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Personally identifiable information (PII) within this document is either removed or redacted (i.e., specific content is masked irreversibly from view with a black bar) to protect personal privacy. Personally identifiable information includes:

- All named persons associated with the study
- Patient identifiers within text, tables, or figures
- By-patient data listings

Anonymized patient data may be made available subject to an approved research proposal submitted. Information which is considered intellectual property or company confidential was also redacted.

1.0 ABSTRACT

Title

Organization of Teratology Information Specialists (OTIS) Entyvio Pregnancy Exposure Registry

Keywords

Pregnancy, registry, cohort, safety, prospective

Rationale and Background

Vedolizumab (Entyvio) is a monoclonal antibody approved by the US Food and Drug Administration (FDA) for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) and Crohn's disease (CD) who achieved an inadequate response, had a loss of response, or were intolerant to conventional and/or other biologic treatments. Currently, there is limited clinical data on the impact of vedolizumab exposure during pregnancy on pregnancy outcome. This pregnancy exposure registry was undertaken to provide information on the impact of vedolizumab exposure during pregnancy on the mother, fetus and infant. The lack of human fetal safety data for vedolizumab made such a monitoring system an important component of post approval research on the safety of this drug.

Research Question and Objectives

The purpose of the OTIS Entyvio Pregnancy Exposure Registry was to monitor planned and unplanned pregnancies in UC or CD female patients exposed to vedolizumab and to evaluate any possible association between this medication and pregnancy outcome, including the health of the mother, fetus, and infant.

The primary objective of the study was:

- To assess the birth prevalence of major structural birth defects in infants of women with UC or CD exposed to vedolizumab during pregnancy, compared to women with UC or CD exposed to other biologic agents.

The secondary objectives of the study were:
To detect any difference in the prevalence/pattern of major and minor birth defects.

- To estimate the risk of spontaneous abortion, elective abortion, stillbirth, preterm delivery, small size for gestational age (SGA), postnatal growth deficiency, and functional development in live born infants to 1 year of age, and
- To estimate the risk of serious infections, opportunistic infections and malignancies in live born infants reported up through 1 year of age.

Study Design

The study was conducted by the Organization of Teratology Information Specialists (OTIS). The study was a prospective, observational cohort study of pregnant women with UC or CD who were exposed to vedolizumab during pregnancy and a comparison group treated with other biological agents for UC or CD.

The analyses compared pregnancy and infant outcomes in the vedolizumab-exposed group to outcomes in the other biological agents group.

The registry included a secondary comparison group of pregnant women without exposure to vedolizumab and without any chronic disease.

In addition, a series of pregnancies with exposure to vedolizumab but who did not meet the cohort inclusion criteria were enrolled and pregnancy and infant outcome data collected. As this case series included retrospective reports, off-label indications, etc., and there was no appropriate comparison group, the findings from the exposure series are included only in the Appendices to the Analysis Report.

Setting

Pregnant women were recruited throughout the US and Canada through referrals from the OTIS network, spontaneous contact with the study research center by potential participants or health care providers, sponsor referral, or participation in other vedolizumab clinical studies.

Subjects and Study Size, Including Dropouts

The study aimed to recruit 100 pregnant women in each of the 3 cohorts: vedolizumab-exposed, vedolizumab-unexposed but with exposure to other biologic agents for UC or CD, and vedolizumab-unexposed without any chronic disease.

Variables and Data Sources

The primary exposure variable was maternal receipt of at least 1 dose of vedolizumab any time from the first day of the last menstrual period (LMP) to the end of the first trimester, with or without continued use later in pregnancy.

Data on exposures, outcomes and covariates were collected directly from participants through telephone interviews, diaries, and a pediatric examination of a subset of live born infants. Data were also abstracted from medical records.

Results

There were no significant increased risks for major structural birth defects, spontaneous abortion, elective abortion, stillbirth, preterm delivery, pre- or postnatal growth deficiency, serious or opportunistic infections, malignancies or developmental concerns in pregnancies and infants prenatally exposed to vedolizumab compared to unexposed pregnancies and infants. Furthermore, there was no pattern of 3 or more minor defects identified in the 27 infants in the exposed cohort who received the physical examination.

Discussion

In this prospective US and Canada-wide cohort study, the overall findings of the study suggested no increased risk for major structural birth defects or any of the secondary outcomes among vedolizumab-exposed pregnancies compared to pregnancies in women with the same underlying disease conditions who were not treated with vedolizumab.

Marketing Authorization Holder(s)

Names and Affiliations of Principal Investigators

See section 3: Investigators