Vedolizumab in Pregnancy

1. Safety of New Biologics (Vedolizumab and Ustekinumab) and Small Molecules (Tofacitinib) During Pregnancy: A Review.

Author(s): Gisbert, Javier P; Chaparro, María

Source: Drugs; Jul 2020; vol. 80 (no. 11); p. 1085-1100

Publication Date: Jul 2020

Publication Type(s): Journal Article Review

PubMedID: 32562207

Available at Drugs - from SpringerLink - Medicine

Abstract: Two new biological drugs (vedolizumab and ustekinumab) and one small molecule (tofacitinib) have been recently approved for the treatment of inflammatory bowel disease. Therefore, we must be familiar with the safety of these "new" drugs during pregnancy and breastfeeding. In the present article, we critically review available data on the safety of new biologics (vedolizumab and ustekinumab) and small molecules (tofacitinib) during pregnancy and breastfeeding, with special focus on women with inflammatory bowel disease. Bibliographical searches (MEDLINE) up to April 2020 were performed. The timing and mechanisms of placental transfer of vedolizumab and ustekinumab are expected to be similar to anti-TNF agents. Animal studies show no evidence of adverse effects on pre- or post-natal development after administration of vedolizumab and ustekinumab. Just a few studies including patients treated with vedolizumab or ustekinumab during pregnancy have been published, reporting uneventful pregnancies in most cases. The clinical programme of both drugs and post-marketing studies showed no new safety concerns. Due to the expected safety of vedolizumab and ustekinumab during pregnancy, it may be recommended to plan the final pregnancy dose approximately 8 or 12 weeks, respectively, before the estimated date of delivery. Live vaccines should be avoided for up to a year in children exposed in utero to vedolizumab or ustekinumab unless drug elimination has been documented. Miniscule amounts of vedolizumab and ustekinumab are transferred to breast milk, so breastfeeding is
probably safe. There is no evidence of adverse effect of vedolizumab or ustekinumab paternal exposure. Regarding tofacitinib, it is reasonable to assume that this molecule crosses the placenta from the beginning of pregnancy. In animal studies, tofacitinib was feticidal and teratogenic in rats and rabbits, although at exposures many times greater than the standard human dose. Reported outcomes of pregnancy cases identified from tofacitinib randomised controlled trials, post-approval and non-interventional studies, and spontaneous adverse-event reporting appear similar to those observed in the general population. Nevertheless, at present, the use of tofacitinib during pregnancy should be avoided. Although no human studies have reported outcomes of breastfeeding with small molecules such as tofacitinib, this drug is present in lactating rat milk so, at present, breastfeeding should be avoided. Pregnancy among patients with paternal exposure to tofacitinib appears to be safe. In summary, we can conclude that new biologic agents (vedolizumab and ustekinumab) and small molecules (tofacitinib) should be used during pregnancy only if the benefits to the mother outweigh the risks to the mother and unborn child.

Database: Medline

2. VEDOLIZUMAB LEVELS IN BREAST MILK: RESULTS FROM A PROSPECTIVE, POSTMARKETING, MILK-ONLY LACTATION STUDY IN NURSING MOTHERS WITH INFLAMMATORY BOWEL DISEASE

Author(s): Sun W.; Fennimore B.; Beaulieu D.; Arsenescu R.; Stein A.C.; Chen J.; Lin T.; McKnight S.; Rosario M.; Lirio R.A.

Source: Gastroenterology; May 2020; vol. 158 (no. 6)

Publication Date: May 2020

Publication Type(s): Conference Abstract

Available at Gastroenterology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

Abstract: Background: The safety of inflammatory bowel disease (IBD) medications during lactation is of significant interest and relevance to female patients of childbearing potential. Available data regarding the safety and transfer of biologic agents via breast milk are limited to case reports. Vedolizumab has a well-established, positive benefit-risk profile in adult IBD patients. Literature data show that vedolizumab is detectable in human milk. Method(s): A prospective, postmarketing, phase 4, open-label, milk-only lactation study was conducted to assess vedolizumab concentrations in breast milk from lactating women with IBD who were on an established vedolizumab maintenance regimen (300 mg intravenous [IV] every 8 weeks [Q8W] or an alternative dose frequency). Maternal milk samples were serially collected throughout the dosing interval on Days 1 (predose and 1 hour after the end of vedolizumab infusion), 4, 8, 15, 29, and 57 to allow the estimation of drug excreted in milk relative to the maternal dosage. Maternal safety data were also collected. Result(s): A total of 11 patients were enrolled in the study. Vedolizumab was detectable in the majority of milk samples collected on Days 1 and 57, and in all samples collected at other time points. Following receipt of vedolizumab 300 mg IV on Day 1, the vedolizumab milk concentration increased with a median time to peak concentration of 3-4 days, and subsequently decreased exponentially. For the 9 patients on the Q8W regimen, median peak concentration was 0.213 micro g/mL (range, 0.098-0.561 micro g/mL); the geometric mean daily infant dosage, calculated using average concentration over 8-week dosing interval (0.13 micro g/mL), was 0.02 mg/kg/day with a corresponding geometric mean percentage of maternal dosage consumed in breast milk by infants of 21%. The maternal safety profile was acceptable and similar to that observed in previous adult studies. Leveraging the mean trough serum concentration of 11.2 micro g/mL from historical studies of vedolizumab, the ratio of mean milk concentration (trough, 0.05 micro g/mL; peak, 0.25 micro g/mL) to serum concentration was approximately 0.4%-2.2%, which is consistent with published data for vedolizumab and
comparable with several other monoclonal antibody therapeutics for IBD. Published vedolizumab studies also showed no increase in general or gastrointestinal tract infections in the infants exposed to vedolizumab in breast milk, and exposed infants reached their acceptable development milestones through up to 10 months of follow-up. Conclusion(s): Vedolizumab was found to be present in human breastmilk at a low level. The impact of vedolizumab IV administration during breastfeeding is expected to be minimal.

**Database:** EMBASE

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### 3. VEDOLIZUMAB DRUG LEVELS IN MATERNAL AND CORD BLOOD FOLLOWING TREATMENT OF INFLAMMATORY BOWEL DISEASE IN PREGNANCY: ONGOING MULTICENTRE PROSPECTIVE STUDY FROM THE CZECH REPUBLIC

**Author(s):** Pipek B.; Duricova D.; Mitrova K.; Bortlik M.; urban O.; Lukas M.

**Source:** Gastroenterology; May 2020; vol. 158 (no. 6)

**Publication Date:** May 2020

**Publication Type(s):** Conference Abstract

**Available at** Gastroenterology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location]: Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

**Abstract:** Background: There is a limited evidence indicating that newborns exposed to vedolizumab (VDZ) in utero have lower drug serum levels compared to other biologicals (1). Our aim was to assess VDZ drug levels in cord blood and maternal blood of women with inflammatory bowel disease (IBD) exposed to VDZ during pregnancy. Method(s): This multicentre, retrospectively - prospective study started in February 2019 to assess the safety of new biologics, including VDZ, during pregnancy for maternal IBD. In prospectively enrolled women, both maternal and cord blood samples were obtained at the time of delivery to measure the drug concentration. Data on patients demographics, clinical characteristics and pregnancy, and newborn outcome were collected by treating physician using predefined questionnaire. ELISA method was used for measurement of VDZ concentrations. Result(s): So far, 15 women exposed to VDZ during pregnancy have been included (11 with Crohns disease). Of them, 12 already terminated their pregnancy with 10 women delivering live infant. Drug levels of VDZ at birth were measured in 7 infant-mother pairs (Table 1). All 7 women were on maintenance VDZ treatment during pregnancy scheduled every 8 weeks. The median time of the last drug infusion before delivery was week 32 (range: 19-38). All children were born at term with a median birth weight of 3120 grams (range: 2945-3780) and had no complications. In all, but one case, VDZ drug levels in cord blood were lower than those in maternal blood at the time of delivery. The median infant/maternal ratio was 0.66 (range: 0.29-1.02). There was a borderline significant correlation between VDZ cord levels and gestational week of last VDZ administration (Spearmans rho=0.75; p=0.05). Conclusion(s): Preliminary results of our study confirm previous limited reports of different pharmacokinetics of VDZ compared to other biologics which results in lower drug levels in cord blood than maternal blood at birth. Further studies should explain this discrepancy.


**Database:** EMBASE
4. **236 INFLIXIMAB, ADALIMUMAB AND VEDOLIZUMAB LEVELS ARE NOT ALTERED BY PREGNANCY PROGRESSION IN IBD PATIENTS AND NEONATAL VEDOLIZUMAB LEVELS ARE LOWER THAN IN MOTHERS: RESULTS FROM THE PICCOLO STUDY**

**Author(s):** Flanagan E.; Gibson P.R.; Ross A.; Rosella O.; Rosella G.; Bell S.J.

**Source:** Gastroenterology; May 2020; vol. 158 (no. 6)

**Publication Date:** May 2020

**Publication Type(s):** Conference Abstract

Available at Gastroenterology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

