 5 μM CC-115 achieved complete inhibition (lane 4). Therefore, CC-115 prevents NHEJ by blocking autophosphorylation of DNA-PKcs and dissociation of DNA-PKcs and the ligase IV/XLF/XRCC4 complex from the dsDNA end. This study suggests the use of ATM deficiency as a patient selection strategy for CC-115 as a single agent.

Reference: Oncotarget. 2017 Sep 26; 8(43): 74688–74702. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5650372/

In vivo activity

The in vivo activity of CC-115 was tested. As described, 786-O cells were s.c. injected into the flanks of the nude mice. Xenografts were established within three weeks (tumor volumes close to 100 mm3, labeled as “Day-0”). The tumor-bearing mice were randomly assigned into three groups, receiving CC-115 or vehicle control. Results demonstrated that oral administration of CC-115, at 2 mg/kg or 5 mg/kg, significantly inhibited subcutaneous 786-O xenograft growth in nude mice (Figure 5A). The estimated daily 786-O tumor growth, calculated by (tumor volume at Day-30 subtracting tumor volume at Day-30)/30, was dramatically inhibited in CC-115-treated mice (Figure 5B). Tumors of all three groups were isolated at Day-30 and weighted (Figure 5C). Tumors with CC-115 treatment were much lighter than the vehicle-treated tumors (Figure 5C). The mouse body weights were not significantly different between the three groups (Figure 5D). Collectively, oral administration of CC-115 inhibited subcutaneous 786-O xenograft growth in mice.

Reference: Aging (Albany NY). 2020 Oct 31; 12(20): 20445–20456. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7655216/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.