

Product Data Sheet

Product Name: MI-773
Cat. No.: GC16296

Chemical Properties

Cas. No. 1303607-07-9

Chemical Name (2'R,3S,4'S,5'R,Z)-6-chloro-4'-(3-chloro-2-fluorophenyl)-2-hydroxy-N-((1r,4R)-4-hydroxy cyclohexyl)-2'-neopentylspiro[indole-3,3'-pyrrolidine]-5'-carbimidic acid

SMILES CC(C)(C[C@](N1)([H])[C@@]([C@@]([C@]1([H])/C(O)=N/[C@]2([H])CC[C@](O)([H])C C2)([H])C3=C(F)C(Cl)=CC=C3)(C(O)=N4)C5=C4C=C(Cl)C=C5)C

Formula C₂₉H₃₄Cl₂FN₃O₃

M.Wt 562.5

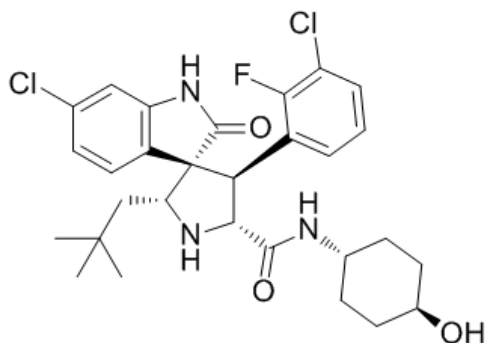
Solubility Soluble in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell experiment: Sulforhodamine B or the WST-1 cytotoxicity assay are performed to determine the effect of MI-773 on ACC cell viability. Briefly, 1 to 3×10³ UM-HACC cells are plated per well, and treated with 0 to 40 µM MI-773 for 24 to 96 hours. To assess apoptosis, 2×10⁵ cells are plated in 60 mm³ dishes, attached overnight, and treated with 0 to 20 µM MI-773 for 72 hours. Cells are lysed with a hypotonic buffer and stained with propidium iodide. Primary low passage ACC cells (UM-HACC-5) are stably transduced with lentiviral vectors expressing shRNA-p53 or scrambled sequence control shRNA-C and selected with 1.0 µg/mL puromycin[1].

Animal experiment: Mice[1] To establish a patient-derived xenograft (PDX) model of ACC, human tumor fragments from the UM-HACC-5 patient are transplanted subcutaneously into the dorsal region of male severe combined immunodeficient (SCID) mice (CB.17.SCID). Two of six initial patient tumor fragments transplant, grow, and are retransplanted in vivo into new male or female mice for up to 12 passages. When tumors reach an average of 250 mm³, mice are randomized into groups and received either vehicle (polyethylene glycol-200 + D-α-tocopherol polyethylene glycol 1000 succinate), or treatment with 10, 50, or 100 mg/kg MI-773 daily by oral gavage. The ACCx6 and ACCx9 models are treated with vehicle or 100 mg/kg MI-773.

References:

- [1]. Warner KA, et al. Targeting MDM2 for Treatment of Adenoid Cystic Carcinoma. Clin Cancer Res. 2016 Jul 15;22(14):3550-9.
[2]. Zhang Q, et al. Targeting p53-MDM2-MDMX loop for cancer therapy. Subcell Biochem. 2014;85:281-319.

Background

MI-773 is a small molecule inhibitor of MDM2 with IC₅₀ value of 62nM [1].

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

MI-773 is a small molecule MDM2 antagonist. It is a spirooxindole derivative. MI-773 shows a high MDM2 affinity with IC₅₀ value of 62nM in the FP competitive binding experiment. In the in vitro cell-based assay, MI-773 shows a similar inhibition efficacy with its enantiomer MI-77301. The GI₅₀ values are 58nM and 33nM for MI-773 and MI-77301, respectively. Both MI-773 and MI-77301 exert considerable activity at dose of 100 mg/kg in mouse xenograft models of osteosarcoma, prostate cancer, colorectal cancer, leukemia or melanoma. Currently, an international and multicenter phase I trial of MI-773 is underway for patients with liposarcomas and other p53-wild-type tumors [1, 2].

References:

- [1] Zak K, Pecak A, Rys B, Wladyka B, Dömling A, Weber L, Holak TA, Dubin G. Mdm2 and MdmX inhibitors for the treatment of cancer: a patent review (2011-present). *Expert Opin Ther Pat.* 2013 Apr;23(4):425-48.
- [2] Shoushtari AN, Van Tine BA, Schwartz GK. Novel treatment targets in sarcoma: more than just the GIST. *Am Soc Clin Oncol Educ Book.* 2014:e488-95.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA