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Date: 27 Oct 2017

Sources Searched: Medline, Embase, BNF, DynaMed Plus.

Ustekinumab in Pregnancy

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Evidence Summary:

Ustekinumab (STELARA) is a human monoclonal antibody against interleukins 12 and 23. It is indicated for the treatment of moderate-to-severe plaque psoriasis (that has not responded to other systemic treatments or photochemotherapy, or when these treatments cannot be used because of intolerance or contra-indications) active psoriatic arthritis and for moderately to severely active Crohn's disease after previous treatment.

There is no adequate data from the use of ustekinumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development. As a precautionary measure, it is preferable to avoid the use of STELARA in pregnancy.

Sources

Electronic Medicines Compendium. STELARA 130 mg concentrate for solution for infusion
<https://www.medicines.org.uk/emc/medicine/32568> [Last Accessed 27/10/2017]

Ustekinumab (BNF October 2017)

<https://www.medicinescomplete.com/mc/bnf/64/PHP34014-ustekinumab.htm> [Last accessed 27/10/2017]

1. Ustekinumab and Anti-Interleukin-23 Agents in Crohn's Disease.

Author(s): Deepak, Parakkal; Sandborn, William J

Source: Gastroenterology clinics of North America; Sep 2017; vol. 46 (no. 3); p. 603-626

Publication Date: Sep 2017

Publication Type(s): Journal Article Review

PubMedID: 28838418

Abstract: This article reviews the available data regarding the efficacy of ustekinumab across published randomized clinical trials and open-label experience from tertiary medical centers, safety data, including in pregnancy, and its use in patients who have failed tumor necrosis factor (TNF) antagonists as well as patients who have not failed TNF antagonists. We have proposed an algorithm for positioning the use of ustekinumab among other agents (TNF antagonists, vedolizumab) in moderate-severe Crohn's disease. The article also enumerates drugs that are specific interleukin-23 blockers, including brazikumab (MEDI2070), risankizumab, LY3074828, tildrakizumab, and guselkumab, and the current status of their clinical trials.

Database: Medline

2. Ustekinumab drug levels in maternal and cord blood in a woman with Crohn's disease treated until 33 weeks gestation.

Author(s): Rowan, Catherine R; Cullen, Garret; Mulcahy, Hugh E; Keegan, Denise; Byrne, Kathryn; Murphy, Deirdre J; Sheridan, Juliette; Doherty, Glen A

Source: Journal of Crohn's & colitis; Oct 2017

Publication Date: Oct 2017

Publication Type(s): Journal Article

PubMedID: 29045603

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

Abstract: A 35-year old woman with ileocolonic, perianal and vulval Crohn's disease was treated with subcutaneous ustekinumab (USK) throughout pregnancy. Dose intervals were shortened from 6-weekly to 4-weekly to maintain clinical remission. The last dose of USK was administered at 33 weeks gestation and a healthy baby boy was delivered by caesarean section at 37 weeks. Maternal trough USK levels remained stable during pregnancy. Cord blood USK levels were nearly two-fold higher than contemporaneous maternal serum levels. To our knowledge, this is the first report of maternal and cord USK levels in a patient with Crohn's disease.

Database: Medline

3. 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; Sep 2017

Publication Date: Sep 2017

Publication Type(s): 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 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

4. Fetal death in utero and miscarriage in a patient with Crohn's disease under therapy with ustekinumab: case-report and review of the literature.

Author(s): Venturin, C; Nancey, S; Danion, P; Uzzan, M; Chauvenet, M; Bergoin, C; Roblin, X; Flourié, B; Boschetti, G

Source: BMC gastroenterology; Jun 2017; vol. 17 (no. 1); p. 80

Publication Date: Jun 2017

Publication Type(s): Journal Article

PubMedID: 28629323

Available at [BMC gastroenterology](#) - from Europe PubMed Central - Open Access

Abstract:BACKGROUND Ustekinumab is a fully human monoclonal antibody against the p40 subunit of interleukin (IL) 12 and 23 which is involved in the pathogenesis of several inflammatory diseases. Ustekinumab is approved for psoriasis and psoriatic arthritis treatment and has been successfully evaluated in phase II and III trials for patients with Crohn's disease (CD). CASE PRESENTATION We report here the case of a patient who became pregnant during treatment with ustekinumab for a refractory CD and which ended in miscarriage. CONCLUSION Ustekinumab is a relatively new pharmacotherapy and in addition to this clinical case, we reviewed the published literature concerning the use of this treatment during pregnancy and its consequences on pregnancy and fetus outcome.

Database: Medline

5. The use of biologics in pregnant patients with rheumatic disease.

Author(s): Østensen, Monika

Source: Expert review of clinical pharmacology; Jun 2017; vol. 10 (no. 6); p. 661-669

Publication Date: Jun 2017

Publication Type(s): Journal Article Review

PubMedID: 28326845

Abstract:INTRODUCTION An increasing number of female patients with autoimmune diseases are treated with biologic drugs. Concerns in regard to safety of biologics during pregnancy arise in patients who have not completed their families. Areas covered: A review of the literature dealing with child outcomes of pregnancies exposed to biologics shows that TNF inhibitors (TNFi) are the best studied in regard to human pregnancy. In studies comparing exposed pregnancies to disease-matched controls no increased risk of spontaneous abortion, low birth weight, prematurity or congenital malformations has been observed. For rituximab, tocilizumab, anakinra, belimumab and ustekinumab no prospective, controlled studies are available, and firm conclusions about their safety during pregnancy cannot be drawn. Expert commentary: TNFi appear fairly safe when given in early pregnancy. For biologics other than TNFi prospective, controlled studies on outcomes after early and late pregnancy exposure are urgently needed. Possible effects of TNFi and all other biologics on children's immune function, infection rate and vaccination responses are either limited or absent and need to be extended. Development of laboratory tests to measure concentrations of biologics routinely in children exposed in utero would facilitate decisions in regard to the time point of vaccination with live vaccines.

Database: Medline

6. Use of TNF-inhibitors and ustekinumab for psoriasis during pregnancy: A patient series.

Author(s): Lund, Tamara; Thomsen, Simon Francis

Source: Dermatologic therapy; May 2017; vol. 30 (no. 3)

Publication Date: May 2017

Publication Type(s): Journal Article

PubMedID: 28071837

Available at [Dermatologic therapy](#) - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:From 2002 to 2016 a total of seven women with severe refractory psoriasis were exposed to the TNF-inhibitors infliximab and adalimumab or to the IL12/23 inhibitor ustekinumab during one or more pregnancies. Maternal, fetal or teratogenic toxicity were not detected during pregnancy and puerperium. All pregnancies were uneventful and resulted in delivery of 10 healthy children in total, one of the women is due February 2017. Postpartum, five of the women were lactating, but none of the women or newborns developed adverse reactions. Data on safety of treatment during breastfeeding are sparse, but so far appears to be safe due to the lack of absorption across the gastrointestinal lining. Currently biological therapy with either TNF-inhibitors or ustekinumab is not recommended during pregnancy, however in selected women with severe psoriasis these treatment modalities may be considered.

Database: Medline

7. Psoriasis in those planning a family, pregnant or breast-feeding. The Australasian Psoriasis Collaboration.

Author(s): Rademaker, Marius; Agnew, Karen; Andrews, Megan; Armour, Katherine; Baker, Chris; Foley, Peter; Frew, John; Gebauer, Kurt; Gupta, Monisha; Kennedy, Debra; Marshman, Gillian; Sullivan, John

Source: The Australasian journal of dermatology; May 2017

Publication Date: May 2017

Publication Type(s): Journal Article Review

PubMedID: 28543445

Available at [The Australasian journal of dermatology](#) - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:The Australasian Psoriasis Collaboration has reviewed the evidence for managing moderate to severe psoriasis in those who are pregnant or are breast-feeding, or planning a family. The severity of the psoriasis, associated comorbidities and specific anti-psoriasis treatment, along with other exposures, can have a deleterious effect on pregnancy outcomes. Psoriasis itself increases the risk of preterm and low birthweight babies, along with spontaneous and induced abortions, but no specific birth defects have been otherwise demonstrated. The baseline risk for a live born baby to have a major birth defect is 3%, and significant neuro-developmental problem is 5%. In Australia, pregnant women with psoriasis are more likely to be overweight or obese, depressed, or smoke in their first trimester, and are also less likely to take prenatal vitamins or supplements. Preconception counselling to improve maternal, pregnancy and baby health is therefore strongly encouraged. The topical and systemic therapies commonly used in psoriasis are each discussed separately, with regards to pregnancy exposure, breast-feeding and effects on male fertility and mutagenicity. The systemic therapies included are acitretin, adalimumab, apremilast, certolizumab, ciclosporin, etanercept, infliximab, ixekizumab, methotrexate, NBUVB, prednisone, PUVA, secukinumab and ustekinumab. The topical therapies include dithranol (anthralin), calcipotriol, coal tar, corticosteroids

(weak, potent and super-potent), moisturisers, salicylic acid, tacrolimus, and tazarotene. As a general recommendation, effective drugs that have been widely used for years are preferable to newer alternatives with less foetal safety data. It is equally important to evaluate the risks of not treating, as severe untreated disease may negatively impact both mother and the foetus.

Database: Medline

8. Ustekinumab therapy for Crohn's disease during pregnancy: a case report and review of the literature.

Author(s): Cortes, X; Borrás-Blasco, J; Antequera, B; Fernandez-Martinez, S; Casterá, E; Martin, S; Molés, J R

Source: Journal of clinical pharmacy and therapeutics; Apr 2017; vol. 42 (no. 2); p. 234-236

Publication Date: Apr 2017

Publication Type(s): Case Reports Journal Article Review

PubMedID: 28004853

Available at [Journal of clinical pharmacy and therapeutics](#) - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:WHAT IS KNOWN AND OBJECTIVEThe safety of continued ustekinumab (UST) therapy during pregnancy remains unclear in patients with Crohn's disease (CD). There are no meta-analysis reports of exposure to UST during pregnancy. The objective was to describe a case of a pregnant patient with CD who was successfully treated with UST maintenance therapy throughout the pregnancy and delivered a baby boy without any congenital malformations, neurological abnormalities or birth defects.CASE SUMMARYA 37-year-old patient with CD treated with UST became pregnant. She had been receiving UST for 8 months at the time. After discussion with the patient and the obstetric team, the UST therapy was continued. The result of treatment was an uneventful pregnancy with delivery, at term, of a healthy boy and the maintenance of clinical, biological and endoscopic remission of CD during and after pregnancy.WHAT IS NEW AND CONCLUSIONTo our knowledge, this is the first reported use of continued UST therapy for CD throughout a pregnancy. The result of treatment was an uncomplicated pregnancy with the mother giving birth to a healthy boy at term and the maintenance of clinical biological and endoscopic remission of CD during and after pregnancy.

Database: Medline

9. Update on biologic safety for patients with psoriasis during pregnancy

Author(s): Porter M.L.; Lockwood S.J.; Kimball A.B.

