

Zimberelimab

Cat. No.:	HY-P99109
CAS No.:	2259860-24-5
Molecular Weight:	146540.00
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	<p>Zimberelimab (GLS-010) is a fully human IgG4 anti-PD-1 monoclonal antibody with an EC₅₀ 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 IC₅₀ 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]}.</p>																														
In Vitro	<p>Zimberelimab has an EC₅₀ of 210 pM for human PD-1 but does not bind to related CD28 family receptors, such as ICOS, CD28 and CTLA-4^[1].</p> <p>Zimberelimab binding to cell-expressed human PD-1 inhibits the interaction of the receptor with both human PD-L1 and PD-L2 with IC₅₀s of 580 pM and 670 pM, respectively^[1].</p> <p>Zimberelimab dose-dependently enhances IFN-γ production and proliferation by CD4⁺ T cells, saturating at concentrations below 100 pM^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>																														
In Vivo	<p>Zimberelimab (10 and 20 mg/kg; i.v.; BIW*3) shows significant anti-tumor effects in mice^[2].</p> <p>PK parameters of Zimberelimab after single vd administrations of 2, 6, and 18 mg/kg in cynomolgus macaques^[2]</p> <table border="1"> <thead> <tr> <th>PK parameters</th> <th>2 mg/kg</th> <th>6 mg/kg</th> <th>18 mg/kg</th> </tr> </thead> <tbody> <tr> <td>C₀ (mg/mL)</td> <td>103 ± 23.7 (23.0%)</td> <td>157 ± 18.7 (11.9%)</td> <td>508 ± 48.0 (9.46%)</td> </tr> <tr> <td>T_{1/2} (h)</td> <td>111 ± 23.7 (30.5%)</td> <td>115 ± 32.8 (28.5%)</td> <td>129 ± 17.0 (13.1%)</td> </tr> <tr> <td>V_{ss} (mL/kg)</td> <td>48.4 ± 7.48 (15.5%)</td> <td>49.4 ± 6.49 (13.1%)</td> <td>46.3 ± 5.49 (11.8%)</td> </tr> <tr> <td>Cl (mL/h/kg)</td> <td>0.288 ± 0.0373 (13.0%)</td> <td>0.278 ± 0.0308 (11.1%)</td> <td>0.183 ± 0.0293 (16.0%)</td> </tr> <tr> <td>T_{last} (h)</td> <td>396 ± 141 (35.5%)</td> <td>704 ± 203 (28.9%)</td> <td>816 ± 0.00</td> </tr> <tr> <td>AUC_{0-last} (h*mg/mL)</td> <td>6300 ± 1320 (21.0%)</td> <td>21300 ± 2570 (12.1%)</td> <td>98100 ± 16300 (16.6%)</td> </tr> </tbody> </table>			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-last} (h*mg/mL)	6300 ± 1320 (21.0%)	21300 ± 2570 (12.1%)	98100 ± 16300 (16.6%)
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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%)

C₀, 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.

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

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