**Abstract:** Background: Optimal timing for the last intrapartum dose of biologic agents is controversial. We established that cord blood levels of anti-TNF agents in exposed infants are greater than maternal levels1, and another study with limited observations suggested maternal infliximab (IFX) levels increased in pregnancy but adalimumab (ADA) levels did not2. The effect of pregnancy on levels of vedolizumab (VDZ), and placental transfer and time to clearance of VDZ in exposed infants remain undefined. Method(s): We performed a prospective observational study of maternal anti-TNF and VDZ levels pre-conception, in each trimester of pregnancy, at delivery and post-partum where possible. Women with IBD on IFX, ADA or VDZ who were pregnant or planning pregnancy were recruited. Serum trough IFX and ADA levels were measured by ELISA (Q-INFLIXI and Q-ADA (Matriks Biotek, Turkey) or Promonitor (Grifols, Spain)) and VDZ levels by ELISA (Theradiag, France). Infant VDZ levels were measured from the umbilical cord at delivery and repeated at around 6-8 weeks and 3 months to assess time to clearance. Result(s): 49 patients (24 IFX, 14 ADA, 11 VDZ) with at least 2 observations on stable dosing were included. The median number of levels per patient was 3 (range 2-5). Infliximab cohort (n=24): Median IFX trough levels were stable (Figure 1). IFX was administered 6-8 weekly at doses of 5 mg/kg (n=21) or 10 mg/kg (n= 2) except for one patient on 4-weekly dosing. The last dose was given at a median 32 weeks; 3 remain pregnant. Adalimumab cohort (n=14): Median ADA levels were stable (Figure 1). 12 were on ADA fortnightly and 2 on weekly. 11 continued ADA throughout pregnancy and 3 stopped at 30-33 weeks; 2 remain pregnant. 3 patients were induced in pregnancy at least 12 weeks before the earliest ADA level. Vedolizumab cohort (n= 11): Trough VDZ levels were stable (Figure 2). 8 patients were on 8-weekly dosing and 3 were on 4-weekly. The last dose was given at a median 30 weeks; 4 remain pregnant (Patients H-K). Vedolizumab in infants (n=8): The median VDZ cord blood level was 4.95 (1-19) mug/mL with median infant:maternal ratio of 0.6 (0.4-0.9). VDZ was cleared at 8 weeks of age in 3 infants and by 15 weeks in 2 infants. Conclusion(s): The stability of maternal levels of IFX, ADA and VDZ during pregnancy indicate that intrapartum dosing adjustment and routine therapeutic drug monitoring for patients in remission are not needed. Unlike anti-TNF, infant VDZ levels were lower in cord blood than in mothers and were cleared by 15 weeks. 1. Julsgaard M et al, Concentrations of Adalimumab and Infliximab in Mothers and Newborns, and Effects on Infection (ERA study); Gastroenterology 2016; 151:110-119 2. Seow CH et al, The effects of pregnancy on the pharmacokinetics of infliximab and adalimumab in inflammatory bowel disease, Aliment Pharmacol Ther 2017; 45:1329-1338Copyright © 2020

**Database:** EMBASE
5. The pre- and post-authorisation data published by the European medicines agency on the use of biologics during pregnancy and lactation

**Author(s):** Ghalandari N.; Dolhain R.J.E.M.; Hazes J.M.W.; Siezen C.L.E.; van der Laan J.W.; Crijns H.J.M.J.; van der Woude C.J.; van Puijenbroek E.P.

**Source:** British Journal of Clinical Pharmacology; Mar 2020; vol. 86 (no. 3); p. 580-590

**Publication Date:** Mar 2020

**Publication Type(s):** Article

**PubMedID:** 31633830

Available at [British journal of clinical pharmacology](https://onlinelibrary.wiley.com/doi/10.1111/bcp.14233) - from Wiley Online Library

Available at [British journal of clinical pharmacology](https://onlinelibrary.wiley.com/doi/10.1111/bcp.14233) - from Unpaywall

**Abstract:** Aims: The effects of biologics on reproduction/lactation are mostly unknown although many patients that receive biologics are women of reproductive age. The first objective of this study was to investigate the publicly available data on pregnancy/lactation before and after marketing authorization in Europe of biologics for the indications of rheumatologic inflammatory autoimmune diseases and inflammatory bowel disease. Secondary objectives included the assessment of the clinical relevance of the provided data and comparison of initial and post-authorization data.

Method(s): Initial and post-authorization data were extracted from the European Public Assessment Reports and the latest versions of Summary of Product Characteristics using publicly available documents on the European Medicines Agency's website. Four sections were categorized regarding pregnancy outcomes: pre-clinical/animal studies, human female fertility, pregnancy-related outcomes and congenital malformations in the human fetus. Three sections were categorized regarding lactation outcomes: pre-clinical/animal studies, excretion in human breast milk and absorption in children through breastfeeding. The clinical applicability of each category was scored by specified criteria, based on scientific literature, and further as defined by the authors. Result(s): For the 16 included biologics, post-authorization data were delivered only for adalimumab, certolizumab pegol, etanercept and infliximab. For the 12 remaining biologics limited data on pregnancy and lactation during the post-marketing period of 2-21 years were available.

Conclusion(s): In this article several suggestions are provided for improving a multidisciplinary approach to these issues. The initiation of suitable registries by marketing authorization holders and data transparency for clinicians and academics are highly endorsed.

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**Database:** EMBASE
Purpose of Review: Treating moderate-to-severe inflammatory bowel disease has become increasingly complex as the array of available biologics increases. Moreover, tofacitinib, the first small molecule approved for IBD, is available for use in ulcerative colitis. Choosing the right biologic, for the right patient, at the right time, can be a confusing and daunting task for clinicians.

Recent Findings: In this review, we summarize the evidence for first-line use of the available biologics by disease state. Special circumstances for consideration including rapidity of action, safety, comparative effectiveness, postoperative Crohn's disease, fertility and pregnancy, and extraintestinal manifestations are discussed. In the moderate-to-severe UC patient, vedolizumab and infliximab are preferred first-line options. In the moderate-to-severe CD patient with a penetrating phenotype or with multiple EIMs, infliximab or adalimumab are the preferred first-line agents. In the moderate-to-severe CD patient with an inflammatory phenotype, anti-TNF, vedolizumab, and ustekinumab are all reasonable options.

Database: Medline
7. Pregnancy outcomes in inflammatory bowel disease patients treated with vedolizumab, anti-TNF or conventional therapy: results of the European CONCEIVE study.

**Author(s):** Moens, Annick; van der Woude, C Janneke; Julsgaard, Mette; Humblet, Evelien; Sheridan, Juliette; Baumgart, Daniel C; Gilletta De Saint-Joseph, Cyrielle; Nancey, Stéphane; Rahier, Jean-François; Bossuyt, Peter; Cremer, Anneline; Dewit, Sophie; Eriksson, Carl; Hoentjen, Frank; Krause, Thomas; Louis, Edouib; Macken, Elisabeth; Milenkovic, Zoran; Nijs, Jochen; Posen, Annelies; Van Hootegem, Anneleen; Van Moerkercke, Wouter; Vermeire, Séverine; Bar-Gil Shitrit, Ariella; Ferrante, Marc

**Source:** Alimentary pharmacology & therapeutics; Jan 2020; vol. 51 (no. 1); p. 129-138

**Publication Date:** Jan 2020

**Publication Type(s):** Research Support, Non-u.s. Gov't Multicenter Study Journal Article

**PubMedID:** 31692017

Available at Alimentary pharmacology & therapeutics - from Wiley Online Library

Available at Alimentary pharmacology & therapeutics - from Unpaywall

**Abstract:**

**BACKGROUND**

Women with inflammatory bowel diseases (IBD) often receive biologicals during pregnancy to maintain disease remission. Data on outcome of vedolizumab-exposed pregnancies (VDZE) are sparse. AIMS To assess pregnancy and child outcomes of VDZE pregnancies and to compare these results to anti-TNF exposed (TNFE) or both immunomodulatory and biologic unexposed (CON IBD) pregnancies. METHODS A retrospective multicentre case-control observational study was performed.

**RESULTS**

VDZE group included 79 pregnancies in 73 IBD women. The TNFE and CON IBD group included 186 pregnancies (162 live births) in 164 IBD women and 184 pregnancies (163 live births) in 155 IBD women, respectively. At conception, cases more often had active disease ([VDZE: 36% vs TNFE: 17%, P = .002] and [VDZE: 36% vs CON IBD: 24%, P = .063]). No significant difference in miscarriage rates were found between groups (VDZE and TNFE: 16% vs 13%, P = .567; VDZE and CON IBD: 16% vs 10%, P = .216). In live-born infants, median gestational age and birthweight were similar between groups. Median Apgar score at birth was numerically equal. Prematurity was similar in the VDZE group compared to the control groups, even when correcting for disease activity during pregnancy. The frequency of congenital anomalies was comparable between groups as were the percentages of breastfed babies. During the first year of life, no malignancies were reported and infants’ infection risk did not significantly differ between groups.

**CONCLUSION**

No new safety signal was detected in VDZE pregnancies although larger, prospective studies are required for confirmation.

**Database:** Medline
8. Editorial: effects of vedolizumab during pregnancy in the CONCEIVE study
Author(s): Winter R.W.
Source: Alimentary Pharmacology and Therapeutics; Jan 2020; vol. 51 (no. 2); p. 307-308
Publication Date: Jan 2020
Publication Type(s): Editorial
PubMedID: 31880010
Available at Alimentary pharmacology & therapeutics - from Wiley Online Library
Available at Alimentary pharmacology & therapeutics - from Unpaywall
Database: EMBASE

9. Insights into the treatment of inflammatory bowel disease in pregnancy
Author(s): Shannahan S.E.; Erlich J.M.; Peppercorn M.A.
Source: Therapeutic Advances in Gastroenterology; 2019; vol. 12
Publication Date: 2019
Publication Type(s): Review
Available at Therapeutic advances in gastroenterology - from Europe PubMed Central - Open Access
Available at Therapeutic advances in gastroenterology - from Free Medical Journals . com
Available at Therapeutic advances in gastroenterology - from Unpaywall
Abstract: Patients diagnosed with inflammatory bowel disease (IBD) are most commonly diagnosed in late adolescence or early adulthood, with half of patients being diagnosed before age 32, thus impacting peak years of reproduction and family planning. While controlled IBD has no negative effects on the ability to conceive, there is overall a trend towards voluntary childlessness due to patients' concerns for adverse fetal outcomes from underlying IBD and from adverse medication effects. Active disease at the time of conception is associated with worsening disease activity during pregnancy and carries a higher risk of poor fetal outcomes. It is therefore important to maintain remission during pregnancy, which is often achieved with pharmacologic therapy. The goal of this paper is to provide a comprehensive review of the current literature and safety data for pharmacologic treatment of IBD in pregnancy, in breastfeeding women, and in men planning to have children. Copyright © The Author(s), 2019.
Database: EMBASE
10. OUTCOMES OF PREGNANCY IN IBD PATIENTS TREATED WITH VEDOLIZUMAB, ANTI-TNF OR CONVENTIONAL THERAPY


Source: Gastroenterology; 2019; vol. 156 (no. 6)

Publication Date: 2019

Publication Type(s): Conference Abstract

Abstract: Background Women with inflammatory bowel diseases (IBD) often receive biologicals during pregnancy to maintain disease remission prior to conception and throughout pregnancy. However, data on vedolizumab exposed pregnancies (VDZE) are scarce. Methods This retrospective multicenter observational study assessed outcomes of VDZE pregnancies in IBD patients (group A). European gastroenterologists were asked to report all VDZE pregnancies. Details of underlying IBD, pre- and postnatal outcomes were collected. Results: were compared to anti-TNF exposed (TNFE, group B) or both immunomodulatory and biologic unexposed (IBU, group C) pregnancies. The control groups were prospectively enrolled from two separate centers with a specialized IBD preconception and pregnancy clinic. Results Group A included 86 pregnancies in 81 women [53% Crohn's disease (CD), 70 live births] from 31 centers in 11 countries. Groups were comparable regarding baseline characteristics, though group A included more women with ileocolonic CD and perianal involvement. At conception 35% of VDZE women had active disease, 17% were on steroids and 20% on immunomodulators. Also, 54% previously failed two biologicals. Group B and C included 186 pregnancies in 155 women and 185 pregnancies in 164 women, respectively (83% vs. 55% CD, 162 vs. 163 live births). Controls had less active disease at conception (B: 16%, C: 24%) and fewer were taking steroids (B: 8%, C: 14%). More miscarriages were seen in group A compared to B (16% vs. 13%, p=0.46) and C (16% vs. 8%, p=0.03). However, after excluding patients with reported active disease in pregnancy, the number of miscarriages was similar in group A compared to B (14% vs. 14%, p=1.0) and C (14% vs. 12%, p=0.80). Neonatal outcomes are displayed in table 1. In live-born infants, median gestational age and birth weight were comparable between groups. Also, median Apgar score at birth was numerically equal in all groups. The number of premature born infants was not significantly different between groups, nor was the amount of reported congenital anomalies. The percentages of breastfed children were similar in all groups. During the first year of life, no malignancies were reported and the infants' infection risk did not significantly differ between groups. Conclusion VDZE pregnancies were associated with more miscarriages, however active disease in pregnancy rather than drug effect seems to have been the driver of this adverse pregnancy outcome, since no significant difference was observed after exclusion of patients with reported active disease in pregnancy. Still, larger prospective studies are needed for confirmation.

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Database: EMBASE
11. No severe neonatal and maternal complications in female patients with inflammatory bowel diseases treated with ustekinumab or vedolizumab during pregnancy

**Author(s):** Wils P.; Seksik P.; Stefanescu C.; Nancey S.; Allez M.; Laharie D.; Pineton De Chambrun G.; Altwegg R.; Gilletta De Saint Joseph C.; Vuitton L.; Viennot S.; Serrero M.; Fumery M.; Savoye G.; Collins M.; Brixi H.; Bouguen G.; Tavernier N.; Boualit M.; Amiot A.; Pariente B.

**Source:** United European Gastroenterology Journal; Oct 2019; vol. 7 (no. 8); p. 15-16

**Publication Date:** Oct 2019

**Publication Type(s):** Conference Abstract

**Available at United European Gastroenterology Journal - from Europe PubMed Central - Open Access**

**Abstract:** Introduction: Inflammatory bowel disease (IBD) has a high incidence in population of childbearing age. Ustekinumab, a fully human monoclonal antibody targeting the p40 subunit of interleukins 12 and 23, and vedolizumab, an anti alpha4 beta7 integrin, are biologics currently used in IBD with immunosuppressant or anti TNF failure. Data concerning use and safety of these new biologics during pregnancy are scarce. Aims & Methods: We conducted a retrospective multicenter study in the GETAID group and collected cases of women with IBD who received at least one injection of ustekinumab or vedolizumab during pregnancy or in the last 2 months before conception. The aims of the study were (1) to evaluate pregnancy and neonatal outcomes in IBD female patients exposed to ustekinumab or vedolizumab during pregnancy, and (2) to observe the impact of ustekinumab or vedolizumab withdrawal on disease activity during pregnancy and postpartum. Result(s): Sixty-seven pregnancies in 62 IBD females (43 for Crohn’s disease and 19 for ulcerative colitis) were reported among 19 centers of the GETAID group. Median age at conception was 29 years. Median time between introduction of ustekinumab or vedolizumab treatment and pregnancy was 12 months. Twenty-five pregnancies occurred on ustekinumab: 7 received ustekinumab in the last 2 months before conception, 11 received 1 injection after conception, and 7 stopped ustekinumab in the 2nd trimester. Among the 25 pregnancies occurred on ustekinumab, there were 22 (88%) live births, 1 elective termination and 2 spontaneous abortions. Maternal complications were reported in 2 women (one gestational diabetes and one threat of premature labor). Fetal complications were reported in 3 pregnancies (intra uterine growth restriction). Four newborns presented a non severe neonatal complication (3 preterm deliveries, one low birth weight) and one a Tetralogy of Fallot. Forty-two pregnancies occurred on vedolizumab: 15 received vedolizumab in the last 2 months before conception, 16 received 1 injection after conception, and 11 stopped vedolizumab (6 during the 2nd trimester and 5 during the 3rd trimester). Among the 42 pregnancies occurred on vedolizumab, there were 36 (86%) live births, 1 elective termination (for Down Syndrom) and 5 (12%) spontaneous abortions. Maternal complications were reported in 5 women (one cholestasis and 4 pre-eclampsia). Fetal complications were reported in one pregnancy (intra uterine growth restriction) and 13 newborns developed a neonatal complication (6 preterm deliveries, 6 low birth weight and one congenital corpus callosum hypoplasia). Concerning IBD activity, 65% of women were in remission at conception. Among them, only 2 patients flared during pregnancy. Conclusion(s): We reported in 67 pregnancies under vedolizumab or ustekinumab exposition, no severe neonatal (except a cardiac malformation) and maternal complications. However, additional prospective evaluations regarding safety concerns pregnancy outcomes in patients directly exposed to ustekinumab or vedolizumab are needed.

**Database:** EMBASE
INTRODUCTION: Vedolizumab is a gut-selective immunoglobulin (Ig) G1 monoclonal antibody that binds to alpha4beta7 integrin; it is approved for the treatment of moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC) in the U.S. and elsewhere. Published studies on the effect of vedolizumab during human pregnancy are limited. Data from the ongoing Vedolizumab Pregnancy Exposure Registry (NCT02678052) in the U.S. and Canada have been collected by the MotherToBaby Pregnancy Studies conducted by the Organization of Teratology Information Specialists (OTIS). This prospective observational cohort study intends to enroll and analyze the outcomes of 100 vedolizumab-exposed participants compared to 100 disease-matched (DM) comparison and 100 healthy comparison (HC) participants. This abstract describes progress of the study through March 1, 2019. METHOD(S): Pregnant women treated with vedolizumab for UC or CD for at least some part of the first trimester were enrolled in the vedolizumab-exposed group. Pregnant women with no exposure to vedolizumab were enrolled in a DM comparison group. Pregnant women with no exposure to any biologic during pregnancy and not diagnosed with an autoimmune disease or any other disease as defined by the OTIS Research Center were enrolled in a HC group. Pregnancy exposure and outcome data were collected from telephone interviews and medical records. The Short Quality of Life in Inflammatory Bowel Disease Questionnaire (SIBDQ) was administered to women with CD or UC at enrollment and 32 weeks' gestation. Follow-up of live born children included a dysmorphological exam, pediatric records review and developmental screening at one year of age. RESULT(S): Between December 2015 and March 2019, outcomes were collected for 223 women, 53 in the vedolizumab group, 88 in the DM group, and 82 in the HC group. Preliminary descriptive data are shown in Table 1. No major structural birth defects were reported in the vedolizumab group, compared to 5 (5.7%) in the DM group, and 4 (5.3%) in the HC group. There was no evidence of a pattern of minor structural defects in the vedolizumab group. CONCLUSION(S): Updated data indicate pregnant women treated with vedolizumab in at least the 1st trimester have similar birth outcomes to disease-matched and healthy comparison women. The Vedolizumab Pregnancy Exposure Registry is ongoing with formal statistical analysis to be performed when the study is completed. (Figure Presented).
13. Peripartum exposure to biologic therapy does not impact wound healing after cesarean section in women with inflammatory bowel disease

Author(s): Aboubakr A.; Riggs A.; Mella M.; Dubinsky M.C.

Source: American Journal of Gastroenterology; Oct 2019; vol. 114

Publication Date: Oct 2019

Publication Type(s): Conference Abstract

Available at American Journal of Gastroenterology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at American Journal of Gastroenterology - from Unpaywall

Abstract: INTRODUCTION: Inflammatory bowel disease (IBD) commonly affects women during their childbearing years, and mode of delivery is a frequent topic of concern. Rates of Cesarean section (C-section) are increased in women with IBD. Biologics are commonly used during pregnancy and data on their effect on C-section outcomes are limited. We investigated whether exposure to biologic agents impacts wound healing after C-section in women with IBD. METHOD(S): Women with IBD seeking consultation at the Marie and Barry Lipman IBD Preconception and Pregnancy Planning (I-PrePP) Clinic between years 2015-2019 were eligible. Delivery data collected as part of the I-PrePP prospective registry were analyzed. Primary outcome was rate of surgical site infection prior to discharge and/or at follow-up visits 2 and 6 weeks after delivery. Timing of biologics were investigated as well as impact of steroids on wound healing. Descriptive statistics summarized patient level data using frequency for categorical variables and median [IQR] for continuous.

RESULT(S): Of the 84 women who presented or became pregnant after their I-PrePP consultation, delivery data was available from 64 (38 (59%) Crohn’s disease, 24 (38%) ulcerative colitis, 2 IBD-U (3%)) pregnancies (median [IQR] age 33 [29-35] years). Indications for the 37 C-sections (58%) included: history of perianal disease (n = 12, 32%), severely active inflammation (n = 1, 3%), ileal pouch anal anastomosis or end ileostomy (n = 2, 5%), previous C-section (n = 7, 19%), other obstetrical indications (large for gestational age, arrest of labor, malpresentation) (n = 14, 38%), or other (n = 1, 3%). Twenty six of 37 (70%) women with C-sections were exposed to biologics during pregnancy: infliximab (n = 13, 35%), adalimumab (n = 5, 14%), ustekinumab (n = 3, 8%), vedolizumab (n = 4, 11%), and certolizumab (n = 1, 3%). Time from last dose to delivery was 6 [4-7] weeks, and 21 of 26 (81%) received therapy at the time of (n = 10) and/or within 2 weeks (n = 11) of delivery. Four (11%) were exposed to systemic steroid therapy, including 2 patients at the time of and/or within 2 weeks of delivery. There was no incidence of surgical site infection in the biologic exposed patients, 1 case of MRSA bacteremia with an intra-abdominal abscess in a patient on systemic steroids, and 1 superficial infection in a non-medicated patient. CONCLUSION(S): Our data suggests that biologics exposure in the peripartum period does not adversely affect wound healing after cesarean section in women with IBD.

Database: EMBASE
Ulcerative colitis and Crohn's disease are the principal forms of inflammatory bowel disease. Both represent chronic inflammation of the gastrointestinal tract, which displays heterogeneity in inflammatory and symptomatic burden between patients and within individuals over time. Optimal management relies on understanding and tailoring evidence-based interventions by clinicians in partnership with patients. This guideline for management of inflammatory bowel disease in adults over 16 years of age was developed by Stakeholders representing UK physicians (British Society of Gastroenterology), surgeons (Association of Coloproctology of Great Britain and Ireland), specialist nurses (Royal College of Nursing), paediatricians (British Society of Paediatric Gastroenterology, Hepatology and Nutrition), dietitians (British Dietetic Association), radiologists (British Society of Gastrointestinal and Abdominal Radiology), general practitioners (Primary Care Society for Gastroenterology) and patients (Crohn's and Colitis UK). A systematic review of 88247 publications and a Delphi consensus process involving 81 multidisciplinary clinicians and patients was undertaken to develop 168 evidence- and expert opinion-based recommendations for pharmacological, non-pharmacological and surgical interventions, as well as optimal service delivery in the management of both ulcerative colitis and Crohn's disease. Comprehensive up-to-date guidance is provided regarding indications for, initiation and monitoring of immunosuppressive therapies, nutrition interventions, pre-, peri- and postoperative management, as well as structure and function of the multidisciplinary team and integration between primary and secondary care. Twenty research priorities to inform future clinical management are presented, alongside objective measurement of priority importance, determined by 2379 electronic survey responses from individuals living with ulcerative colitis and Crohn's disease, including patients, their families and friends. Copyright © Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.
15. The use of vedolizumab in pregnancy and breastfeeding in women with inflammatory bowel disease

Author(s): Glassner K.; Abraham B.P.
Source: Practical Gastroenterology; Sep 2019; vol. 43 (no. 9); p. 13-18
Publication Date: Sep 2019
Publication Type(s): Article
Database: EMBASE


Author(s): Picardo, Sherman; Seow, Cynthia H
Source: Drugs; Jul 2019; vol. 79 (no. 10); p. 1053-1063
Publication Date: Jul 2019
Publication Type(s): Journal Article Review
PubMedID: 31183768
Available at Drugs - from SpringerLink - Medicine

Abstract: The inflammatory bowel diseases commonly affect individuals during their peak reproductive years. Patients are often concerned about the impact of medical therapies on their ability to conceive, effect on the fetus, as well as the ability to breastfeed, which has led to poor medical adherence during pregnancy. However, most medications are safe, and discontinuation may lead to active disease, which is associated with adverse materno-fetal outcomes. The anti-TNF biologic therapies, infliximab and adalimumab have been extensively studied in the context of pregnancy. They are actively transferred to the placenta during the second and third trimesters; these have not been associated with an increased rate of congenital abnormalities or fetal death. The minimal amounts of drug that are transferred to breast milk are proteolyzed by the infant’s digestive system with no reported short- or long-term adverse effects. There is a paucity of clinical data for the other approved anti-TNF agents or newer anti-integrin (vedolizumab) and anti-interleukin (ustekinumab) therapies used in the management of inflammatory bowel disease; however, no significant safety signals have been documented thus far. The new oral small molecule therapy, tofacitinib is teratogenic in animal models and is contra-indicated in patients attempting pregnancy. It is important that patients, as well as physicians managing patients with these conditions, be aware of the impact of these medical therapies during pregnancy.

Database: Medline
17. Exposure to Vedolizumab in IBD Pregnant Women Appears of Low Risk for Mother and Neonate: A First Prospective Comparison Study.

**Author(s):** Bar-Gil Shitrit, Ariella; Ben Ya’acov, Ami; Livovsky, Dan Meir; Cuker, Tzufit; Farkash, Rivka; Hoyda, Aviya; Granot, Tami; Avni-Biron, Irit; Lahat, Adi; Goldin, Eran; Grisaru-Granovsky, Sorina

**Source:** The American journal of gastroenterology; Jul 2019; vol. 114 (no. 7); p. 1172-1175

**Publication Date:** Jul 2019

**Publication Type(s):** Journal Article

**PubMedID:** 30920987

Abstract: **OBJECTIVES**

Despite encouraging data gathered in inflammatory bowel diseases (IBD) patients, Vedolizumabs' (VDZ) safety profile in pregnancy is not established. **DESIGN**

Data of 330 consecutive pregnancies with IBD was prospectively collected. **RESULTS**

Women with IBD were treated with: VDZ (n = 24), anti-tumor necrosis factors (n = 82) or conventional therapy (n = 224). Gravidity and parity were similar among the 3 groups. The VDZ group was comprised mostly of Crohn's disease patients who were all not naïve to biological treatment. They had significantly higher conception rates during active disease (P < 0.05), with fewer flares during pregnancy. **DISCUSSION**

Although further study is needed, VDZ appears of low risk during pregnancy.

**Database:** Medline

18. Pregnancy outcomes in IBD patients treated with vedolizumab, anti-TNF, or conventional therapy


**Source:** Journal of Crohn's and Colitis; Mar 2019; vol. 13

**Publication Date:** Mar 2019

**Publication Type(s):** Conference Abstract

Abstract: **Background:**

Women with inflammatory bowel diseases (IBD) often receive biologicals during pregnancy to maintain disease remission prior to conception and throughout pregnancy. However, data on vedolizumab exposed pregnancies (VDZE) are scarce. **Method(s):**

This retrospective multi-centre observational study assessed outcomes of VDZE pregnancies in IBD patients (group A). European gastroenterologists were asked to report all VDZE pregnancies. Details of underlying IBD, pre- and postnatal outcomes were collected. Results were compared with anti-TNF exposed (TNFE, group B) or both immunomodulatory and biologic unexposed (IBU, group C) pregnancies. The control groups were prospectively enrolled from two separate centres. **Result(s):**

Group A included 86 pregnancies in 81 women [53% Crohn's disease (CD), 70 live births] from 31 centres in 11 countries. Groups were comparable regarding baseline characteristics though group A included more women with ileocolonic CD and perianal involvement. At conception 35% of VDZE women had active disease, 17% were on steroids and 20% on immunomodulators. Also, 54% previously failed two biologicals. Group B and C included 186 pregnancies in 155 women and 185 pregnancies in 164 women respectively (83% vs. 55% CD, 162 vs. 163 live births). Controls had less active disease at conception (B:16%, C:24%) and fewer were taking steroids (B: 8%, C: 14%). More
miscarriages were seen in group A compared with B (16% vs. 13%, \(p = 0.46\)) and C (16% vs. 8%, \(p = 0.03\)). However, after excluding patients with reported active disease in pregnancy, the number of miscarriages was similar in group A compared with B (14% vs. 14%, \(p = 1.0\)) and C (14% vs. 12%, \(p = 0.80\)). Neonatal outcomes are displayed in Table 1. In live-born infants, median gestational age and birth weight were similar between groups. Also median Apgar score at birth was numerically equal in all groups. The number of premature born infants was not significantly different between groups nor was the amount of reported congenital anomalies. The percentages of breastfed children were similar in all groups. During the first year of life, no malignancies were reported and the infants' infection risk did not significantly differ between groups. Conclusion(s): VDZE pregnancies were associated with more miscarriages; however, active disease in pregnancy rather than drug effect seems to have been the driver of this adverse pregnancy outcome, since no significant difference was observed after exclusion of patients with reported active disease. Still, larger prospective studies are needed for confirmation. (Figure Presented).

