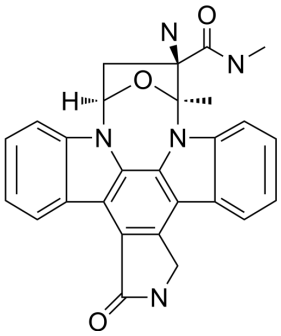
TTT 3002

Cat. No.:	HY-111249
CAS No.:	871037-95-5
Molecular Formula:	$C_{27}H_{23}N_5O_3$
Molecular Weight:	465.5
Target:	FLT3
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

TTT 3002 is a potent and orally active FLT3 inhibitor. TTT 3002 potently inhibits FLT3 phosphorylation by activating mutations at residue D835, with an IC_{50} of 0.2 nM. TTT 3002 can be used for AML (acute myeloid leukemia) research[1].

In Vitro

TTT 3002 downregulates FLT3 phosphorylation (pFLT3) in Molm14 and MV4-11 cells[1].
TTT 3002 induces cell cycle arrest followed by marked induction of apoptosis[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	Molm14 and MV4-11 cells
Concentration:	0, 0.25, 0.5, 1, 2 nM
Incubation Time:	1 h
Result:	Downregulated FLT3 phosphorylation (pFLT3) in Molm14 and MV4-11 cells in a dose-dependent manner. The IC_{50} for FLT3 phosphorylation in both cell lines was six- to seven fold lower for TTT 3002 compared with Quizartinib (HY-13001) at 0.2 vs 1.3 nM, respectively.

Cell Cycle Analysis[1]

Cell Line:	Molm14 and MV4-11 cells
Concentration:	0, 1, 2, 5, 10 nM
Incubation Time:	24 h
Result:	Showed cell cycle arrest followed by marked induction of apoptosis, along with concurrent activation of caspase 3 and poly ADP ribose polymerase cleavage.

In Vivo

TTT 3002 (6 mg/kg, Oral gavage, twice per day, for 2 to 4 weeks) is effective in vivo in several mouse tumor models of FLT3/ITD-associated AML (acute myeloid leukemia) with minimal toxicity[1].
TTT 3002 (6 mg/kg, Oral gavage, single) is rapidly absorbed with a biphasic maximum serum concentration (C_{max}) followed by a monoexponential decay[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	BALB/C mice (female, age 6 to 8 weeks, received Ba/F3-ITD Luc+ cells by tail vein injection on day 0)[1]
Dosage:	6 mg/kg
Administration:	Oral gavage, twice per day, for 2 to 4 weeks
Result:	Showed no significant changes in animal weight and was sufficient to eliminate the presence of Ba/F3-ITD Luc+ cells by day 17 (10 days of treatment).

Animal Model:	Leukemic engrafted mice (female, age 6 to 8 weeks)[1]
Dosage:	6 mg/kg
Administration:	Oral gavage, single (Pharmacokinetic Analysis)
Result:	After oral administration, TTT 3002 was rapidly absorbed with a biphasic maximum serum concentration (C_{max}) followed by a monoexponential decay. The C_{max} and area under the concentration-time curve from time 0 to infinity ($AUC_{0\to\infty}$) were 613 nM and 3127 nM·h, respectively. The half-life, apparent volume of distribution, and apparent clearance were 3.6 hours, 21 L/kg, and 4.1 L/h per kilogram, respectively.

REFERENCES

[1]. Ma H, et al. TTT-3002 is a novel FLT3 tyrosine kinase inhibitor with activity against FLT3-associated leukemias in vitro and in vivo. Blood. 2014 Mar 6;123(10):1525-34

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