Source: International Journal of Women's Dermatology; Mar 2017; vol. 3 (no. 1); p. 21-25

Publication Date: Mar 2017

Publication Type(s): Review

Available at [International Journal of Women's Dermatology](#) - from Europe PubMed Central - Open Access

Abstract:Biologic agents have become more common to treat patients with psoriasis, but concerns about their effect on pregnancy and lactation often preclude this treatment during these time periods. During the past decade, we have gained a much better understanding of the course of psoriasis during pregnancy and the safety of the use of biologic agents during pregnancy and lactation. Under certain circumstances, biologic agents can be considered appropriate treatment options for patients who are pregnant or lactating. Copyright © 2016 Women's Dermatologic Society

Database: EMBASE

10. Systemic medications used in treatment of common dermatological conditions: Safety profile with respect to pregnancy, breast feeding and content in seminal fluid.

Author(s): Brown, S M; Aljefri, K A; Waas, R; Hampton, P J

Source: The Journal of dermatological treatment; Jan 2017 ; p. 1-53

Publication Date: Jan 2017

Publication Type(s): Journal Article

PubMedID: 28092212

Abstract:Prescribing for pregnant or lactating patients and male patients wishing to father children can be a difficult area for dermatologists. There is a lack of review articles of commonly used systemic medications in dermatology with respect to their effects on developing embryogenesis and their potential transfer across the placenta, in breast milk and in seminal fluid. This paper aims to provide an up to date summary of evidence to better equip dermatologists to inform patients about the effects of systemic medications commonly used in dermatology to treat conditions such as atopic dermatitis, psoriasis and acne, on current and future embryogenesis and fertility. RESULTS/DISCUSSION We have provided detailed evidence about the safety profile for the use of systemic medication used in the treatment of common dermatological conditions, such as atopic dermatitis, psoriasis and acne with respect to pregnancy, breastfeeding and spermatogenesis. The following medications are completely contraindicated in pregnancy: retinoids, methotrexate, mycophenolate and fumaric acid esters, whilst ciclosporin and hydroxychloroquine are considered safer options. Azathioprine and biologics have been considered on a case by case scenario. There is an association with impaired neonatal immunity and a possible VACTERL association with biologics. There is insufficient evidence to recommend ustekinumab. Dapsone should also be considered on a case by case basis as it is associated with haemolysis and hyperbilirubinaemia in the neonate. The following medications are contraindicated in breastfeeding: retinoids, methotrexate, mycophenolate, fumaric acid esters and ciclosporin. There is conflicting information about the use of azathioprine. Dapsone use during breastfeeding is associated with haemolysis and hyperbilirubinaemia in the neonate. The use of hydroxychloroquine is felt to be safe. The data associated with the use of biologic agents is limited, specific guidance for each biological medication is detailed in the relevant section. Methotrexate is completely contraindicated in male patients actively trying for children and needs to be suspended for at least 3 months prior to contraception. The following medications are felt to be low risk: biologics, ciclosporin and retinoids, there are some concerns however regarding isotretinoin use in males when their female partner is already pregnant

and recent advice recommends contraception. There is insufficient information regarding the use of mycophenolate, fumaric acid esters, azathioprine, hydroxychloroquine, dapsone and ustekinumab in order to consider their safety profile.

Database: Medline

11. Successful pregnancy outcome under prolonged ustekinumab treatment in a patient with Crohn's disease and paradoxical psoriasis.

Author(s): Galli-Novak, E; Mook, S-C; Büning, J; Schmidt, E; Zillikens, D; Thaci, D; Ludwig, R J

Source: Journal of the European Academy of Dermatology and Venereology : JEADV; Dec 2016; vol. 30 (no. 12); p. e191

Publication Date: Dec 2016

Publication Type(s): Letter Case Reports

PubMedID: 26559393

Available at [Journal of the European Academy of Dermatology and Venereology : JEADV](#) - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Database: Medline

12. Critical review of the current recommendations for the treatment of systemic inflammatory rheumatic diseases during pregnancy and lactation.

Author(s): Levy, Roger A; de Jesús, Guilherme R; de Jesús, Nilson R; Klumb, Evandro M

Source: Autoimmunity reviews; Oct 2016; vol. 15 (no. 10); p. 955-963

Publication Date: Oct 2016

Publication Type(s): Journal Article Review

PubMedID: 27490204

Abstract:The crucial issue for a better pregnancy outcome in women with autoimmune rheumatic diseases is appropriate planning, with counseling of the ideal timing and treatment adaptation. Drugs used to treat rheumatic diseases may interfere with fertility or increase the risk of miscarriages and congenital abnormalities. MTX use post-conception is clearly linked to abortions as well as major birth defects, so it should be stopped 3months before conception. Leflunomide causes abnormalities in animals even in low doses. Although in humans, it does not seem to be as harmful as MTX, when pregnancy is detected in a patient on leflunomide, cholestyramine is given for washout. Sulfasalazine can be used safely and is an option for those patients who were on MTX or leflunomide. Azathioprine is generally the immunosuppressive of choice in many high-risk pregnancy centers because of the safety profile and its steroid-sparing property. Cyclosporine and tacrolimus can also be used as steroid-sparing agents, but experience is smaller. Although prednisone and prednisolone are inactivated in the placenta, we try to limit the dose to the minimal effective one, to prevent side effects. Antimalarials have been broadly studied and are safe during pregnancy and breastfeeding. Among biologic disease modifying anti-rheumatic agents (bDMARD), the anti-TNFs that have been used for longer are the ones with greater experience. The large monoclonal antibodies do not cross the placenta in the first trimester, and after conception, the decision to continue medication should be taken individually. The experience is larger in women with inflammatory bowel diseases, where anti-TNF is generally maintained at least until 30weeks to reduce fetal exposure. Live vaccines should not be administered to the infant in the first 6months of life. Pregnancy data for rituximab, abatacept, anakinra, tocilizumab, ustekinumab, belimumab, and tofacitinib are limited and their use in pregnancy cannot currently be recommended.

