West Middlesex University Hospital

Epirubicin/ cyclophosphamide chemotherapy in pregnancy (breast cancer)

Date of Search: 04/08/2016
Sources Searched: Medline, Embase, NICE Evidence, DynaMed.

Search History:
1. Medline; pregn*.ti,ab; 406421 results.
2. Medline; exp PREGNANCY/; 790329 results.
3. Medline; 1 OR 2; 873358 results.
4. Medline; (breast adj2 cancer*).ti,ab; 214361 results.
5. Medline; exp BREAST NEOPLASMS/; 240272 results.
6. Medline; (breast adj2 neoplas*).ti,ab; 2377 results.
7. Medline; (breast adj2 carcinoma*).ti,ab; 35781 results.
8. Medline; 4 OR 5 OR 6 OR 7; 301256 results.
9. Medline; epirubicin.ti,ab; 4617 results.
10. Medline; exp EPIRUBICIN/; 4629 results.
11. Medline; 9 OR 10; 6230 results.
12. Medline; exp CYCLOPHOSPHAMIDE/; 49152 results.
13. Medline; cyclophosphamide.ti,ab; 41636 results.
14. Medline; 12 OR 13; 65414 results.
15. Medline; 3 AND 8 AND 11 AND 14; 18 results.
16. Medline; 3 AND 11 AND 14; 23 results.
17. EMBASE; pregn*.ti,ab; 506321 results.
18. EMBASE; exp PREGNANCY/; 623464 results.
19. EMBASE; 17 OR 18; 799144 results.
20. EMBASE; (breast adj2 cancer*).ti,ab; 289588 results.
21. EMBASE; exp BREAST NEOPLASMS/; 411879 results.
22. EMBASE; (breast adj2 neoplas*).ti,ab; 2108 results.
23. EMBASE; (breast adj2 carcinoma*).ti,ab; 35297 results.
24. EMBASE; 20 OR 21 OR 22 OR 23; 446957 results.
25. EMBASE; exp EPIRUBICIN/; 24242 results.
26. EMBASE; epirubicin.ti,ab; 6645 results.
27. EMBASE; 25 OR 26; 24719 results.
28. EMBASE; exp CYCLOPHOSPHAMIDE/; 176356 results.
29. EMBASE; cyclophosphamide.ti,ab; 55994 results.
30. EMBASE; 28 OR 29; 181989 results.
31. EMBASE; 19 AND 24 AND 27 AND 30; 209 results.
32. EMBASE; exp SECOND TRIMESTER PREGNANCY/; 17358 results.
33. EMBASE; 31 AND 32; 25 results.
34. EMBASE; 24 AND 27 AND 30 AND 32; 25 results.

35. EMBASE; (cyclophosphamide OR epirubicin).ti; 16804 results.
36. EMBASE; 19 AND 24 AND 35; 26 results.
37. EMBASE; *CYCLOPHOSPHAMIDE/; 47296 results.
38. EMBASE; *EPIRUBICIN/; 5257 results.
39. EMBASE; 19 AND 24 AND 37 AND 38; 11 results.
40. EMBASE; 24 AND 32 AND 37 AND 38; 1 results.
41. EMBASE; exp THIRD TRIMESTER PREGNANCY/; 20078 results.
42. EMBASE; 24 AND 37 AND 38 AND 41; 0 results.
43. EMBASE; 35 AND 41; 4 results.
44. EMBASE; 19 AND 24 AND 37; 70 results.
45. EMBASE; exp PLACENTAL TRANSFER/; 7128 results.
46. EMBASE; 37 AND 38 AND 45; 1 results.
47. EMBASE; 37 AND 45; 19 results.
48. EMBASE; 38 AND 45; 3 results.
49. EMBASE; exp FETOTOXICITY/; 2231 results.
50. EMBASE; 37 AND 38 AND 49; 1 results.
51. EMBASE; 38 AND 49; 2 results.
52. EMBASE; 37 AND 49; 16 results.
53. Medline; (cyclophosphamide OR epirubicin).ti; 13966 results.
54. Medline; 3 AND 53; 344 results.
55. Medline; pregn*.ti; 194984 results.
56. Medline; 53 AND 55; 62 results.
57. Medline; 3 AND 8 AND 11; 32 results.
58. Medline; 3 AND 8 AND 14; 98 results.
59. Medline; exp MATERNAL-FETAL EXCHANGE/; 28242 results.
60. Medline; 8 AND 11 AND 14 AND 59; 0 results.
61. Medline; 8 AND 11 AND 59; 1 results.
62. Medline; 8 AND 14 AND 59; 3 results.

Additional evidence:

In May 2013, the National Toxicology Program (US) completed a Monograph on Developmental Effects and Pregnancy Outcomes Associated With Cancer Chemotherapy Use During Pregnancy. The Monograph is intended as a resource for clinicians and their pregnant patients and provides a comprehensive literature review of the human data, including all available data on follow-up evaluations in gestationally exposed offspring. The Monograph does not provide medical advice or guidance. **(Sections 5.11 and 5.17 cover the administration of Epirubicin and cyclophosphamide during pregnancy.)**

Title: Epirubicin: A new entry in the list of fetal cardiotoxic drugs? Intrauterine death of one fetus in a twin pregnancy. Case report and review of literature

Citation: BMC Cancer, December 2015, vol./is. 15/1(no pagination), 1471-2407 (December 16, 2015)

Author(s): Framarino-dei-Malatesta M., Perrone G., Giancotti A., Ventriglia F., Derme M., Iannini I., Tibaldi V., Galoppi P., Sammartino P., Cascialli G., Brunelli R.

Language: English

Abstract: Background: Current knowledge indicate that epirubicin administration in late pregnancy is almost devoid of any fetal cardiotoxicity. We report a twin pregnancy complicated by breast cancer in which epirubicin administration was causatively linked to the death of one twin who was small for gestational age (SGA) and in a condition of oligohydramnios and determined the onset of a transient cardiotoxicity of the surviving fetus/newborn. Case presentation: A 38-year-old caucasic woman with a dichorionic twin pregnancy was referred to our center at 20 and 1/7weeks for a suspected breast cancer, later confirmed by the histopathology report. At 31 and 3/7weeks, after the second chemotherapy cycle, ultrasound examination evidenced the demise of one twin while cardiac examination revealed a monophasic diastolic ventricular filling, i.e. a diastolic dysfunction of the surviving fetus who was delivered the following day due to the occurrence of grade II placental abruption. The role of epirubicin cardiotoxicity in the death of the first twin was supported by post-mortem cardiac and placental examination and by the absence of structural or genomic abnormalities that may indicate an alternative etiology of fetal demise. The occurrence of epirubicin cardiotoxicity in the surviving newborn was confirmed by the report of high levels of troponin and transient left ventricular septal hypokinesia. Conclusion: Based on our findings we suggest that epirubicin administration in pregnancy should be preceded by the screening of some fetal conditions like SGA and oligohydramnios that may increase its cardiotoxicity and that, during treatment, the diastolic function of the fetal right ventricle should be specifically monitored by a pediatric cardiologist; also, epirubicin and desamethasone for lung maturation should not be closely administered since placental effects of glucocorticoids may increase epirubicin toxicity.

Publication Type: Journal: Article

Source: EMBASE

Title: Chemotherapy for breast cancer during pregnancy: Is epirubicin safe?

Citation: Annals of Oncology, 2008, vol./is. 19/10(1814-1815), 0923-7534;1569-8041 (2008)

Author(s): Mir O., Berveiller P., Rouzier R., Goffinet F., Goldwasser F., Treluyer J.M.

Language: English

Publication Type: Journal: Letter

Source: EMBASE

Full Text:
Available from *Highwire Press* in Annals of Oncology
Available from *Oxford University Press* in Annals of Oncology; Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Exploring the safety of chemotherapy for treating breast cancer during pregnancy

Citation: Expert Opinion on Drug Safety, September 2015, vol./is. 14/9(1395-1408), 1474-0338;1744-764X (02 Sep 2015)

Author(s): Lambertini M., Kamal N.S., Peccatori F.A., Del Mastro L., Azim H.A.

Language: English

Abstract: Introduction: The diagnosis of breast cancer during pregnancy (BCP) represents a unique challenge to the patient, her family and the treating physician. The proper management of this critical clinical situation is crucial, and requires a multidisciplinary approach. A proper understanding of the safety of chemotherapy during pregnancy is a vital step to avoid detrimental consequences on the mother and the fetus.Areas covered: The aim of this article is to review the available evidence on the safety of chemotherapy administration in managing BCP. Expert opinion: The rule of thumb of chemotherapy - avoiding first trimester exposure and starting therapy in the second trimester - can be considered applicable for classic agents that are used in managing pregnant breast cancer patients. Anthracycline-based regimens are considered the standard of care in managing BCP. Recently, a growing amount of data suggests the safety of taxanes during pregnancy. Pregnancy in cancer patients should be considered as "high risk": once the systemic treatment is initiated, regular fetal monitoring is highly recommended. Emerging data are available on the relative long-term safety secondary to anthracycline exposure during pregnancy. A continued monitoring of the health of individuals with prenatal exposure to chemotherapy into adulthood is recommended for the possible occurrence of long-term side effects.

Publication Type: Journal: Review

Source: EMBASE

Title: Optimizing anticancer drug treatment in pregnant cancer patients: pharmacokinetic analysis of gestation-induced changes for doxorubicin, epirubicin, docetaxel and paclitaxel.

Citation: Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, Oct 2014, vol. 25, no. 10, p. 2059-2065, 1569-8041 (October 2014)

Author(s): van Hasselt, J G C, van Calsteren, K, Heyns, L, Han, S, Mhallem Gziri, M, Schellens, J H M, Beijnen, J H, Huitema, A D R, Amant, F

Abstract: Pregnant patients with cancer are increasingly treated with anticancer drugs, although the specific impact of pregnancy-induced physiological changes on the pharmacokinetics (PK) of anticancer drugs and associated implications for optimal dose regimens remains unclear. Our objectives were to quantify changes in PK during pregnancy for four frequently used anticancer agents doxorubicin, epirubicin, docetaxel and paclitaxel, and to determine associated necessary dose adjustments. A pooled analysis of PK data was carried out for pregnant (Pr) and nonpregnant (NPr) patients for doxorubicin (n = 16 Pr/59 NPr), epirubicin (n = 14 Pr/57 NPr), docetaxel (n = 3 Pr/32 NPr) and paclitaxel (n = 5 Pr/105 NPr). Compartmental nonlinear mixed effect models were used to describe the PK and gestational effects. Subsequently, we derived optimized dose regimens aiming to match to the area under the concentration-time curve (AUC) in nonpregnant patients. The effect of pregnancy on volumes of distribution for doxorubicin, epirubicin, docetaxel and paclitaxel were estimated as fold-change of <1.32, <2.08, <1.37 and <4.21, respectively, with adequate precision [relative standard error (RSE) <37%]. For doxorubicin, no gestational effect could be estimated on clearance (CL). For epirubicin, docetaxel and paclitaxel, a fold-change of 1.1 (RSE 9%), 1.19 (RSE 7%) and 1.92 (RSE 21%) were, respectively, estimated on CL. Calculated dose adjustment requirements for doxorubicin, epirubicin, docetaxel and paclitaxel were +5.5%, +8.0%, +16.9% and +37.8%, respectively. Estimated changes in infusion duration were marginal (<4.2%) except for paclitaxel (-21.4%). Clinicians should be aware of a decrease in drug exposure during pregnancy and should not a priori reduce dose. The decrease in exposure was most apparent for docetaxel and paclitaxel which is supported by known physiological changes during pregnancy. The suggested dose adaptations should only be implemented after conduct of further confirmatory studies of the PK during pregnancy.

Source: Medline

Full Text:
Available from *Highwire Press* in Annals of Oncology
Available from *Oxford University Press* in Annals of Oncology; Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Antineoplastic and immunomodulating agents use during pregnancy: A retrospective study in TERAPPEL database

Citation: Fundamental and Clinical Pharmacology, May 2014, vol./is. 28/(6), 0767-3981 (May 2014)

Author(s): Bourgeois I., Thompson-Bos M.A., Bonenfant S., Vial T., Damase-Michel C., Bavoux F., Despas F., Dautriche A., Montastruc J.L., Lacroix I.

Language: English

Abstract: Objective: Few clinical data are available regarding the effects of antineoplastic and immunomodulating agents in pregnant woman. The objective of the present study was to describe the outcome of pregnancies exposed to 'antineoplastic and immunomodulating agents' using TERAPPEL database. Material and methods: We performed a retrospective descriptive study using TERAPPEL, a French database which records requests from health professionals and patients to Regional Centres of PharmacoVigilance about women exposed to drugs during pregnancy and/or breastfeeding.TERAPPEL registers the outcome of pregnancy. We analyzed all cases of women exposed during pregnancy to 'antineoplastic and immunomodulating agents' (L01 to L03 ATC class) from 1984 to 2009. Results: Fifty eight women exposed to 'antineoplastic and immunomodulating agents' during pregnancy were identified of whom 56.9% (n = 33) were exposed during the first trimester. The most common cancers were breast cancer (n = 37, 63.8%) and leukemia (n = 7, 12.1%). The most frequent used drug classes were alkylating agents (n = 28, 48.3%) among 'antineoplastic agents' (L01) and hormone antagonists and related agents (n = 17, 29.3%) among 'endocrine therapy' (L02). Immunostimulants (L03) were used in only 6.9% of cases (n = 4). The most cited drugs were cyclophosphamide (n = 21, 36.2%), epirubicin (n = 17, 29.3%), tamoxifen (n = 17, 29.3%), fluorouracil (n = 17, 27.6%) and doxorubicin (n = 8, 13.8%). The outcome of these pregnancies was as follows: 43 livebirths (74.1%), 8 medical terminations (13.8%), 3 voluntary terminations (5.1%), 2 miscarriages (3.5%) and 2 intrauterine deaths (3.5%). The 4 (6.8%) newborns and fetus (2 medical terminations) with congenital malformations were exposed during organogenesis. Neonatal complications were evidenced in 13 neonates (29.5%), of whom 11 were exposed during the second and third trimesters. Cardiorespiratory diseases were the most common (9 cases) complications. One case of urinary tract infection, 1 hypothermia-hypoglycemia and tremors, 1 cervical tumefaction and 1 hypotonia were also observed. Discussion: In our study, chemotherapy administered after the first trimester seems to imply little risk to the fetus. Data about 'antineoplastic and immunomodulating agents' during pregnancy should be notified and registered.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Fetal cyclophosphamide exposure induces testicular cancer and reduced spermatogenesis and ovarian follicle numbers in mice

Citation: PLoS ONE, April 2014, vol./is. 9/4(no pagination), 1932-6203 (01 Apr 2014)

Author(s): Comish P.B., Drumond A.L., Kinnell H.L., Anderson R.A., Matin A., Meistrich M.L., Shetty G.

Language: English

Abstract: Exposure to radiation during fetal development induces testicular germ cell tumors (TGCT) and reduces spermatogenesis in mice. However, whether DNA damaging chemotherapeutic agents elicit these effects in mice remains unclear. Among such agents, cyclophosphamide (CP) is currently used to treat breast cancer in pregnant women, and the effects of fetal exposure to this drug manifested in the offspring must be better understood to offer such patients suitable counseling. The present study was designed to determine whether fetal exposure to CP induces testicular cancer and/or gonadal toxicity in 129 and in 129.MOLF congenic (L1) mice. Exposure to CP on embryonic days 10.5 and 11.5 dramatically increased TGCT incidence to 28% in offspring of 129 mice (control value, 2%) and to 80% in the male offspring of L1 (control value 33%). These increases are similar to those observed in both lines of mice by radiation. In utero exposure to CP also significantly reduced testis weights at 4 weeks of age to ~70% of control and induced atrophic seminiferous tubules in ~30% of the testes. When the in utero CP-exposed 129 mice reached adulthood, there were significant reductions in testicular and epididymal sperm counts to 62% and 70%, respectively, of controls. In female offspring, CP caused the loss of 77% of primordial follicles and increased follicle growth activation. The results indicate that i) DNA damage is a common mechanism leading to induction of testicular cancer, ii) increased induction of testis cancer by external agents is proportional to the spontaneous incidence due to inherent genetic susceptibility, and iii) children exposed to radiation or DNA damaging chemotherapeutic agents in utero may have increased risks of developing testis cancer and having reduced spermatogenic potential or diminished reproductive lifespan © 2014 Comish et al.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in PLoS ONE
Available from *ProQuest* in PLoS One
Available from *National Library of Medicine* in PLoS ONE
Available from *Allen Press* in PLoS One

Title: Breast cancer during pregnancy and chemotherapy: A systematic review [English;Portuguese] Cancer de mama na gravidez e quimioterapia: Revisao sistematica

Citation: Revista da Associacao Medica Brasileira, March 2013, vol./is. 59/2(174-180), 0104-4230 (March/April 2013)

Author(s): Leite Maia Monteiroa D., Trajano A.J.B., Menezes D.C.S., Silveira N.L.M., Magalhaes A.C., de Miranda F.R.D., Caldas B.