Database: EMBASE

19. Outcome of Pregnancies in Female Patients With Inflammatory Bowel Diseases Treated With Vedolizumab.

Author(s): Moens, Annick; van Hoeve, Karen; Humblet, Evelien; Rahier, Jean-François; Bossuyt, Peter; Dewit, Sophie; Franchimont, Denis; Macken, Elisabeth; Nijs, Jochen; Posen, Annelies; Strubbe, Beatrijs; Van Hootegem, Anneleen; Van Moerkercke, Wouter; Vermeire, Séverine; Ferrante, Marc; Belgian IBD Research and Development group (BIRD)

Source: Journal of Crohn's & colitis; Jan 2019; vol. 13 (no. 1); p. 12-18

Publication Date: Jan 2019

Publication Type(s): Multicenter Study Journal Article Observational Study

PubMedID: 30281093

Available at Journal of Crohn's & colitis - from Oxford Journals - Medicine

Available at Journal of Crohn's & colitis - from Unpaywall

Abstract: Background and Aims: Vedolizumab is an IgG1 anti-α4β7 integrin antibody approved for the treatment of inflammatory bowel diseases [IBD], but without clear safety data during conception, pregnancy and nursing. Animal studies showed that mucosal vascular addressin cell adhesion molecule 1 [MAdCAM-1] is expressed by maternal vessels in the placenta and recruits α4β7-expressing cells that are considered important for maternal/fetal tolerance. Blocking this interaction by vedolizumab might affect this process. We aimed to evaluate pregnancy outcomes in vedolizumab-treated female IBD patients. Methods: We conducted a retrospective, multicentre Belgian observational study. Details on disease activity, prenatal complications, delivery and neonatal outcome were collected through a case report form. Results: Twenty-four pregnancies were reported. Five women had active disease at conception and one patient flared during pregnancy. There were 23 live births. Complications were observed in 25% of pregnancies [premature rupture of membranes, pre-eclampsia, miscarriage, elective termination and stillbirth] and in 35% of infants [prematurity, intra-uterine growth retardation, small for gestational age and congenital malformations including hip dysplasia, pulmonary valve stenosis and Hirschprung's disease]. Vedolizumab was continued throughout pregnancy in two females and stopped in the 1st and 2nd trimester in five and 16 patients, respectively. For live born children, the median [interquartile range] gestational age, weight and Apgar score 5 min after birth were 39 [37-39.6] weeks, 3270 [3080-3585] grams and 10 [9-10], respectively. Conclusions: Although several complications were observed, both in mothers and in newborns, no firm conclusions can be drawn. Awaiting prospective and controlled registries, vigilance and strict follow-up of pregnant patients treated with vedolizumab seems mandatory.
20. Immunosuppressives and biologics during pregnancy and lactation: A consensus report issued by the Austrian Societies of Gastroenterology and Hepatology and Rheumatology and Rehabilitation


Source: Wiener Klinische Wochenschrift; Jan 2019; vol. 131 (no. 1); p. 29-44

Publication Date: Jan 2019

Publication Type(s): Article

PubMedID: 30643992

Available at Wiener klinische Wochenschrift - from SpringerLink - Medicine
Available at Wiener klinische Wochenschrift - from UnpayWall

Abstract: An increasing and early-onset use of immunosuppressives and biologics has become more frequently seen among patients with inflammatory bowel diseases (IBD) and rheumatic disorders. Many women in their childbearing years currently receive such medications, and some of them in an interdisciplinary setting. Many questions arise in women already pregnant or wishing to conceive with respect to continuing or discontinuing treatment, the risks borne by the newborns and their mothers and long-term safety. Together with the Austrian Society of Rheumatology and Rehabilitation, the IBD working group of the Austrian Society of Gastroenterology and Hepatology has elaborated consensus statements on the use of immunosuppressives and biologics in pregnancy and lactation. This is the first Austrian interdisciplinary consensus on this topic. It is intended to serve as a basis and support for providing advice to our patients and their treating physicians. Copyright © 2019, The Author(s).

Database: EMBASE
21. Vedolizumab drug levels during pregnancy and in neonates following intrauterine exposure

**Author(s):** Flanagan E.; Bell S.J.; Gibson P.R.; Rosella O.; Rosella G.; Begun J.; Ghaly S.; Garg M.

**Source:** Journal of Gastroenterology and Hepatology; Sep 2018; vol. 33; p. 92-93

**Publication Date:** Sep 2018

**Publication Type(s):** Conference Abstract

Available at Journal of Gastroenterology and Hepatology - from Wiley Online Library

**Abstract:**

Introduction: Vedolizumab is an anti-integrin monoclonal antibody increasingly used for moderately to severely active inflammatory bowel disease (IBD). Currently, there are no data regarding drug levels during pregnancy and time to clearance in the exposed neonate. Aim(s): We aimed to present the first report of vedolizumab drug levels in the mother during pregnancy, together with neonatal outcomes, including drug levels, over the first 3 months. Method(s): Clinical monitoring and neonatal outcomes were documented. Serum drug levels were measured by ELISA (Theradiag) for the mother intrapartum at trough and at delivery, and, for the neonate, at birth, 6 weeks (or 2 months), and 3 months, until not detectable. Result(s): Four patients with IBD (one with Crohn’s disease and three with ulcerative colitis) aged 24-40 years on stable maintenance vedolizumab therapy (duration, 1.3-2.2 years) became intentionally pregnant following appropriate pre-conception counseling. Three patients remained in remission during pregnancy. Patient 1 elected to stop vedolizumab at 24 weeks, as she was in sustained remission, while Patients 2 and 3 continued vedolizumab throughout pregnancy. Patient 4 had planned to cease at 26 weeks, but, due to a mild flare in the third trimester, vedolizumab was given at 35 weeks. Figure 1 shows the drug levels. All four patients delivered healthy babies at term, with normal birthweight and APGAR scores. One infant had hip dysplasia; all four infants were otherwise well up to 6 weeks of age. Infant drug levels are shown in Table 1. Conclusion(s): Our data suggest that maternal vedolizumab levels are likely to remain stable in pregnancy. Neonatal vedolizumab levels at birth are lower than the levels in mothers. Time to clearance has not yet been established, but our early data suggest that vedolizumab is cleared faster than infliximab and adalimumab. Ongoing case study and registry data remain important to inform appropriate use of vedolizumab in pregnancy.

**Database:** EMBASE
22. Pregnant women with inflammatory bowel disease: the effects of biologicals on pregnancy, outcome of infants, and the developing immune system.

**Author(s):** Wieringa, Jantien W; Driessen, Gertjan J; Van Der Woude, C Janneke

**Source:** Expert review of gastroenterology & hepatology; Aug 2018; vol. 12 (no. 8); p. 811-818

**Publication Date:** Aug 2018

**Publication Type(s):** Journal Article Review

**PubMedID:** 29972674

**Abstract:** INTRODUCTION Relapse of inflammatory bowel disease (IBD) during conception and pregnancy has been associated with a negative pregnancy outcome. Therefore, it is advised to maintain drugs in order to prevent relapse. The effect of drugs, which cross the placenta, on children who have been exposed during pregnancy will be discussed in this review. Areas covered: A literature search was performed using the following search terms: inflammatory bowel disease, pregnancy, infant, antitumor necrosis factor alpha, infliximab, adalimumab, golimumab, certolizumab, anti-integrins, vedolizumab, anti-interleukin (IL)-12/23 ustekinumab, placenta, vaccination. Other studies were identified by using references from articles identified through our original literature search. The occurrence of unfavorable pregnancy outcome and congenital malformations does not seem to be increased after exposure to anti-TNFα, but the effects on the developing immune system are largely unknown. For anti-integrins and anti IL-12/23, the numbers of exposed pregnancies are too small to draw any conclusions. Expert commentary: Follow-up of the developing immune system in children exposed to these drugs seems warranted, preferably in a prospective study design.

**Database:** Medline

23. OUTCOME OF PREGNANCIES IN VEDOLIZUMAB TREATED FEMALE IBD PATIENTS

**Author(s):** Moens A.; van Hoeve K.; Humblet E.; Rahier J.-F.; Bossuyt P.; Dewit S.; Franchimont D.; Elisabeth M.; Nijs J.; Posen A.; Van Hootegem A.; Van Moerkercke W.; Vermeire S.; Ferrante M.

**Source:** Gastroenterology; May 2018; vol. 154 (no. 6)

**Publication Date:** May 2018

**Publication Type(s):** Conference Abstract

**Available at** Gastroenterology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

**Abstract:** Background Vedolizumab (VDZ) is a gut-targeted IgG1 anti-alpha4beta7 integrin approved for treatment of inflammatory bowel disease (IBD). As IBD typically affects women at a childbearing age, studies reporting on pregnancy outcomes in patients under VDZ are important. Animal studies showed that MAdCAM-1, the ligand for alpha4beta7-integrin, is expressed by maternal vessels during placental development and alpha4beta7-expressing cells of the macrophage/monocyte lineage are therefore considered to play an important role in maternal/fetal tolerance. Blocking this interaction by VDZ might affect this process. Methods We conducted a retrospective, national observational study to evaluate the outcome of pregnancies in IBD patients under VDZ. Details on disease activity, prenatal complications, delivery and neonatal outcome were collected. Results A total of 23 pregnancies were reported. All but five women had disease remission during conception. There were 18 live births (72% female, including 2 twins), two interrupted pregnancies and five pregnancies are still ongoing. Maternal characteristics are displayed in table 1. Patients, who remained in remission (n=12), reported the following complications: intra-uterine growth retardation (n=1), eclampsia (n=1), premature rupture of the membranes (n=2) and congenital
malformation (n=2, hip dysplasia and pulmonary valve stenosis). Of the five patients with active disease at conception, three pregnancies were unaffected, one female lost her fetus due to chorioamnionitis at week 22 and one had an active termination due to relational problems. One patient had an IBD flare during pregnancy and delivered a child with Hirschsprung's disease. VDZ was continued throughout pregnancy in two females and was stopped in the 1st, 2nd and 3rd trimester in 4, 11 and 1 patient respectively. The median (IQR) gestational age, Apgar score at birth and birth weight were respectively 39 (37-39.4) weeks, 9 (9-9) and 3305 (2823-3698) grams. Eight children were breastfed and this for a median (IQR) of 10 (4-26) weeks. All newborns were vaccinated according to the standard Belgian regimen, but only 44% received Rotavirus vaccination. No serious infections or malignancies were reported in the children during the first year of life. Conclusion This is the largest cohort study reporting on pregnancy outcomes in patients treated with VDZ. Although the number of pregnancies remains low, we observed a number of prenatal complications and congenital malformations, which urges more studies on the function of alpha4beta7-MAdCAM1 interaction in the placenta. In the meanwhile, vigilance and strict follow-up of pregnant IBD patients treated with VDZ is necessary. [Table Presented]Copyright © 2018 AGA Institute. All rights reserved.

