2.0 Synopsis

AbbVie Inc.	Individual Study Table Referring to Part of Dossier: Volume: Page:	(For National Authority Use Only)
Name of Study Drug: Not applicable		
Name of Active Ingredient: Not applicable		
Title of Study: A Multicenter, Observational Cohort Study of Women Receiving Standard of Care (SOC) for the Treatment of Pelvic Pain Attributable to Suspected or Confirmed Endometriosis		
Investigator: [redacted]		
Study Site(s)**:** 23 sites in the United States (US)		
Publications: Not applicable		
Studied Period (Years): First Subject First Visit: 1/20/2020 Last Subject Last Visit: 11/19/2020	**Phase of Development:** 4	

Objective(s):

Primary Objective:

- To describe historic, current, and evolving treatment pathways, treatments, and interventions in women with a suspected or confirmed endometriosis (EM) diagnosis.

Exploratory Objectives:

- To characterize the associations between:
  - Patients' demographic and clinical characteristics at onset of EM-related symptoms (chronic pelvic pain (CPP) and/or dysmenorrhea (DYS) [index date]), treatment sequence during follow-up, and time to diagnosis of EM
  - Clinical characteristics at index date, and outcomes from index date as measured by pain, treatment, and treatment patterns
  - Clinical characteristics at index date and treatment satisfaction at enrollment
  - Patient-reported pain symptoms and comorbid conditions at enrollment and treatment for CPP and/or DYS
- To examine how the various interventions during the study impact the experience of patients with suspected or confirmed EM.
- To describe health care resource utilization (HCRU) (including opioid prescription) for the management of CPP, DYS and EM.
- To examine the use of procedures characterizing phenotypic details of the disease.

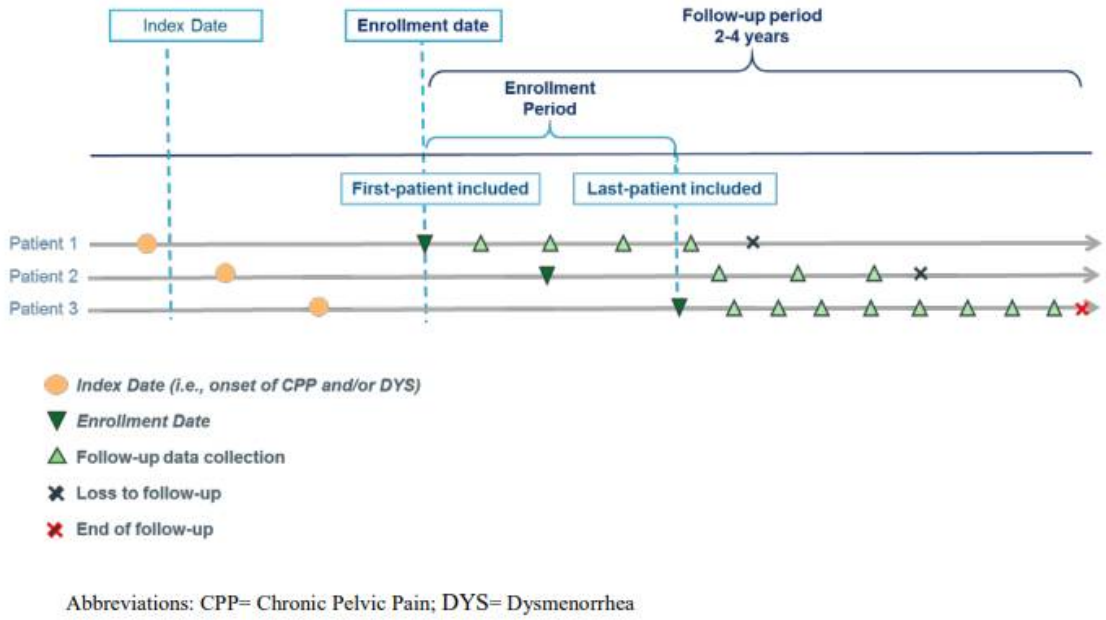
In a subgroup of patients on Orilissa:

- To understand real-world data associated with Orilissa usage in routine clinical practice (dose escalation, duration of treatment, re-treatment, pain relief, quality of life [QoL], geographic region, etc.).

Methodology:

This was a United States (US)-based non-interventional, multicenter, cohort study of reproductive-aged women suffering from suspected or confirmed EM for at least 6 months and having failed nonsteroidal anti-inflammatory drugs (NSAIDs) or initial hormonal/medical therapy. Participating sites assessed all patients who presented during the enrollment period for eligibility for the study. In addition to consenting to participation in the study, all eligible patients provided consent to link their primary-collected data (i.e., electronic case report form [eCRF] from physician and patient-reported outcomes [PROs] provided by the patients) with Longitudinal Prescription Claims (LRx)/Professional Fee Claims (Dx) and, when possible, to PharMetrics Plus (PMTX+) using a unique encrypted identifier that allowed for deterministic linkage across the different data sources (linkage not completed due to early study termination for business reasons by Sponsor). Patients were enrolled at routine clinic visit presentation and all initial assessments were performed at the time of a routine clinical encounter or by referencing the medical record. Participants were followed periodically from enrollment until study termination (with plans to continue through 2-4 years of follow-up) or withdrawal, whichever occurred first. No additional clinic visits were required as part of study participation.

Figure 1. Study Design and Example Patient profiles



Abbreviations: CPP= Chronic Pelvic Pain; DYS= Dysmenorrhea

Number of Subjects (Planned and Analyzed):

The study enrolled 291 women (from an original target of 2,000) from 23 sites in the US. Patients were enrolled in the study based on the inclusion and exclusion criteria described below.