Language: English, Portuguese

Abstract: This study aimed to establish the safety of chemotherapy use in pregnant women with breast cancer, and to find possible effects in the fetus. A search of MEDLINE/PubMed, LILACS, SciELO, Cochrane, UpToDate, and Google Scholar databases was performed to identify publications., 86 articles published from 2001 to 2012 were retrieved and evaluated by two readers in accordance predetermined exclusion and inclusion criteria; 39 articles were selected. All the chemotherapy drugs used to treat breast cancer during pregnancy belonged to class D, and consisted of 5-fluorouracil (F), doxorubicin (A) or epirubicin (E) and cyclophosphamide (C), or the combination doxorubicin and cyclophosphamide (AC), a safe regimen when used after the first trimester of pregnancy. Few studies evaluated the use of taxanes (T), such as docetaxel (D) and paclitaxel (P), with no increase in the occurrence of fetal defects and other maternal complications when used in the second and third trimesters of pregnancy. The use of trastuzumab in pregnant women is associated with oligohydramnios and anhydramnios; thus, it is not recommended during pregnancy. As almost all studies were observational and retrospective, new prospective studies on the subject are needed. © 2013 Elsevier Editora Ltda. All rights reserved.

Publication Type: Journal: Review

Source: EMBASE
Full Text Link http://www.scielo.br/pdf/ramb/v59n2/en_v59n2a18.pdf

---

Title: Outcomes of children exposed in utero to chemotherapy for breast cancer.

Citation: Breast cancer research : BCR, Jan 2014, vol. 16, no. 6, p. 500., 1465-542X (2014)

Author(s): Murthy, Rashmi K, Theriault, Richard L, Barnett, Chad M, Hodge, Silvia, Ramirez, Mildred M, Milbourne, Andrea, Rimes, Sue A, Hortobagyi, Gabriel N, Valero, Vicente, Litton, Jennifer K

Abstract: The incidence of breast cancer diagnosed during pregnancy is expected to increase as more women delay childbearing in the United States. Treatment of cancer in pregnant women requires prudent judgment to balance the benefit to the cancer patient and the risks to the fetus. Prospective data on the outcomes of children exposed to chemotherapy in utero are limited for the breast cancer population. Between 1992 and 2010, 81 pregnant patients with breast cancer were treated in a single-arm, institutional review board-approved study with 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC) in the adjuvant or neoadjuvant setting. Labor and delivery records were reviewed for each patient and neonate. In addition, the parents or guardians were surveyed regarding the

health outcomes of the children exposed to chemotherapy in utero. In total, 78% of the women (or next of kin) answered a follow-up survey. At a median age of 7 years, most of the children exposed to chemotherapy in utero were growing normally without any significant exposure-related toxicity or health problems. Three children were born with congenital abnormalities: one each with Down syndrome, ureteral reflux or clubfoot. The rate of congenital abnormalities in the cohort was similar to the national average of 3%. During the second and third trimesters, pregnant women with breast cancer can be treated with FAC safely without concerns for serious complications or short-term health concerns for their offspring who are exposed to chemotherapy in utero. Continued long-term follow-up of the children in this cohort is required. ClinicalTrials.gov Identifier: NCT00510367. Other Study ID numbers: ID01-193, NCI-2012-01578. Registration date: 31 July 2007.

Source: Medline

Full Text:
Available from *National Library of Medicine* in Breast Cancer Research : BCR
Available from *Free Access Content* in Breast Cancer Research
Available from *National Library of Medicine* in Breast Cancer Research : BCR

Title: Effects of fetal exposure to maternal chemotherapy

Citation: Pediatric Drugs, 2013, vol./is. 15/5(329-334), 1174-5878;1179-2019 (2013)

Author(s): Dekrem J., Van Calsteren K., Amant F.

Language: English

Abstract: Approximately 1 in 1,000-2,000 pregnancies are complicated by cancer. Today, different treatment options are considered as safe during pregnancy: chemotherapy, radiotherapy, surgery, or a combination of these. Surgery is considered safe during all trimesters of pregnancy; radiotherapy can be administered during the first and the second trimester, and chemotherapy after the first trimester of pregnancy. The placenta, acting as a barrier between the mother and the fetus, plays a key role in the safe administration of chemotherapy during pregnancy. A few studies have investigated the short- as well as the long-term health, general development, and cognitive and cardiac outcomes on children exposed to chemotherapy in utero. In general, these results were reassuring. Nevertheless, better safety data are required. This means data with longer follow-up periods and comparison with appropriate control groups. Moreover, important biasing factors should be taken into account when interpreting these results. Firstly, a great proportion of children were born prematurely due to the maternal condition. Preterm birth in general has been associated with cognitive impairment. Secondly, cancer during pregnancy is clearly a stressful situation, and maternal stress is associated with attention deficits. In sum, we state that chemotherapy can be administered safely after the first trimester of pregnancy. Moreover, iatrogenic prematurity in order to start postpartum administration of chemotherapy should be avoided. Nonetheless, decisions concerning treatment in these specific cases should always be made in a multidisciplinary setting with internationally

recognized expertise in the coexistence of cancer and pregnancy. © 2013 Springer International Publishing Switzerland.

Publication Type: Journal: Review

Source: EMBASE

Full Text:
Available from *ProQuest* in Pediatric Drugs

Title: Maternal and neonatal outcomes of dose-dense chemotherapy for breast cancer in pregnancy

Citation: Obstetrics and Gynecology, December 2012, vol./is. 120/6(1267-1272), 0029-7844 (December 2012)

Author(s): Cardonick E., Gilmandyar D., Somer R.A.

Language: English

Abstract: OBJECTIVE: To estimate the effect of dose-dense chemotherapy during pregnancy on maternal and neonatal outcomes. METHODS: This is a retrospective cohort study in which women were identified from the international Cancer and Pregnancy Registry at Cooper Medical School at Rowan University in Camden, New Jersey. A chart analysis was completed and FisherEs exact test and independent t test were used in comparing patient outcomes. RESULTS: Ten women received dose-dense chemotherapy, received every 2 weeks, and 99 women received conventional chemotherapy, received with at least 3-week intervals, for breast cancer during pregnancy. Birth weight, gestational age at delivery, rate of growth restriction, congenital anomalies, and incidence of maternal and neonatal neutropenia were not statistically different between the two groups. CONCLUSION: In the small cohort of women in our registry, dose-dense chemotherapy does not appear to increase the risk of fetal or maternal complications. © 2012 by The American College of Obstetricians and Gynecologists.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Obstetrics and Gynecology* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *Ovid* in Obstetrics and Gynecology
Available from *Ovid* in Obstetrics and gynecology.

Title: Maternal and fetal outcomes of taxane chemotherapy in breast and ovarian cancer during pregnancy: Case series and review of the literature

Citation: Annals of Oncology, December 2012, vol./is. 23/12(3016-3023), 0923-7534;1569-8041 (December 2012)

Author(s): Cardonick E., Bhat A., Gilmandyar D., Somer R.

Language: English

Abstract: Background: The purpose of this study was to evaluate the use of taxane chemotherapy during pregnancy and compare maternal and neonatal outcomes with those in women who did not receive taxanes during pregnancy, and review current existing data. Study design: This is a retrospective cohort study in which women were identified from the Cancer and Pregnancy Registry at Robert Wood Johnson Medical Center. A retrospective chart analysis and an independent t-test were carried out comparing patient outcomes. A literature search in Ovid, Medline and PubMed was then carried out using the terms 'breast or ovarian cancer', 'pregnancy', 'paclitaxel', 'docetaxel', 'taxanes' and 'chemotherapy'. Results: Twelve of 129 women with breast cancer were exposed to taxanes during pregnancy. Three of nine women with ovarian cancer received taxane-based treatment during pregnancy. Birth weight, gestational age at delivery, rate of growth restriction, congenital anomalies and incidence of maternal and neonatal neutropenia were not statistically different between the two groups. Conclusions: Taxane-based chemotherapy does not appear to increase the risk of fetal or maternal complications when compared with conventional chemotherapy in the small cohort of women in our Registry.© The Author 2012. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved.

Publication Type: Journal: Review

Source: EMBASE

Full Text:
Available from *Highwire Press* in Annals of Oncology
Available from *Oxford University Press* in Annals of Oncology; Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Treatment of breast cancer during pregnancy: an observational study.

