Breast Cancer: Chemotherapy Drugs and Pregnancy

Drugs	Use in pregnancy	Comments
Chemotherapy		
Capecitabine	2	It has not been studied in humans although there is considerable experience with the use of fluorouracil, an analog. Animal studies have shown teratogenicity and fetal loss.[10]
Carboplatin	2	It has not been studied in humans during 1st trimester. Animal studies have demonstrated teratogenicity.[21] Several case reports supporting the use after the period of organogenesis (2nd and 3rd trimester).[22]
Cyclophosphamide	1	There is considerable clinical experience (usually with fluorouracil and doxorubicin) during 2nd and 3rd trimesters.[1-4] No significant complications were reported for the fetus and infant in women treated with the MD Anderson protocol (cyclophosphamide, fluorouracil and doxorubicin every 21 days)[2]
Docetaxel	2	Several case reports suggest short-term clinical safety[5,6,17] but international guidelines suggest avoiding taxanes during pregnancy[9]. There are also no data on the safety of dose-dense anthracycline-containing regimens with or without taxanes, during pregnancy.
Doxorubicin	1	There is considerable clinical experience (usually with fluorouracil and cyclophosphamide) during 2nd and 3rd trimesters.[1-4,**16**] No significant complications were reported for the fetus and infant in women treated with the MD Anderson protocol (cyclophosphamide, fluorouracil and doxorubicin every 21 days).[2]
Epirubicin	2	Doxorubicin is preferred if equally effective for a particular indication. Clinical case reports have shown 23% of cases exposed to epirubicin died either as fetuses or as neonates.[3] Animal studies have shown teratogenicity and embryotoxicity.
Fluorouracil	1	There is considerable clinical experience (usually with doxorubicin and cyclophosphamide) during 2nd and 3rd trimesters.[1-4] No significant complications were reported for the fetus and infant in women treated with the MD Anderson protocol (cyclophosphamide, fluorouracil and doxorubicin every 21 days).[2]

Breast Cancer: Chemotherapy Drugs and Pregnancy

Drugs	Use in pregnancy	Comments
Gemcitabine	2	Animal studies have shown embryotoxicity and fetal malformations.[10]
Methotrexate	3	It is abortifacient and associated with severe fetal malformations such as the "aminopterin syndrome" and cranial dysostosis.[13,14]
Paclitaxel	2	Several case reports suggest short-term clinical safety[3,15,18,19] but international guidelines suggest avoiding taxanes during pregnancy[9]. There are also no data on the safety of dose-dense anthracycline-containing regimens with or without taxanes, during pregnancy.
Vinorelbine	2	Several case reports suggest short-term clinical safety.[6,7] Vinca alkaloids are highly protein bound and considered less potent teratogens than antimetabolites.[3]
Hormonal agents		
Anastrozole	3	Animal studies have shown fetotoxicity[10]
Exemestane	3	Animal studies have shown embryotoxicity and fetotoxicity[10]
Letrozole	3	Animal studies have shown embryotoxicity and fetotoxicity[10]
Tamoxifen	3	Clinical studies have shown birth defects (e.g. Goldenhar syndrome, ambiguous genitalia) [11,12]
Others		
Pamidronate	3	Animal studies have shown fetal risks.
Trastuzumab	2	Several clinical reports have shown inconsistent short-term clinical safety.[18, 20] Animal studies have not shown fetal risks.

1 = has been safely used during pregnancy
2 = may be (insufficient data)
3 = not indicated during pregnancy

Breast Cancer: Chemotherapy Drugs and Pregnancy

References

1. Illidge TM, Hussey M, Godden CW. Malignant hypercalcaemia in pregnancy and antenatal administration of intravenous pamidronate. Clin Oncol (R Coll Radiol) 1996; 8(4):257-8.
2. Berry DL, Theriault RL et al. Management of breast cancer during pregnancy using a standardized protocol. J Clin Oncol 1999; 17(3):855-61
3. Andreadis C, Charalampidou M, Diamantopoulos N, et al. Combined chemotherapy and radiotherapy during conception and first two trimesters of gestation in a woman with metastatic breast cancer. Gynecol Oncol 2004; 95(1):252-5.
4. Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. Lancet Oncol 2004; 5(5):283-91.
5. Vitoratos N, Salamalekis E, Makrakis E, et al. Sigmoid colon cancer during pregnancy. Eur J Obstet Gynecol Reprod Biol 2002; 104(1):70-2.
6. De Santis M, Lucchese A, De Carolis S, et al. Metastatic breast cancer in pregnancy: first case of chemotherapy with docetaxel. Eur J Cancer Care (Engl) 2000; 9(4):235-7.
7. Cuvier C, Espie M, Extra JM, et al. Vinorelbine in pregnancy. Eur J Cancer 1997;33(1):168-9.
8. Janne PA, Rodriguez-Thompson D, Metcalf DR, et al. Chemotherapy for a patient with advanced non-small-cell lung cancer during pregnancy: a case report and a review of chemotherapy treatment during pregnancy. Oncology 2001; 61(3):175-83.
9. Loibl S et al. Breast carcinoma during pregnancy. International recommendations from an expert meeting. Cancer. 2006 Jan 15; 106(2):237-46.
10. UpToDate. Breast cancer during pregnancy and lactation.
11. Cullins,SL, Pridjian G, et al. Goldenhar's syndrome associated with tamoxifen given to the mother during gestation. *JAMA.*1994; 271:1905-1906.
12. Tewari K, Bonebrake RG, et al. Ambiguous genitalia in infant exposed to tamoxifen in utero. Lancet. 1997;350:183
13. Doll DC, Ringerberg QS, et al. Antineoplastic agents in pregnancy. Semin Oncol.1989; 16:337-346.
14. Ebert U, Loffler H, et al. Cytotoxic therapy and pregnancy. Pharmacol Ther. 1997; 74:207-220.
15. Theriault R, Hahn K, et al. Management of Breast Cancer in Pregnancy. Current Oncology Reports. 2007, 9:17-21
16. Gonzales-Angulo AM, Walters RS et al. Paclitaxel chemotherapy in a pregnant patient with bilateral breast cancer. Clin Breast Cancer 2004, 5:317-319
17. Nieto Y, Santisteban M et al. Docetaxel administered during pregnancy for inflammatory breast carcinoma. Clin Breast Cancer 2006; 6: 533-534
18. Bader AA, Schlembach D et al. Anhydramnios associated with administration of trastuzumab and paclitaxel for metastatic breast cancer during pregnancy. Lancet Oncol 2007; 8: 79-81
19. Lycette JL, Dul CL et al. Effect of pregnancy on the pharmacokinetics of paclitaxel: a case report. Clin Breast Cancer 2006; 7: 342-344
20. Fanale MA, Uyei AR et al. Treatment of metastatic breast cancer with trastuzumab and vinorelbine during pregnancy. Clin Breast Cancer 2005; 61:175-356
21. Kai S, et al. Teratogenic effects of carboplatin, an oncostatic drug, administered during the early organogenetic period in rats. J Toxicol Sci 1989; 14:115-30
22. Mendez L, Mueller E et al. Paclitaxel and Carboplatin chemotherapy administered during pregnancy for advanced epithelial ovarian cancer. Obstet Gynecol 2003;102:1200-2