A Phase 1 Study Evaluating the Bioequivalence Between HLX11, a China-manufactured Pertuzumab Biosimilar Candidate, and Pertuzumab from Three Different Sources in Healthy Chinese Male Subjects

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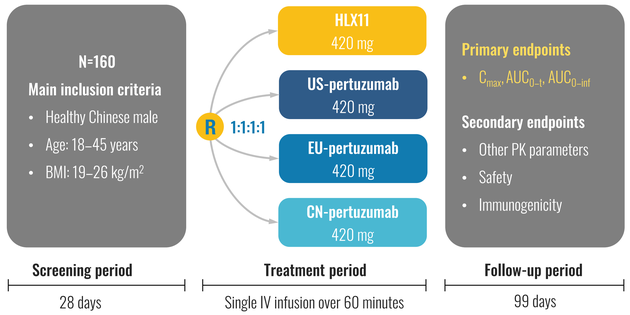
BACKGROUND

- Breast cancer has surpassed lung cancer as the most commonly diagnosed cancer, with an estimated 2.3 million new cases (11.7%) occurred in 2020 worldwide[1].
- Pertuzumab (Perjeta®), an anti-HER2 recombinant humanized monoclonal antibody, has been approved in the United States (US), the European Union (EU) and China (CN) for the treatment of HER2 positive breast cancer in combination with trastuzumab and chemotherapy[2–4].
- HLX11, a proposed pertuzumab biosimilar, has been demonstrated to be highly similar to the EU-approved pertuzumab in both *in vitro*, *in vivo* and toxicity studies.
- Here we report the results of a phase 1 study (HLX11-001, NCT04411550) comparing HLX11 to US-, EU- and CN-approved pertuzumab.

METHODS

- This randomized, double-blind, four-arm phase 1 study aimed to compare pharmacokinetics (PK), safety and immunogenicity between HLX11, US-, EU- and CN-approved pertuzumab (Figure 1).

Figure 1. HLX11-001 study design



AUC_{0-inf}, area under the concentration-time curve from time zero to infinity; AUC_{0-t}, area under the concentration-time curve from time zero to the last quantifiable concentration; **BMI**, body mass index; C_{max}, maximum serum concentration; **CN**, China; **EU**, the European Union; **IV**, intravenous; **PK**, pharmacokinetics; **US**, the United States;

- Eligible subjects were randomized 1:1:1:1 to receive a single dose of 420 mg HLX11, US-, EU-, or CN-pertuzumab by intravenous infusion, respectively.
- The primary endpoints were area under the concentration-time curve from time zero to infinity (AUC_{0-inf}), area under the concentration-time curve from time zero to the last quantifiable concentration (AUC_{0-t}), and maximum serum concentration (C_{max}). PK bioequivalence was established if 90% confidence interval (CI) of the geometric mean ratio of AUC_{0-inf}, AUC_{0-t}, and C_{max} fell within the range of 0.80–1.25.
- Secondary endpoints included other PK parameters, safety and immunogenicity (anti-drug antibody [ADA]).

HLX11 is comparable with US-pertuzumab, EU-pertuzumab and CN-pertuzumab in PK and safety

PK

Figure 2. Statistical comparison of PK parameters

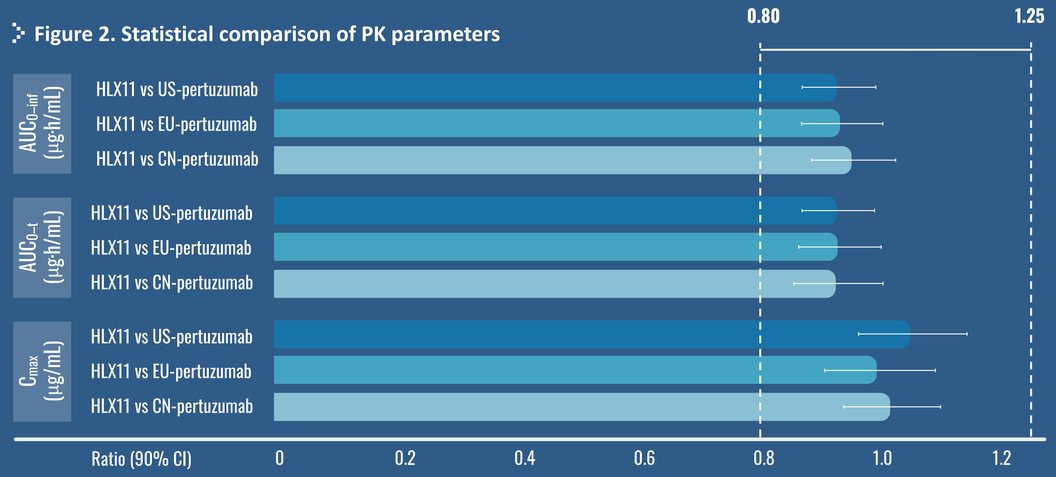
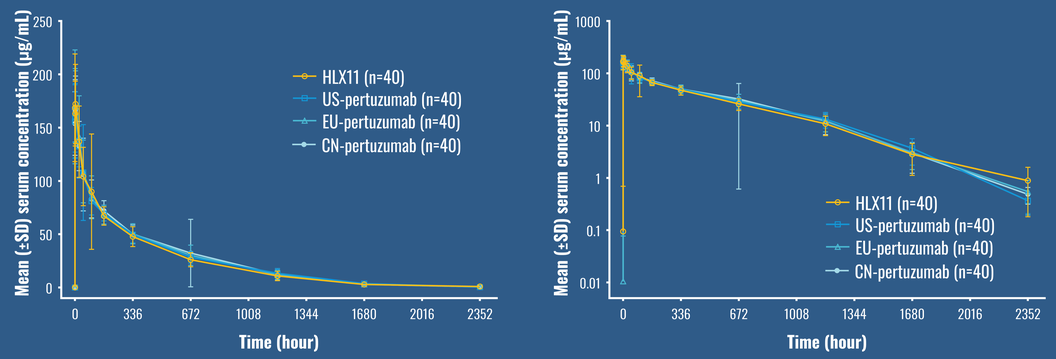