Citation: The Lancet. Oncology, Sep 2012, vol. 13, no. 9, p. 887-896, 1474-5488 (September 2012)

Author(s): Loibl, Sibylle, Han, Sileny N, von Minckwitz, Gunter, Bontenbal, Marijke, Ring, Alistair, Giermek, Jerzy, Fehm, Tanja, Van Calsteren, Kristel, Linn, Sabine C, Schlehe, Bettina, Gziri, Mina Mhallem, Westenend, Pieter J, Müller, Volkmar, Heyns, Liesbeth, Rack, Brigitte, Van Calster, Ben, Harbeck, Nadia, Lenhard, Miriam, Halaska, Michael J, Kaufmann, Manfred, Nekljudova, Valentina, Amant, Frederic

Abstract: Little is known about the treatment of breast cancer during pregnancy. We aimed to determine whether treatment for breast cancer during pregnancy is safe for both mother and child. We recruited patients from seven European countries with a primary diagnosis of breast cancer during pregnancy; data were collected retrospectively if the patient was diagnosed before April, 2003 (when the registry began), or prospectively thereafter, irrespective of the outcome of pregnancy and the type and timing of treatment. The primary endpoint was fetal health for up to 4 weeks after delivery. The registry is ongoing. The study is registered with ClinicalTrials.gov, number NCT00196833. From April, 2003, to December, 2011, 447 patients were registered, 413 of whom had early breast cancer. Median age was 33 years (range 22-51). At the time of diagnosis, median gestational age was 24 weeks (range 5-40). 197 (48%) of 413 women received chemotherapy during pregnancy with a median of four cycles (range one to eight). 178 received an anthracycline, 15 received cyclophosphamide, methotrexate, and fluorouracil, and 14 received a taxane. Birthweight was affected by chemotherapy exposure after adjustment for gestational age (p=0·018), but not by number of chemotherapy cycles (p=0·71). No statistical difference between the two groups was observed for premature deliveries before the 37th week of gestation. 40 (10%) of 386 infants had side-effects, malformations, or new-born complications; these events were more common in infants born before the 37th week of gestation than they were in infants born in the 37th week or later (31 [16%] of 191 infants vs nine [5%] of 195 infants; p=0·0002). In infants for whom maternal treatment was known, adverse events were more common in those who received chemotherapy in utero compared with those who were not exposed (31 [15%] of 203 vs seven [4%] of 170 infants; p=0·00045). Two infants died; both were exposed to chemotherapy and delivered prematurely, but both deaths were thought not to be related to treatment. Median disease-free survival for women with early breast cancer was 70·6 months (95% CI 62·1-105·5) in women starting chemotherapy during pregnancy and 94·4 months (lower 95% CI 64·4; upper 95% CI not yet reached) in women starting chemotherapy after delivery (unadjusted hazard ratio 1·13 [95% CI 0·76-1·69]; p=0·539). Although our data show that infants exposed to chemotherapy in utero had a lower birthweight at gestational age than did those who were unexposed, and had more complications, these differences were not clinically significant and, since none of the infants was exposed to chemotherapy in the first trimester, were most likely related to premature delivery. Delay of cancer treatment did not significantly affect disease-free survival for mothers with early breast cancer. Because preterm birth was strongly associated with adverse events, a full-term delivery seems to be of paramount importance. BANSS Foundation, Biedenkopf, Germany and the Belgian Cancer Plan, Ministry of Health, Belgium.

Source: Medline

Title: Increased evidence for use of chemotherapy in pregnancy

Citation: The Lancet Oncology, September 2012, vol./is. 13/9(852-854), 1470-2045;1474-5488 (September 2012)

Author(s): Mir O., Berveiller P.

Language: English

Publication Type: Journal: Letter

Source: EMBASE

Full Text:
Available from *ProQuest* in Lancet Oncology

Title: Breast Cancer during Pregnancy: An Interdisciplinary Approach in Our Institution.

Citation: Breast care (Basel, Switzerland), Aug 2012, vol. 7, no. 4, p. 311-314, 1661-3791 (August 2012)

Author(s): Pirvulescu, Cristina, Mau, Christine, Schultz, Holger, Sperfeld, Antje, Isbruch, Annette, Renner-Lützkendorf, Heike, Loibl, Sybille, Freitag, Ulrike, Klühs, Gabriele, Fleige, Barbara, Untch, Michael

Abstract: Breast cancer is the most common cancer diagnosed during pregnancy. We report on a case of a 26-year-old woman who was diagnosed with right-sided breast cancer in her 15th week of gestation. We discussed possible treatment scenarios and the patient opted for neoadjuvant therapy with taxanes and anthracyclines during pregnancy, followed by delivery and then followed by surgery, antibody therapy, and radiotherapy. The patient received neoadjuvant chemotherapy with paclitaxel 80 mg/m(2) weekly for 12 cycles, followed by 4 cycles of epirubicin and cyclophosphamide (90/600 mg/m(2)) every 3 weeks. Complete clinical response was seen after preoperative chemotherapy. After delivery of a healthy child at 40 weeks of gestation, she received breast-conserving surgery and axillary dissection. Anti-HER2 antibody treatment with trastuzumab was started concomitantly with adjuvant radiotherapy. Endocrine treatment with a gonadotropin-releasing hormone (GnRH) analog and tamoxifen for 5 years was planned to be started after radiotherapy. Treatment of breast cancer during pregnancy requires an interdisciplinary approach and careful consideration of the patient's stage of disease, the gestational age, and the preferences of the patient and her family.

Source: Medline

Full Text:
Available from *National Library of Medicine* in Breast Care

Title: Pre-eclampsia following chemotherapy for breast cancer during pregnancy: case report and review of the literature.

Citation: Archives of gynecology and obstetrics, Jul 2012, vol. 286, no. 1, p. 89-92, 1432-0711 (July 2012)

Author(s): Massey Skatulla, L, Loibl, S, Schauf, B, Müller, T

Abstract: There has been some discussion about the effect of antineoplastic agents on the trophoblast, and whether this is associated with abnormal placental function such as an increased risk of pre-eclampsia/eclampsia. We discuss a possible causal relationship between chemotherapy for breast cancer during pregnancy and the development of pre-eclampsia based on the occurrence of both in a recent pregnancy. We report the case of a 34-year-old gravida 4, para 1 with unilateral ductal invasive breast cancer, treated by surgery and subsequent chemotherapy during pregnancy. At 36 + 2 weeks of gestation a growth restricted male infant (1,680 g, <5th percentile) was born by urgent caesarean section because of acute pre-eclampsia, pathologic CTG and umbilical end-diastolic reverse flow. This case is reported in detail, and literature and databases reviewed. So far there have been no reports suggesting an increased risk of pre-eclampsia following chemotherapy for breast cancer in pregnancy from the second trimester onwards, and the most probable is an accidental occurrence from pre-eclampsia and chemotherapy. Whenever possible, pregnant patients with breast cancer should receive the same treatment as those who are not pregnant. Should chemotherapy for breast cancer be indicated in pregnancy from the second trimester onwards only, contraindications would be other risks for pre-eclampsia and intrauterine growth restriction, such as smoking and gestational diabetes.

Source: Medline

Title: Cancer in pregnancy: Fetal and neonatal outcomes

Citation: Clinical Obstetrics and Gynecology, December 2011, vol./is. 54/4(574-590), 0009-9201;1532-5520 (December 2011)

Author(s): Backes C.H., Moorehead P.A., Nelin L.D.

Language: English

Abstract: Cancer during pregnancy represents a potential conflict between optimal maternal treatment and fetal development. Traditionally, clinicians operated under the assumption that cancer treatment during pregnancy is incompatible with normal fetal development. However, recent evidence suggests that many diagnostic and treatment modalities cause little or no harm to the developing fetus. As such, both maternal and neonatal interests should be considered when developing management strategies for pregnant cancer patients. In this review, we will discuss issues related to fetal and neonatal health associated with conventional diagnostic and treatment approaches in the care of pregnant women with cancer. In addition, we offer recommendations on strategies to maximize fetal outcomes in pregnancies complicated by cancer. © 2011 Lippincott Williams & Wilkins.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Ovid* in Clinical Obstetrics and Gynecology

Title: Chemotherapy for breast cancer in pregnancy:Evidence and guidance for oncologists

Citation: Therapeutic Advances in Medical Oncology, March 2011, vol./is. 3/2(73-83), 1758-8340;1758-8359 (March 2011)

Author(s): McGrath S.E., Ring A.

Language: English

Abstract: It has been estimated that up to 3.8 of breast cancers may be diagnosed in women who are pregnant, with an estimated 1 in 3000-3500 deliveries occurring in women with breast cancer. Owing to the lack of large randomized trials available to guide our clinical practice, our decisions regarding adjuvant systemic management are based on retrospective analyses, case reports and a small number of prospective studies. A tailored approach to treatment is required with careful consideration given at all stages to the needs of the mother and risks to the foetus. Management is critically influenced by the stage of pregnancy, especially the first trimester. Anthracycline-based chemotherapy may be administered during the second and third trimesters, with apparently few short-term implications. Limited data shows the taxanes may also be given with few adverse events at these stages. Weekly fractionation regimens may allow closer monitoring of pregnancy with prompt termination of agents, if necessary. Data concerning the long-term risks of systemic anticancer treatment are limited. All stages of patient management should be discussed within a multidisciplinary team and a clear consensus of treatment options communicated to the mother. Delaying chemotherapy until after delivery may be reasonable in some cases, but where the delay is likely to be prolonged, a decision must be made on the basis of risks versus benefits. © The Author(s), 2011.

