West Middlesex University Hospital

Date: 20 Jul 2017
Sources Searched: Medline, Embase, PubMed.

Ustekinumab in Pregnancy

See full search strategy

Summary:

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.

Source: Electronic Medicines Compendium. STELARA 130 mg concentrate for solution for infusion
URL: https://www.medicines.org.uk/emc/medicine/32568 [Last Accessed 20/07/2017]

1. 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 in full text at BMC Gastroenterology - from BioMed Central

Available in full text at BMC Gastroenterology - from ProQuest

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.CONCLUSIONUstekinumab 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

2. 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

3. 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 in full text at Dermatologic Therapy - from John Wiley and Sons

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

4. 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 in full text at Australasian Journal of Dermatology - from John Wiley and Sons

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

5. 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

PubMedID: 28004853

Available in full text at Journal of Clinical Pharmacy and Therapeutics - from John Wiley and Sons

Abstract:WHAT IS KNOWN AND OBJECTIVESThe 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

6. 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 in full text at International Journal of Women's Dermatology - from National Library of Medicine

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.

Database: EMBASE

7. 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/DISCUSSIONWe 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, ciclopsorin 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

8. Psoriasis and pregnancy in the era of biologics. Case report of ustekinumab treatment during pregnancy

Author(s): Fierens H.; Baeck M.

Source: Louvain Medical; 2016; vol. 135 (no. 4); p. 231-235

Publication Date: 2016

Publication Type(s): Article

Abstract: We report the case of a successful delivery following exposure to ustekinumab during pregnancy. Though psoriasis is not uncommon in pregnant women, its treatment may prove challenging during pregnancy, especially in severe psoriasis cases. While the disease usually improves during pregnancy, its treatment must often be continued. Besides local treatment, UVB phototherapy remains the treatment of choice in moderate-to-severe psoriasis. In patients requiring a systemic treatment, biologics can be considered. Whereas limited safety results are available from studies, various follow-up registers provide reassuring data. Unexpected exposure to biologics during the first trimester of pregnancy proves unproblematic.

Database: EMBASE

9. 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 in full text at Journal of the European Academy of Dermatology and Venereology - from John Wiley and Sons

Database: Medline

10. 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 administrated 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

11. Managing inflammatory bowel disease in pregnancy: Current perspectives

Author(s): Pinder M.; Lummis K.; Selinger C.P.

Source: Clinical and Experimental Gastroenterology; Oct 2016; vol. 9 ; p. 325-335

Publication Date: Oct 2016

Publication Type(s): Review

Available in full text at Clinical and Experimental Gastroenterology - from National Library of Medicine

Abstract: Inflammatory bowel disease (IBD) affects many women of childbearing age. The course of IBD is closely related to pregnancy outcomes with poorly controlled IBD increasing the risk of prematurity, low weight for gestation, and fetal loss. As such, women with IBD face complex decision making weighing the risks of active disease versus those of medical treatments. This review summarizes the current evidence regarding the safety and efficacy of IBD treatments during pregnancy and lactation aiming to provide up-to-date guidance for clinicians. Over 50% of women have poor IBD- and pregnancy-related knowledge, which is associated with views contrary to medical evidence and voluntary childlessness. This review highlights the effects of poor patient

knowledge and critically evaluates interventions for improving patient knowledge and outcomes.

Database: EMBASE

12. 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, Josè; 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

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

13. 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 USTexposure may not impact pregnancy outcomes but additional experience is needed.

Database: EMBASE

14. 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 in full text at Journal of the European Academy of Dermatology and Venereology - from John Wiley and Sons

Database: Medline

15. The Toronto Consensus Statements for the Management of Inflammatory Bowel Disease in Pregnancy

Author(s): Nguyen G.C.; Maxwell C.; Seow C.H.; Leung Y.; Huang V.; Jones J.; Leontiadis G.I.; Tse F.; Mahadevan U.; Van Der Woude C.J.

Source: Gastroenterology; Mar 2016; vol. 150 (no. 3); p. 734

Publication Date: Mar 2016

Publication Type(s): Article

PubMedID: 26688268

Available in print at Patricia Bowen Library and Knowledge Service West Middlesex university Hospital - from Gastronterology

Abstract: Background & Aims The management of inflammatory bowel disease (IBD) poses a particular challenge during pregnancy because the health of both the mother and the fetus must be considered. Methods A systematic literature search identified studies on the management of IBD during pregnancy. The quality of evidence and strength of recommendations were rated using the Grading of Recommendation Assessment, Development and Evaluation (GRADE) approach. Results Consensus was reached on 29 of the 30 recommendations considered. Preconception counseling and access to specialist care are paramount in optimizing disease management. In general, women on 5-ASA, thiopurine, or anti-tumor necrosis factor (TNF) monotherapy for maintenance should continue therapy throughout pregnancy. Discontinuation of anti-TNF therapy or switching from combination therapy to monotherapy may be considered in very select low-risk patients. Women who have a mild to moderate disease flare while on optimized 5-ASA or thiopurine therapy should be managed with systemic corticosteroid or anti-TNF therapy, and those with a corticosteroid-resistant flare should start anti-TNF therapy. Endoscopy or urgent surgery should not be delayed during pregnancy if indicated. Decisions regarding cesarean delivery should be based on obstetric considerations and not the diagnosis of IBD alone, with the exception of women with active perianal Crohn's disease. With the exception of methotrexate, the use of medications for IBD should not influence the decision to breast-feed and vice versa. Live vaccinations are not recommended within the first 6 months of life in the offspring of women who were on anti-TNF therapy during pregnancy. Conclusions Optimal management of IBD before and during pregnancy is essential to achieving favorable maternal and neonatal outcomes.

Database: EMBASE

16. Disease-modifying anti-rheumatic drug use in pregnant women with rheumatic diseases: A systematic review of the risk of congenital malformations

Author(s): Baldwin C.; Avina-Zubieta A.; Rai S.K.; Carruthers E.; De Vera M.A.

Source: Clinical and Experimental Rheumatology; Mar 2016; vol. 34 (no. 2); p. 172-183

Publication Date: Mar 2016

Publication Type(s): Article

PubMedID: 26940667

Abstract: Objective Despite the high incidence of rheumatic diseasesDespite the high incidence of rheumatic diseases during the reproductive years, little is known about the impact of diseasemodifying anti-rheumatic drug (DMARD) use during pregnancy. Our objective was to systematically review and appraise evidence in women with rheumatic disease on the use of traditional and biologic DMARDs during pregnancy and the risk of congenital malformation outcomes. Methods We conducted a systematic search of MEDLINE, EMBASE, and INTERNATIONAL PHARMACEUTICAL ABSTRACTS databases. Inclusion criteria were: 1) study sample including women

with rheumatic disease; 2) use of traditional and/or biologic DMARDs during pregnancy; and 3) congenital malformation outcome(s) reported. We extracted information on study design, data source, number of exposed pregnancies, type of DMARD, number of live births, and number of congenital malformations. Results Altogether, we included 79 studies; the majority were based on designs that did not involve a comparison group, including 26 case reports, 17 case series, 20 cross-sectional studies, and 4 surveys. Studies that had a comparator group included 1 case control, 10 cohort studies, and 1 controlled trial. Hydroxychloroquine and azathioprine represent the most studied traditional DMARD exposures and, among biologics, most of the reports were on infliximab and etanercept. Conclusion This is the first systematic review on the use of both traditional and biologic DMARDs during pregnancy among women with rheumatic diseases and congenital malformation outcomes, with a focus on study design and quality. Findings confirm the limited number of studies, as well as the need to improve study designs.

Database: EMBASE

17. Challenges in vaccinating infants born to mothers taking immunoglobulin biologicals during pregnancy

Author(s): Ling J.; Koren G.

