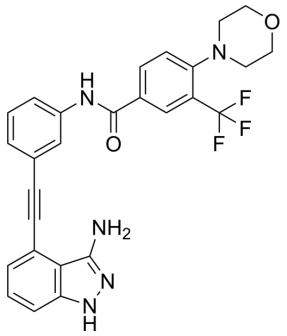
BCR-ABL-IN-6

Cat. No.:	HY-150569
CAS No.:	2499499-26-0
Molecular Formula:	$C_{27}H_{22}F_3N_5O_2$
Molecular Weight:	505.49
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	BCR-ABL-IN-6 (9h) is a selective Bcr-Abl kinase inhibitor with IC_{50}s of 4.6 and 227 nM for Bcr-Abl^{WT} and Bcr-Abl^{T3151} respectively. BCR-ABL-IN-6 inhibits Bcr-Abl kinase with strong affinity inside the cells with an EC_{50} of 14.6 nM. BCR-ABL-IN-6 is an imatinib derivative which can be used for research of chronic myelogenous leukemia[1]. BCR-ABL-IN-6 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.
IC_{50} & Target	IC50: 4.6 nM (Bcr-Abl^{WT}), 227 nM (Bcr-Abl^{T3151})[1]

In Vitro

BCR-ABL-IN-6 (10 μM; 1 h) againts with c-Src which is a closely related kinase domain of Bcr-Abl and exerts superior cellular potencies to imatinib[1].

BCR-ABL-IN-6 (10 μM; 1 h) suppresses Bcr-Abl phosphorylation dose dependenly and results underscored selective antiproliferative effects towards Bcr-Abl [1].

BCR-ABL-IN-6 (10 μM; 1 h) shows great selectivity cytotoxic between K562 and L132 cells[1].

BCR-ABL-IN-6 (10 μM) shows strong cytostatic activity against K562 and HL60 cells[1].

BCR-ABL-IN-6 (10 μM) shows exceptional selective antiproliferative effects towards the Bcr-Abl positive leukemia cell K562[1].

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

Western Blot Analysis[1]

Cell Line:	K562 cell line
Concentration:	0.003, 0.01, 0.03, 0.1 and 0.3 μM
Incubation Time:	1 h
Result:	Showed a dose-dependent suppression of Bcr-Abl phosphorylation.

Cell Viability Assay[1]

Cell Line:	K562 and L132 cell lines
Concentration:	10 μM
Incubation Time:	1 h

Result:	Exerted cellular activity with GI_{50} less than 160 nM against the Bcr-Abl positive leukemia K562 cells and exerted superior cellular potencies to imatinib with GI_{50} of 0.02 μM. Showed selectivity cytotoxic effects to the normal cell L132 with GI_{50} of 9.27 μM.

In Vivo

BCR-ABL-IN-6 (5 and 10 mg/kg; male ICR mice; for 9 h) takes 0.6 h to reach the maximum concentration (C_{max}). With intravenous and oral administration, the AUC_{last} values of BCR-ABL-IN-6 are 14018.7 ng·h/mL and 174.7 ng·h/mL. BCR-ABL-IN-6 intravenous administration is better, but unfavorable oral administration[1].

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

Animal Model:	Male ICR mice[1]
Dosage:	5 mg/kg and 10 mg/kg
Administration:	Intravenous and oral; 5 and 10 mg/kg; for 9h
Result:	Oral administration is not as effective as intravenous injection, intravenous injection is better.

REFERENCES

[1]. El-Damasy AK, et al. Design, synthesis, and biological evaluations of novel 3-amino-4-ethynyl indazole derivatives as Bcr-Abl kinase inhibitors with potent cellular antileukemic activity[J]. European Journal of Medicinal Chemistry, 2020, 207:112710.

[2]. El-Damasy AK, et al. Design, synthesis, and biological evaluations of novel 3-amino-4-ethynyl indazole derivatives as Bcr-Abl kinase inhibitors with potent cellular antileukemic activity[J]. European Journal of Medicinal Chemistry, 2020, 207:112710.

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