**Database:** EMBASE

**24. Safety Analysis of Vedolizumab During Pregnancy: Findings from a Reproductive Study in Monkeys**

**Author(s):** Crawford D.; Friedman M.

**Source:** Gastroenterology; May 2018; vol. 154 (no. 6)

**Publication Date:** May 2018

**Publication Type(s):** Conference Abstract

Available at Gastroenterology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

**Abstract:**Background Vedolizumab (VDZ) is a gut-selective humanized monoclonal antibody targeting alpha4 beta7 integrin, approved for adults with moderate-to-severe ulcerative colitis and Crohn's disease. The few publications reporting on VDZ use in pregnancy have not identified any incidence of maternal or fetal toxicity. The objective of this study was to evaluate the effects of VDZ on pregnancy, parturition, and lactation in cynomolgus monkeys and on survival, growth, and postnatal development of the offspring. Methods Non-fasted pregnant cynomolgus monkeys were randomly assigned to receive 0 mg/kg (saline control), 10 mg/kg (human equivalent dose [HED]: 3.2 mg/kg), or 100 mg/kg (HED: 32.3 mg/kg) of VDZ (n=12/group) every 2 weeks (total of nine intravenous infusions between gestational Days [GD] 20 and 140). Dams and infants were monitored for clinical signs, development, neurobehavior, and grip strength, then euthanized at 181+/-1 days postpartum. Levels of VDZ and primate anti-human antibody (PAHA) were assessed by direct enzyme-linked immunosorbent assay (ELISA) in the serum at GD 20 and 132 and in the breast milk at 28+/-1 days postpartum of the dams, and in the serum of the infants at postpartum Days 20 and 120. Results The number of pregnant females was similar across the three groups. There were no VDZ-related maternal deaths and no increase in the incidence of prenatal loss or stillbirth in any group. No VDZ-related effects on the number of infants born, clinical signs, or infant development were noted. In the dams at GD 132, time to the maximum serum concentration of VDZ after administration was 3.4+/-6.7 hours in the 100 mg/kg group (Table 1). At necropsy, no VDZ-related maternal organ toxicity was found. Low levels of VDZ (0.16-0.27 mug/mL) were found in the breast milk of 3/11 monkeys in the 100 mg/kg group. No VDZ-related effects were found on grip strength, neurobehavioral, or morphologic assessments in the infants. In the 10 and 100 mg/kg groups, positive PAHA titers were detected in 9/12 dams (each group), and 2/7 and 1/9 infants, respectively.
Neutralizing effects on VDZ toxicokinetics and pharmacodynamics were strongest in pregnant monkeys dosed at 10 mg/kg. Conclusion Administration of VDZ to pregnant monkeys resulted in no evidence of effects on teratogenicity, prenatal or postnatal neurobehavioral, and overall development in infants up to 6 months of age. At the no-observed-adverse-effect-level of 100 mg/kg, the serum exposure was 346 times higher in monkeys than in humans dosed at VDZ 300 mg. [Table Presented]Copyright © 2018 AGA Institute

Database: EMBASE

25. Vedolizumab is safe for use in pregnant patients with IBD; Report of our preliminary data

Author(s): Bar-Gil Shitrit A.; Koslowsky B.; Milgrom Y.; Goldin E.; Lahat A.; Granovsky-Grisaru S.

Source: Journal of Crohn's and Colitis; Feb 2018; vol. 12

Publication Date: Feb 2018

Publication Type(s): Conference Abstract

Abstract: Background: Knowledge regarding safety of new biologics during pregnancy is sparse. The recent 2015 ECCO guidelines have no recommendations for or against use of vedolizumab (VDZ) during pregnancy. Aim: To evaluate the safety profile of VDZ during pregnancy. Methods: Prospective data of pregnant women with IBD between January 2015 and November 2017 were collected. The study group comprised patients treated with VDZ during pregnancy. The two control groups included patients treated with an anti-TNF (control 1) and patients not treated by any biologic (control 2). Results: The VDZ group included 21 pregnancies. The control groups included 83 and 196 pregnancies in control groups 1 and 2, respectively. Disease flare at conception was seen in 5/21 (24%) patients in the VDZ group compared with 12/83 (14%) and 33/196 (16%) in control groups 1 and 2, p = 0.27, p = 0.35, respectively. Disease flare during pregnancy, when in remission at conception, occurred in 1/16 (6.3%) patients receiving VDZ compared with 21/71 (29%), and 57/163 (35%), in control groups 1 and 2, p = 0.06, p = 0.02, respectively. Early pregnancy loss, between 6-12 weeks, occurred in 6 (28.5%) of VDZ treated patients, three had active disease at conception, two pregnancies were by in-vitro fertilisations in a woman 45 years old with active disease, and one occurred by a patient in remission. One patient had induced early termination of pregnancy. One preterm delivery was reported in the VDZ group, due to severe pre-eclampsia. Mean gestational age at birth was similar among all groups. Neonatal mean birth weight was found to be appropriate for gestational age and similar between the groups. All neonates had a 5' Apgar score of 8 and above. One newborn from the VDZ group who was born at 32 weeks of pregnancy developed an atypical Kawasaki disease with eosinophilia at 3 months old. He responded well to corticosteroids and his development was normal. One newborn from control group 2 (exposed to thiopurines) had tetralogy of Fallot. He underwent a successful surgical repair. No other major congenital malformations were reported. Conclusions: VDZ continued throughout pregnancy was found to be safe. More patients had active disease at conception. The high rates of early pregnancy loss may reflect disease severity at conception.

Database: EMBASE
26. Outcome of pregnancies in female IBD patients treated with vedolizumab

**Author(s):** Moens A.; Vermeire S.; Ferrante M.; Van Hoeve K.; Humblet E.; Rahier J.-F.; Bossuyt P.; Dewit S.; Franchimont D.; Macken E.; Nijs J.; Posen A.; Van Hootegem A.; Van Moerkercke W.

**Source:** Journal of Crohn's and Colitis; Feb 2018; vol. 12

**Publication Date:** Feb 2018

**Publication Type(s):** Conference Abstract

Available at Journal of Crohn's and Colitis - from Oxford Journals - Medicine
Available at Journal of Crohn's and Colitis - from Unpaywall

**Abstract:** Background: Vedolizumab (VDZ) is a gut-targeted IgG1 anti-alpha4beta7 integrin approved for treatment of inflammatory bowel disease (IBD). As IBD typically affects women at childbearing age, studies on pregnancy outcomes in patients under VDZ are important. Animal studies showed that MAdCAM-1, the ligand for alpha4beta7-integrin, is expressed by maternal vessels during placental development and alpha4beta7-expressing cells of the macrophage/monocyte lineage are therefore considered important in maternal/foetal tolerance. Blocking this interaction by VDZ might affect this process. Methods: This retrospective, national observational study evaluated the outcome of pregnancies in IBD patients under VDZ. Details on disease activity, prenatal complications, delivery and neonatal outcome were collected. Results: A total of 23 pregnancies were reported. All but five women had disease remission at conception. There were 18 live births (72% female, incl. two twins), two interrupted pregnancies and five pregnancies are still ongoing. Maternal characteristics are displayed in Table 1. Patients, who remained in remission (n = 12), reported the following complications: intra-uterine growth retardation (n = 1), eclampsia (n = 1), premature rupture of the membranes (n = 2) and congenital malformation (n = 2, hip dysplasia and pulmonary valve stenosis). Of the five patients with active disease at conception, three pregnancies were unaffected, one female lost her foetus due to chorioamnionitis at week 22 and one had an active termination due to relational problems. One patient flared during pregnancy and delivered a child with Hirschsprung's disease. VDZ was continued throughout pregnancy in two females and was stopped in the first, second and third trimester in 4, 11, and 1 patient, respectively. The median (IQR) gestational age, Apgar score at birth and birth weight were respectively 39 (37-39.4) weeks, 9 (9-9) and 3305 (2823-3698) grams. Eight children were breastfed for a median (IQR) of 10 (4-26) weeks. All newborns were vaccinated according to the standard Belgian regimen with 44% receiving Rotavirus vaccination. No serious infections or malignancies were reported during the first year of life. Conclusions: This is the largest cohort study on pregnancy outcomes in patients treated with VDZ. Despite the still low number of pregnancies, we observed a number of prenatal complications and congenital malformations, which urges more studies on the function of alpha4beta7-MAdCAM1 interaction in the placenta. In the meanwhile, vigilance and strict follow-up of pregnant IBD patients treated with VDZ is necessary.

**Database:** EMBASE
27. Vedolizumab Levels in Breast Milk of Nursing Mothers With Inflammatory Bowel Disease.

**Author(s):** Lahat, Adi; Shitrit, Ariella Bar-Gil; Naftali, Timna; Milgrom, Yael; Elyakim, Rami; Goldin, Eran; Levhar, Nina; Selinger, Limor; Zuker, Tzufit; Fudim, Ella; Picard, Orit; Yavzori, Miri; Ben-Horin, Shomron

**Source:** Journal of Crohn's & colitis; Jan 2018; vol. 12 (no. 1); p. 120-123

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article Observational Study

**PubMedID:** 28961712

Available at Journal of Crohn's & colitis - from Oxford Journals - Medicine

**Abstract:**

IntroductionThere are no data on the transfer of vedolizumab in breast milk of nursing mothers. We aimed to assess the presence of vedolizumab in breast milk of nursing inflammatory bowel disease [IBD] patients.

