Zimberelimab

Cat. No.: HY-P99109

CAS No.: 2259860-24-5

Target: PD-1/PD-L1

Pathway: Immunology/Inflammation

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description

Zimberelimab (GLS-010) is a fully human IgG4 anti-PD-1 monoclonal antibody with an EC_{50} of 210 pM for human PD-1. Zimberelimab effectively blocks the binding of PD-L1 and PD-L2 to cell-surface PD-1 in CHO-S cells, with IC_{50} values of 580 pM and 670 pM, respectively. Zimberelimab shows antitumor activities, and can be used for various cancers research, including cervical cancer, non-small cell lung cancer and classical Hodgkin's lymphoma[1][2].

In Vitro

Zimberelimab has an EC_{50} of 210 pM for human PD-1 but does not bind to related CD28 family receptors, such as ICOS, CD28 and CTLA-4[1].

Zimberelimab binding to cell-expressed human PD-1 inhibits the interaction of the receptor with both human PD-L1 and PD-L2 with IC_{50}s of 580 pM and 670 pM, respectively[1].

Zimberelimab dose-dependently enhances IFN-γ production and proliferation by $CD4^+$ T cells, saturating at concentrations below 100 pM[1].

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

In Vivo

Zimberelimab (10 and 20 mg/kg; i.v.; BIW*3) shows significant anti-tumor effects in mice[2].

PK parameters of Zimberelimab after single vd administrations of 2, 6, and 18 mg/kg in cynomolgus macaques[2]

PK parameters	2 mg/kg	6 mg/kg	18 mg/kg
C_0 (mg/mL)	103 ± 23.7 (23.0%)	157 ± 18.7 (11.9%)	508 ± 48.0 (9.46%)
$T_{1/2}$ (h)	111 ± 23.7 (30.5%)	115 ± 32.8 (28.5%)	129 ± 17.0 (13.1%)
V_{ss} (mL/kg)	48.4 ± 7.48 (15.5%)	49.4 ± 6.49 (13.1%)	46.3 ± 5.49 (11.8%)
Cl (mL/h/kg)	0.288 ± 0.0373 (13.0%)	0.278 ± 0.0308 (11.1%)	0.183 ± 0.0293 (16.0%)
T_{last} (h)	396 ± 141 (35.5%)	704 ± 203 (28.9%)	816 ± 0.00
$AUC_{0\text{-}last}$ (h*mg/mL)	6300 ± 1320 (21.0%)	21300 ± 2570 (12.1%)	98100 ± 16300 (16.6%)

AUC_{0-inf} (h*mg/mL)	7060 ± 1020 (14.5%)	21800 ± 2310 (10.6%)	101000 ± 16700 (16.6%)
MRT_{0-last} (h)	126 ± 23.3 (18.4%)	164 ± 31.2 (19.0%)	236 ± 14.8 (6.27%)
MRT_{0-inf} (h)	170 ± 29.7 (17.5%)	180 ± 29.4 (16.4%)	255 ± 17.4 (6.82%)
AUC_{0-inf}/AUC_{0-last} (%)	113 ± 11.8 (10.4%)	103 ± 0.940 (0.916%)	103 ± 0.940 (0.916%)

C_0, initial drug concentration; $T_{1/2}$, half-life; V_{ss}, apparent volume of distribution in the steady-state; Cl, clearance; T_{last}, the last time; AUC, area under the curve; MRT, mean residence time.

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

Animal Model:	The human PD-1 knock-in mouse model of MC38 tumors[2]
Dosage:	10 and 20 mg/kg
Administration:	Intravenous injection, BIW*3
Result:	Showed statistically significant anti-tumor effects comparable with Pembrolizumab (HY-P9902).

Animal Model:	Nine male and nine female cynomolgus monkeys[2]
Dosage:	2, 6, and 18 mg/kg
Administration:	Intravenous injection (Pharmacokinetic Analysis)
Result:	Displays long-term effects in cynomolgus monkeys, without differences between males and females.

REFERENCES

[1]. Lou B, et al. Preclinical Characterization of GLS-010 (Zimberelimab), a Novel Fully Human Anti-PD-1 Therapeutic Monoclonal Antibody for Cancer. Front Oncol. 2021 Sep 15;11:736955.

[2]. Markham A. Zimberelimab: First Approval. Drugs. 2021 Nov;81(17):2063-2068.

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