Goals: This Phase I/IIb study compared the pharmacokinetics (PK) and safety of trastuzumab and CT-P6, a biosimilar to trastuzumab, in women with HER2+ metastatic breast cancer (MBC).

Methods: In this double blind, randomized, parallel-group study, 174 patients with HER2+ MBC were randomized 1:1 to receive either CT-P6 (n = 86) or trastuzumab (n = 88) 8 mg/kg intravenously (day 1), followed by CT-P6 or trastuzumab 6 mg/kg every 3 weeks. Paclitaxel (175 mg/m² 3-weekly) was co-administered. The primary endpoint, area under the concentration-time curve at steady state (AUC_{SS}), was measured during treatment cycle 8, although treatment was continued until disease progression, death or patient withdrawal. Serum blood samples for PK analysis were obtained immediately prior to the study treatment infusion and at the end of the study treatment infusion on dosing days. For primary PK analysis, a total of 10 serum blood samples were obtained during cycle 8. Patients were monitored for safety and tolerability throughout the study.

Results: Primary PK analysis was performed in 100 patients who reached steady state. Geometric mean AUC_{SS} (% coefficient of variation [%CV]) was 32,000 ?gh/mL (43.5%) for CT-P6 and 30,600 ?gh/mL (30.9%) for trastuzumab. The ratio of geometric means was 104.57% (90% CI: 93.64, 116.78) for AUC_{SS}. The limits of the 90% CIs for the ratio of AUC_{SS} geometric means were contained within the established margin (80–125%) required for bioequivalence. Geometric mean C_{troughSS} was 19.5 ?g/mL for CT-P6 and 19.2 ?g/mL for trastuzumab. The ratio of geometric means was 101.35% (90% CI: 87.94, 116.82) for C_{troughSS}. PK parameters including C_{max}, C_{min}, C_{av}, T_{max}, CL, V_{Z}, MRT, PTF and T_{1/2} were not different in CT-P6 and trastuzumab. Serious adverse events (SAEs) were reported in 15.8% of CT-P6 and 20.9% of trastuzumab patients; 2.6% and 3.0% were treatment-related, respectively. Overall, treatment-related AEs were reported in 40.8% of CT-P6 and 46.3% of trastuzumab patients. Hypersensitivity, infusion reaction, cardiotoxicity, and infection (any grade) were reported in 1.3%, 19.7%, 2.6% and 1.3% of CT-P6 and 1.5%, 35.8%, 7.5% and
Conclusion: CT-P6 and trastuzumab were equivalent for $AUC_{SS}$ in patients with HER2+ MBC. $C_{troughSS}$ and other PK parameters further confirmed CT-P6 and trastuzumab comparability. CT-P6 was well tolerated, with a safety profile comparable to that of trastuzumab. All authors have received research funding, and/or travel support directly related to this clinical trial from Celltrion Inc.