Methods

This was a prospective observational study of vedolizumab-treated breastfeeding patients with IBD. Serum and breast milk samples were obtained at pre-defined time points. The in-house developed enzyme-linked immunosorbent assay [ELISA] for measuring vedolizumab in blood was adapted and validated for measurement of the drug in breast milk. The level of vedolizumab was also measured in breast milk of a control group of nursing healthy mothers.

Results

Vedolizumab was undetectable in breast milk in IBD patients before the first infusion of vedolizumab \( [n = 3] \) and in all of the healthy controls \( [n = 5] \). Vedolizumab was measurable in all lactating women who received vedolizumab \( [n = 5] \). However, on serial measurements in breast milk after an infusion, drug levels did not surpass 480 ng/ml, which was roughly 1/100 of the comparable serum levels.

Conclusions

Vedolizumab can be detected in the breast milk of nursing mothers. Although more data are imperative, the concentrations of vedolizumab in breast milk are minute and are therefore unlikely to result in systemic or gastrointestinal immune-suppression of the infant.

**Database:** Medline


**Author(s):** Engel, Tal; Ungar, Bella; Yung, Diana E; Ben-Horin, Shomron; Eliakim, Rami; Kopylov, Uri

**Source:** Journal of Crohn's & colitis; Jan 2018; vol. 12 (no. 2); p. 245-257

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article Review Systematic Review

**PubMedID:** 29077833

Available at Journal of Crohn's & colitis - from Oxford Journals - Medicine

Available at Journal of Crohn's & colitis - from Unpaywall

**Abstract:**

Background

Vedolizumab [VDZ] is an anti-integrin monoclonal antibody effective in ulcerative colitis [UC] and Crohn's disease [CD]. Several real-world experience [RWE] studies with VDZ have been published to date. The aim of this systematic review was to summarise the available real-life experience with VDZ.

Methods

We performed a systematic review of the available RWE studies of VDZ in CD and UC. We performed a pooled analysis of the available efficacy and safety data for induction and maintenance treatment in adult cohorts. A narrative review of VDZ use in special clinical settings was also performed.

Results

Nine studies including 1565 [571 UC, 994 CD] adult patients were identified. In CD, clinical response and remission were achieved in 54% (95% confidence interval [CI] 41-66%) and 22% [95% CI 13-35%] by Week 6 and in 49% [95% CI 37-51%] and 32% [95% CI 23-42%] by Week 14; at Week 52, 45% [95% CI 28-64%] and 32% [95% CI 12-62%] of the patients responded, and were in clinical remission, respectively. In UC, clinical response and
remission were achieved in 43% [95% CI 37-49] and 25% [95% CI 12-45] by Week 6, respectively, and in 51% [95% CI 43-61] and 30% [95% CI 24-36] by Week 14/22, respectively; at week 52, clinical response and remission were achieved in 48% and 39% of the patients, respectively. Adverse effects were mostly minor and occurred in 30.6% of the patients; infections were reported in 3.4% of the patients.

Conclusions
VDZ is efficacious in CD and UC and has a favourable safety profile in RWE studies.

Database: Medline

29. Use of Biologic Therapy by Pregnant Women With Inflammatory Bowel Disease Does Not Affect Infant Response to Vaccines.

Author(s): Beaulieu, Dawn B; Ananthakrishnan, Ashwin N; Martin, Christopher; Cohen, Russell D; Kane, Sunanda V; Mahadevan, Uma

Source: Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association; Jan 2018; vol. 16 (no. 1); p. 99-105

Publication Date: Jan 2018

Publication Type(s): Multicenter Study Journal Article

PubMedID: 28870657

Abstract: BACKGROUND & AIMS In women with inflammatory bowel diseases (IBDs), exposure to immunomodulator or biologic therapy has not been associated with adverse events during pregnancy or outcomes of newborns. We investigated whether exposure of patients to these agents during pregnancy affects serologic responses to vaccines in newborns.

METHODS We collected data from the Pregnancy in IBD and Neonatal Outcomes registry, which records outcomes of pregnant women with diagnosis of IBD receiving care at multiple centers in the United States, from 2007 through 2016. Serum samples collected from infants at least 7 months old were analyzed for titers of antibodies to Haemophilus influenzae B (HiB) or tetanus toxin; mothers completed a survey of vaccine practices and outcomes from July 2013 through October 2016. Umbilical cord blood samples from 33 infants were assayed for concentration of biologic agents. Vaccination response was compared between infants born to mothers exposed to biologic therapy (infliximab, adalimumab, certolizumab pegol, golimumab, natalizumab, vedolizumab, or ustekinumab—either as a single agent or in combination with an immunomodulator, at any time between conception and delivery) and infants born to unexposed mothers.

RESULTS A total of 179 women completed the vaccine survey (26 biologic unexposed, 153 exposed to a biologic agent). We found no significant difference in proportions of infants with protective antibody titers against HiB born to exposed mothers (n = 42, 71%) vs unexposed mothers (n = 8, 50%) (P = .41). We also found no difference in the proportion of infants with protective antibody titers to tetanus toxoid born to exposed mothers (80%) vs unexposed mothers (75%) (P = .66). The median concentration of infliximab in cord blood did not differ significantly between infants with vs without protective antibody titers to HiB (P = .30) or tetanus toxoid (P = .93). Mild reactions were observed in 7/40 infants who received rotavirus vaccine and whose mothers had been exposed to biologic therapies.

CONCLUSIONS Vaccination of infants against HiB and tetanus toxoid, based on antibody titers measured when infants were at least 7 months old, does not appear to be affected by in utero exposure to biologic therapy.

Database: Medline
30. Vedolizumab safety in pregnancy and newborn outcomes.

Author(s): Julsgaard, Mette; Kjeldsen, Jens; Baumgart, Daniel C

Source: Gut; Oct 2017; vol. 66 (no. 10); p. 1866-1867

Publication Date: Oct 2017

Publication Type(s): Letter Comment

PubMedID: 28073891

Available at Gut - from BMJ Journals - NHS
Available at Gut - from Free Medical Journals . com
Available at Gut - from ProQuest (Health Research Premium) - NHS Version

Database: Medline


Author(s): Bye, W A; Jairath, V; Travis, S P L

Source: Alimentary pharmacology & therapeutics; Jul 2017; vol. 46 (no. 1); p. 3-15

Publication Date: Jul 2017

Publication Type(s): Journal Article Review Systematic Review

PubMedID: 28449273

Available at Alimentary pharmacology & therapeutics - from Wiley Online Library

Abstract: BACKGROUND Vedolizumab specifically recognises the α4β7 integrin and selectively blocks gut lymphocyte trafficking: potentially, it offers gut-specific immunosuppression. AIM To review the safety of vedolizumab and summarise post-marketing data to assess if any safety concerns that differ from registration trials have emerged. METHOD A systematic bibliographic search identified six registration trials and nine cohort studies. RESULTS Integrated data from registration trials included 2830 vedolizumab-exposed patients (4811 person-years exposure [PYs]) and 513 placebo patients. This reported lower exposure-adjusted incidence rates of infection (63.5/100 PYs; 95% CI: 59.6-67.3) and serious adverse events (20.0/100 PYs; 95% CI: 18.5-21.5) compared to placebo (82.9/100 PYs; 95% CI: 68.3-97.5) and (28.3/100 PYs 95% CI: 20.6-35.9) respectively. Higher, but statistically insignificant rates of enteric infections occurred in vedolizumab-exposed patients (7.4/100 PYs; 95% CI: 6.6-8.3) compared to placebo (6.7 PYs; 95% CI: 3.2-10.1). Six post-marketing cohort studies (1049 patients, 403 PYs) demonstrated rates of infection of 8% (82/1049); enteric infection of 2% (21/1049) and adverse events of 16% (166/1049). Multivariate analysis in one cohort study suggested increased risk of surgical site infection with perioperative VDZ. Human experience in pregnancy is limited. CONCLUSION Post-marketing data confirm the excellent safety of vedolizumab observed in registration trials. The signal of post-operative complications should be interpreted with caution, but warrants further study. Although comparative studies are needed, Vedolizumab may be a safe alternative in patients who best avoid systematic immunosuppression, including those predisposed to infection, malignancy or the elderly.

Database: Medline
32. Editorial: vedolizumab in pregnancy - is gut selectivity as good for baby as it is for mum?

