Abstract: CT144
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Pharmacokinetics of spevatamig (PT886), a bispecific antibody targeting CLDN18.2 and CD47, in patients with advanced gastrointestinal cancers as monotherapy or combination therapy

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Background

Introduction

Spevatamig is an IgG1-based bispecific antibody (bsAb) targeting claudin 18.2 (CLDN18.2) and CD47 with an optimized anti-CD47 arm that has higher binding to CD47 on cancer cells than on human red blood cells. Spevatamig is expected to mediate enhanced killing of CLDN18.2-expressing cancer cells by innate immune cells and potentially by T cells. In addition, the binding of CD47 on cancer cells by spevatamig potentially enables anti-tumor activity against low CLDN18.2-expressing cancer cells. In combination with chemotherapy which induces “eat me” signals, the immune-activation and cancer killing activities of spevatamig are expected to be further stimulated. **As of March 2026, more than 160 patients globally have been dosed with spevatamig collectively in monotherapy and combination therapy settings.**

Design of spevatamig, a native IgG1-like bsAb

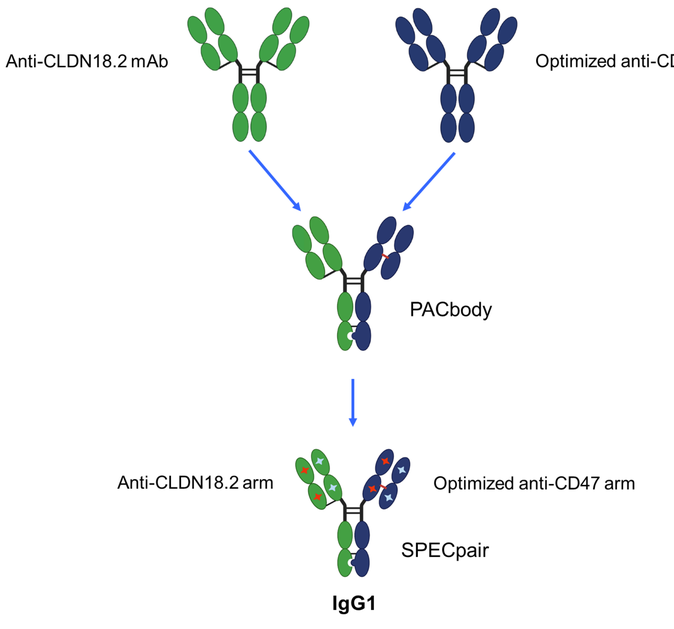

Figure 1: Spevatamig is a bsAb on a native IgG1-like backbone, with one arm binding to CLDN18.2, and an optimized anti-CD47 arm with reduced binding to human red blood cells.

Spevatamig was constructed with PACbody and SPECpair

- **PACbody** is a native IgG-like bispecific antibody platform invented by Phanes Therapeutics, Inc.
- **SPECpair** is a technology platform invented by Phanes Therapeutics, Inc.; it enables manufacturing of native IgG-like bispecific antibodies with the mAb manufacturing process

Results

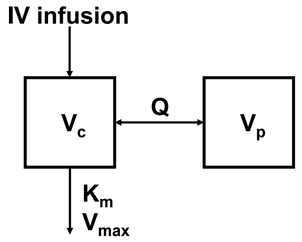

Figure 2: Two-compartment population PK model.

