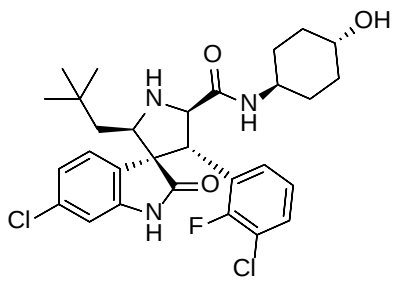
Product data sheet

MedKoo Cat#: 206069 Name: MI-773 CAS: 1303607-07-9 Chemical Formula: $C_{29}H_{34}Cl_2FN_3O_3$ Exact Mass: 561.1961 Molecular Weight: 562.5074	
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:
MI-773 is a new small molecule inhibitor of the MDM2-p53 interaction, binds to MDM2 with high affinity (Ki=0.88 nM) and blocks the p53-MDM2 interaction. MI-773 is an isomer of MI-77301 (SAR405838).

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	53.0	94.22

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.78 mL	8.89 mL	17.78 mL
5 mM	0.36 mL	1.78 mL	3.56 mL
10 mM	0.18 mL	0.89 mL	1.78 mL
50 mM	0.04 mL	0.18 mL	0.36 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. Vuaroqueaux V, Hendriks HR, Al-Hasani H, Peille AL, Das S, Fiebig HH. Pharmacogenomics characterization of the MDM2 inhibitor MI-773 reveals candidate tumours and predictive biomarkers. NPJ Precis Oncol. 2021 Oct 28;5(1):96. doi: 10.1038/s41698-021-00235-7. PMID: 34711913; PMCID: PMC8553758.
2. Chen YL, Zhang ZM, Li XL, Tao YF, Wu SY, Fang F, Xie Y, Liao XM, Li G, Wu D, Wang HR, Zuo R, Cao HB, Pan JJ, Yu JJ, Zhang Z, Chu XR, Zhang YP, Feng CX, Wang JW, Lu J, Hu SY, Li ZH, Pan J. MI-773, a breaker of the MDM2/p53 axis, exhibits anticancer effects in neuroblastoma via downregulation of INSM1. Oncol Lett. 2021 Dec;22(6):838. doi: 10.3892/ol.2021.13099. Epub 2021 Oct 18. PMID: 34712362; PMCID: PMC8548782.

In vivo study

1. Andrews A, Warner K, Rodriguez-Ramirez C, Pearson AT, Nör F, Zhang Z, Kerk S, Kulkarni A, Helman JI, Brenner JC, Wicha MS, Wang S, Nör JE. Ablation of Cancer Stem Cells by Therapeutic Inhibition of the MDM2-p53 Interaction in Mucoepidermoid Carcinoma. Clin Cancer Res. 2019 Mar 1;25(5):1588-1600. doi: 10.1158/1078-0432.CCR-17-2730. Epub 2018 Nov 29. PMID: 30498096; PMCID: PMC6397688.
2. Warner KA, Nör F, Acasigua GA, Martins MD, Zhang Z, McLean SA, Spector ME, Chepeha DB, Helman J, Wick MJ, Moskaluk CA, Castilho RM, Pearson AT, Wang S, Nör JE. Targeting MDM2 for Treatment of Adenoid Cystic Carcinoma. Clin Cancer Res. 2016 Jul 15;22(14):3550-9. doi: 10.1158/1078-0432.CCR-15-1698. Epub 2016 Mar 2. PMID: 26936915; PMCID: PMC4947417.

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7. Bioactivity

Biological target:

MI-773 is a potent MDM2-p53 protein-protein interaction (PPI) inhibitor with high binding affinity against MDM2 (K_d=8.2 nM).

In vitro activity

The molecular mechanisms by which MI-773 exerted its effects were investigated using a microarray. The results showed that disturbance of the MDM2/p53 axis by MI-773 resulted in potent suppression of proliferation, induction of apoptosis and cell cycle arrest in NB cells. In addition, microarray analysis showed that MI-773 led to significant downregulation of genes involved in the G2/M phase checkpoint and upregulation of hallmark gene associated with the p53 pathway.

Reference: Oncol Lett. 2021 Dec;22(6):838. https://pubmed.ncbi.nlm.nih.gov/34712362/

In vivo activity

To evaluate the anti-tumor effect of MI-773, this study administered it to mice harboring three different patient-derived xenograft (PDX) models of ACC expressing functional p53. Single-agent MI-773 caused tumor regression in the 3 PDX models of ACC studied here. The number of p53-positive cells was increased in MI-773-treated PDX tumors ($P < 0.001$), with a correspondent shift in p53 localization from the nucleus to the cytoplasm.

Reference: Clin Cancer Res. 2016 Jul 15;22(14):3550-9. https://pubmed.ncbi.nlm.nih.gov/26936915/

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.