**Author(s):** Shim, H H; Seow, C H  
**Source:** Alimentary pharmacology & therapeutics; May 2017; vol. 45 (no. 9); p. 1283-1284  
**Publication Date:** May 2017  
**Publication Type(s):** Editorial Comment  
**PubMedID:** 28370049  
Available at Alimentary pharmacology & therapeutics - from Wiley Online Library  
Available at Alimentary pharmacology & therapeutics - from Unpaywall  
**Database:** Medline

33. Vedolizumab exposure in pregnancy: outcomes from clinical studies in inflammatory bowel disease.

**Author(s):** Mahadevan, U; Vermeire, S; Lasch, K; Abhyankar, B; Bhayat, F; Blake, A; Dubinsky, M  
**Source:** Alimentary pharmacology & therapeutics; Apr 2017; vol. 45 (no. 7); p. 941-950  
**Publication Date:** Apr 2017  
**Publication Type(s):** Journal Article  
**PubMedID:** 28169436  
Available at Alimentary pharmacology & therapeutics - from Wiley Online Library  
**Abstract:** BACKGROUND Vedolizumab is a gut-selective immunoglobulin G1 monoclonal antibody to α4 β7 integrin for the treatment of Crohn's disease (CD) and ulcerative colitis (UC). Prospective clinical studies of vedolizumab in pregnancy have not been conducted; therefore, existing safety data of vedolizumab in pregnancy were examined. AIM To assess pregnancy outcomes in females and partners of males who received vedolizumab. METHODS All pregnancy data collected during the clinical programme (from 14 May 2007 to 27 June 2013) and in the post-marketing setting (to 19 November 2015) were analysed. RESULTS Across six studies, there were 27 pregnancies in female participants and 19 pregnancies in partners of male participants. Among 24 vedolizumab-treated females (23 with CD/UC, one healthy volunteer), there were 11 live births, five elective terminations, four spontaneous abortions and four undocumented outcomes. A congenital corpus callosum agenesis anomaly was reported in one live birth from a healthy volunteer with extensive obstetric history exposed to single-dose vedolizumab 79 days before estimated conception. Of 19 pregnancies in partners of male participants, there were 11 live births, two spontaneous abortions, three elective terminations and three undocumented outcomes. Post-marketing reports recorded 81 pregnancies, resulting in four live births, 11 spontaneous abortions and 66 pregnancies that were on-going or reported undocumented outcomes. CONCLUSIONS Initial analysis, limited by sample size and follow-up, identified no new safety concerns for pregnancy outcomes in females directly or indirectly exposed to vedolizumab. However, vedolizumab should be used during pregnancy only if the benefits to the mother outweigh the risks to the mother/unborn child.  
**Database:** Medline
34. Safety of treatments for inflammatory bowel disease: Clinical practice guidelines of the Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD).

**Author(s):** Biancone, Livia; Annese, Vito; Ardizzone, Sandro; Armuzzi, Alessandro; Calabrese, Emma; Caprioli, Flavio; Castiglione, Fabiana; Comberlato, Michele; Cottone, Mario; Danese, Silvio; Daperno, Marco; D'Incà, Renata; Frieri, Giuseppe; Fries, Walter; Gionchetti, Paolo; Kohn, Anna; Latella, Giovanni; Millà, Monica; Orlando, Ambrogio; Papi, Claudio; Petruzzello, Carmelina; Riegler, Gabriele; Rizzello, Fernando; Saibeni, Simone; Scribano, Maria Lia; Vecchi, Maurizio; Vernia, Piero; Meucci, Gianmichele; Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD)

**Source:** Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver; Apr 2017; vol. 49 (no. 4); p. 338-358

**Publication Date:** Apr 2017

**Publication Type(s):** Practice Guideline Journal Article

**PubMedID:** 28161290

**Abstract:** Inflammatory bowel diseases are chronic conditions of unknown etiology, showing a growing incidence and prevalence in several countries, including Italy. Although the etiology of Crohn's disease and ulcerative colitis is unknown, due to the current knowledge regarding their pathogenesis, effective treatment strategies have been developed. Several guidelines are available regarding the efficacy and safety of available drug treatments for inflammatory bowel diseases. Nevertheless, national guidelines provide additional information adapted to local feasibility, costs and legal issues related to the use of the same drugs. These observations prompted the Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD) to establish Italian guidelines on the safety of currently available treatments for Crohn's disease and ulcerative colitis. These guidelines discuss the use of aminosalicylates, systemic and low bioavailability corticosteroids, antibiotics (metronidazole, ciprofloxacin, rifaximin), thiopurines, methotrexate, cyclosporine A, TNFα antagonists, vedolizumab, and combination therapies. These guidelines are based on current knowledge derived from evidence-based medicine coupled with clinical experience of a national working group.

**Database:** Medline

35. Placental madcam1 expression-potential consequences for the treatment with vedolizumab during pregnancy

**Author(s):** Zelinkova Z.; Berakova K.; Podmanicky D.; Kadleckova B.

**Source:** United European Gastroenterology Journal; Oct 2016; vol. 4 (no. 5)

**Publication Date:** Oct 2016

**Publication Type(s):** Conference Abstract

**Available at** United European Gastroenterology Journal - from Europe PubMed Central - Open Access

**Available at** United European Gastroenterology Journal - from Unpaywall

**Abstract:** Introduction: Inflammatory bowel diseases (IBD) affect patients in reproductive age. Over the past two decades, the experience with the treatment of IBD during pregnancy has been increasing and most of the IBD drugs have been shown to be effective and safe for the use by the mothers-to-be. Vedolizumab, a monoclonal antibody against alpha4beta7 integrin has been shown to be effective in inducing and maintaining remission in IBD. By blocking alpha4beta7, it is preventing the homing of lymphocytes to the gut mucosa through binding to mucosal vascular adrenergic cell adhesion molecule 1 (MadCAM1) localised on the endothelial cells. As with other biologicals in the past, the question arises on the safety of the use of this novel molecule during
pregnancy. Embryonic implantation is a complex process orchestrated by maternal immune response. It is not clear whether MadCAM1 is expressed in human placenta which could have consequences for the local immune response during pregnancy in case of alpha4beta7 blockade. Therefore, the aim of this study was to determine the expression of MadCAM1 in the placental tissue. Aims & Methods: Placental tissue of 15 placenta's from spontaneous abortions occurring during the first trimester and 12 mature placenta's were stained by immunohistochemistry for the expression of MadCAM1. The localization of positive cells was determined based on the comparison with the hematoxylineosin staining. Samples from small intestinal wall were used as positive controls. Results: MadCAM1 was expressed invariably by decidual vessels, syntiotrophoblast and cytotrophoblast in all samples from the first trimester. In contrast, there was no expression of MadCAM1 in the samples from mature placenta's. Conclusion: MadCAM1 is expressed in human placenta during the first trimester. Blocking alpha4beta7 integrins may thus interfere with the maternal immune surveillance crucial for the successful course of early stages of the pregnancy.

Database: EMBASE

36. Treating Inflammatory Bowel Disease in Pregnancy: The Issues We Face Today.

Author(s): Damas, Oriana M; Deshpande, Amar R; Avalos, Danny J; Abreu, Maria T

Source: Journal of Crohn's & colitis; Oct 2015; vol. 9 (no. 10); p. 928-936

Publication Date: Oct 2015

Publication Type(s): Journal Article Review

PubMedID: 26129693

Available at Journal of Crohn's & colitis - from Oxford Journals - Medicine

Abstract: Many women of childbearing age are living with inflammatory bowel disease [IBD], yet there are limited studies on the use of IBD medications in pregnancy. In this review, we provide a comprehensive update on the safety of these medications during pregnancy, particularly thiopurines and biologicals. Antibiotics, steroids, and aminosalicylates are relatively low risk for use in pregnancy, and growing evidence supports the safety of immunomodulators and anti-tumour necrosis factor agents as well. Available studies on infliximab, adalimumab, and certolizumab pegol show no increase in adverse events during pregnancy or perinatally. Similarly, studies on lactation demonstrate that concentrations of subcutaneous anti-tumour necrosis factor biologicals are undetectable, and levels of thiopurines and infliximab are negligible in breast milk. Less is known about anti-integrins in pregnancy [eg natalizumab and vedolizumab] but currently available data suggest they may be safe as well. Although more studies are needed to examine the long-term effects of these medications on offspring, the available data provide reassuring information for providers caring for women of childbearing age.

Database: Medline
37. Vedolizumab exposure in pregnancy: Outcomes from clinical studies in ulcerative colitis and crohn’s disease

**Authors:** Mahadevan U.; Dubinsky M.; Vermeire S.; Abhyankar B.; Lasch K.

**Source:** American Journal of Gastroenterology; Oct 2015; vol. 110

**Publication Date:** Oct 2015

**Publication Type(s):** Conference Abstract

Available at American Journal of Gastroenterology - from SpringerLink - Medicine
Available at American Journal of Gastroenterology - from Ovid (LWW Total Access Collection 2019 - with Neurology)
Available at American Journal of Gastroenterology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location]: Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.
Available at American Journal of Gastroenterology - from Unpaywall

**Abstract:** Introduction: Vedolizumab (VDZ) is a gut-selective immunoglobulin G1 (IgG1) monoclonal antibody to a4b7 integrin with demonstrated efficacy and safety in the treatment of ulcerative colitis (UC) and Crohn's disease (CD). Placental transfer of VDZ is anticipated to be similar to all other IgG1 therapeutic antibodies and increase in a linear fashion as pregnancy progresses, with the largest amount transferred during the third trimester. There are no controlled studies with VDZ in pregnant women. Here we report the pregnancy outcomes for female study participants and partners of male patients exposed to VDZ in clinical studies. Methods: Data from the VDZ clinical development program up to June 27, 2013, were reviewed. According to study protocols, female participants who became pregnant were to discontinue the study. The outcomes of pregnancies for female participants who became pregnant during the study and male patients with pregnant partners were summarized descriptively. Results: A total of 27 pregnancies were reported in study participants-25 in patients with UC or CD, 2 in healthy volunteers (Table 1) and 19 in the partners of male study participants (Table 2). These pregnancies were reported in 6 clinical studies: placebo and VDZ were administered in 2 single-dose studies and 2 multiple-dose 1-year studies; VDZ was also administered in 2 open-label multiple-dose studies of 78 weeks and 4 years (ongoing). Of the 24 VDZ-treated females, 11 resulted in live births (2 premature) (Table 1). A congenital anomaly of agenesis of the corpus callosum was reported in the healthy volunteer with an obstetric history of 2 spontaneous abortions and 1 ectopic pregnancy who had received a single dose of VDZ 79 days prior to the estimated date of conception. Among the 15 VDZ-exposed partner pregnancies, there were 8 live births (Table 2). Conclusion: Although treatment was discontinued for female participants if they became pregnant during the study, data from the VDZ clinical development program provide some insight into pregnancy outcomes of VDZ-treated patients. An observational pregnancy registry enrolling patients with UC or CD on VDZ is currently in development to observe and evaluate the long-term safety of VDZ in pregnancy. (Table Presented).

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