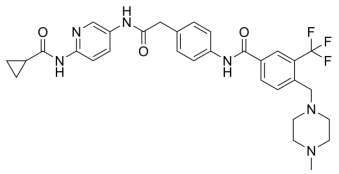
CHMFL-ABL-039

Cat. No.:	HY-126143
CAS No.:	2304344-56-5
Molecular Formula:	$C_{31}H_{33}F_3N_6O_3$
Molecular Weight:	594.63
Target:	Bcr-Abl
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	CHMFL-ABL-039 is a type II native ABL kinase and drug-resistant V299L mutant BCR-ABL inhibitor with the IC_{50}s of 7.9 nM and 27.9 nM, respectively. CHMFL-ABL-039 is used in the research of chronic myeloid leukemia[1].
IC_{50} & Target	IC50: 27.9 nM (BCR-ABL), 7.9 nM (ABL kinase)[1] Kd: 228 nM (ABL V299L mutant)[1]

In Vitro

CHMFL-ABL-039 (0-10 μM; 72 hours) is 6-10 fold more sensitive than Imatinib to BCRABL driven cancer cell lines, and BCR-ABL independent cell lines display a great selectivity window comparing to BCRABL driven cancer cell lines. CHMFL-ABL-039 exhibits no general cytotoxicity[1].

CHMFL-ABL-039 (0.01-3 μM; 4 hours) can dose dependently inhibit the ABL Y245 phosphorylation and the subsequent downstream signaling mediators[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	K562, KU812, MEG-01 (BCRABL driven cancer cell lines); HL-60, MOLM-14, MV4-11, U937 (BCR-ABL independent cell lines); CD34+ (Normal cell)
Concentration:	0-10 μM
Incubation Time:	72 hours
Result:	6-10 fold more sensitive to BCRABL driven cancer cell lines including K562, KU812, and MEG01 compared Imatinib. HL-60, MOLM-14, MV4-11 and U937 displayed a great selectivity window comparing to the BCR-ABL driven cell lines. CHMFL-ABL-039 exhibited a similar range of anti-proliferative effect against CD34+ cells, which indicated there was no general cytotoxicity.

Western Blot Analysis[1]

Cell Line:	BaF3-BCR-ABL-V299L cells, KU812 cells, MEG-01 cells, K562 cells
Concentration:	0.01 μM, 0.03 μM, 0.1 μM, 0.1 μM, 0.3 μM, 1 μM, 3 μM
Incubation Time:	4 hours

Result:	Dose dependently inhibited the ABL Y245 phosphorylation and the subsequent downstream signaling mediators such as pSTAT5 Y694, pERK T202/204 in K562, KU812, MEG-01, and BaF3-BCR-ABL-V299L.

In Vivo

CHMFL-ABL-039 (25-100 mg/kg; given i.p.injection; daily for 28 days in K562 mediated five weeks old female nu/nu mice models, daily for 11 days in BaF3-BCR-ABL-V299L mediated five weeks old female nu/nu mice models) do not exhibit any apparent general toxicity and do not affect the mouse weight. CHMFL-ABL-039 can dose dependently suppress the tumor progression for both models at either dosage[1].

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Animal Model:	BaF3-BCR-ABL-V299L (Imatinib insensitive) and K562 cells inoculated xenograft mouse model (Five weeks old female nu/nu mice)[1]
Dosage:	25 mg/kg, 50 mg/kg, 100 mg/kg
Administration:	Given i.p.injection; daily for 28 days (K562 mediated models), daily for 11 days (BaF3-BCR-ABL-V299L mediated models)
Result:	Did not exhibit any apparent general toxicity and did not affect the mouse weight. Dose dependently suppressed the tumor progression for both models at the dosage of 25, 50 and 100 mg/kg. 25 mg/kg daily administration of CHMFL-ABL-039 could achieve 77% tumor growth inhibition (TGI) in K562 mediated models and 100 mg/kg dosage even almost completely eliminated the tumor (TGI: about 100%). In the Imatinib insensitive BaF3- BCR-ABL-V299L mutant cells mediated xenograft model, 25 mg/kg dosage of CHMFL-ABL-039 displayed similar efficacy as 100 mg/kg.

REFERENCES

[1]. Wu J, et al. Discovery and characterization of a novel highly potent and selective type II native and drug-resistant V299L mutant BCR-ABL inhibitor (CHMFL-ABL-039) for Chronic Myeloid Leukemia(CML). Cancer Biol Ther. 2019;20(6):877-885.

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

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