Database: Medline

13. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation.

Author(s): Götestam Skorpen, Carina; Hoeltzenbein, Maria; Tincani, Angela; Fischer-Betz, Rebecca; Elefant, Elisabeth; Chambers, Christina; da Silva, José; Nelson-Piercy, Catherine; Cetin, Irene; Costedoat-Chalumeau, Nathalie; Dolhain, Radboud; Förger, Frauke; Khamashta, Munther; Ruiz-Irastorza, Guillermo; Zink, Angela; Vencovsky, Jiri; Cutolo, Maurizio; Caeyers, Nele; Zumbühl, Claudia; Østensen, Monika

Source: Annals of the rheumatic diseases; May 2016; vol. 75 (no. 5); p. 795-810

Publication Date: May 2016

Publication Type(s): Journal Article Consensus Development Conference

PubMedID: 26888948

Available at [Annals of the rheumatic diseases](#) - from BMJ Journals - NHS

Available at [Annals of the rheumatic diseases](#) - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract: A European League Against Rheumatism (EULAR) task force was established to define points to consider on use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Based on a systematic literature review and pregnancy exposure data from several registries, statements on the compatibility of antirheumatic drugs during pregnancy and lactation were developed. The level of agreement among experts in regard to statements and propositions of use in clinical practice was established by Delphi voting. The task force defined 4 overarching principles and 11 points to consider for use of antirheumatic drugs during pregnancy and lactation. Compatibility with pregnancy and lactation was found for antimalarials, sulfasalazine, azathioprine, ciclosporin, tacrolimus, colchicine, intravenous immunoglobulin and glucocorticoids. Methotrexate, mycophenolate mofetil and cyclophosphamide require discontinuation before conception due to proven teratogenicity. Insufficient documentation in regard to fetal safety implies the discontinuation of leflunomide, tofacitinib as well as abatacept, rituximab, belimumab, tocilizumab, ustekinumab and anakinra before a planned pregnancy. Among biologics tumour necrosis factor inhibitors are best studied and appear reasonably safe with first and second trimester use. Restrictions in use apply for the few proven teratogenic drugs and the large proportion of medications for which insufficient safety data for the fetus/child are available. Effective drug treatment of active inflammatory rheumatic disease is possible with reasonable safety for the fetus/child during pregnancy and lactation. The dissemination of the data to health professionals and patients as well as their implementation into clinical practice may help to improve the management of pregnant and lactating patients with rheumatic disease.

Database: Medline

14. Pregnancy outcomes in women with psoriasis and psoriatic arthritis exposed to ustekinumab

Author(s): Naureckas S.; Slater J.; Gearhart N.; Ramachandran P.; Nissinen R.; Geldhof A.; Hopkins L.

Source: Journal of the American Academy of Dermatology; May 2016; vol. 74 (no. 5)

Publication Date: May 2016

Publication Type(s): Conference Abstract

Abstract:Background: Ustekinumab (UST) is indicated for moderate to severe psoriasis (PSO) and psoriatic arthritis (PsA) in adult patients, with a Food and Drug Administration pregnancy class B designation. No adverse developmental outcomes (pre- and postnatal) were observed in preclinical (animal) studies of UST, and limited published data exist concerning the effects of UST on human pregnancies. Studies have suggested PSO may be a potential risk factor for adverse pregnancy outcomes. To characterize pregnancy outcomes in women treated with UST for approved indications, data from clinical trials, registries, and spontaneous reports are presented. Methods: This dataset includes individual patient cases within the company safety database through 31 December 2014. Cases retrieved include prospectively reported (ie, pregnancy outcome not known when first reported) and retrospectively reported (ie, pregnancy outcome known when first reported) cases with maternal UST use for PSO or PsA during pregnancy or within 2 months prior to conception and with a known pregnancy outcome. Results: Eighty seven pregnancy reports (86 PSO, 2 PsA, some cases may report >1 indication, 58 prospective, 29 retrospective) were identified. Average maternal age was 31 years. Of the 87 reports, the majority of pregnancies (57/87; 65.5%) resulted in live births (LB, [including 3 premature births]). Congenital anomalies (CA) were reported in 1 pregnancy (1.2%): stenosis (spontaneous report). Spontaneous abortion (SA) was reported in 16 pregnancies (18.4%). Elective termination (ET) was reported in 14 pregnancies (16.1%). Of the 87 pregnancy reports, 16 reported exposure in all 3 trimesters (12 LBs, 3 SAs, 1 ET) and 37 reported exposure in the first trimester: 23 LBs (including 3 premature), 6 SAs, and 8 ETs. Conclusion: Review of pregnancy outcomes after maternal exposure to UST for PSO and PsA indications identified 87 pregnancies with known outcomes: 57 LBs (including 3 premature) and 1 CA. The rate of SAs was generally comparable to the rate reported for the general population (15% to 20%). Consistent with the literature, SAs in this case series were associated with older maternal age (34.42 yrs). The limited available data suggest that UST exposure may not impact pregnancy outcomes but additional experience is needed.

