

Product Data Sheet

Product Name: APTO-253 (LOR-253)

Cat. No.: GC32692

Chemical Properties

Cas. No. 916151-99-0

SMILES CC(N1)=C(C(N2)=NC3=C2C4=CC=CN=C4C5=NC=CC=C53)C6=C1C=CC(F)=C6

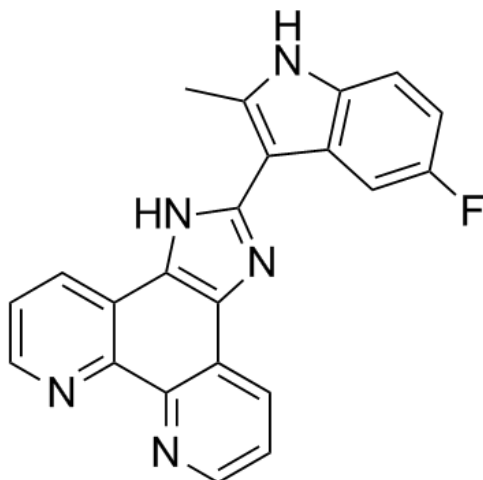
Formula $C_{22}H_{14}FN_5$ M.Wt 367.38

Solubility DMSO : 33.33 mg/mL (90.72 mM); Water : < 0.1 mg/mL (insoluble) 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

Cell experiment [1]:

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Cell lines	AML and lymphoma cell lines, including MV4-11, EOL-1, and KG-1 cells
Preparation Method	Cells were seeded in 96-well plates and treated with DMSO vehicle or a 10-point concentration series of APTO-253 (LOR-253). Cell viability was measured using the CellTiter 96 AQueous One Solution (MTS) assay, and IC ₅₀ values were calculated using GraphPad Prism 7.
Reaction Conditions	1nM-100μM; 5 days
Applications	APTO-253 (LOR-253) inhibited proliferation of AML and lymphoma cell lines with IC ₅₀ values of 57nM-1.75μM.
Animal experiment [2]:	
Animal models	Collagen-induced arthritis in 6-week-old male DBA/1J mice
Preparation Method	Treatment was initiated after arthritis onset. The APTO-253 (LOR-253) group received intravenous dosing, and controls received vehicle. Arthritis severity scores were recorded, and hind paws were collected at endpoint to assess inflammation, pannus, cartilage damage, and bone erosion.
Dosage form	15mg/kg; intravenous injection; twice daily on 2 consecutive days per week for 2 weeks
Applications	APTO-253 (LOR-253) reduced arthritis severity scores and histopathologic severity in collagen-induced arthritis mice.

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References:

- [1] Local A, Zhang H, Benbatoul KD, Folger P, Sheng X, Tsai CY, et al. APTO-253 stabilizes G-quadruplex DNA, inhibits MYC expression, and induces DNA damage in acute myeloid leukemia cells. *Mol Cancer Ther.* 2018;17(6):1177-1186. doi:10.1158/1535-7163.MCT-17-1209.
- [2] Tsuchiya H, Ota M, Sumitomo S, Ishigaki K, Suzuki A, Sakata T, et al. Parsing multiomics landscape of activated synovial fibroblasts highlights drug targets linked to genetic risk of rheumatoid arthritis. *Ann Rheum Dis.* 2021;80(4):440-450. doi:10.1136/annrheumdis-2020-218189.

Background

APTO-253 (LOR-253) is a small-molecule inducer of Krüppel-like factor 4 (KLF4) with antiproliferative activity against acute myeloid leukemia and lymphoma cell lines, with IC₅₀ values of 57nM-1.75µM^[1]. APTO-253 (LOR-253) induces KLF4 and stabilizes G-quadruplex DNA, thereby suppressing MYC-associated transcription and promoting cell-cycle arrest, DNA-damage responses, and apoptosis^[1] [3]. APTO-253 (LOR-253) is used in research on hematologic malignancies, KLF4/NOXA-regulated apoptosis, ovarian cancer cell responses, fibroblast activation and fibrosis, inflammatory synovial biology, T-cell acute lymphoblastic leukemia, and vascular smooth-muscle-cell phenotype regulation^{[2][3][4][5][6][7]}.

