Protocol Synopsis

Protocol Number: CT-P13 4.4	
Title of Study: An Observational, Prospective Cohort Study to Evaluate Safety and Efficacy of Remsima™ in Patients with Ankylosing Spondylitis	
Marketing Authorization Holder: Celltrion Healthcare Hungary Kft, 1023 Budapest, Regus Óbuda Gate, Árpád fejedelem útja 26-28 Hungary	
Study Center(s): Approximately 50 centers in Europe and South Korea	
Length of Study: A 5-year period (2 years initially, followed by an additional 3 years for patients who consent to participate in an extension study)	**Phase of Development:** IV
Objectives: The primary objective of this study is to assess the safety of Remsima™ in ankylosing spondylitis (AS) patients, in comparison with patients receiving other anti-TNF drugs, by evaluation of events of special interest (ESI) for up to 5 years from the first visit of each patient. The secondary objectives of this study are to evaluate efficacy and additional safety of Remsima™ in AS patients, in comparison with patients receiving other TNF blockers. Health-economics parameters will also be assessed.	
Study Design: This is a longitudinal, observational, prospective cohort study to assess the safety and efficacy of Remsima™ in patients with AS in comparison with patients receiving other TNF blockers.	
Sample size: Approximately 1000 male or female patients with confirmed diagnosis of AS (approximately 500 patients treated with Remsima™, 500 patients treated with other anti-TNF drugs).	
Study Drug, Dose and Regimen: Remsima™ (5 mg/kg) will be administered intravenously during this study. Dose and treatment schedule are recommended to comply with the approved posology in each regulatory authority or investigator's clinical decision and time intervals between doses are controlled flexibly upon the investigator's clinical decision according to the product label of Remsima™.	
Comparator, Dose and Regimen: The first comparator cohort will be patients recruited with AS who are being treated with other anti-TNFs. Dose and regimen are recommended to comply with the approved posology in each regulatory authority.	
Main selection criteria: Male or female patients with active AS will be considered for enrolment in the study if they meet all of the inclusion criteria and none of the exclusion criteria.	
Safety Assessment: Safety will be assessed by collection of data in the patient medical records as part of routine clinical practice.	
Efficacy Assessments: Efficacy will be assessed by collection of data recorded in the patient medical records as part of routine clinical practice.	
Data analysis: *Statistical analysis*: The statistical analysis will be performed using SAS software Version 9.1.3 or later (SAS Institute, Inc, Cary, North Carolina). Interim analysis and an annual regulatory report will be generated if it is required from a regulatory perspective. Descriptive analysis will be performed for safety data including drug exposure and data will be presented for Remsima™ cohort, and other anti-TNF drug cohort. The data documented in this study and the clinical parameters measured will be described using descriptive statistics (n, mean, median, SD, minimum, and maximum) for quantitative variables and frequencies for qualitative variables. For descriptive purpose, incidence rates per 100 patient-years or 10,000 patient-years will be calculated and analysis items will be specified on statistical analysis plan. For missing data, appropriate imputation methods will be used, if required. The statistical considerations summarized in this section outline the plan for data analysis of this study. A final and complete statistical analysis plan will be prepared prior to data analysis.	
Milestones:	

Milestones	Planned Date
Start of data collection	・Korea: 3Q 2014 ・European region: 2Q 2014
End of data collection	・Korea: 2026 ・European region: 2026
Study progress report(s)	・Included in Periodic Safety Update Report and/or; ・Upon request from the national competent authorities
Final report of study results	・2026