Figure 3. Mean (±SD) serum concentration-time profiles (linear and semi-logarithmic scales)



❖ Furthermore, PK parameters stratified by ADA status were comparable among four treatment groups.

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The American Society for Clinical Pharmacology and Therapeutics (ASCPT) 2022 Annual Meeting, March 16–18, 2022

RESULTS

Demographics

- 160 eligible subjects were enrolled and randomized 1:1:1:1 to receive HLX11, US-pertuzumab, EU-pertuzumab or CN-pertuzumab, respectively.
- All subjects received treatment and were included in the PK analysis set and the safety analysis set.
- Baseline characteristics were well-balanced among the four groups (Table 1).

Table 1. Baseline characteristics

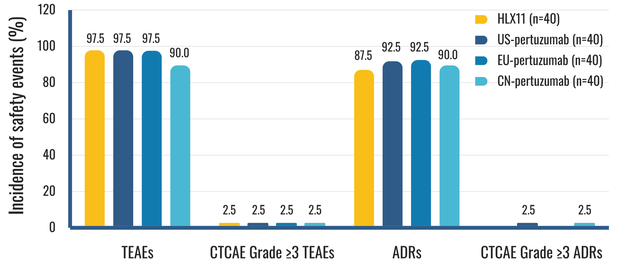
Characteristic		HLX11 (n=40)	US-pertuzumab (n=40)	EU-pertuzumab (n=40)	CN-pertuzumab (n=40)	Overall (N=160)
Age, years	Mean (SD)	28.7 (6.4)	29.5 (6.1)	29.4 (5.9)	27.7 (6.2)	28.8 (6.1)
Weight, kg	Mean (SD)	68.1 (7.9)	65.5 (7.0)	64.3 (7.4)	65.0 (7.2)	65.7 (7.4)
Height, cm	Mean (SD)	173.1 (6.0)	171.5 (6.4)	169.2 (7.2)	172.5 (6.1)	171.6 (6.6)
BMI, kg/m²	Mean (SD)	22.7 (2.0)	22.2 (1.7)	22.4 (1.6)	21.8 (1.6)	22.3 (1.8)

BMI, body mass index; **CN**, China; **EU**, the European Union; **SD**, standard deviation; **US**, the United States;

Safety

- The incidence and severity of treatment-emergent adverse events (TEAEs) were comparable among four treatment groups. Only one (2.5%) subject from each treatment group experienced CTCAE Grade 3 TEAEs. Two subjects had Grade ≥3 adverse drug reactions (ADRs), with one (2.5%) in each of US-pertuzumab group and CN-pertuzumab group. No TEAEs leading to deaths or drug discontinuation were reported in the study (Figure 4).
- In all eligible subjects, the most frequently reported TEAEs by preferred term (PT) were leukocytosis (54.4%), proteinuria (36.9%), hypertriglyceridemia (30.6%), urinary tract infection (28.1%), diarrhea (26.3%), mouth ulceration (18.8%), and hyperuricemia (15.6%).
- By PT, the most common ADRs were leukocytosis (54.4%), proteinuria (36.9%), urinary tract infection (28.1%), diarrhea (26.3%), and mouth ulceration (18.8%).

Figure 4. Incidence of safety events in each treatment group



ADR, adverse drug reaction; **CN**, China; **CTCAE**, the Common Terminology Criteria for Adverse Events; **EU**, the European Union; **SAE**, serious adverse event; **TEAE**, treatment-emergent adverse event; **US**, the United States;

REFERENCES

1. Sung H, *et al*. *CA Cancer J Clin*. **2021**;71(3):209–249.
2. Perjeta® Food and Drug Administration (FDA) Label.
3. Perjeta® National Medical Products Administration (NMPA) Approval.
4. Perjeta® European Medicines Agency (EMA) Label.

DISCLOSURES

- This study is sponsored by Shanghai Henlius Biotech, Inc.
- G. Sun, L. Zhou, W. Kang and J. Zhu are employees of Shanghai Henlius Biotech, Inc. All other authors declare no conflict of interest.

ACKNOWLEDGEMENTS

- The authors would like to acknowledge the participants and their families, investigators and staff at all study sites, as well as the members of the Independent Data Monitoring Committee.