# Supplementary Materials

**Title:** Pharmacokinetics, Safety, Tolerability, and Immunogenicity of BP02 (Trastuzumab Biosimilar) Compared to EU- and US-approved Trastuzumab in Healthy Adult Male Volunteers: A Phase 1 Randomized, Double-blind Study


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***Supplementary Table 1:*** *Detailed inclusion and exclusion criteria*

| **Inclusion criteria** |
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| 1. Signed and dated written informed consent prior to any study-specific procedures, ability to understand, and willingness to comply with the study procedures, restrictions, and requirements as judged and confirmed by the Principal Investigator.<br>2. Healthy adult male subjects, 18 to 65 years (both inclusive) of age at the time of signing informed consent.<br>3. Having body mass index between 18 to 30 kg/m2 and body weight between 50 to 100 kg (all inclusive).<br>4. Subjects with no clinically relevant abnormalities detected during baseline history, physical examination, and vital signs (blood pressure, pulse rate, body temperature, including respiratory rate) as judged by the Principal Investigator (PI).<br>5. Subjects who were considered healthy as determined by clinically acceptable findings of hematology, biochemistry, coagulation tests, urinalysis, 12-lead ECG, and echocardiogram.<br>6. Subjects with normal thyroid function (subjects on thyroid supplementation therapy were not eligible) at screening.<br>7. Subjects were to refrain from donating sperm or fathering a child from the day of signing the consent form until 9 months after administration of BP02, EU-Herceptin or US Herceptin administration by agreeing to use (with their female partner) 2 acceptable contraceptives (see Appendix 6 of the protocol [Appendix 16.1.1]).<br>8. Non-smokers or casual smokers who smoke no more than 5 cigarettes (or equivalent quantity of any other nicotine containing substance) per week. Subject were to abstain from smoking 48 hours prior to admission to in-patient component of treatment period. |
| **Exclusion criteria** |
| 1. Known history of hypersensitivity or allergic reactions to trastuzumab or any of its excipients.<br>2. History of cardiovascular, hepatic, ophthalmic, pulmonary, neurological, metabolic, hematologic, gastrointestinal, endocrine, immunological, psychiatric or any other disease which in the opinion of the Principal Investigator made the subject inappropriate for study participation.<br>3. Abnormal and clinically relevant (in the opinion of the Principal Investigator) ECG, history of angina, exertional dyspnea, orthopnea, congestive heart failure, or myocardial infarction.<br>4. Subjects with left ventricular ejection fraction (LVEF) of < 55% on screening echocardiogram were to be excluded from the study.<br>5. Sites were to adhere to local and institutional guidelines for exclusion of subjects with severe acute respiratory syndrome coronavirus 2 infection and suspected coronavirus disease-2019 (COVID-19) infection/testing regarding the enrollment of subjects.<br>6. History of any cancer, including carcinoma in situ.<br>7. Had a positive test result for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV)-suggestive of Active Hepatitis B or C infection, or human immunodeficiency virus I and II at screening.<br>8. Use of prescription or non-prescription drugs, including herbal and dietary supplements (including St. John's Wort, grapefruit) within 14 days or 5 half-lives (whichever is longer) prior to the start of study treatment until completion of the follow-up visit, unless in the opinion of the Principal Investigator and Sponsor, the medication was not to be interfere with the study procedures or compromise subject safety.<br>9. Received COVID-19 vaccine within 14 days prior to study drug administration or planned to receive COVID-19 vaccine until Day 15 of the study. Any live attenuated vaccine was not allowed during the study. |

10. Use of hematopoietic growth factors, monoclonal antibodies, or immunoglobulins within 6 months prior to screening or 5 half-lives, whichever is longer.
11. Major surgery or major trauma within past one year of screening or anticipated need for any surgery during the study duration.
12. Difficulty in blood sampling or difficulty in accessibility of veins.
13. Prior history of or current alcohol abuse or excessive intake of alcohol as judged by the Principal Investigator and/or a positive test result in breath alcohol done before check-in.
14. Subjects with a history of drug abuse or positive drug test at screening or admission. Drug of abuse test was reported to be positive for casual smokers who smoke no more than 5 cigarettes or equivalent quantity of any other nicotine containing substance per week. In such cases, site needs to document that subject met inclusion/exclusion criteria as per smoking history.
15. Blood donation within 90 days or platelet/plasma donation within 14 days prior to commencement of study (from the time of signing the consent form at screening visit) and during the study.
16. Participation in an investigational antibody-based study within 6 months (from post dose follow-up) and any other investigational study within 90 days prior to dosing.
17. Participation in a study with trastuzumab or HER2 targeted antibody or any prior exposure to these drugs.
18. Subjects who, in the opinion of the Principal Investigator, were not likely to complete the study for whatever reason.
19. Any persons who were:
    a. an employee of the Principal Investigator, clinical center, contract research organization (CRO) or Sponsor
    b. a relative of an employee of the clinical center, the Principal Investigators, CRO, or the Sponsor.