Characterization of Patients With Ulcerative Colitis in a Post-Authorization Safety Study of Golimumab Based in the Spanish ENEIDA Registry

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BACKGROUND

- Simponi (golimumab) is an anti–tumor necrosis factor alpha (anti-TNFα) agent authorized for the treatment of moderately to severely active ulcerative colitis (UC).
- As part of its risk management plan, Merck Sharp & Dohme Corp. (MSD), a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA as the study sponsor is conducting a post-authorization safety study (PASS) using data from ENEIDA, a large, prospectively maintained registry of patients with inflammatory bowel disease in Spain in the setting of routine clinical practice. Founded in 2006, ENEIDA has not previously been used in a PASS.

OBJECTIVE

Overall Study Objectives

- At planned completion in 2023 (using data from September 2013 until May 2022), the study intends to provide comparative data on the **risk of colectomy due to intractable disease** and of **advanced colonic neoplasia (ACN)** in patients with UC treated with golimumab, other anti-TNFα agents, or thiopurines. The incidence of **hepatosplenic T-cell lymphoma (HSTCL)** will be described. Figure 1 shows the overall PASS objectives, including the scope of the annual progress reports and the final analysis.

Objectives for This Presentation

- Using data from September 2013 until May 2017, we present the following:
  - Characteristics of the ENEIDA registry
  - Ongoing study cohorts' assembly
  - Baseline characteristics of currently enrolled patients with UC
  - Number of study outcomes

Figure 1. Study Objectives for the Annual and Final Analyses

Study: Among new users of treatments for UC

Annual analyses, **2016-2021**	Final analysis, **2022**
Describe and compare patient profiles of new users: –Golimumab –Thiopurines –Other anti-TNF agents	**Annual analyses** AND **Compare risk of ACN:** –Golimumab vs. other anti-TNF agents **Compare risk of colectomy for intractable disease:** –Golimumab vs. other anti-TNF agents
Describe incidence of colectomy for intractable disease	
Describe incidence of ACN: –Golimumab –Thiopurines –Other anti-TNF agents	
Describe incidence of colorectal cancer: –Golimumab, thiopurines, other anti-TNF agents	**Describe incidence of colorectal cancer:** –Golimumab, thiopurines, other anti-TNF agents **Compare risk of colorectal cancer:** –Golimumab vs. other anti-TNF agents **Compare risk of ACN:** –Golimumab vs. thiopurines (if comparable)
Describe incidence of HSTCL: –Golimumab, thiopurines, other anti-TNF agents	**Describe incidence of HSTCL:** –Golimumab, thiopurines, other anti-TNF agents

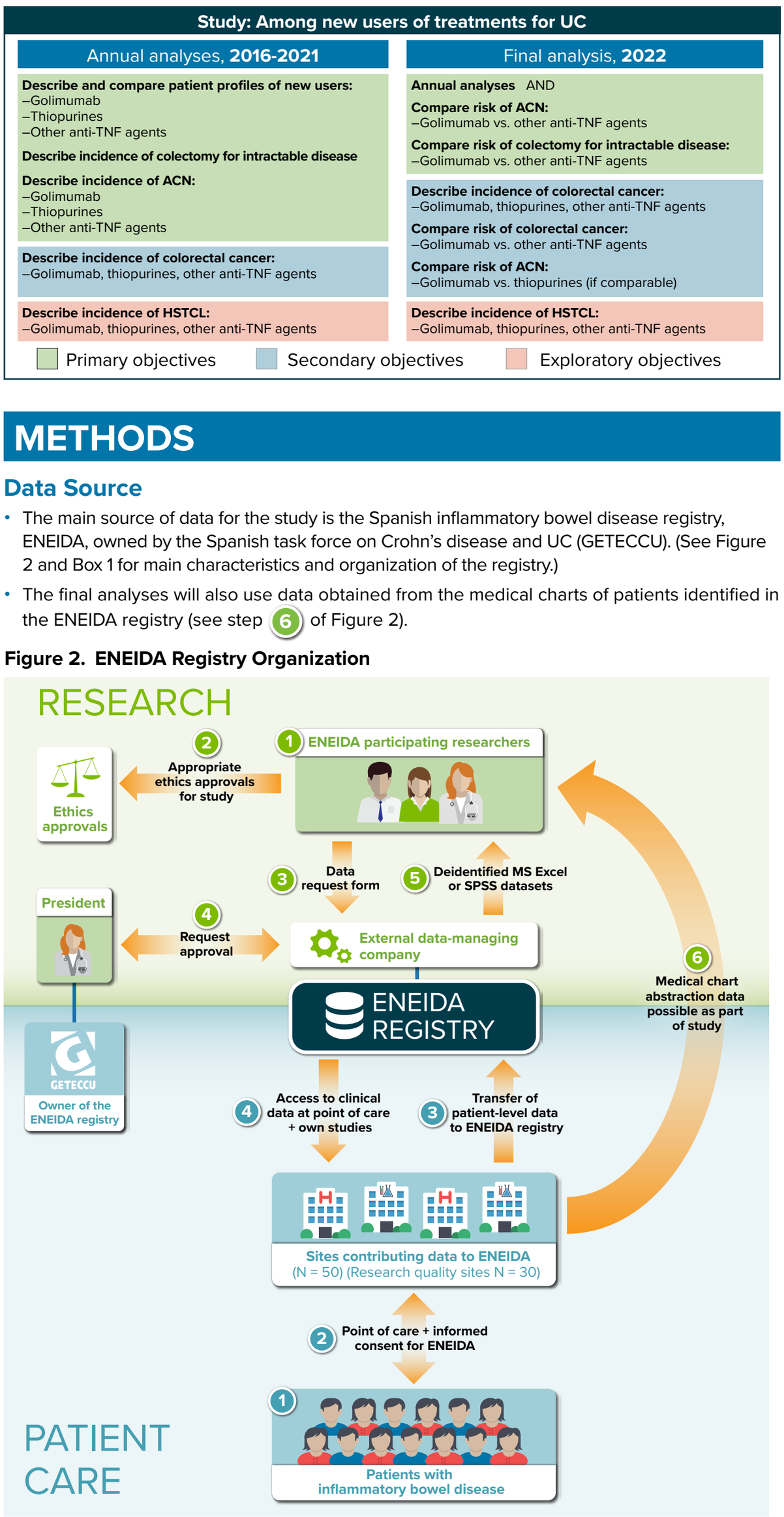
Primary objectives · Secondary objectives · Exploratory objectives

