Outcome of breast cancer patients treated with chemotherapy during pregnancy compared with non-pregnant controls

Frédéric Amant[1], Valentina Nekljudova[2], Charlotte Maggen[3], Fenja Seither[2], Patrick Neven[4], Elyce H. Cardonick[5], Sabine Schmatloch[6], Kristel Van Calsteren[7], Tatjana Cordes[8], Jorine de Haan[9], Christianne A.R. Lok[10], Christina Bechtner[11], Ingrid A. Boere[12], Mina Mhallem Gziri[13], Christine Solbach[14], Hanne Lefrère[3], Andreas Schneeweiss[15], Isabel Witzel[16], Sabine Seiler[2], Sibylle Loibl[2]

[1]Department of Oncology, KULeuven, Leuven, Belgium, and Center for Gynecologic Oncology Amsterdam, Amsterdam University Medical Centers and Center for Gynecologic Oncology Amsterdam, Antoni van Leeuwenhoek–Netherlands Cancer Institute, Amsterdam, Netherlands; [2]German Breast Group, Neu-Isenburg, Germany; [3]Department of Oncology, KU Leuven, Leuven, Belgium; [4]Multidisciplinary Breast Center, Universitair Ziekenhuis, Leuven, Belgium; [5]Department of Obstetrics and Gynecology, Cooper University Health Care, Camden, NJ, USA; [6]Elisabeth Krankenhaus Kassel, Germany; [7]Department of Development and Regeneration, KU Leuven, Leuven, Belgium; Department of Obstetrics and Gynecology, University Hospitals Leuven, Leuven, Belgium; [8]HSK Wiesbaden, Germany; [9]Department of Obstetrics and Gynecology, VU University Medical Center, Amsterdam, Netherlands; [10]Center for Gynecologic Oncology Amsterdam, Antoni van Leeuwenhoek-Netherlands Cancer Institute, Amsterdam, Netherlands; [11]Klinikum Memmingen, Germany; [12]Department of Medical Oncology, Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, Netherlands; [13]Department of Obstetrics, Cliniques Universitaires St Luc, UCL, Sint-Lambrechts-Woluwe, Belgium[14]Goethe Universität Frankfurt, Germany; [15]Nationales Centrum für Tumourerkrankungen, Heidelberg, Germany; [16]Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany

Poster #515

Background

Overall, a diagnosis of breast cancer during pregnancy (BCP) appears not to impact maternal prognosis if standard treatment is offered (1-3). However, caution is warranted as gestational changes in pharmacokinetics with respect to the distribution, metabolism and excretion of drugs may lead to reduced chemotherapy concentration in pregnant patients (4,5). This cohort study was designed to focus on the maternal prognosis of BCP patients that receive chemotherapy during pregnancy.

Patients and Methods

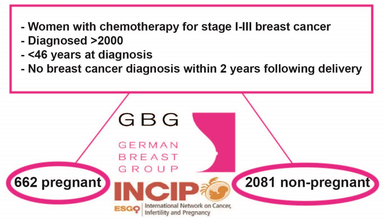
Trial design

The outcome of BCP patients treated with chemotherapy during pregnancy was compared to non-pregnant breast cancer patients treated with chemotherapy, diagnosed after 2000, excluding postpartum diagnosis and with an age limit of 45 years. The data was registered by two multicentric registries (the International Network of Cancer, Infertility and Pregnancy and the German Breast Cancer Group) that collect both retro-and prospectively breast cancer data. **Primary and secondary objectives** were to compare disease-free (DFS) and overall survival (OS), respectively, between patients treated with chemotherapy during pregnancy for BCP and patients not diagnosed in association with a pregnancy.

Statistical consideration

Cox proportional hazards regression was used to compare DFS and OS between both groups, adjusting for stage (I, II or III), grading (gr 1-2 versus gr 3), histologic tumor type (lobular versus non-lobular), estrogen receptor (ER)/progesterone receptor (PR) status (positive or negative), human epidermal growth factor receptor 2 (HER2) status (HER2-negative vs HER2-positive without or unknown anti-HER2 treatment vs HER2-positive with single anti-HER2 agent treatment) and type of chemotherapy (anthracycline-based only, anthracyclines and taxanes, non-standard treatment); and weighted by propensity scoring in order to account for the differences in baseline characteristics between pregnant patients and controls. Missing values for covariates were imputed.

Figure 1. Study Design



Results

- **662 pregnant** and **2081 non-pregnant** women who received chemotherapy for breast cancer, were eligible for analysis (Figure 1).
- Pregnant patients were more likely to have **stage II breast cancer**, **grade 3** tumors, **hormone receptor-negative** tumors or **triple-negative** breast cancer (Table 1).
- With a median follow-up of 66 months, the observed 5-year DFS was 76.9% (73.2% for pregnant and 78.1% for non-pregnant) and 5-year OS was 88.1% (84.2% and 89.2% respectively). **DFS and OS were comparable for pregnant and non-pregnant patients** (Figure 2).
- A **subgroup** analysis of 339 women that received more than 60% of chemotherapy during pregnancy (cut-off at median) revealed a comparable survival compared to non-pregnant women. Proportion of chemotherapy during pregnancy did not impact survival in the pregnant group (Figure 2).