Source: Expert Review of Vaccines; Feb 2016; vol. 15 (no. 2); p. 239-256

Publication Date: Feb 2016

Publication Type(s): Review

PubMedID: 26642867

Abstract: While immunoglobulin biologicals are increasingly used during pregnancy, there have been concerns on the immune function and vaccination of infants born to mothers taking immunoglobulin biologicals. In addition to the detection of biologicals in cord blood, cases of severe neonatal neutropenia and fatal dissemination of Bacillus Calmette-Guerin (BCG) have been reported. With increasing number of infants exposed to immunoglobulin biologicals in utero, there is a need to address the challenges in vaccinating these infants. This review summarizes the available evidence to discuss the issues of immunoglobulin biological exposure in utero, neonatal immune function, long-term immune development, and the challenges and strategies of vaccinating newborns and infants who were born to mothers taking biologicals during pregnancy.

Database: EMBASE

18. 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 in full text at Dermatology - from ProQuest

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

19. 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 in full text at American Journal of Clinical Dermatology - from ProQuest

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

20. Treatment of psoriasis and psoriatic arthritis during pregnancy and breastfeeding

Author(s): Kurizky P.S.; Da Henrique Mota L.M.; Castro Ferreira C.D.; Carmo Nogueira L.S.

Source: Anais Brasileiros de Dermatologia; Jul 2015; vol. 90 (no. 3); p. 367-375

Publication Date: Jul 2015

Publication Type(s): Article

PubMedID: 26131868

Available in full text at Anais Brasileiros de Dermatologia - from National Library of Medicine

Abstract: Psoriasis is a chronic infl ammatory disease that affects primarily the skin and joints, with a worldwide incidence of 2-3%. Fifty percent of patients are women, most still diagnosed during childbearing years. Current-ly,the estimate is that up to 107 thousand deliveries are performed annually in women with psoriasis, a percentage of them in women with moderate to severe disease. Fetal risks in pregnant women with psoriasis derive both from maternal disease and the medications used to control the illness. The purpose of this review is to study the effect of the main drugs used in the treatment of psoriasis and psoriatic arthritis during pregnancy and lactation, with particular focus on disease-modifying anti-rheumatic biological drugs, biological therapies, immunobiolog-ics or biologics.Copyright © 2015, by Anais Brasileiros de Dermatologia.

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 in full text at Australasian Journal of Dermatology - from John Wiley and Sons

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 in full text at Australasian Journal of Dermatology - from John Wiley and Sons

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

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 inadvertedly 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-a 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

Available in full text at American Journal of Gastroenterology, The - from ProQuest

Available in print at Patricia Bowen Library and Knowledge Service West Middlesex university Hospital - from American Journal of Gastroenterology

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

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

Available in full text at Birth Defects Research Part B: Developmental and Reproductive Toxicology - from John Wiley and Sons

Abstract:BACKGROUNDUstekinumab 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.METHODSUstekinumab 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.RESULTSUstekinumab 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.CONCLUSIONSExposure of macaque fetuses and infants to ustekinumab had no adverse effects on pre- and postnatal development.

Database: Medline

Strategy 243556

#	Database	Search term	Results
1	Medline	(Stelara).ti,ab	17
2	Medline	(Ustekinumab).ti,ab	925
3	Medline	exp USTEKINUMAB/	542
4	Medline	(1 OR 2 OR 3)	1033
5	Medline	(pregnan*).ti,ab	425559
6	Medline	exp PREGNANCY/	812240
7	Medline	(5 OR 6)	901578
8	Medline	(4 AND 7)	24
9	EMBASE	(Stelara).ti,ab	40
10	EMBASE	(Ustekinumab).ti,ab	1935
11	EMBASE	exp USTEKINUMAB/	3661
12	EMBASE	(9 OR 10 OR 11)	3721
13	EMBASE	(pregnan*).ti,ab	550239
14	EMBASE	exp PREGNANCY/	670484
15	EMBASE	(13 OR 14)	860617
16	EMBASE	(12 AND 15)	123
17	PubMed	(Stelara).ti,ab	1048
18	PubMed	(Ustekinumab).ti,ab	1048
19	PubMed	(pregnan*).ti,ab	903662

20	PubMed	(17 OR 18)	1048
21	PubMed	(19 AND 20)	27