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POS0287

A PHASE III, RANDOMISED, DOUBLE-BLIND, ACTIVE-CONTROLLED CLINICAL TRIAL TO COMPARE BAT1806/BIIB800, A PROPOSED TOCILIZUMAB BIOSIMILAR, WITH TOCILIZUMAB REFERENCE PRODUCT IN SUBJECTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS WITH AN INADEQUATE RESPONSE TO METHOTREXATE THERAPY

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Background: BAT1806/BIIB800 is a proposed biosimilar to reference tocilizumab (TCZ). A Phase III randomised, double-blind, active-controlled clinical trial was conducted as part of a biosimilar development programme.
Objectives: To evaluate the efficacy, pharmacokinetics (PK), safety and immunogenicity of BAT1806/BIIB800 in comparison with EU-sourced TCZ in subjects with moderate to severe rheumatoid arthritis with inadequate response to methotrexate (MTX).
Methods: The study was conducted at 55 centres in China and Europe, between June 2018 and January 2021. Eligible subjects were randomised in a 2:1:1 ratio to one of three treatment groups: (1) BAT1806/BIIB800 up to Week 48, (2) TCZ up to Week 48, or (3) TCZ up to Week 24, followed by BAT1806/BIIB800 from Week 24 to Week 48, administered intravenously every 4 weeks at a dose of 8mg/kg. The primary endpoint was the proportion of subjects achieving an ACR20 response at timepoints pre-specified to meet the requirements of different Regulatory Agencies: Week 12, for EMA; Week 24, for FDA and NMPA. Equivalence margins applied to differences in ACR20 response rates in the BAT1806/BIIB800 and TCZ treatment groups were pre-specified as follows: +/- 14.5% for EMA (95% confidence interval (CI)); -12.0%,15% for FDA (90% CI); +/- 13.6% for NMPA (95% CI). Secondary endpoints included pharmacokinetics, safety and immunogenicity.
The ICH E9(R1) estimands framework including intercurrent events (related or unrelated to the COVID19 pandemic) was implemented for the ACR20 evaluation. A logistic regression model including 'region' (China and Eastern Europe) and 'previous biologic or targeted synthetic DMARD use' (Yes/No) as captured in Interactive Web Response System as stratification factors was utilised to assess equivalence for the primary endpoint. The difference in response rates was estimated and corresponding confidence intervals were derived to assess equivalence for the primary endpoint. This abstract presents results up to Week 24.
Results: In total, 621 subjects were randomised to receive BAT1806/BIIB800 (N=312), TCZ (N=155), or TCZ followed by BAT1806/BIIB800 (N=154). The groups were comparable in terms of baseline demographics and disease characteristics, including age, gender, disease activity and disease duration. The estimated proportions of subjects achieving an ACR20 response in the BAT1806/BIIB800 vs. the TCZ groups, respectively, were 68.97% vs. 64.82% at Week 12 and 69.89% vs. 67.94% at Week 24. The estimated difference between ACR response rates was 4.15% (95% CI -3.63, 11.93) at week 12, and 1.94% (90% CI -4.04, 7.92; 95% CI -5.18, 9.07) at Week 24. The CIs for the estimated differences between the treatment groups were within the pre-defined equivalence margins (Figure 1). The treatment groups were comparable in terms of serum trough levels, incidence of TEAEs and ADA/NAb positivity (Table 1).

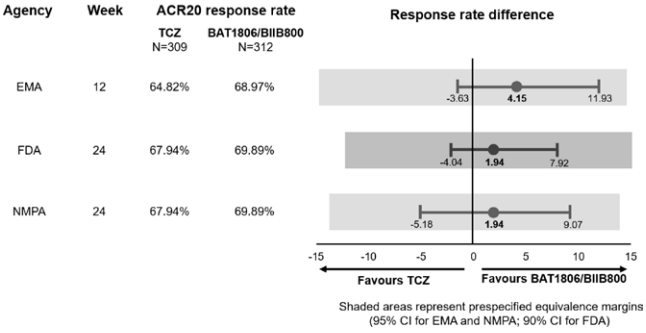
Table 1. Safety and Immunogenicity up to Week 24, and Pharmacokinetics at Week 24

	TCZ (N =309) n (%)	BAT1806/BIIB800 (N=312) n (%)
TEAE	196 (63.4)	201 (64.4)
Related TEAE	151 (48.9)	148 (47.4)
Serious TEAE	13 (4.2)	11 (3.5)
Related Serious TEAE	7 (2.3)	2 (0.6)
Fatal TEAE	1 (0.3)	3 (1.0)
ADA positive [a]	42 (13.6%)	64 (20.5%)
NAb positive [a]	42 (13.6%)	63 (20.2%)
PK, n	271	276
Serum trough level (ug/mL), mean (SD)	15.4 (17.1)	15.8 (12.3)
Serum trough level (ug/mL), geometric mean (CV%)	12.3 (140.3)	12.9 (121.3)
Below limit of quantification, n (%)	43 (15.9)	28 (10.1)

TEAE, treatment emergent adverse events[a] subjects with ≥1 ADA/NAb positive results up to week 24

Conclusion: BAT1806/BIIB800 has demonstrated equivalent efficacy at Week 12 and Week 24 and a similar PK, safety and immunogenicity profile as reference tocilizumab up to Week 24.

Figure 1. Forest Plot of Primary Efficacy Results



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POS0288

A CANADIAN RETROSPECTIVE CHART REVIEW EVALUATING CONCOMITANT METHOTREXATE DE-ESCALATION PATTERNS IN RA PATIENTS TREATED WITH BIOLOGIC OR TARGETED SYNTHETIC DMARDS

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Background: Rheumatoid arthritis (RA) guidelines recommend methotrexate (MTX) as anchor therapy in combination with biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs). However, its tolerability is challenging with a significant proportion of patients not adhering to their prescribed MTX regimen following b/tsDMARD initiation. Rates of MTX tapering and withdrawal have been reported elsewhere but Canadian data are lacking.
Objectives: This multi-centre, retrospective chart-based cohort study assessed the frequency of MTX withdrawal or tapering following initiation of a b/tsDMARD in Canadian adults with RA.