Database: EMBASE

15. Inadvertent pregnancy during ustekinumab therapy in a patient with plaque psoriasis and impetigo herpetiformis.

Author(s): Alsenaid, A; Prinz, J C

Source: Journal of the European Academy of Dermatology and Venereology : JEADV; Mar 2016; vol. 30 (no. 3); p. 488-490

Publication Date: Mar 2016

Publication Type(s): Letter Case Reports

PubMedID: 25413895

Available at [Journal of the European Academy of Dermatology and Venereology : JEADV](#) - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Database: Medline

16. Pregnancy during Ustekinumab Treatment for Severe Psoriasis.

Author(s): Rocha, Katiucia; Piccinin, Mariana Carolina; Kalache, Luciana F; Reichert-Faria, Adriane; Silva de Castro, Caio César

Source: Dermatology (Basel, Switzerland); 2015; vol. 231 (no. 2); p. 103-104

Publication Date: 2015

Publication Type(s): Case Reports Journal Article

PubMedID: 25790947

Available at [Dermatology \(Basel, Switzerland\)](#) - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract:We report the case of a 25-year-old patient who became pregnant during ustekinumab therapy. Treatment was suspended immediately after pregnancy had been confirmed. The patient had an uneventful pregnancy and her child is currently 14 months old, with adequate development to her age. Four reports of pregnancy during ustekinumab treatment have been reported and one resulted in miscarriage.

Database: Medline

17. Treating Psoriasis During Pregnancy: Safety and Efficacy of Treatments.

Author(s): Bangsgaard, Nannie; Rørbye, Christina; Skov, Lone

Source: American journal of clinical dermatology; Oct 2015; vol. 16 (no. 5); p. 389-398

Publication Date: Oct 2015

Publication Type(s): Journal Article Review

PubMedID: 26149091

Available at [American journal of clinical dermatology](#) - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract:Psoriasis is a chronic inflammatory disease with a well-documented negative effect on the quality of life of affected patients. Psoriasis often occurs in the reproductive years, during which the issue of pregnancy needs to be addressed. The course of psoriasis during pregnancy is unpredictable, and many patients face the challenge of needing treatment during pregnancy. In this review we provide an overview of the key considerations for managing psoriasis in pregnant women, covering the potential effects of active psoriasis and co-morbid conditions on the health of the mother and fetus, as well as the effects of psoriasis treatment options on the developing fetus. Although there are no robust data on the safety of systemic treatment of pregnant women, increasing evidence regarding the safety of cyclosporine (ciclosporin) treatment as well as anti-tumor necrosis factor- α is available and should be considered in pregnant women with moderate to severe psoriasis unresponsive to local corticosteroids and UVB light treatment.

Database: Medline

18. Treatment in RA and SPA during pregnancy: Present and future

Author(s): Ostensen M.

Source: Annals of the Rheumatic Diseases; Jun 2015; vol. 74 ; p. 10

Publication Date: Jun 2015

Publication Type(s): Conference Abstract

Available at [Annals of the Rheumatic Diseases](#) - from BMJ Journals - NHS

Available at [Annals of the Rheumatic Diseases](#) - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract:New effective therapies during the last 15 years have improved outcome and quality of life in patients with rheumatoid arthritis (RA) and spondylarthropathies (SpA). More female patients consider pregnancy. However, adjustments of therapy before and during pregnancy are required. Classical disease modifying drugs (cDMARDs), prednisone, and non-steroidal anti-inflammatory drugs (NSAIDs) remain valid options for treatment of pregnant patients because their safety profile in regard to the fetus is known. Among cDMARDs antimalarials, sulfasalazine, azathioprine, and cyclosporine are compatible with use throughout pregnancy. Methotrexate and cyclophosphamide are teratogenic and must be discontinued before a planned pregnancy. In spite of no indication for teratogenicity in humans, child safety has still not been established for leflunomide, so a washout procedure should be completed before conception. Prolonged and high doses (>7.5 mg/day) of prednisone carry risk for side effects in mother and fetus and should be avoided during pregnancy. In contrast to cDMARDs, child safety is a concern for new biologics with no or little pregnancy experience, and for combination therapies which include methotrexate or leflunomide. TNF α - inhibitors (TNFi) are the best studied biologics. Related to their differences in structure transplacental passage varies with high amounts of transfer in late pregnancy for monoclonal TNFi that possess a Fc part of IgG1. TNFi with either small affinity to the fetal Fc receptor or with no Fc part show low transplacental passage to the child. TNFi can be given before conception and during the

first and early 2nd trimester of pregnancy. When possible Fc containing TNFi should be avoided in the third trimester. Studies that investigate child health, particularly infection rate in the first year after antenatal exposure to TNFi are in progress and will provide answers how best to use TNFi in pregnant patients. For most other biologics data on human pregnancy exposure are sparse. Decisions for treatment during pregnancy in regard to biologics targeting B-cells, T cell activation or cytokines like IL-6, IL-23, IL-17 or IL-1beta must be based on the severity of maternal disease and have to be reserved for cases where no other safe options are available. Publications on fetal side effects or long term outcomes of in utero exposed children for rituximab, abatacept, tocilizumab, ustekinumab and anakinra are few and cannot guarantee safety for the child. They are therefore best avoided during pregnancy. In order to prevent unintended pregnancy exposure to insufficiently studied biologics, often in combination with MTX, family planning should be discussed and counseling given on contraception to patients of fertile age.