In vitro, APTO-253 (LOR-253) treatment of acute myeloid leukemia and lymphoma cell lines (1nM-100µM; 5 days) inhibited proliferation with IC₅₀ values of 57nM-1.75µM; in MV4-11 cells, APTO-253 (LOR-253) (1µM; 24h) induced CDKN1A expression and G0/G1 cell-cycle arrest and reduced MYC expression^[1]. In MDA-MB-231 and BT-549 human triple-negative breast cancer cells, APTO-253 (LOR-253) (5, 10, and 20µM; 24h) increased KLF4 and NOXA expression and cleaved caspase-3; NOXA knockdown attenuated the loss of viability produced by APTO-253 (LOR-253) (5µM; 24h)^[3]. In normal human lung fibroblasts, APTO-253 (LOR-253) (250nM; 36h) increased KLF4 without detectable cytotoxicity and reduced fibroblast proliferation and α-smooth muscle actin expression after profibrotic stimulation^[5].

In vivo, male DBA/1J mice with collagen-induced arthritis received APTO-253 (LOR-253) (15mg/kg;

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intravenous injection twice daily on 2 consecutive days per week for 2 weeks), which reduced arthritis severity scores and histopathologic inflammation, pannus formation, cartilage damage, and bone erosion^[2]. In a persistent bleomycin-induced pulmonary fibrosis mouse model, APTO-253 (LOR-253) (25mg/kg; intraperitoneal injection every other day from day 42 to day 60, with lungs collected on day 63) reduced lung fibrosis, hydroxyproline content, and profibrotic gene expression^[5].

References:

- [1] Local A, Zhang H, Benbatoul KD, Folger P, Sheng X, Tsai CY, et al. APTO-253 stabilizes G-quadruplex DNA, inhibits MYC expression, and induces DNA damage in acute myeloid leukemia cells. *Mol Cancer Ther.* 2018;17(6):1177-1186. doi:10.1158/1535-7163.MCT-17-1209.
- [2] Tsuchiya H, Ota M, Sumitomo S, Ishigaki K, Suzuki A, Sakata T, et al. Parsing multiomics landscape of activated synovial fibroblasts highlights drug targets linked to genetic risk of rheumatoid arthritis. *Ann Rheum Dis.* 2021;80(4):440-450. doi:10.1136/annrheumdis-2020-218189.
- [3] Nakajima W, Miyazaki K, Asano Y, Kubota S, Tanaka N. Krüppel-like factor 4 and its activator APTO-253 induce NOXA-mediated, p53-independent apoptosis in triple-negative breast cancer cells. *Genes (Basel).* 2021;12(4):539. doi:10.3390/genes12040539.
- [4] Wang B, Shen A, Ouyang X, Zhao G, Du Z, Huo W, et al. KLF4 expression enhances the efficacy of chemotherapy drugs in ovarian cancer cells. *Biochem Biophys Res Commun.* 2017;484(3):486-492. doi:10.1016/j.bbrc.2017.01.062.
- [5] Penke LR, Speth JM, Huang SK, Fortier SM, Baas J, Peters-Golden M. KLF4 is a therapeutically tractable brake on fibroblast activation that promotes resolution of pulmonary fibrosis. *JCI Insight.* 2022;7(16):e160688. doi:10.1172/jci.insight.160688.
- [6] Noura M, Matsuo H, Yasuda T, Tsuzuki S, Kiyoi H, Hayakawa F. Suppression of super-enhancer-driven TAL1 expression by KLF4 in T-cell acute lymphoblastic leukemia. *Oncogene.* 2024;43(6):447-456. doi:10.1038/s41388-023-02913-1.
- [7] Xiang L, Zhang Y, Wang Y, Liu J, Zhang X, Zhang J, et al. Quercetin attenuates KLF4-mediated phenotypic switch of VSMCs to macrophage-like cells in atherosclerosis: a critical role for the JAK2/STAT3 pathway. *Int J Mol Sci.* 2024;25(14):7755. doi:10.3390/ijms25147755.

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