財團法人生物技術開發中心
Development Center for Biotechnology

Precision Medicine : Selective FLT3 Inhibitor DCBCO1901

DCBCO1901 with a **novel chemical structure exhibits highly potent and selective inhibitory activity against FLT3 and its mutants**. DCBCO1901 exhibits selective cytotoxicity and effectively suppresses the intracellular FLT3 signaling in AML cell lines harboring FLT3 mutant. **Once-daily oral administration of DCBCO1901 completely suppresses FLT3-ITD mutant tumor growth in the xenograft model and PDX model.**

Hence, DCBCO1901 can be a precision medicine for the treatment of cancer patients with FLT3 mutation.

Indication
- **Precision medicine**
- **Acute myeloid leukemia (AML) with FLT3 mutation**

Highlights

- Novel chemical structure
- Highly potent/ selective against FLT3 & FLT3 mutants
- Monotherapy & orally active
- Well-tolerance in preclinical Tox study; GLP Tox study in progress
- Kilogram level production

DCBCO1901 exhibited highly selective and potent inhibition activity

Biochemical activity(Mean IC_{50}, nM)

Compound	FLT3	FLT3-ITD	FLT3* (D835Y)	KIT	CSF-1R	PDGFRβ	AXL	Met	VEGFR2
Quizartinib	3	15	47	132	26	142	> 10μM	> 10 μM	235
Gilteritinib	2	3	1	805	258	> 3 μM	28	1008	606
DCBCO1901	0.3	1	0.5	> 10 μM	> 10 μM	> 3 μM	> 10 μM	> 10 μM	> 3 μM

*FLT3 (D835 mutation):quizartinib-resistant activation loop mutation

DCBCO1901 exhibited selective cytotoxicity

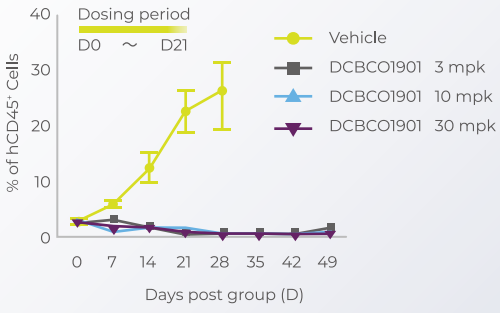
Cancer Cell line	Cancer Type	Stimulating growth factor	Target	Cytotoxicity (Mean IC_{50}, nM)	
				Gilteritinib	DCBCO1901
MV4-11	Leukemia		FLT3-ITD	2	12
Molm-13	Leukemia		FLT3-ITD	24	38
Molm-14	Leukemia		FLT3-ITD	15	49
OCI-AML5	Leukemia	FL(10 ng/mL)	FLT3 Signal	16	78
OCI-AML5	Leukemia	M-CSF(10 ng/mL)	CSF-1R Signal	56	>10,000
OCI-AML5	Leukemia	GM-CSF(10 ng/mL)	GM-CSF Signal	340	>10,000
M-07e	Leukemia	SCF(10 ng/mL)	KIT Signal	425	>10,000
M-07e	Leukemia	IL-3(10 ng/mL)	IL-3 Signal	1,084	>10,000
HCC827	NSCLC		EGFR(Exon19del)	345	>10,000

Normal cell line	Tissue	Cell Type	Cytotoxicity (Mean IC_{50}, nM)	
			Gilteritinib	DCBCO1901
HUVEC	Vein	Endothelial cell	1,797	>10,000
HAoSMC	Heart	Smooth muscle cell	3,168	>10,000

DCBCO1901 completely suppressed FLT3-ITD mutant tumor growth in PDX model

Model: AM7577 FLT3-ITD positive PDX model
Strain: Female NOD-SCID (n=10)
Frequency: Once daily oral dosing for 21 days
Execution: CrownBio

AM7577 tumor growth in peripheral blood



No death or body weight loss was observed in all dosing groups after 28 days dose cessation

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