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Date: 30 October 2019

Sources Searched: Medline, EMBASE

Vedolizumab in Pregnancy & Breastfeeding

[See full search strategy](#)

1. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults

Author(s): Lamb C.A.; Kennedy N.A.; Raine T.; Davies R.J.; Parkes M.; Hendy P.A.; Faiz O.; Smith P.J.; Limdi J.K.; Hayee B.; Lomer M.C.E.; Sanderson J.; Parkes G.C.; Selinger C.; Barrett K.J.; Bennett C.; Gittens S.; Dunlop M.G.; Fraser A.; Garrick V.; Hansen R.; Johnston P.D.; Terry H.; Gaya D.R.; Iqbal T.H.; Taylor S.A.; Smith M.; Brookes M.; Hawthorne A.B.

Source: Gut; Sep 2019

Publication Date: Sep 2019

Publication Type(s): Article

PubMedID: 31562236

Available at [Gut](#) - from BMJ Journals - NHS

Abstract: 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.

Database: EMBASE

2. A Pharmacological Approach to Managing Inflammatory Bowel Disease During Conception, Pregnancy and Breastfeeding: Biologic and Oral Small Molecule Therapy.

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

3. 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

Available at [The American journal of gastroenterology](#) - from SpringerLink - Medicine

Available at [The American journal of gastroenterology](#) - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract:OBJECTIVESDespite encouraging data gathered in inflammatory bowel diseases (IBD) patients, Vedolizumab's (VDZ) safety profile in pregnancy is not established.DESIGNData of 330 consecutive pregnancies with IBD was prospectively collected.RESULTSWomen 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.DISCUSSIONAlthough further study is needed, VDZ appears of low risk during pregnancy.

Database: Medline

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

Author(s): Moens A.; Vermeire S.; Ferrante M.; Van Der Woude C.; Julsgaard M.; Sebastian S.; Arebi N.; Alzinaty M.; Humblet E.; Kok K.B.; Sheridan J.; Gilletta De Saint-Joseph C.; Nancey S.; Rahier J.-F.; Bossuyt P.; Cremer A.; Dewit S.; Eriksson C.; Hoentjen F.; Krause T.; Louis E.; Macken E.; Milenkovic Z.; Nijs J.; Posen A.; Van Hootegem A.; Van Moerkercke W.; Bar-Gil Shitrit A.

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

Publication Date: Mar 2019

Publication Type(s): Conference Abstract

Available at [Journal of Crohn's and Colitis](#) - from Oxford Journals - Medicine

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

5. 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 Hootegeem, 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 AimsVedolizumab is an IgG1 anti- $\alpha 4\beta 7$ 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 $\alpha 4\beta 7$ -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.MethodsWe conducted a retrospective, multicentre Belgian observational study. Details on disease activity, prenatal complications, delivery and neonatal outcome were collected through a case report form.ResultsTwenty-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 Hirschsprung'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.ConclusionsAlthough 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.

Database: Medline

6. 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

7. 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:INTRODUCTIONRelapse 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-TNF α , 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

8. 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- $\alpha 4\beta 7$ 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 $\alpha 4\beta 7$ -integrin, is expressed by maternal vessels during placental development and $\alpha 4\beta 7$ -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 $\alpha 4\beta 7$ -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

9. 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

10. 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

11. 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.MethodsThis 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.ResultsVedolizumab 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.ConclusionsVedolizumab 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

12. Vedolizumab in IBD-Lessons From Real-world Experience; A Systematic Review and Pooled Analysis.

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:BackgroundVedolizumab [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.MethodsWe 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.ResultsNine 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.ConclusionsVDZ is efficacious in CD and UC and has a favourable safety profile in RWE studies.

Database: Medline

13. 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

Available at [Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association](#) - from Unpaywall

Abstract:BACKGROUND & AIMSIn 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.METHODSWe 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.RESULTSA 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.CONCLUSIONSVaccination of infants against HiB and tetanus toxin, 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

14. Systematic review: the safety of vedolizumab for the treatment of inflammatory bowel disease.

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 $\alpha 4 \beta 7$ 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. CONCLUSIONS 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 pre-disposed to infection, malignancy or the elderly.

