SYNOPSIS OF CLINICAL STUDY REPORT

Name of Sponsor/Company: Genentech, Inc.	**Individual Study Table Referring to Part of the Dossier**	*(For National Authority Use Only)*
Name of Finished Product: MLTA3698A (Pateclizumab)	**Volume:**	
Name of Active Ingredient: MLTA3698A (Pateclizumab)	**Page:**	

Title of Study: A Phase II, Randomized, Double-Blind, Parallel-Group Study to Evaluate the Efficacy and Safety of MLTA3698A In Combination with a Disease-Modifying Anti-Rheumatic Drug (DMARD) Compared with Adalimumab in Combination with a DMARD in Patients with Active Rheumatoid Arthritis

Phase of Development: II

Study Period: 5 Oct 2010 to 17 Dec 2012

Objectives

Primary:

- To evaluate the efficacy of MLTA3698A compared with adalimumab (ADA), used in combination with stable doses of methotrexate (MTX) or leflunomide (LFU), in patients with active rheumatoid arthritis (RA) who have had an inadequate response to either of these DMARDs at Day 85
- To evaluate the safety and tolerability of MLTA3698A

Secondary:

- To characterize the pharmacokinetic (PK) profile of MLTA3698A used in combination with stable doses of MTX or LFU in patients with active RA
- To characterize the immunogenicity of MLTA3698A by measurement of anti-therapeutic antibodies (ATAs)
- To evaluate the effects of MLTA3698A compared with ADA, used in combination with stable doses of MTX or LFU, upon patient-reported outcome measures (visual analog scale [VAS] scores, Stanford Health Assessment Questionnaire Disability Index [HAQ-DI], and Short Form Health Survey [SF-36])

Methodology

Details of the study can be found in the protocol (see Appendix 11.1.1).

Efficacy Evaluations

The primary endpoint, the change from baseline in DAS28(4)-ESR at Day 85, with mean values, was 1.89, 2.52, and 1.54 for the MLTA3698A, ADA, and placebo groups, respectively. The differences of DAS28(4)-ESR mean change from baseline between ADA and the other two treatment groups were statistically significant (p-value <0.01) whereas the difference between MLTA3698A and placebo groups was not statistically significant (p-value >0.05).

The key secondary efficacy endpoint, the American College of Rheumatology 50% (ACR50) response, was achieved at Day 85, was 26 (33.3%), 43 (57.3%), and 9 (24.3%) patients from the MLTA3698A, ADA, and placebo groups, respectively. The differences of ACR50 between ADA and two other treatment groups were statistically significant (p<0.01), but the difference between MLTA3698A and placebo was not statistically significant (p>0.05).

Other secondary efficacy variables, both ACR20 and ACR70, as well as SF-36 individual and component summary scores, also showed a statistically significant difference between ADA and MLTA3698A but no statistically significant difference between MLTA3698A and placebo. These secondary variables include ACR20 and ACR70, SF-36 individual and component summary scores, European League Against Rheumatism (EULAR) score, DAS28-CRP, global VAS, pain VAS, DAS28(4)-ESR score, CRP, and ESR score.

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Safety Conclusions

Overall, MLTA3698A appears well tolerated and safe within the dose range employed in Study ALT4864g. There were no deaths during the conduct of the study. There were six serious adverse events (SAEs) reported during the conduct of the study. There were five SAEs in the ADA-treated cohort and one in the placebo-treated cohort. There were no SAEs reported with patients who received MLTA3698A. Adverse events (AEs) in the MLTA3698a cohort were comparable in frequency to the placebo rates. There were no time-related patterns of adverse events or clinical abnormalities associated with MLTA3698a. In general, there were fewer treatment-emergent AEs (TEAEs) associated with MLTA3698a than with either ADA or placebo. No clinically significant changes in laboratory parameters or vital signs were observed.

Overall Summary and Conclusions

MLTA3698A treatment did not meet the primary or secondary efficacy endpoints as pre-specified in the Statistical Analysis Plan. MLTA3698A treatment had statistically significantly smaller DAS28(4)-ESR change from baseline than ADA, but not statistically significantly larger than placebo. Other secondary efficacy variables, including ACR50 response rate; DAS28(4)-ESR change from baseline; and ACR20, ACR70, and SF-36 individual and component summary scores, also showed a statistically significant difference between ADA and MLTA3698A, but no statistically significant difference between MLTA3698A and placebo.

Study ALT4864g did not demonstrate any clinically significant safety signals associated with MLTA3698A treatment. Exposure of MLTA3698A was confirmed and was consistent with predictions from a population PK model based on the PK data from the Phase I study (ALT4623g) in RA patients. Overall, the occurrence of ATAs to MLTA3698A was low and there did not appear to have any impact on the exposure of MLTA3698A during the dosing period in treated patients who tested ATA positive at posttreatment.

Date of the Report

7 May 2013