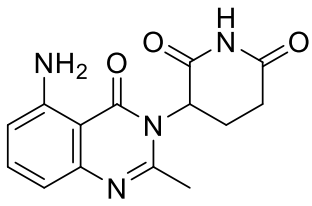
Product data sheet

MedKoo Cat#: 205830 Name: Avadomide free base CAS#: 1015474-32-4 (free base) Chemical Formula: $C_{14}H_{14}N_4O_3$ Exact Mass: 286.1066 Molecular Weight: 286.291	
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:

Avadomide, also known as CC-122, is an orally available pleiotropic pathway modulator with potential antineoplastic activity. CC-122 mimics an interferon response and has antitumor activity in DLBCL CC-122 binds Cereblon (CRBN) and promotes degradation of Aiolos and Ikaros in diffuse large B-cell lymphoma (DLBCL) and T cells in vitro, in vivo, and in patients, resulting in both cell autonomous as well as immunostimulatory effects.

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	40.11	140.10
DMSO:PBS (pH 7.2) (1:1)	0.33	1.15
DMF	30.0	104.79

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.49 mL	17.46 mL	34.93 mL
5 mM	0.70 mL	3.49 mL	6.99 mL
10 mM	0.35 mL	1.75 mL	3.49 mL
50 mM	0.07 mL	0.35 mL	0.70 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

Ioannou N, Hagner PR, Stokes M, Gandhi AK, Apollonio B, Fanous M, Papazoglou D, Sutton LA, Rosenquist R, Amini RM, Chiu H, Lopez-Girona A, Janardhanan P, Awan FT, Jones J, Kay NE, Shanafelt TD, Tallman MS, Stamatopoulos K, Patten PEM, Vardi A, Ramsay AG. Triggering interferon signaling in T cells with avadomide sensitizes CLL to anti-PD-L1/PD-1 immunotherapy. Blood. 2021 Jan 14;137(2):216-231. doi: 10.1182/blood.2020006073. PMID: 33024998; PMCID: PMC7820876.

In vivo study

Ioannou N, Hagner PR, Stokes M, Gandhi AK, Apollonio B, Fanous M, Papazoglou D, Sutton LA, Rosenquist R, Amini RM, Chiu H, Lopez-Girona A, Janardhanan P, Awan FT, Jones J, Kay NE, Shanafelt TD, Tallman MS, Stamatopoulos K, Patten PEM, Vardi A, Ramsay AG. Triggering interferon signaling in T cells with avadomide sensitizes CLL to anti-PD-L1/PD-1 immunotherapy. Blood. 2021 Jan 14;137(2):216-231. doi: 10.1182/blood.2020006073. PMID: 33024998; PMCID: PMC7820876.

7. Bioactivity

Product data sheet

Biological target:

Avadomide (CC 122) is an orally active cereblon modulator.

In vitro activity

Antibody arrays revealed that avadomide, as well as its combination with anti-PD-1, induced the secretion of several proinflammatory (IL-2, tumor necrosis factor-α) and chemotactic cytokines (CXCL10, CCL5) (Figure 5A-B). In contrast, anti-PD-1 alone had little effect on the production of cytokines from xenografted patient T cells. Multiplex immunoassays confirmed the consistent enrichment of immunoregulatory and chemoattractant cytokines including CXCL10 within the culture supernatants of T cells treated with avadomide alone or in combination with anti-PD-1 or anti-PD-L1 (including significantly increased CXCL10 production with combination therapy compared with avadomide alone) (Figure 5C). Time-lapse microscopy assays showed that avadomide, as well as anti-PD-1 or anti-PD-L1 alone, enhanced T-cell motility compared with vehicle treatment (Figure 5D). However, compared with these drugs alone, avadomide plus anti-PD-1 or anti-PD-L1 increased T-cell migration rates. The conditioned media of avadomide-treated T cells increased the recruitment of T cells, which was further enhanced when avadomide was paired with PD-L1/PD-1 blockade (Figure 5E). This augmented T-cell migration was reduced by cotreating xenografted patient T cells with a neutralizing antibody targeting CXCR3, the receptor for CXCL9-11 (Figure 5F). Collectively, data suggest that the ability of avadomide to activate IFN-activated chemokine and cytoskeletal signaling in patient T cells could enhance the recruitment and functionality of immune cells in the TME.

Reference: Blood. 2021 Jan 14; 137(2): 216–231. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7820876/

In vivo activity

Mice with established tumors (3 weeks after xenografting) were treated with a single dose of avadomide or anti-PD-L1 alone or in combination for 6 days. The splenic TME, the percentage of CD25+ CD8+ T cells increased following avadomide and combination anti-PD-L1 therapy (Figure 6A). In contrast, this stimulatory effect was less evident in the patient CD4+ T-cell compartment (supplemental Figure 6A). Notably, avadomide therapy increased the frequency of PD-L1+ CD8+ T cells and CLL cells (Figure 6B; supplemental Figure 6C), whereas expression of PD-1 did not change (supplemental Figure 6B). Confocal microscopy corroborated the ability of avadomide to induce PD-L1 expression within the immune TME (Figure 6C) and triggered CD8+ T cells to increase in number and infiltrate tumor areas more vigorously (Figure 6D). CD4+ T cells localized mainly within CLL nodules at baseline (vehicle) intermixed with tumor cells, in keeping with their pro-tumor role. In contrast, CD8+ T cells exhibited a tumor-excluded localization pattern at baseline that converted to a tumor-infiltrated pattern following avadomide treatment, maximally augmented with combination therapy.

Reference: Blood. 2021 Jan 14; 137(2): 216–231. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7820876/

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.