Database: Medline

15. 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 $\alpha 4 \beta 7$ 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

16. 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; Milla, 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, TNF α 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

17. 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 adressin 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

18. 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

19. Vedolizumab exposure in pregnancy: Outcomes from clinical studies in ulcerative colitis and crohn's disease

Author(s): 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 Unpaywall

Abstract:Introduction: Vedolizumab (VDZ) is a gut-selective immunoglobulin G1 (IgG1) monoclonal antibody to $\alpha 4\beta 7$ 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).

Database: EMBASE

20. Vedolizumab exposure in pregnancy: Outcomes from clinical studies in inflammatory bowel disease

Author(s): Dubinsky M.; Mahadevan U.; Vermeire S.; Abhyankar B.; Lasch K.

Source: Journal of Crohn's and Colitis; Feb 2015; vol. 9

Publication Date: Feb 2015

Publication Type(s): Conference Abstract

Available at [Journal of Crohn's and Colitis](#) - from Oxford Journals - Medicine

Abstract:Background: Vedolizumab (VDZ) is a gut-selective immunoglobulin G1 monoclonal antibody to alpha4beta7 integrin with demonstrated efficacy and safety in the treatment of Crohn's disease (CD) and ulcerative colitis (UC) in adults. Placental transfer of VDZ is anticipated to be similar to all other immunoglobulin G1 therapeutic antibodies and increases 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 effect of VDZ on pregnancy outcomes for female study participants and partners of male patients exposed in clinical studies. Methods: Data from the VDZ clinical development programme up to 27 June 2013 were reviewed. According to the 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 summarised descriptively. Results: The number of pregnancies reported were 27 in females (25 in patients with UC or CD, 2 in healthy volunteers) and 20 pregnancies in the partners of male patients 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 long-term, open-label, multiple dose studies of 78 weeks and 4 years [ongoing]; Table). Of the 24 VDZ-treated females, 11 resulted in live births (2 premature). 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 16 VDZ-exposed partner pregnancies, there were 9 live births, 2 spontaneous abortions, 2 elective terminations, and 3 undocumented outcomes at the last follow-up. Conclusions: Although female participants were discontinued if they became pregnant during the study, data from the VDZ clinical development programme 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. The clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc. (table present).

Database: EMBASE

Strategy 742733

#	Database	Search term	Results
1	Medline	(Vedolizumab).ti,ab	680
2	Medline	(ENTYVIO).ti,ab	10
3	Medline	(1 OR 2)	681
4	Medline	(pregnan*).ti,ab	474209
5	Medline	exp PREGNANCY/	874185
6	Medline	(breastfeeding OR "breast feeding").ti,ab	33168
7	Medline	exp "BREAST FEEDING"/	36328
8	Medline	exp "MILK, HUMAN"/	18632
9	Medline	(4 OR 5 OR 6 OR 7 OR 8)	1018817
10	Medline	(3 AND 9)	26
11	EMBASE	(Vedolizumab).ti,ab	2243
12	EMBASE	(ENTYVIO).ti,ab	29
13	EMBASE	(11 OR 12)	2246
14	EMBASE	(pregnan*).ti,ab	611705
15	EMBASE	exp PREGNANCY/	645798
17	EMBASE	exp "PREGNANCY OUTCOME"/	56211
18	EMBASE	exp "PREGNANCY COMPLICATION"/	118359
20	EMBASE	(breastfeeding OR "breast feeding").ti,ab	42845
21	EMBASE	exp "BREAST FEEDING"/	50452

22	EMBASE	exp "BREAST MILK"/	26385
23	EMBASE	(14 OR 15 OR 17 OR 18 OR 20 952483 OR 21 OR 22)	
24	EMBASE	(13 AND 23)	61
25	EMBASE	exp VEDOLIZUMAB/	3062
26	EMBASE	(23 AND 25)	105
27	EMBASE	26 not 24	45