Simulated PK profiles for spevatamig + GnP

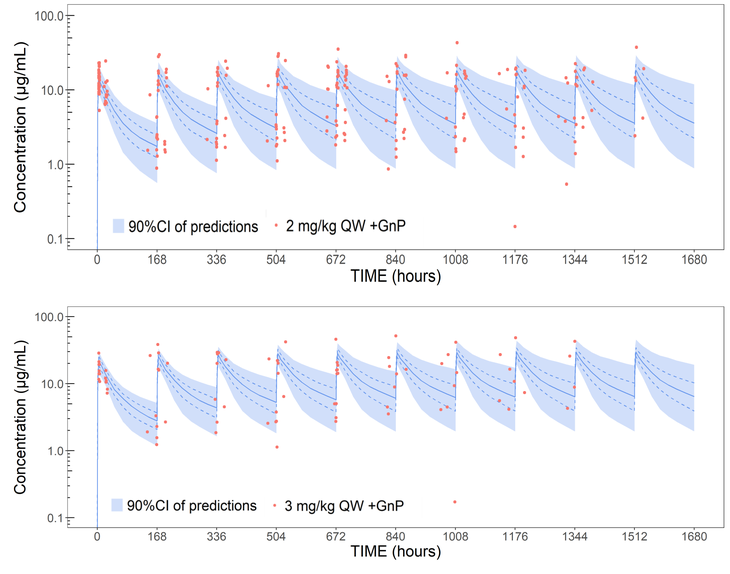

Figure 3: Simulated PK profiles for the 2 mg/kg QW spevatamig + GnP dose level (upper panel) and 3 mg/kg QW spevatamig + GnP dose level (lower panel). Simulated PK profiles (blue) are overlaid with measured concentrations from patient PK samples (red).

Table 1: Nonlinear (Michaelis-Menten) clearance parameters

Parameter	All cohorts N = 67	Spevatamig monotherapy N = 31	Spevatamig + GnP N = 36
K_m (μg/mL)	35.52	35.52	35.52
V_{max} (mg/h)	5.23	4.77	5.63
V_C (L)	8.06	6.51	9.39
Q (L/h)	0.136	0.136	0.136
V_P (L)	11.53	11.53	11.53

V_{max}: Maximum elimination rate in the Michaelis-Menten equation; K_m: Concentration at which 50% of maximum elimination rate in MM equation can be reached; Vc: central volume of distribution; Q: inter-compartmental clearance; V_p: peripheral volume of distribution. Inter-individual variabilities are observed for V_{max} and Vc; Inter-individual variabilities for K_m, Q, and V_P are insignificant and therefore, the values for these parameters are the same across different cohorts as estimated by the model.

Non-compartmental analysis (NCA) of the simulated PK profiles

Table 2: NCA parameters for 2 mg/kg QW spevatamig + GnP

Parameter	Cycle 1		Cycle 5	
	Spevatamig	%CV	Spevatamig	%CV
$AUC_{0\text{-}168h}$ (h*μg/mL)	892.3	25.4	1,531.3	38.2
C_{trough} (μg/mL)	2.2	41.7	4.9	56.0
C_{max} (μg/mL)	16.8	22.8	21.5	23.4
$t_{1/2}$ (h)	123.1	20.8	143.7	27.2
λ_z (h^{-1})	0.006	20.0	0.005	25.8

Note: T_{max} is 2 hours, as the duration of infusion used for simulation is set as 2 hours.

Table 3: NCA parameters for 3 mg/kg QW spevatamig + GnP

Parameter	Cycle 1		Cycle 5	
	Spevatamig	%CV	Spevatamig	%CV
$AUC_{0\text{-}168h}$ (h*μg/mL)	1,344.4	30.3	2,441.8	46.9
C_{trough} (μg/mL)	3.3	49.3	8.2	68.0
C_{max} (μg/mL)	25.5	27.4	33.1	28.2
$t_{1/2}$ (h)	123.3	23.2	150.2	34.2
λ_z (h^{-1})	0.006	23.0	0.005	31.2

Note: T_{max} is 2 hours, as the duration of infusion used for simulation is set as 2 hours.

A statistically significant difference was observed between the estimated $AUC_{0\text{-}168}$ of 2 mg/kg QW spevatamig + GnP and that of 3 mg/kg QW spevatamig + GnP (p = 2.4e-6, two-sample T-test).

Conclusions

- PK analysis suggests that higher doses of spevatamig correlate with increased exposure.
- Analysis of the simulated PK profiles showed a significant difference in spevatamig exposure between the 2 mg/kg QW and 3 mg/kg QW spevatamig dose levels when combined with GnP.
- Overall, spevatamig exhibits PK characteristics suitable for clinical development in combination with GnP.