

## Protocol Synopsis

<b>Protocol Number:</b> CT-P13 4.3	
<b>Title of Study:</b> An observational, prospective cohort study to evaluate the safety and efficacy of Remsima™ in patients with Crohn’s disease (CD), or Ulcerative Colitis (UC)	
<b>Sponsor:</b> CELLTRION, Inc.	
<b>Marketing Authorization Holder:</b> Celltrion Healthcare Hungary Kft. 1023 Budapest, Regus Óbuda Gate, Árpád Fejedelem útja 26-28, Hungary	
<b>Study Center(s):</b> Approximately 50 centers in South Korea and EU	
<b>Length of Study:</b> A 5-year continuous period from initiation of treatment for each patient	<b>Phase of Development:</b> IV
<p><b>Objectives:</b> The primary objective of this study is to assess the safety of Remsima™ by evaluation of Events of Special Interest (ESI) in IBD patients, who have active Crohn’s disease (CD), fistulizing Crohn’s disease (CD), or Ulcerative Colitis (UC) for up to 5 years for each patient.</p> <p>The secondary objectives of this study are to evaluate additional safety and efficacy of Remsima™ in IBD patients, who have active CD, fistulizing CD or UC. Health-economic parameters will also be assessed.</p>	
<b>Study Design:</b> This is a longitudinal, observational, prospective cohort study to assess the safety and efficacy of Remsima™ in patients with IBD, who have active Crohn’s disease (CD), fistulizing Crohn’s disease (CD), or Ulcerative Colitis (UC).	
<b>Sample Size:</b> At least 500 male and female patients with confirmed diagnosis of CD or UC.	
<b>Study Drug, Dose and Regimen:</b> Remsima™ (5 mg/kg) will be administered intravenously at weeks 0, 2, 6, and every 8 weeks thereafter. Dose escalation is permitted in accordance with the local guidelines of the institution in which the patient is receiving treatment. Dose and treatment schedule are recommended to comply with the approved posology in each regulatory authority or investigator’s clinical decision.	
<b>Main Selection Criteria:</b> Male or female patients with either moderate to severe active CD, fistulizing active CD, or moderate to severe active UC will be considered for enrollment in the study if they meet all of the inclusion criteria and none of the exclusion criteria.	
<b>Safety Assessment:</b> Safety will be assessed by collection of data in the patient medical records as part of routine clinical practice.	
<b>Efficacy Assessments:</b> Efficacy will be assessed by collection of data recorded in the patient medical records as part of routine clinical practice.	
<p><b>Data Analysis:</b> <i>Statistical analysis:</i> The statistical analysis will be performed using SAS software Version 9.1.3 or later (SAS Institute, Inc, Cary, North Carolina). The data documented in this study including exposure to Remsima™ 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. Periodic interim analyses are planned for regulatory reporting purposes. An annual regulatory report will be generated and reported to the regulatory authority. This will contain safety and efficacy data observed since the start of the study until December of each year. The first annual regulatory report is planned to be submitted in May 2015.</p> <p>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.</p>	

<b>Milestones:</b>	
<b>Milestones</b>	<b>Planned Date</b>
Start of data collection	<ul style="list-style-type: none"><li>• Korea: April 2014</li><li>• European region: 4Q 2014</li></ul>
End of data collection	<ul style="list-style-type: none"><li>• Korea: 2026</li><li>• European region: 2026</li></ul>
Study progress report(s)	<ul style="list-style-type: none"><li>• Included in Periodic Safety Update Report and/or;</li><li>• Upon request from the national competent authorities</li></ul>
Interim report(s) of study results	<ul style="list-style-type: none"><li>• Annual report: every May from 2015</li></ul>
Final report of study results	<ul style="list-style-type: none"><li>• 2026</li></ul>