Database: EMBASE

19. Management of moderate to severe plaque psoriasis in pregnancy and lactation in the era of biologics.

Author(s): Mervic, Liljana

Source: Acta dermatovenerologica Alpina, Pannonica, et Adriatica; 2014; vol. 23 (no. 2); p. 27-31

Publication Date: 2014

Publication Type(s): Journal Article

PubMedID: 24964946

Abstract:Psoriasis is not uncommon in the reproductive years and therefore in pregnant patients. There are limited data about the impact of psoriasis on the course and prognosis of pregnancy and about the impact of pregnancy on the course of psoriasis. Usually the disease improves during pregnancy and patients experience worsening between 4 and 6 weeks after delivery. A safe option for patients with limited disease is topical therapy, including moisturizers and topical steroids as well as UVB phototherapy. In the case of active psoriasis or even psoriasis worsening during pregnancy, there might be a need for continuation or even introduction of systemic therapy. Methotrexate and acitretin are known teratogens and mutagens, and they must be avoided. Ciclosporin may be regarded as a possible rescue therapy for pregnant psoriasis patients in the case of severe disease. Post-marketing experience regarding the safety of biologics is accumulating, with largely reassuring results. All four biologics approved for the treatment of moderate to severe psoriasis--etanercept, infliximab, adalimumab, and ustekinumab--are not currently recommended in pregnant psoriasis patients. The existing evidence implies that the risk of biologics in pregnancy is relatively low and that the risk of fetal drug exposure may be outweighed by the benefits for the mother.

Database: Medline

20. Biologics in the Treatment of Skin Diseases During Pregnancy and Lactation

Author(s): Matz H.

Source: Current Dermatology Reports; Sep 2014; vol. 3 (no. 3); p. 144-148

Publication Date: Sep 2014

Publication Type(s): Review

Available at [Current Dermatology Reports](#) - from SpringerLink

Abstract: Dermatologists are frequently faced with questions about the safety of commonly prescribed topical and systemic medications during pregnancy and lactation. Safety data, particularly regarding medications that are unique to dermatology, can be difficult to find as no unified database or reference guides for clinicians are currently available. In the absence of definitive data, it is prudent to recommend to avoid if possible treatment with biologics during pregnancy. The tumor necrosis factor (TNF)-alpha antagonists and ustekinumab have been labeled pregnancy category B, which allows for their use in pregnant patients with severe psoriasis or psoriatic arthritis. In contrast, rituximab is classified as pregnancy category C (although anecdotal data indicate that rituximab has been used safely in pregnancy as well). Regarding lactation, it has been shown that biologics are secreted into breast milk, but whether they are absorbed by the infant's gastrointestinal system is unlikely. Although no adverse outcomes have been demonstrated in all case reports available, it may be prudent to advise against breastfeeding while on anti-TNF, ustekinumab, or rituximab therapy until further evidence is collected. © 2014 Springer Science+Business Media New York.

Database: EMBASE

21. Pregnancy outcomes of two patients exposed to ustekinumab in the first trimester.

Author(s): Sheeran, Claire; Nicolopoulos, Jennifer

Source: The Australasian journal of dermatology; Aug 2014; vol. 55 (no. 3); p. 235-236

Publication Date: Aug 2014

Publication Type(s): Letter Case Reports

PubMedID: 25117169

Available at [The Australasian journal of dermatology](#) - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Database: Medline

22. Pregnancy outcomes in women exposed to ustekinumab in the psoriasis clinical development program

Author(s): Cather J.C.; Horn E.J.; Rahawi K.W.; Schaufelberger B.W.; Chan D.; Goyal K.

Source: Australasian Journal of Dermatology; May 2014; vol. 55 ; p. 30

Publication Date: May 2014

Publication Type(s): Conference Abstract

Available at [Australasian Journal of Dermatology](#) - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:Introduction: To characterize pregnancy outcomes in women exposed to UST during pregnancy, data from the UST PsO clinical development program are presented. Method: Pregnancies reported with maternal use of UST from 4 PsO studies (Ph2 [n = 320] and Ph3 [PHOENIX 1; n = 766, PHOENIX 2; n = 1230, ACCEPT; n = 903]) were evaluated. Pregnancy outcomes were summarized using descriptive statistics. Results: 981 female patients received ≥ 1 dose of UST, and 29 pregnancies were reported (despite agreement to use adequate birth control measures). Per protocol, UST treatment was discontinued upon report of pregnancy in all cases. Mean maternal age (MMA) was 30 years (range 21-44), and mean duration of UST exposure prior to reported pregnancy was 72 +/- 61 weeks. Pregnancy outcomes were reported for 26 of 29 pregnancies, including 14 (54%) live births (LBs), 5 (19%) spontaneous abortions (SAs), and 7 (27%) elective abortions (EAs). All 5 SAs occurred in the 1st trimester. MMA was older for patients who had SAs (35 +/- 5 years) vs. LBs (29 +/- 4 years), and UST treatment duration prior to pregnancy report was shorter for patients who had SAs (36 +/- 25 weeks) vs. LBs (98 +/- 57 weeks). Among LBs, there were no congenital anomalies, and 2 infants had neonatal jaundice treated with phototherapy. Neonatal outcomes were generally healthy with mean birth weight of 7 +/- 1 lbs (n = 12), gestation age of 38 +/- 0.7 weeks (n = 9), and mean 5-min APGAR of 9 +/- 0.6 (n = 8). Rate of SAs was generally comparable to rate reported for the general population (15-20%). SAs in this case series were associated with older maternal age. Longer duration of UST exposure prior to the reported pregnancy was not associated with adverse outcomes. The limited available data suggest that UST exposure may not impact pregnancy outcomes but additional experience is needed.