Publication Type: Journal: Review

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in Therapeutic Advances in Medical Oncology

---

Title: Treatment of breast cancer during pregnancy: Regimen selection, pregnancy monitoring and more ..

Citation: Breast, February 2011, vol./is. 20/1(1-6), 0960-9776 (February 2011)

Author(s): Azim H.A., Del Mastro L., Scarfone G., Peccatori F.A.

Language: English

Abstract: Breast cancer is uncommonly diagnosed during pregnancy but when encountered, it poses several clinical conflicts. Managing patients with gestational breast cancer should not be associated with considerable risk of morbidity provided the choice of the right drug in the right time for the right patient. Due to its relative rarity, we lack a standardized approach to manage these patients. Previous reports have suggested that women can be offered treatment strategies similar to those offered in the " non-pregnant" setup. Nevertheless, generalizing treatment decisions is too hard and treatment of these cases should be tailored according to the clinical situation. In order to ensure proper counseling of these patients, there are several key points that need to be addressed. These include timing of chemotherapy administration, the scheduling of agents, and pregnancy monitoring. In this review, we provide some guidance on how to select the chemotherapy regimen and address the feasibility and safety of administering trastuzumab during pregnancy. We also discuss some practical points on monitoring these patients during the course of pregnancy. © 2010 Elsevier Ltd.

Publication Type: Journal: Review

Source: EMBASE

Title: Specific congenital malformations after exposure to cyclophosphamide, epirubicin and 5-fluorouracil during the first trimester of pregnancy.

Citation: Gynecologic and obstetric investigation, Jan 2011, vol. 71, no. 2, p. 141-144, 1423-002X (2011)

Author(s): Leyder, Mina, Laubach, Monika, Breugelmans, Maria, Keymolen, Katelijn, De Greve, Jacques, Foulon, Walter

Abstract: The treatment of pregnant women with chemotherapeutic drugs leads to congenital malformations in 10-20% of newborn children. We present a case of an ongoing 19-week-long pregnancy which was diagnosed in a 39-year-old woman who was being treated with CEF (cyclophosphamide, epirubicin, 5-fluorouracil) chemotherapy for an infiltrating ductal carcinoma of the breast. After termination of the pregnancy, subsequent examination of the fetus revealed micrognathia and bilateral malformations of the hands and feet. The peak exposure of the fetus to the chemotherapeutic agents was in the 5th to 6th week of the pregnancy. Both the nature of the malformations and the timing of the administration of chemotherapy are similar to another case reported previously. We conclude that chemotherapy treatments with CEF in the 5th to 6th week of pregnancy specifically generate hand and foot abnormalities and micrognathia, which is consistent with an inhibition of proliferation, leading to cell death at this embryonic stage. Copyright © 2010 S. Karger AG, Basel.

Source: Medline

Full Text:

Title: Management of cancer during pregnancy emphasizing maternal and fetal effects

Citation: European journal of Clinical and Medical Oncology, 2011, vol./is. 3/5(1-6), 1759-8958;1759-8966 (2011)

Author(s): Gziri M.M., van Calsteren K., Heyns L., Han S., Debieve F., Amant F.

Language: English

Abstract: One in 1000 pregnancies is complicated by maternal cancer. The most frequently encountered malignancies are breast cancer, hematologic tumors, and skin cancer. Cancer management implies multidisciplinary decisions taking into account the (sub)type and stage of cancer, the gestational age at diagnosis, and patient's wish to preserve the pregnancy. Oncological treatment modalities including surgery, radiotherapy, and chemotherapy are possible during pregnancy, however, under strict conditions. Actually, pregnant patients receive the same dosages of chemotherapeutic agents as nonpregnant women, despite gestational changes in hemodynamics and drug pharmacokinetics. Data on the outcome of the children are limited. Neonatal outcome seems reassuring, albeit data on long-term outcomes are lacking. Cancer during pregnancy poses a real challenge for obstetricians, oncologists, and pediatricians to balance fetal and maternal risks and benefices. Here, we address some important clinical issues related to the management of cancer complicating pregnancy.

Publication Type: Journal: Review

Source: EMBASE

Title: Transplacental transfer of anthracyclines, vinblastine, and 4-hydroxy-cyclophosphamide in a baboon model

Citation: Gynecologic Oncology, December 2010, vol./is. 119/3(594-600), 0090-8258;1095-6859 (December 2010)

Author(s): Van Calsteren K., Verbesselt R., Beijnen J., Devlieger R., De Catte L., Chai D.C., Van Bree R., Heyns L., De Hoon J., Amant F.

Language: English

Abstract: Objective: The paucity of data on the fetal effects of prenatal exposure to chemotherapy prompted us to study transplacental transport of chemotherapeutic agents. Methods: Fluorouracil-epirubicin-cyclophosphamide (FEC) and doxorubicin-bleomycin-

vinblastine-dacarbazine (ABVD) were administered to pregnant baboons. At predefined time points over the first 25 h after drug administration, fetal and maternal blood samples, amniotic fluid (AF), urine, fetal and maternal tissues, and cerebrospinal fluid (CSF) were collected. High-performance liquid chromatography (HPLC) and liquid chromatography-mass spectrometry (LC-MS) were used for bioanalysis of doxorubicin, epirubicin, vinblastine, and cyclophosphamide. Results: In nine baboons, at a median gestational age of 139 days (range, 93-169), FEC 100% (n = 2), FEC 200% (n = 1), ABVD 100% (n = 5), and ABVD 200% (n = 1) were administered. The obtained ratios of fetal/maternal drug concentration in the different simultaneously collected samples were used as a measure for transplacental transfer. Fetal plasma concentrations of doxorubicin and epirubicin averaged 7.5 +/- 3.2% (n = 6) and 4.0 +/- 1.6% (n = 8) of maternal concentrations, respectively. Fetal tissues contained 6.3 +/- 7.9% and 8.7 +/- 8.1% of maternal tissue concentrations for doxorubicin and epirubicin, respectively. Vinblastine concentrations in fetal plasma averaged 18.5 +/- 15.5% (n = 9) of maternal concentrations. Anthracyclines and vinblastine were neither detectable in maternal nor in fetal brain/CSF. 4-Hydroxy-cyclophosphamide concentrations in fetal plasma and CSF averaged 25.1 +/- 6.3% (n = 3) and 63.0% (n = 1) of the maternal concentrations, respectively. Conclusion: This study shows limited fetal exposure after maternal administration of doxorubicin, epirubicin, vinblastine, and 4-hydroxy-cyclophosphamide. © 2010 Elsevier Inc. All rights reserved.

Publication Type: Journal: Article

Source: EMBASE

Title: Breast cancer in pregnancy: recommendations of an international consensus meeting.

Citation: European journal of cancer (Oxford, England : 1990), Dec 2010, vol. 46, no. 18, p. 3158-3168, 1879-0852 (December 2010)

Author(s): Amant, Frédéric, Deckers, Sarah, Van Calsteren, Kristel, Loibl, Sibylle, Halaska, Michael, Brepoels, Lieselot, Beijnen, Jos, Cardoso, Fatima, Gentilini, Oreste, Lagae, Lieven, Mir, Olivier, Neven, Patrick, Ottevanger, Nelleke, Pans, Steven, Peccatori, Fedro, Rouzier, Roman, Senn, Hans-Jörg, Struikmans, Henk, Christiaens, Marie-Rose, Cameron, David, Du Bois, Andreas

Abstract: To provide guidance for clinicians about the diagnosis, staging and treatment of breast cancer occurring during an otherwise uncomplicated pregnancy. An international expert Panel convened to address a series of questions identified by a literature review and personal experience. Issues relating to the diagnosis and management of breast cancer after delivery were outside the scope. There is a paucity of large and/or randomized studies. Based on cohort studies, case series and case reports, the recommendations represent the best available evidence, albeit of a lower grade than is optimal. In most circumstances, serious consideration should be given to the option of treating breast cancer whilst continuing with the pregnancy. Each woman should ideally be referred to a centre with sufficient expertise, given a clear explanation of treatment options. Most diagnostic and staging examinations can be performed adequately and safely during pregnancy. Treatment should however be adapted to the clinical presentation and the trimester of the pregnancy:

surgery can be performed during all trimesters of pregnancy; radiotherapy can be considered during the first and second trimester but should be postponed during the third trimester; and standard chemotherapies can be used during the second and third trimester. Since neonatal morbidity mainly appears to be related to prematurity, delivery should not be induced before 37 weeks, if at all possible. The treatment of breast cancer in pregnancy should be executed by experienced specialists in a multidisciplinary setting and should adhere as closely as possible to standard protocols.

Source: Medline
Full Text Link URL:
https://www.cancerinpregnancy.org/combell/docs/Artikels/Amant.%20Breast%20cancer%20in%20pregnancy_Recommendations%20of%20an%20international%20consensus%20meeting.pdf

---

Title: Breast cancer and pregnancy: Current concepts in diagnosis and treatment

Citation: Oncologist, December 2010, vol./is. 15/12(1238-1247), 1083-7159;1549-490X (December 2010)

Author(s): Litton J.K., Theriault R.L.

Language: English

Abstract: The treatment of breast cancer diagnosed during pregnancy presents a challenging situation for the patient, family, and caregivers. Case series have demonstrated the efficacy and safety of using anthracycline-based chemotherapy during the second and third trimesters. Additionally, patients should be seen, evaluated, and treated in a multidisciplinary setting with facilitated communication among the medical oncologist, surgical oncologist, obstetrician, radiation oncologist, pathologist, and radiologist. This review details the available data regarding the diagnosis and management of the pregnant breast cancer patient. © AlphaMed Press.

Publication Type: Journal: Review

Source: EMBASE

Full Text:
Available from *Free Access Content* in Oncologist, The
Available from *Highwire Press* in Oncologist, The
Available from *National Library of Medicine* in Oncologist, The

---

Title: Perinatal outcomes of a pregnancy complicated by cancer, including neonatal follow-up after in utero exposure to chemotherapy: Results of an international registry

Citation: American Journal of Clinical Oncology: Cancer Clinical Trials, June 2010, vol./is. 33/3(221-228), 0277-3732;1537-453X (June 2010)

Author(s): Cardonick E., Usmani A., Ghaffar S.

Language: English

Abstract: Objective: Because of few cases at any 1 institution, pooling information on the treatment of pregnant women diagnosed with cancer and long-term follow-up of their children is important. Methods: Women diagnosed with cancer between their last menstrual period and end of pregnancy were voluntarily enrolled in the Cancer and Pregnancy Registry. Details of cancer treatment and pregnancy outcomes were collected. Neonatal follow-up is obtained yearly. Results: Two hundred thirty-one women were enrolled over a 13-year period. Thirteen women elected termination. One hundred fifty-seven neonates were exposed to chemotherapy in utero. Mean gestational age at delivery for neonates exposed to chemotherapy was 35.8 +/- 2.8 weeks, mean birth weight was 2647 +/- 713 g. Six children (3.8%) were born with a congenital anomaly. An intrauterine fetal demise and a neonatal death occurred in 1 case each (0.7% in each). In 12 cases (7.7%), the neonate measured <10% for gestational age at birth. Nine cases (5.8%) delivered spontaneously premature. Sixty-seven women did not receive chemotherapy during pregnancy and delivered 70 neonates. The mean gestational age at delivery was 36.5 +/- 3.3 weeks, mean birth weight was 2873 +/- 788 g. Mean neonatal follow-up is 3 years postpartum and is provided by cancer type and chemotherapy regimen. Conclusions: In pregnancies exposed to chemotherapy after the first trimester, congenital anomalies, preterm delivery, and growth restriction were not increased as compared with general population norms. Mean gestational age at delivery was not significantly different than neonates who were not exposed to chemotherapy. There was a statistical significant difference in the birth weight between groups, which may not be clinically significant. Copyright © 2010 by Lippincott Williams & Wilkins.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Ovid* in American Journal of Clinical Oncology

---

Title: Weekly epirubicin in the treatment of gestational breast cancer (GBC)

Citation: Breast Cancer Research and Treatment, June 2009, vol./is. 115/3(591-594), 0167-6806;1573-7217 (June 2009)

Author(s): Peccatori F.A., Azim Jr. H.A., Scarfone G., Gadducci A., Bonazzi C., Gentilini O., Galimberti V., Intra M., Locatelli M., Acaia B., Rossi P., Cinieri S., Calabrese L., Goldhirsch A.

Language: English

Abstract: Background GBC is a rare disease and chemotherapy in this setting lacks a standardized approach. Patients and Methods Patients 16-30 weeks pregnant with locally

advanced/metastatic disease or with high risk of recurrence after surgery were evaluated. Results Twenty patients received weekly epirubicin 35 mg/m². Median maternal age was 37 years (23-42). Median gestational age at chemotherapy was 19 weeks. Thirteen patients were treated after surgery while 7 had locally advanced tumours of which one had liver metastases. Mean total epirubicin dose was 420 mg/m² with a median number of 12 administrations (4-16). No grade 3-4 toxicities were observed. No foetal adverse events were observed except 1 premature delivery at 28 weeks. Births were induced by caesarean section in 12 patients at a median gestational age of 35 weeks. No malformations were reported except 1 newborn with polycystic kidney. At a median age of 2 years, neurological, cardiological and immunological development was normal in all children as reported by their parents. In 7/20 patients with evaluable disease, five had an objective response. At a median follow-up of 38 months, 17 patients are alive; 14 are disease free. Conclusions Weekly epirubicin appears safe and effective with low foetal toxicity and could be considered in GBC. © 2008 Springer Science+Business Media, LLC.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Springer Link Journals* in Breast Cancer Research and Treatment
Available from *ProQuest* in Breast Cancer Research and Treatment

---

Title: Successful pregnancy outcome with 5-flurouracil, epirubicin, cyclophospamide chemotherapy, and hemostatic radiotherapy with abdominal shielding for metastatic invasive intraductal breast carcinoma

Citation: Archives of Gynecology and Obstetrics, March 2009, vol./is. 279/3(415-417), 0932-0067 (March 2009)

Author(s): Sharma J.B., Pushparaj M., Kumar S., Roy K.K., Raina V., Malhotra N.

Language: English

Abstract: A case of metastatic infiltrating breast cancer in a young multiparous lady with 33 weeks pregnancy is presented who was treated with combination chemotherapy and hemostatic radiotherapy and had successful pregnancy outcome. © 2008 Springer-Verlag.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Springer Link Journals* in Archives of Gynecology and Obstetrics

---

Title: Weekly epirubicin in pregnant breast cancer patients: A cooperative study on 20 patients

Citation: Annals of Oncology, September 2008, vol./is. 19/S8(viii81), 0923-7534 (September 2008)

Author(s): Locatelli M., Peccatori F., Galimberti V., Scarfone G., Cinieri S., Gadducci A., Bonazzi C., Gentilini O., Azim H.A., Goldhirsch A.

Language: English

Abstract: Background: Gestational breast cancer (GBC) is a rare disease, with less than 3% of breast cancers diagnosed during pregnancy. Methods: Single agent weekly Epirubicin, at an average dose of 35 mg/sqm was administered because of shorter terminal half-life and lower cardio toxicity compared to Doxorubicin. Patients (pts) were eligible if they had locally advanced or metastatic disease, high risk of recurrence after surgery and pregnant between 16 and 30 weeks of gestational age. Results: 20/88 pts with GBC were treated with weekly Epirubicin since 1.2002. Median maternal age was 37 years (23-42). Median gestational age at chemotherapy was 19 weeks (16-30). 13/20 pts were treated after surgery because of high risk of relapse. 5/13 pts had positive axillary nodes, with 3 having > 5 positive nodes. 6/20 pts had locally advanced tumours and 1 patient had a locally advanced tumour with synchronous liver metastases. 10/20 pts had endocrine responsive diseases, with 4/20 over expressing HER-2. Ki-67 was >20% in 13/15 pts. Mean total Epirubicin dose was 420 mg/sqm with a median number of 12 (4-16) administrations. No G3-4 toxicities were observed. Chemotherapy was administered with thorough fetal monitoring, and no adverse fetal effects were observed, but 1 premature delivery at 28 weeks. Births were induced by caesarean section in 12/20 pts at a median gestational age of 35 weeks (28-40). 2/20 newborns required neonatal intensive care, but none had pulmonary, cerebral or infectious complications. No malformations were observed, except 1 newborn with polycystic kidney. With a median age of 2 years (0-4), neurological and immunological development was normal in all 20 children, as reported by parents. In the 7/20 pts with evaluable disease, 5/7 had an objective response. With a median follow-up of 38 months, 17/20 pts are alive, 14/17 disease free. Conclusions: Weekly Epirubicin is a safe and effective in pregnant breast cancer pts who need chemotherapy, with low acute toxicity for the fetus. A cardiologic follow up is planned for all children, to exclude late onset of cardiac damage.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Breast cancer and pregnancy: Challenges of chemotherapy

Citation: Critical Reviews in Oncology/Hematology, September 2008, vol./is. 67/3(196-203), 1040-8428 (September 2008)

Author(s): Lenhard M.S., Bauerfeind I., Untch M.

