A comparative clinical study of PF-06410293, a candidate adalimumab biosimilar, and reference adalimumab for the treatment of active rheumatoid arthritis

R. Allen1, R.M. Fleischmann2, M. Pileckyte4, S.Y. Hua5, C. Cronenberger6, A. E. Bod2, K.L. Sewell2, 3Lithuanian University of Health Sciences, Lithuania; 4Pfizer Inc, San Diego; 5Pfizer Inc, Collegeville; 6Pfizer Inc, Cambridge, USA

Background: To confirm the efficacy, safety and immunogenicity of biosimilars, a comparative clinical study is typically required.

Objectives: This double-blind, randomised, 78 week (wk) study compared the efficacy, safety and immunogenicity of PF-06410293, a candidate adalimumab biosimilar, with reference adalimumab sourced from the EU (ADA-EU), in biologic-naïve patients (pts) with active rheumatoid arthritis (RA) despite methotrexate (MTX; 10–25 mg/wk).

Methods: Pts with active RA (n=597) were stratified by region and randomised (1:1) to PF-06410293 or ADA-EU (40 mg subcutaneous injection every 2 wks), with continued MTX. The primary endpoint was American College of Rheumatology (ACR)20 response at Wk 12. Therapeutic equivalence was confirmed if the 2–sided 95% confidence interval (CI) for the difference in Wk 12 ACR20 response was within the symmetric equivalence margin of ±14%. Additionally, a 2–sided 90% CI was requested by the US Food and Drug Administration, using the asymmetric equivalence margin of –12% to +15%. Secondary efficacy endpoints to Wk 26 included ACR20/50/70, change from baseline Disease Activity Score in 28 joints (DAS28), European League Against Rheumatism (EULAR) response, achievement of DAS28 CRP <2.6, and ACR/EULAR remission.

Results: Pts with active RA (78.7% female, 81.6% seropositive) had a mean age of 52.5 years, and mean RA duration of 6.8 years. Mean baseline DAS28 CRP was 5.9 (PF-06410293) and 6.1 (ADA-EU). The observed Wk 12 ACR20 was 68.7% (PF-06410293) and 72.7% (ADA-EU) in the intent-to-treat population (figure 1). Using non-responder imputation (n=19; 3.2%), the treatment difference in Wk 12 ACR20 was –2.98%, and the corresponding CIs (95% CI (–10.38%,+4.44%); 90% CI (–9.25%,+3.28%)) were entirely contained within both equivalence margins (symmetric and asymmetric). The ACR20 difference ranged from –3.98% to +5.50% (Wks 2–26). Mean DAS28 CRP change from baseline at Wk 26 was –2.7 and –2.8 in the PF-06410293 and ADA-EU arms, respectively. ACR50/70, EULAR response, DAS28 CRP <2.6 and ACR/EULAR remission were similar between arms at each visit. Incidence of treatment-emergent adverse events (AEs) was 48.1% vs 47.8%, serious AEs were 4.0% vs 4.3% (with a fatal myocardial infarction in the ADA-EU arm) and serious infections were 0.7% vs 1.3% for PF-06410293 and ADA-EU, respectively. Injection site reactions occurred at 1.7% vs 2.0%, hypersensitivity events at 4.4% vs 8.4%, pneumonia at 0.7% vs 2.0%, and latent tuberculosis (based on specialist consultation for Wk 26 QuantiFERON-TB + ) at 1.7% vs 0.3% for PF-06410293 and ADA-EU, respectively. Post-dose anti-drug antibody rates to Wk 26 were 44.4% (PF-06410293) and 50.5% (ADA-EU).

Conclusions: The efficacy, safety and immunogenicity of PF-06410293 and ADA-EU were similar up to Wk 26 in pts with active RA on MTX. At Wk 26, pts on ADA-EU were blindly re-randomised (1:1) to continue ADA-EU or transition to PF-06410293 for ongoing treatment in the study.


Figure 1. ACR20 response rates (ITT population)