Figure 2: Forest plot with results of multivariable Cox proportional hazard regression of Disease-free (DFS) and Overall Survival (OS) by subgroups of interest

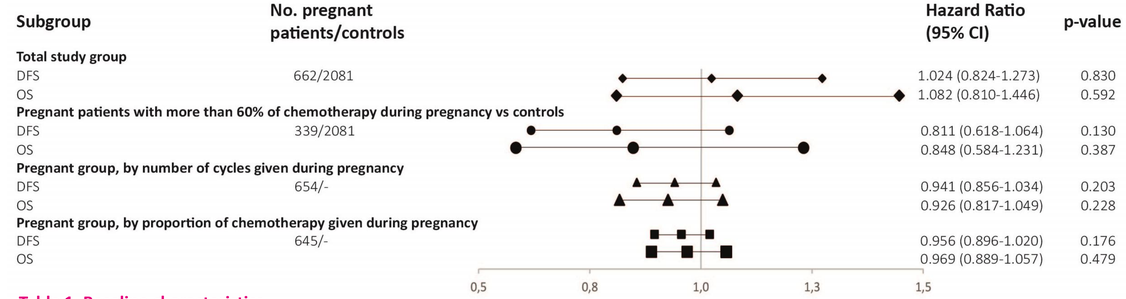


Table 1. Baseline characteristics

Characteristic	Overall No.	%	Pregnant No.	%	Non-pregnant No.	%	p-value
No. of patients	*2743*		*662*		*2081*		
Age (years)							
Median, range	37, 19-47		34, 22-47		38, 19-45		<.001
Stage							
stage I	516	19.8	97	16.1	419	20.9	0.035
stage II	1486	57.0	361	60.1	1125	56.1	
stage III	603	23.1	143	23.8	460	23.0	
missing	*138*		*61*		*77*		
Histological tumor type							
Non-lobular	2581	95.2	634	96.9	1947	94.6	0.016
Lobular invasive	131	4.8	20	3.1	111	5.4	
missing	*31*		*8*		*23*		
Grading, dichotomized							
G1-2	928	35.1	159	26.0	769	37.8	<.001
G3	1718	64.9	453	74.0	1265	62.2	
missing	*97*		*50*		*47*		
HER2 status							
negative	1937	72.6	443	71.5	1494	73.0	0.472
positive	730	27.4	177	28.5	553	27.0	
missing	*76*		*42*		*34*		
Hormone receptor status							
both ER and PgR negative	1014	37.4	310	48.4	704	34.0	<.001
ER and/or PgR positive	1696	62.6	330	51.6	1366	66.0	
missing	*33*		*22*		*11*		
Chemotherapy							
Anthracycline	579	21.1	147	22.2	432	20.8	0.089
Anthracycline + taxane	1916	69.9	469	70.8	1447	69.5	
Non-standard chemotherapy	248	9.0	46	6.9	202	9.7	
missing	*0*		*0*		*0*		

Abbreviations: BC: breast cancer, ER: estrogen receptor, PR: progesterone receptor, HER2: Human Epidermal growth factor Receptor 2

Conclusions

Pregnancy-induced alternations in chemotherapy concentration does not seem to affect maternal prognosis in breast cancer patients. These results support initiation of chemotherapy for BCP where indicated for oncological reasons.

References

1. Loibl S, Schmidt A, Gentilini O, et al. Breast Cancer Diagnosed During Pregnancy: Adapting Recent Advances in Breast Cancer Care for Pregnant Patients. JAMA Oncol 2015;1:1145-53.

2. Stensheim H, Moller B, van Dijk T, Fossa SD. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. J Clin Oncol 2009;27:45-51.

3. Amant F, von Minckwitz G, Han SN, et al. Prognosis of women with primary breast cancer diagnosed during pregnancy: results from an international collaborative study. J Clin Oncol 2013;31:2532-9.

4. van Hasselt JG, van Calsteren K, Heyns L, et al. Optimizing anticancer drug treatment in pregnant cancer patients: pharmacokinetic analysis of gestation-induced changes for doxorubicin, epirubicin, docetaxel and paclitaxel. Ann Oncol 2014;25:2059-65.

5. Janssen JM, Van Calsteren K, Dorlo TPC, et al. Population Pharmacokinetics of Docetaxel, Paclitaxel, Doxorubicin and Epirubicin in Pregnant Women with Cancer: A Study from the International Network of Cancer, Infertility and Pregnancy (INCIP). Clin Pharmacokinet 2021.

Presented at: ASCO 2021, June 4-8, 2021

This study was financially supported by the European Research Council, Research foundation Flanders, Kom op tegen Kanker