Language: English

Abstract: Background: Breast cancer is the second most frequently occurring malignancy during pregnancy. As evidence-based data on diagnostics and treatment is lacking, current recommendations mostly derive from nonrandomized experiences. We reviewed the current literature with focus on chemotherapy during pregnancy and lactation. Results: The diagnosis of pregnancy associated breast cancer implies the challenge to balance between a life-saving therapy for the mother's breast cancer and a potentially life-threatening therapy for the fetus. With few limitations, surgery and chemotherapy can be performed during pregnancy, preferably in the second and third trimester, whereas radiotherapy and endocrine or antibody treatment should be postponed until after delivery. Conclusion: Breast cancer during pregnancy and lactation remains a therapeutic and ethical multidisciplinary challenge. Close cooperation between all disciplines is inevitable to find an optimal treatment strategy for the mother and her unborn child. © 2008 Elsevier Ireland Ltd. All rights reserved.

Publication Type: Journal: Review

Source: EMBASE

Title: Anthracyclines for gestational breast cancer: course and outcome of pregnancy.

Citation: Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, Aug 2008, vol. 19, no. 8, p. 1511-1512, 1569-8041 (August 2008)

Author(s): Azim, H A, Peccatori, F A, Scarfone, G, Acaia, B, Rossi, P, Cascio, R, Goldhirsch, A

Source: Medline

Full Text:
Available from *Highwire Press* in Annals of Oncology
Available from *Oxford University Press* in Annals of Oncology; Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Breast cancer diagnosed during pregnancy

Citation: Anticancer Research, May 2007, vol./is. 27/3 B(1705-1707), 0250-7005 (May/June 2007)

Author(s): Bodner-Adler B., Bodner K., Zeisler H.

Language: English

Abstract: Cancer is rare during pregnancy, but breast cancer is the second most common cancer in pregnant women. Pregnancy-associated breast cancer (PABC) is defined as breast cancer that occurs during pregnancy or within one year of delivery. Five cases of PABC occurring during the second and third trimester of pregnancy managed at the University Hospital of Vienna during the year 2005/2006 are reported. A review of the available literature is also presented. Five patients were diagnosed with PABC which was detected in completely different weeks of pregnancy. In two women, the diagnosis was made during the second trimester of pregnancy and in three during the third trimester. The treatment depended, among other things, on the gestational age at diagnosis. The patients diagnosed during the second trimester received six courses of neoadjuvant chemotherapy type FEC (5-fluorouracil, epirubicin, cyclophosphamide). Locoregional radiotherapy and surgery were postponed until after delivery. The three patients diagnosed during the third trimester received adequate therapy after delivery. The mean age of the patients at the time of diagnosis was 37 years (range: 33-40 years) and all patients were diagnosed at an advanced stage. All patients were alive and free of symptoms and signs at the time of writing. All infants are healthy and no congenital malformation or stillbirth was observed. In conclusion, late diagnosis and poor prognosis of PABC are common in literature. Ttreatment options seem to be reduced in pregnant women and mainly depend on the patient's condition as well as on the gestational age at presentation. In a multidisciplinary approach, an optimal therapy schedule should be assessed depending on these two conditions.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Highwire Press* in Anticancer Research
Available from *Free Access Content* in Anticancer Research

Title: Treatment of pregnant breast cancer patients and outcomes of children exposed to chemotherapy in utero

Citation: Cancer, September 2006, vol./is. 107/6(1219-1226), 0008-543X;1097-0142 (15 Sep 2006)

Author(s): Hahn K.M.E., Johnson P.H., Gordon N., Kuerer H., Middleton L., Ramirez M., Yang W., Perkins G., Hortobagyi G.N., Theriault R.L.

Language: English

Abstract: BACKGROUND. As women in the US delay childbearing, it has been hypothesized that the incidence of breast cancer diagnosed during pregnancy will increase. There are very

little prospective data on the treatment of pregnant women with breast cancer with chemotherapy and even less data on the outcomes of their children who were exposed to chemotherapy in utero. METHODS. Fifty-seven pregnant breast cancer patients were treated on a single-arm, multidisciplinary, institutional review board-approved protocol with FAC (5-fluorouracil, doxorubicin, cyclophosphamide) in the adjuvant (n = 32) or neoadjuvant (n = 25) setting. Parents/guardians were surveyed by mail or telephone regarding outcomes of children exposed to chemotherapy in utero. RESULTS. Of the 57 women, 40 are alive and disease-free, 3 have recurrent breast cancer, 12 died from breast cancer, 1 died from other causes, and 1 was lost to follow-up. Of the 25 patients who received neoadjuvant FAC, 6 had a pathologic complete response, whereas 4 had no tumor response to chemotherapy and eventually died from their disease. All women who delivered had live births. One child has Down syndrome and 2 have congenital anomalies (club foot; congenital bilateral ureteral reflux). The children are healthy and those in school are doing well, although 2 have special educational needs. CONCLUSIONS. Breast cancer can be treated with FAC chemotherapy during the second and third trimesters without significant short-term complications for the majority of children exposed to chemotherapy in utero. Longer follow-up of the children is needed to evaluate possible late side effects such as impaired cardiac function and fertility. © 2006 American Cancer Society.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Wiley-Blackwell Free Backfiles NHS* in Cancer
Available from *John Wiley and Sons* in Cancer
Available from *Cancer* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *John Wiley and Sons* in Cancer
Available from *John Wiley and Sons* in Cancer
Available from *John Wiley and Sons* in Cancer Cytopathology

Title: Combined chemotherapy and teratogenicity.

Citation: Birth defects research. Part A, Clinical and molecular teratology, Sep 2005, vol. 73, no. 9, p. 634-637, 1542-0752 (September 2005)

Author(s): Paskulin, Giorgio Adriano, Gazzola Zen, Paulo Ricardo, de Camargo Pinto, Louise Lapagesse, Rosa, Rafael, Graziadio, Carla

Abstract: The concomitant occurrence of breast cancer and pregnancy is relatively uncommon. We report the case of a patient with syndactyly, cleft hands, and absence of distal finger phalanges associated with maternal exposure to chemotherapeutic agents during the first trimester of pregnancy. These associations have not been previously described. The patient was born by normal delivery after 38 weeks of pregnancy. His mother became pregnant while receiving chemotherapy (cyclophosphamide, 5-fluorouracil, and adriamycin) for breast cancer, and the fetus was exposed to these drugs from conception to

the 16th week of pregnancy. At birth, anomalies were observed, including a high-arched palate, microcephaly, a flat nasal bridge, bilateral syndactyly in the first and second fingers with a hand cleft between the second and third fingers and hypoplasia of the fifth fingers, and dystrophic nail of the fourth finger of the left hand. The patient's growth and development were deficient. The malformations associated with in utero exposure to these chemotherapeutic agents are highly variable, but growth deficiency and anomalies of the craniofacial region and limbs are the most common. The pattern of malformations in children who were congenitally exposed to chemotherapeutic agents appears to be directly related to the age at and duration of exposure, rather than to the specific drug itself. Effective contraception is essential for the safe use of a potential teratogen in nonpregnant women of reproductive age. Birth Defects Research (Part A), 2005. (c) 2005 Wiley-Liss, Inc.

Source: Medline

Full Text:
Available from *John Wiley and Sons* in Birth Defects Research Part A: Clinical and Molecular Teratology

---

Title: Chemotherapy for breast cancer during pregnancy: an 18-year experience from five London teaching hospitals.

Citation: Journal of clinical oncology : official journal of the American Society of Clinical Oncology, Jun 2005, vol. 23, no. 18, p. 4192-4197, 0732-183X (June 20, 2005)

Author(s): Ring, Alistair E, Smith, Ian E, Jones, Alison, Shannon, Catherine, Galani, Eleni, Ellis, Paul A

Abstract: The rare association between breast cancer and pregnancy means that few oncologists gain an expertise in this area. In particular, there are few published data concerning the use of chemotherapy for breast cancer during pregnancy. In this retrospective case series, we describe the experiences of five hospitals in London, United Kingdom, and how they manage this condition. Retrospective searches were performed at five London hospitals in order to identify women who received chemotherapy for breast cancer while pregnant. Twenty-eight women were identified who had received chemotherapy for breast cancer during pregnancy. Twenty-four women received adjuvant or neoadjuvant chemotherapy for early breast cancer, and four women received palliative chemotherapy for metastatic disease. A total of 116 cycles of chemotherapy were administered during pregnancy. Sixteen women were treated with anthracycline-based chemotherapy and 12 received cyclophosphamide, methotrexate, and fluorouracil. All but one of the women were treated after the first trimester. One spontaneous abortion occurred in the woman treated during her first trimester; otherwise, there were no serious adverse consequences for the mothers or neonates. These data provide evidence that in terms of peripartum complications and immediate fetal outcome, chemotherapy can be safely administered to women during the second and third trimesters of pregnancy.

