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A RANDOMIZED, SINGLE-BLIND, SINGLE-DOSE, THREE-ARM, PARALLEL GROUP STUDY IN HEALTHY SUBJECTS TO DEMONSTRATE PHARMACOKINETIC EQUIVALENCE OF ABP 501 AND ADALIMUMAB: RESULTS OF COMPARISON WITH ADALIMUMAB (EU)

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Background: Adalimumab (Humira®) is a recombinant IgG1 monoclonal antibody that binds to TNFα blocking its interaction with p55 and p75 cell surface receptors. ABP 501 is being developed as a biosimilar candidate to adalimumab, contains a fully human recombinant monoclonal antibody with same amino acid sequence and similar post-translational modifications. Evidence from analytical comparisons indicates that ABP 501 is highly similar to adalimumab. We describe the pharmacokinetic results of ABP 501 compared with adalimumab (EU).

Objectives: To demonstrate pharmacokinetic equivalence of ABP 501 to adalimumab

Methods: This was a single-blind, single-dose, 3-arm, parallel-group study. Subjects were randomized to receive 40-mg subcutaneous (SC) injection of ABP 501, adalimumab (US) or adalimumab (EU). Subjects included healthy male and female subjects, 18 to 45 years of age with a body mass index of 18 to 30 kg/m². Primary endpoint was demonstration of pharmacokinetic equivalence of ABP 501 relative to adalimumab, based on area under the serum concentration-time curve (AUC) from time 0 extrapolated to infinity (AUC_inf) and the maximum observed serum concentration (C_max). Pre-specified equivalence criterion for all parameters was 90% confidence interval (CI) for geometric means (GM) ratio within 0.80 to 1.25. Secondary endpoints included the safety, tolerability, and immunogenicity.

Results: A total of 67 subjects received ABP 501 and 67 subjects received adalimumab (EU). Following single dose, the GM of C_max, AUC_last and AUC_inf for ABP 501 were 3.22 ng/ml, 2002.27 ng.h/ml and 2136.95 ng.h/ml and a median t_max of 190.82 hr. The GM of C_max, AUC_last and AUC_inf for adalimumab (EU) were 3.37 ng/ml, 2022.62 ng.h/ml and 2046.82 ng.h/ml and a median t_max of 168.00 hr. Ratio of adjusted least square geometric means (90% CIs) between ABP 501 and adalimumab (EU) for C_max was 0.96 (0.89, 1.03); AUC_inf was 1.04 (0.93, 1.17) and AUC_last was 0.99 (0.89, 1.10). The 90% CIs of GM ratio for C_max, AUC_inf, and AUC_last were fully contained within 0.80 to 1.25, confirming the bioequivalence between ABP 501 and adalimumab (EU).

There were no treatment related serious adverse events, or treatment related adverse events leading to discontinuation from the study. The most frequently reported treatment-related AEs included headache, nausea, nasopharyngitis, and oropharyngeal pain.

No pre-existing anti-drug antibodies (ADA) were detected at baseline. In the ABP 501 treatment group, 36 (54%) subjects developed binding antibodies and 12 (18%) developed neutralizing antibodies. In the adalimumab (EU) treatment group, 45 (67%) subjects developed binding antibodies and 14 (21%) developed neutralizing antibodies.

Conclusions: Results of this phase 1 study demonstrated bioequivalence of ABP 501 following a single 40-mg SC injection relative to that from a 40-mg SC injection of adalimumab (EU). No new safety signals with ABP 501 treatment were identified.


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