Database: EMBASE

23. Spontaneous abortion during ustekinumab therapy.

Author(s): Fotiadou, Christina; Lazaridou, Elizabeth; Sotiriou, Eleni; Ioannides, Demetrios

Source: Journal of dermatological case reports; Dec 2012; vol. 6 (no. 4); p. 105-107

Publication Date: Dec 2012

Publication Type(s): Journal Article

PubMedID: 23329988

Available at [Journal of dermatological case reports](#) - from Europe PubMed Central - Open Access

Abstract:BACKGROUNDPsoriasis affects a considerable proportion of women in their reproductive years. Limited published data exist about the possible negative impact of the disease itself in the prognosis of pregnancy. On this background, the emergence of newer biologic agents for psoriasis treatment - such as ustekinumab - raises safety issues concerning the exposure to the drug during pregnancy. To our knowledge this is the first report in the literature describing a pregnancy outcome under ustekinumab treatment.OBSERVATIONWe report a 35-year-old female psoriasis patient who was under treatment with ustekinumab for a year when she inadvertently became pregnant. The drug was discontinued immediately and the patient did not opt for termination. During the 12th week of gestation she experienced a spontaneous abortion.CONCLUSIONAlthough the patient's profile fulfilled 2 general risk factors for spontaneous abortion - she was a smoker and this was her third pregnancy - one could not underestimate the possible role of the drug and of psoriasis per se in this adverse pregnancy outcome. Pregnancy registries and large prospective studies are needed in order to determine whether poorer pregnancies outcomes in psoriatic women are due to the disease itself, associated comorbidities or side-effects of new therapies such as ustekinumab.

Database: Medline

24. Treatment of severe psoriasis with ustekinumab during pregnancy.

Author(s): Andrulonis, Ryan; Ferris, Laura Korb

Source: Journal of drugs in dermatology : JDD; Oct 2012; vol. 11 (no. 10); p. 1240

Publication Date: Oct 2012

Publication Type(s): Case Reports Journal Article

PubMedID: 23134993

Abstract:We present the case of a female, aged 22 years, with a long history of recalcitrant pustular psoriasis and psoriatic arthritis, treated with ustekinumab during pregnancy. The result of treatment was an uncomplicated pregnancy with delivery, at term, of a healthy boy. To our knowledge, this is the first reported use of ustekinumab in a human during pregnancy. Following a description of the case, we discuss the characteristics of ustekinumab and review the known information from human case reports, case series, and animal studies regarding the use of TNF- α inhibitors and ustekinumab during pregnancy. We also provide a short discussion of administration of ustekinumab during the time period when a mother is nursing and the potential for complications to infants in this setting.

Database: Medline

**25. A case of ustekinumab for the treatment of Crohn's disease during pregnancy
ACG/AstraZeneca clinical vignette award presidential poster**

Author(s): Rosen M.; Scherl E.; Bosworth B.

Source: American Journal of Gastroenterology; Oct 2012; vol. 107

Publication Date: Oct 2012

Publication Type(s): Conference Abstract

Abstract: Purpose: Therapies for the treatment of steroid- and anti-TNF-refractory Crohn's disease are limited and even further restricted and concerning in pregnant patients. This is the first case of a patient with Crohn's disease (CD) treated with ustekinumab for a flare during her pregnancy. Case: The patient is a 34-year-old woman with steroid-refractory Crohn's ileocolitis. She was intolerant to azathioprine with the development of leukopenia without significant response to the medication and she had attenuated her response to infliximab. After her first pregnancy, she developed a severe flare and was started on certolizumab, to which she was only minimally responsive. After another ineffective course of steroids, she was started on open label ustekinumab at 45 mg subcutaneously for the treatment of her Crohn's disease. The patient achieved clinical and endoscopic remission maintained on 45 mg every 8 weeks. She discovered she was pregnant and decided to discontinue her medication, having received her last dose at week 3 of her pregnancy. The patient then began to develop symptoms of abdominal pain, bloody diarrhea, and arthralgias during her second trimester. At 34 weeks into her pregnancy, she represented and was given a dose of ustekinumab 45 mg subcutaneously in order to reinduce remission. The patient responded with improvement in symptoms with resolution of her bloody diarrhea and improvement in stool frequency within 1 week. The patient had a successful full-term pregnancy and delivered a healthy baby of 3,543 grams. Conclusion: Ustekinumab is a monoclonal antibody against the shared p40 subunit of interleukin-12/23 and has been demonstrated to produce clinical response in patients with moderate-to-severe CD with induction dosing in a phase 2a study. Since its approval by the FDA in September 2009 for the treatment of psoriasis, the drug has been used off-label as a treatment for anti-TNF refractory CD outside the context of clinical trials. To date, there is a paucity of data describing the use of this medication in the pregnant population. Studies in the macaque monkey have shown that there are no teratogenic effects of ustekinumab up to doses of 45 mg/kg and thus it has been determined to be pregnancy category B. Our therapeutic options were limited in this patient, as she has failed anti-TNF therapy (pregnancy category B), corticosteroids (category C), and azathioprine (category D) in the past. In this patient, the administration of ustekinumab in both the first and the third trimesters was proven to be safe and effective in first maintaining and then re-inducing remission. The patient was enrolled in the PIANO registry and she and her daughter will be followed prospectively.

Database: EMBASE

26. The safety of ustekinumab in psoriasis.

Author(s): Famenini, Shannon; Wu, Jashin J

Source: Journal of drugs in dermatology : JDD; Aug 2012; vol. 11 (no. 8); p. 907-910

Publication Date: Aug 2012

Publication Type(s): Journal Article Review

PubMedID: 22859234

Abstract:Ustekinumab is effective in the treatment of a variety of autoimmune conditions including psoriasis. As a relatively new therapeutic agent, its long-term effects are still under investigation. Short-term studies, however, have revealed ustekinumab to be generally well tolerated and safe. This article provides a comprehensive review of the pharmacokinetics of ustekinumab, its safety profile, adverse effects, and use in pregnancy. The effect of diabetes and prior immunosuppressant therapy is also addressed.