Diagnosis and Main Criteria for Inclusion:

Inclusion criteria

1. Women of reproductive age (i.e., between the first onset of their menses and before the onset of menopause) aged ≥12 years
2. Women who experienced CPP and/or DYS for at least 6 months prior to enrollment and did not show any sustained symptom improvement with NSAIDs or initial hormonal/medical therapy
3. Women with a suspected or confirmed diagnosis of EM at the time of enrollment
4. Women with CPP and/or DYS impacting daily activities as judged by the treating physician

Exclusion criteria

1. Women with CPP and/or DYS attributable **primarily** to a known etiology other than EM
2. Current participation in an interventional clinical trial
3. Women who have had a hysterectomy and/or bilateral oophorectomy
4. Currently pregnant, planning to become pregnant, or utilizing assisted reproductive technologies such as in vitro fertilization
5. History of or active malignancy (with or without systemic chemotherapy), except treated basal cell carcinoma of the skin

Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:

This was an observational study to evaluate the real-world treatment practices and outcomes in patients suffering from suspected or confirmed EM. This study did not recommend the use of any specific treatments; study medication was not provided as part of participation.

Duration of Treatment: Treatment was not evaluated in this study.

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:

A reference therapy was not evaluated in this study.

Criteria for Evaluation

The following variables were captured to describe historic and current treatments in a population of women with suspected or confirmed EM: demographics (e.g., age at enrollment and menarche, race, ethnicity, body mass index [BMI]), clinical and treatment characteristics (e.g., EM characteristics and duration, menstrual bleeding, pain), HCRU (e.g., OTC pain medications, prescription drug use, Orilissa use), PROs, and patient-perceived treatment satisfaction. Demographics, as well as some medical history and menstrual cycle characteristics, were captured using a tailored self-reported survey. Captured PROs included: Endometriosis disease burden assessment tool (EndoDisc), designed to capture pelvic pain burden; Central Sensitization Inventory (CSI), designed to capture central sensitization pain-related symptoms; Pain Catastrophizing Scale (PCS), designed to capture pain catastrophizing; Work Productivity and Activity Impairment-Specific Health Problems (WPAI-SHP), designed to capture QoL and work impairment and productivity; and Patient-Reported Outcomes Measurement Information Systems (PROMIS), designed to capture fatigue. Patient-perceived treatment satisfaction was captured using the Endometriosis Treatment Satisfaction Questionnaire.

Efficacy:

The study was terminated early for business reasons and no study drug was administered; therefore, efficacy was not evaluated in this study.

Pharmacokinetic:

Pharmacokinetics were not evaluated in this study as no study drug was administered.

Safety:

All safety data was summarized by treatment at the time of the event. All adverse events (AEs) (serious and non-serious) among users of AbbVie or non-AbbVie products, during the follow-up period were captured in the eCRF. AEs were classified using standardized terminology from the verbatim description (Investigator term) according to the Medical Dictionary for Regulatory Activities (MedDRA) Coding Dictionary to assign a system organ class (SOC) and preferred term for each event.

The safety reporting followed all applicable external laws, regulatory requirements, and IQVIA internal Standard Operating Procedures. Sites were responsible for reporting safety events associated with AbbVie or non-AbbVie products directly to the manufacturer. Product complaints with non-AbbVie products were reported to the Market Authorization Holder’s safety department by the site.

Statistical Methods

Descriptive statistics, including demographics, menstrual cycle characteristics, and clinical characteristics, were evaluated separately among the overall population and among a subgroup of Orilissa users. Summaries of continuous variables, such as PROs and time since pelvic pain onset, are provided using frequency, mean, median, standard deviation, minimum, and maximum values. Summaries of categorical variables, such as treatment medications and comorbid conditions, are provided using the number and percentage of patients. The proportion of missing data and the main reasons for missing data are summarized where appropriate. As applicable, 2-sided binomial exact confidence intervals (CIs) for proportions, and 95% CIs for means of normally distributed variables are provided. No formal hypothesis testing was performed. In general, missing data was not imputed, and the data was analyzed as recorded in the study. The full analytic set was used for all primary, secondary, and exploratory analyses, unless otherwise indicated. All computations and generation of tables, listings and data for figures were performed using Statistical Analysis Software (SAS®) version 9.2 or higher (SAS Institute, Cary, NC, USA).

Efficacy:

Efficacy was not evaluated in this study as no study drug was administered.

Pharmacokinetic:

Pharmacokinetics were not evaluated in this study as no study drug was administered.

Safety:

The proportion of patients with AEs within specific time intervals were reported along with severity and resolution.

Summary/Conclusions

In this study, 291 patients were eligible and enrolled. No investigational treatment was provided in this study and all treatments were prescribed as SOC. The most common treatment medications from the patient's index date until the end of enrollment for CPP and/or DYS, were NSAID prescriptions (86%) and combined hormonal contraception including pills, patches, and rings (63%). A minority (8%) of patients had an Orilissa prescription. This study was terminated early for business reasons by the sponsor, not due to any safety concerns, and results were incomplete.

Safety Results:

The most common AEs (experienced by >1 patient) were endometriosis (n=2), nausea (n=2), and hot flush (n=2). The current safety profile of Orilissa remains unchanged. At the time of study discontinuation, there were no deaths or serious AEs identified.

Conclusions:

In conclusion, this study is a prospective observational cohort of women with suspected or confirmed EM that was terminated early for business reasons. This is a summary of the methods and data collected up until the point of termination. The current safety profile of Orilissa remains unchanged.