Source: Medline

Full Text:
Available from *Free Access Content* in Journal of Clinical Oncology

---

Title: Neonatal effects of breast cancer chemotherapy administered during pregnancy

Citation: Pharmacotherapy, March 2005, vol./is. 25/3(438-441), 0277-0008 (March 2005)

Author(s): Kerr J.R.

Language: English

Abstract: A human fetus is most susceptible to teratogenic agents during the first trimester of pregnancy. Cyclophosphamide and doxorubicin are pregnancy category D agents; however, potential benefits may warrant treatment with these agents during pregnancy under special circumstances. During her first trimester of pregnancy, a 37-year-old Caucasian woman was diagnosed with stage IIIB infiltrating ductal carcinoma in situ (breast cancer) that was estrogen and progesterone receptor negative and human epidermal growth factor receptor-2 positive. The patient was treated with doxorubicin and cyclophosphamide in the second and third trimesters and delivered a premature baby boy at 31 weeks' gestation. The neonate was intubated on delivery because of respiratory distress and failure; however, no physical anomalies were observed. He had neutropenia and anemia, quite possibly as a result of his mother's chemotherapy 1 week before delivery. He was prophylactically treated for sepsis, but all cultures were negative. The infant grew and developed normally during his first year of life and remained in good health. An objective causality assessment revealed that it was probable that the infant's adverse events (prematurity, neutropenia, and anemia) were related to his mother's doxorubicin and cyclophosphamide therapy; however, these were the only adverse events potentially linked to in utero exposure to chemotherapy during the second and third trimesters. Due to the special considerations of both mother and infant, optimal treatment for patients with pregnancy-associated breast cancer requires the expert opinion of a multidisciplinary care team.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Pharmacotherapy, The Journal Of Human Pharmacology And Drug Therapy
Available from *John Wiley and Sons* in Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy

---

Title: Combined chemotherapy and radiotherapy during conception and first two trimesters of gestation in a woman with metastatic breast cancer.

Citation: Gynecologic oncology, Oct 2004, vol. 95, no. 1, p. 252-255, 0090-8258 (October 2004)

Author(s): Andreadis, Charalampos, Charalampidou, Martha, Diamantopoulos, Nikolaos, Chouchos, Nikolaos, Mouratidou, Despina

Abstract: A 33-year-old woman with T(4c)N(3) breast cancer with metastases in the skeleton (M(1)) received five cycles of 5-fluorouracil, epirubicin, and cyclophosphamide (FEC regimen) before conception and during the first trimester. Salvage radiotherapy (28 Gy) was delivered during the 17th week. Tamoxifen and zolendronic acid were also administered throughout the second and third trimesters. The patient was not aware of her pregnancy until the 28th week. A female phenotypically normal infant was delivered in the 35th week of gestation by cesarean section. The child is functioning normally 12 months after delivery. The literature of anthracycline treatment during conception and the first trimester is reviewed. The effects of tamoxifen and biphosphonate therapy on the fetus during pregnancy are also discussed.

Source: Medline

Title: Chemotherapy during pregnancy: what is really safe?

Citation: The Lancet. Oncology, Jul 2004, vol. 5, no. 7, p. 398., 1470-2045 (July 2004)

Author(s): Peccatori, Fedro, Martinelli, Giovanni, Gentilini, Oreste, Goldhirsch, Aron

Source: Medline

Full Text:
Available from *ProQuest* in Lancet Oncology

Title: Use of chemotherapy during human pregnancy

Citation: Lancet Oncology, May 2004, vol./is. 5/5(283-291), 1470-2045 (01 May 2004)

Author(s): Cardonick E., Iacobucci A.

Language: English

Abstract: When cancer is diagnosed in a pregnant woman, life-saving chemotherapy for the mother poses life-threatening concerns for the developing fetus. Depending on the type of cancer and the stage at diagnosis, chemotherapy cannot necessarily be delayed until after delivery. Women diagnosed with acute lymphoblastic leukaemia who decline both termination and chemotherapy often die with the previable fetus in utero. Safe use of chemotherapy, especially during the second and third trimester, have been reported, and pregnant women with cancer can accept therapy without definite neonatal harm. Here, we review the use of chemotherapy in pregnancy by trimester of exposure and summarise neonatal outcomes, including malformations, perinatal complications, and oldest age of

neonatal follow-up. We will also discuss the modes of action of the drugs used and look at the multiagent regimens recommended for use during pregnancy.

Publication Type: Journal: Review

Source: EMBASE

Full Text:
Available from *ProQuest* in Lancet Oncology

Title: Chemotherapy with epirubicin and paclitaxel for breast cancer during pregnancy: case report and review of the literature.

Citation: Anticancer research, Nov 2003, vol. 23, no. 6D, p. 5225-5229, 0250-7005 (2003 Nov-Dec)

Author(s): Gadducci, Angiolo, Cosio, Stefania, Fanucchi, Antonio, Nardini, Vincenzo, Roncella, Manuela, Conte, Pier Franco, Genazzani, Andrea Riccardo

Abstract: Breast cancer diagnosed during pregnancy is a challenging clinical situation. Little data are currently available about chemotherapy in pregnant women with this malignancy. We report the case of a 36-year-old pregnant woman with a T2N1M0 breast cancer who received sequential chemotherapy including epirubicin (120 mg/m2 every three weeks for four cycles) and paclitaxel (175 mg/m2 every three weeks for three cycles) from the 14th to the 32nd week of gestation. The patient delivered a normal female baby by caesarean section at the 36th week. The immunohistochemical examination of the placenta showed a diffuse, strong P-glycoprotein expression. Thirty-six months after the delivery, the mother was disease-free and the infant showed normal development and growth. Sequential chemotherapy including epirubicin and paclitaxel should be taken into consideration as adjuvant treatment for pregnant women with high-risk breast cancer. The strong placental expression of P-glycoprotein may play a major role in limiting fetal exposure to anthracyclines and taxanes.

Source: Medline

Full Text:
Available from *Free Access Content* in Anticancer Research

Title: Eclampsia after polychemotherapy for nodal-positive breast cancer during pregnancy.

Citation: European journal of obstetrics, gynecology, and reproductive biology, Aug 1996, vol. 67, no. 2, p. 197-198, 0301-2115 (August 1996)

Author(s): Müller, T, Hofmann, J, Steck, T

Abstract: We report the case of a 39-year-old para-4 gravida-4 who received polychemotherapy 5-fluorouracil 600 mg/m2, cyclophosphamide 600 mg/m2 and epirubicin

50 mg/m2 for invasive breast cancer (pT2N2Mo) with extensive metastatic involvement of all 23 axillary lymph nodes removed at 29 gestational weeks. Soon after the second course of chemotherapy at 35 weeks, she developed two eclamptic tonic-clonic seizures which were treated by antihypertensive and anticonvulsive drugs and delivery of a healthy infant, 1650 g (< 10th percentile) by cesarean section. That this patient indeed suffered from eclampsia was supported by the findings of transient postpartum severe hypertension (peak 170/110 mmHg), proteinuria (peak 3.2 g/24 h), incomplete features of the HELLP syndrome (thrombocytopenia 81,000/mm3, haptoglobin < 10 mg/dl) and of DIC, and by the results of cerebral CT scanning showing two 1-cm ischemic lesions. Since the detrimental effect of antineoplastic agents on the rapidly proliferating trophoblast is well known and as abnormal placental function, such as in triploidy, trisomy or hydatiform mole, has been associated with an increased risk for preeclampsia/eclampsia, a possible causal relationship between polychemotherapy and the subsequent development of this rare disorder is suggested.

Source: Medline

Title: [Transplacental passage of epirubicin].

Citation: Journal de gynécologie, obstétrique et biologie de la reproduction, Jan 1995, vol. 24, no. 1, p. 63-68, 0368-2315 (1995)

Author(s): Gaillard, B, Leng, J J, Grellet, J, Ducint, D, Saux, M C

Abstract: We studied the transplacental transfer of epirubicin, an anthracycline used for the treatment of different neoplastic disorders, in particular breast cancers, by in vitro perfusion of term human placenta. Placenta from women with uncomplicated pregnancy were collected immediately after vaginal delivery and put into 37 degrees C thermostated hood. Perfusion of foetal surface of the placenta by modified Earle's solution was started immediately after catheterisation at a flow rate of 6 ml/min and then so was the perfusion of the intervillous space at the rate of 12 ml/min. Samples were collected at different times after the initiation of the perfusion from arterial inflow and venous outflow respective of the maternal and foetal compartment. The transplacental transfer of epirubicin was investigated for two doses: 5 and 9 micrograms/ml. The mean transfer value of epirubicin is low (3.66 +/- 1.07%) for the two tested doses and is only slightly higher than doxorubicin transfer, which drug has provided rare accidents in the clinical reports. These results are in favour of a low placental toxicity of epirubicin. Clinical data have to be collected from pregnant women to confirm the low foetal toxicity of epirubicin.

Source: Medline