Database: Medline

27. Consensus guidelines for the management of plaque psoriasis.

Author(s): Hsu, Sylvia; Papp, Kim Alexander; Lebwohl, Mark G; Bagel, Jerry; Blauvelt, Andrew; Duffin, Kristina Callis; Crowley, Jeffrey; Eichenfield, Lawrence F; Feldman, Steven R; Fiorentino, David F; Gelfand, Joel M; Gottlieb, Alice B; Jacobsen, Carmen; Kalb, Robert E; Kavanaugh, Arthur; Korman, Neil J; Krueger, Gerald G; Michelson, Melissa A; Morison, Warwick; Ritchlin, Christopher T; Stein Gold, Linda; Stone, Stephen P; Strober, Bruce E; Van Voorhees, Abby S; Weiss, Stefan C; Wanat, Karolyn; Bebo, Bruce F; National Psoriasis Foundation Medical Board

Source: Archives of dermatology; Jan 2012; vol. 148 (no. 1); p. 95-102

Publication Date: Jan 2012

Publication Type(s): Research Support, Non-u.s. Gov't Practice Guideline Journal Article

PubMedID: 22250239

Available at [Archives of dermatology](#) - from Free Medical Journals . com

Abstract:The Canadian Guidelines for the Management of Plaque Psoriasis were reviewed by the entire National Psoriasis Foundation Medical Board and updated to include newly approved agents such as ustekinumab and to reflect practice patterns in the United States, where the excimer laser is approved for psoriasis treatment. Management of psoriasis in special populations is discussed. In the updated guidelines, we include sections on children, pregnant patients or pregnant partners of patients, nursing mothers, the elderly, patients with hepatitis B or C virus infections, human immunodeficiency virus-infected patients, and patients with malignant neoplasms, as well as sections on tumor necrosis factor blockers, elective surgery, and vaccinations.

Database: Medline

28. Development in the cynomolgus macaque following administration of ustekinumab, a human anti-IL-12/23p40 monoclonal antibody, during pregnancy and lactation.

Author(s): Martin, Pauline L; Sachs, Clifford; Imai, Noritaka; Tsusaki, Hideshi; Oneda, Satoru; Jiao, Qun; Treacy, George

Source: Birth defects research. Part B, Developmental and reproductive toxicology; Oct 2010; vol. 89 (no. 5); p. 351-363

Publication Date: Oct 2010

Publication Type(s): Journal Article

PubMedID: 20540088

Abstract:BACKGROUND Ustekinumab is a human monoclonal antibody that binds to the p40 subunit of interleukin (IL) 12 and IL-23 and inhibits their pharmacological activity. To evaluate potential effects of ustekinumab treatment during pregnancy, developmental studies were conducted in cynomolgus macaques. METHODS Ustekinumab was tested in two embryo/fetal development (EFD) studies and in a combined EFD/pre and postnatal development (PPND) study. In the EFD studies, pregnant macaques (12/group) were dosed with saline or ustekinumab (9 mg/kg IV, 22.5 mg/kg SC, or 45 mg/kg IV or SC during the period of major organogenesis, gestation day [GD] 20-50). Fetuses were harvested on GD100-102 and examined for any effects on development. In the EFD/PPND study, pregnant macaques were injected with saline or ustekinumab (22.5 or 45 mg/kg SC) from GD20 through lactation day 33. Infants were examined from birth through 6 months of age for morphological and functional development. Potential effects on the immune system were evaluated by immunophenotyping of peripheral blood lymphocytes and immunohistopathology of lymphoid tissues in fetuses and infants and by T-dependent antibody response (TDAR) to KLH and TTX and by DTH response in infants. Ustekinumab concentrations were measured in serum from dams, fetus, and infants and in breast milk. RESULTS Ustekinumab treatment produced no maternal toxicity and no toxicity in the fetuses or infants, including no effects on the TDAR or DTH responses. Ustekinumab was present in serum from GD100 fetuses and was present in infant serum through day 120 post-birth. Low levels of ustekinumab were present in breast milk. CONCLUSION Exposure of macaque fetuses and infants to ustekinumab had no adverse effects on pre- and postnatal development.

Database: Medline

Strategy 301357

#	Database	Search term	Results
1	Medline	(Ustekinumab).ti,ab	985
2	Medline	exp USTEKINUMAB/	566
3	Medline	(Stelara).ti,ab	19
4	Medline	(1 OR 2 OR 3)	1093
5	Medline	(pregnan*).ti,ab	431053
6	Medline	exp PREGNANCY/	818330
7	Medline	(5 OR 6)	909364
8	Medline	(4 AND 7)	27
9	EMBASE	(Ustekinumab).ti,ab	2091
10	EMBASE	exp USTEKINUMAB/	3933
11	EMBASE	(Stelara).ti,ab	42
12	EMBASE	(9 OR 10 OR 11)	4006
13	EMBASE	(pregnan*).ti,ab	564508
14	EMBASE	exp PREGNANCY/	683090
15	EMBASE	(13 OR 14)	879226
16	EMBASE	(12 AND 15)	128
17	EMBASE	*USTEKINUMAB/	1185
18	EMBASE	(15 AND 17)	33
19	EMBASE	*PREGNANCY/	137473
20	EMBASE	*"PREGNANCY OUTCOME"/	14733

21	EMBASE	*"PREGNANCY COMPLICATION"/	43619
22	EMBASE	(19 OR 20 OR 21)	192372
23	EMBASE	(12 AND 22)	41
24	EMBASE	(Ustekinumab AND pregnan*).ti,ab	41