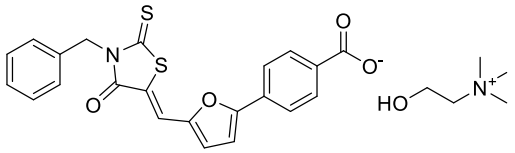
Product data sheet

MedKoo Cat#: 408039 Name: ADH-503 CAS#: 2055362-74-6 (choline) Chemical Formula: $C_{27}H_{28}N_2O_5S_2$ Molecular Weight: 524.65	
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:

ADH-503 is a potent agonist of the integrin CD11b to mitigate myeloid cell immunosuppression. The partial activation of CD11b by ADH-503 leads to the repolarization of tumor-associated macrophages, reduction in the number of tumor-infiltrating immunosuppressive myeloid cells, and enhanced dendritic cell responses. These actions, in turn, improve antitumor T cell immunity and render checkpoint inhibitors effective in previously unresponsive PDAC models.

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	21.43	40.85

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.91 mL	9.53 mL	19.06 mL
5 mM	0.38 mL	1.91 mL	3.81 mL
10 mM	0.19 mL	0.95 mL	1.91 mL
50 mM	0.04 mL	0.19 mL	0.38 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

Panni RZ, Herndon JM, Zuo C, Hegde S, Hogg GD, Knolhoff BL, Breden MA, Li X, Krisnawan VE, Khan SQ, Schwarz JK, Rogers BE, Fields RC, Hawkins WG, Gupta V, DeNardo DG. Agonism of CD11b reprograms innate immunity to sensitize pancreatic cancer to immunotherapies. Sci Transl Med. 2019 Jul 3;11(499):eaau9240. doi: 10.1126/scitranslmed.aau9240. PMID: 31270275; PMCID: PMC7197026.

In vivo study

Panni RZ, Herndon JM, Zuo C, Hegde S, Hogg GD, Knolhoff BL, Breden MA, Li X, Krisnawan VE, Khan SQ, Schwarz JK, Rogers BE, Fields RC, Hawkins WG, Gupta V, DeNardo DG. Agonism of CD11b reprograms innate immunity to sensitize pancreatic cancer to immunotherapies. Sci Transl Med. 2019 Jul 3;11(499):eaau9240. doi: 10.1126/scitranslmed.aau9240. PMID: 31270275; PMCID: PMC7197026.

7. Bioactivity

Biological target:

ADH-503 ((Z)-Leukadherin-1 choline) is an orally active and allosteric CD11b agonist.

In vitro activity

Product data sheet

To examine the direct effects of ADH-503 on the responses of macrophages to tumor-derived factors, this study treated bone marrow-derived macrophages with conditioned medium from KPC-derived PDAC cells in the presence or absence of ADH-503, and then examined the gene expression levels of key cytokines by Q-PCR and RNA sequencing (RNA-seq). RNA-seq analysis showed that greater than 8000 RNAs were changes by 2 fold within 6 hours of ADH-503 exposure (Fig. 2F). Ontological analyses of these gene sets showed key changes in genes involved in antigen presentation and processing, lysosomal trafficking, phagocytosis and interleukin (IL)-8 signaling (Fig. 2G). Further analyses of these data also show that ADH-503 rapidly decreased the genes involved in IL-1 signaling, increased the expression of cytokines involved in T cell and DC trafficking, and reduced the regulatory T cell recruitment of cytokines CCL17 and 22 (Fig. 2H). Results from a parallel Q-PCR analysis in a second experiment revealed that ADH-503 down-regulated TGFβ1, IL1α, and IL1β, and reduced the levels of alternative activation markers Arg1, YM1, and Retnlα, while upregulating type I interferons (IFNα1 and β) and T cell recruitment factors (CXCL9, 10, and 11, Fig. 2I). Taken together, these data suggest that ADH-503 results in the repolarization of macrophages towards a phenotype that could support anti-tumor T cell responses.

Reference: Sci Transl Med. 2019 Jul 3; 11(499): eaau9240. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7197026/

In vivo activity

To determine whether CD11b agonism can improve anti-tumor immunity, this study explored changes in tumor T cell infiltration and phenotype in two orthotopic PDAC models and in KPC mice. This study analyzed tumor-infiltrating T cells and found that ADH-503 treatment resulted in increased numbers of total $CD8^+$ cytotoxic T lymphocytes (CTLs) and $CD4^+$ T effectors (Figs. 4A–D and S4A). In addition to increasing T cell frequency, ADH-503 also increased $CD8^+$ CTL and $CD4^+$ effector cell proliferation ($Ki67^+$ $CD8^+$ CTLs) and activation ($CD44^{Hi}$ $CD62L^{neg}$) (Fig. 4A–D). In contrast, this study found reduced numbers of $FOXP3^+$ regulatory T cells (T_{reg}) and a better $CD8^+$ CTL to T_{reg} ratio in PDAC tissues from ADH-503-treated mice (Figs. 4B and S4A–B). This study found that although the distribution of $CD8^+$ T cells was not markedly changed over distances of 30–150 μm, the number and frequency of $CD8^+$ T cells in close proximity to PDAC cells were changed by ADH-503 treatment (Fig. 4E). In vehicle-treated mice, $CD8^+$ T cells were in very limited numbers at distances of less than 25 μm, with nearly no CTLs at distances <10 μm. In contrast, ADH-503 treatment significantly increased the number of $CD8^+$ CTLs in direct contact (< 5 μm) and in close proximity (< 25 μm) to $CK19^+$ PDAC cells.

Reference: Sci Transl Med. 2019 Jul 3; 11(499): eaau9240. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7197026/