METHODS

Data Source

- The main source of data for the study is the Spanish inflammatory bowel disease registry, ENEIDA, owned by the Spanish task force on Crohn's disease and UC (GETECCU). (See Figure 2 and Box 1 for main characteristics and organization of the registry.)
- The final analyses will also use data obtained from the medical charts of patients identified in the ENEIDA registry (see step 6 of Figure 2).

Figure 2. ENEIDA Registry Organization



PASS Study Population

- Adults with UC newly prescribed golimumab, other anti-TNFα agents, or thiopurines from September 2013 through May 2017 (through May 2022 for the final analyses) were included.
- Figure 3 presents the assembly of the 3 study cohorts and the specific inclusion and exclusion criteria.
- Patients may have qualified for up to 3 study cohorts based on first use of each study drug during the study period. Patients could have switched therapies and, if so, were included in all qualifying cohorts.

Box 1. List of Mandatory Variables in the ENEIDA Registry

List of variables whose transfer in Step 3 of Figure 2 is mandatory for hospitals contributing data to the ENEIDA registry

Demographic data:
- Name
- Date of birth
- Sex
- Date of inclusion in the registry
- Date of last visit

Clinical data:
- Date of the first diagnosis of UC
- Current IBD diagnosis
- Disease location

Immunosuppressive therapy:
- Drug type
- Start date
- Active treatment (yes/no)
- Indication
- Adverse events

Biologic therapy:
- Drug type
- Start date
- Active treatment (yes/no)
- Indication
- Secondary loss of response
- Adverse events

Surgical therapy:
- Date of surgery
- Urgent vs. programmed
- Abdominal vs. perianal
- Indication

Risk factors:
- Family history
- Smoking habit

"Research quality" status of contributing hospitals is based on the percentage of completeness of these variables in the transfers to the ENEIDA registry.

Analysis

- Descriptive statistics of patient characteristics at study cohort entry

RESULTS

- Figure 3 and Figure 4 show cohort description and overall number of identified outcomes as of May 2017, respectively.

Figure 3. Cohort Description

Number of patients with UC diagnosis in ENEIDA = **21,253 as of May 2017**

Number of patients with UC diagnosis in ENEIDA from research quality centers = **14,297 as of May 2017**

Inclusion criteria:
- Research quality site
- ≥ 18 years at study drug start
- Not lost to follow-up

Exclusion criteria:
- Study outcomes before cohort entry
- For each cohort, use of the corresponding drug before September 2013
- Use of any novel biological agent before cohort entry

DESCRIPTION OF INCEPTION COHORTS

Golimumab	Other anti-TNF	Thiopurines	
193	638	610	**N**
12.9	14.4	17.3	**Median follow-up (yrs)**
43	44	42	**Median age at enrollment (yrs)**
48	48	45	**Female (%)**
6.5	4.2	2.4	**Median duration of UC (yrs)**
52	52	45	**Extensive UC (%)**

Figure 4. Outcomes Identified

	TOTAL NUMBER OF OUTCOMES IN THE INCEPTION COHORTS
Colectomy due to intractable disease	45
ACN	2
CRC	0
HSTCL	0

Outcomes have been counted more than once if identified in patients enrolled in more than 1 inception cohort.

DISCUSSION

- The Spanish ENEIDA registry has allowed for the following:
  - Accrual of patients in the 3 study cohorts
  - Identification of study outcomes
  - Acquisition of the information required for the conduct of this EMA-requested PASS
- Until May 2017, the number of patients exposed to golimumab and the number of outcomes have been limited. Patients will be enrolled in the study through May 2022.
- Patients with UC enrolled in the 2 anti-TNFα agent cohorts (i.e., golimumab and other anti-TNFα agents) appear to have similar characteristics. Those enrolled in the thiopurines cohort appear to have less severe UC, which is expected because treatment guidelines recommend the use of an anti-TNFα agent when thiopurines are not sufficient to control the disease.
- The 3 study cohorts were not mutually exclusive, and patients could be in more than 1 cohort if inclusion and exclusion criteria were met. Thus, robust comparability of cohorts is currently limited. Time-dependent analytic methods will be employed in the final analysis to address this limitation.
- Importantly, outcomes may have been counted several times in patients enrolled in > 1 inception cohort (i.e., exposed to > 1 study drug) and thus may not necessarily represent individual outcomes.

CONCLUSIONS

- Based on the preliminary results presented:
  - The ENEIDA registry is a useful data source to study patients with UC in Spain.
  - Extended study periods are needed for less common outcomes.

DISCLOSURE

JF, LR, AT, and SPG, are full-time employees of RTI Health Solutions (RTI-HS). The contract between RTI-HS and the sponsor, MSD, includes independent publication rights. RTI-HS conducts work for government, public, and private organizations. As an RTI-HS employee, SPG has also participated in scientific advisory boards that are funded by pharmaceutical companies. DM and EE are employees of MSD. ED and JPG are employees of Spanish public hospitals.

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