Pregnancy in breast cancer patients: Timing, safety, and treatment approaches (during and post-cancer)

Fedro A Peccatori, MD PhD
European Institute of Oncology
European School of Oncology
MILAN, ITA
Disclosures

No relevant relationships to disclose

Lecture outline

- Safety and timing of spontaneous pregnancy in BC survivors
- Safety and feasibility of ART pregnancy in BC survivors
- Pregnancy outcome in BC survivors
- Breast cancer during pregnancy: a need for action
SAFETY AND TIMING OF SPONTANEOUS PREGNANCY IN BC SURVIVORS
Attitudes on fertility issues in breast cancer patients: an Italian survey
Nicoletta Biglia, Rosalba Tomisi, Marta D’Alonzo, Giovanni Codacci Pisanelli, Selene Rota, and
Federico Alessandro Peccatori

10. May a pregnancy in women previously affected by BCa increase the risk of recurrence?

Only 51% of oncologists believed that pregnancy does not affect the prognosis of BCa patients, while 49% of them supports that an increase in estrogen levels during pregnancy could stimulate the growth of hidden tumor cells (Statement 10).

Pregnancy after breast cancer
Safety of pregnancy following breast cancer diagnosis: A meta-analysis of 14 studies
Hatem A. Azim Jr., Luigi Santoro, Nicholas Pawlidis, Shari Gelber, Niels Kroman, Hamdy Azim, and Federico A. Peccatori

Safety: meta-analysis

14 studies
7 case control studies
4 population based studies
3 hospital based studies

1244 cases e 18145 controls
Median time to pregnancy: 33 months
Follow-up 5-30 years

Data pooling using random effect

Sensitivity analysis and subgroup analysis

Safety: meta-analysis

All studies, 41% reduction of death

Pooled Relative Risk

0.59 (0.59, 0.70)
Safety: meta-analysis

15% reduction of death with more stringent criteria

Time to pregnancy

187 patients who became pregnant within 6-24 months
353 patients who became pregnant after 2 years

Shorter time to pregnancy not associated with a worse prognosis
Pregnancy after breast cancer

Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study


J Clin Oncol. 2013 Jan 1;31(1):73-9

Pregnancy after breast cancer

BRIEF COMMUNICATION

Long-term Safety of Pregnancy Following Breast Cancer According to Estrogen Receptor Status


**Multicenter study in ER+/ER- patients**

Retrospective, multicenter cohort study (7 Institutions)

Primary endpoint: DFS ER+ pts.  
(Two sided test a= 5%, b=20%, 226 events 645 pts for HR 0.65)

Secondary endpoints: DFS in ER- pts., OS

---

**Multicenter study in ER+/ER- patients**

333 cases with pregnancy after breast cancer  
874 non pregnant controls  
matched for ER, stage, adjuvant treatment, age, year at diagnosis

Mean age: 32y (21–44)  
Node positive: 43%  
ER+: 58%  
Chemo: 79%

323 pregnancies  
188 live birth  
135 abortions or miscarriages  
Median time to pregnancy: 27 months
RFS in ER+ patients

Estrogen receptor-positive cohort (n = 696)

HR 0.91 (95% CI 0.67-1.24)

Favorable outcome of Pregnancy in 184
Malignant outcome of Pregnancy in 402
HR, 0.91; 95% CI, 0.67 to 1.26; P = .55

Median time from diagnosis to pregnancy 2.4 years

Median follow-up 7.2 years after pregnancy

HR 0.94 (95% CI 0.70-1.26)

OS in ER+/ER- patients

HR 0.72 (95% CI 0.55-0.94)

OS in ER+/ER- patients

HR 0.72 (95% CI 0.54-0.97)
SAFETY AND TIMING OF SPONTANEOUS PREGNANCY IN BC SURVIVORS

- Pregnancy in breast cancer survivors is safe: no increased risk of relapse or mortality in ER negative or ER positive tumors
- Timing of pregnancy after breast cancer is still debated: no increased risk when pregnancy occurred after 6 months from diagnosis, but most data are for pregnancy after 2 years.
SAFETY AND FEASIBILITY OF ART PREGNANCY IN BC SURVIVORS

Pregnancy with ART in BC survivors

Pregnancy following breast cancer using assisted reproduction and its effect on long-term outcome

Oranite Goldrat a,b, Niels Kroman c, Pedro A. Peccatori d, Octavi Cordoba e, Barbara Pistili f, Oeonind Lidegaard g, Isabelle Demeestere h, Hatem A. Azim Jr. b,c

Eur J Cancer. 2015;51:1490-1496
### Safety of pregnancy with ART in BC survivors

#### Table 1

<table>
<thead>
<tr>
<th>Institution/Group</th>
<th>Spontaneous preg, n</th>
<th>ART, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>173</td>
<td>25</td>
</tr>
<tr>
<td>Mean age at diagnosis (range)</td>
<td>31.4 (29-34)</td>
<td>33.7 (31-37)</td>
</tr>
<tr>
<td>Tumor size &gt; T2</td>
<td>10 (5.8%)</td>
<td>0</td>
</tr>
<tr>
<td>Nodal status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Negative</td>
<td>100 (58%)</td>
<td>19 (76%)</td>
</tr>
<tr>
<td>• Positive</td>
<td>75 (42%)</td>
<td>6 (4%)</td>
</tr>
<tr>
<td>Histological grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>16 (9%)</td>
<td>5 (20%)</td>
</tr>
<tr>
<td>• 2</td>
<td>43 (25%)</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>• 3</td>
<td>103 (60%)</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>• unknown</td>
<td>11 (6%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>ER status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Negative</td>
<td>81 (53%)</td>
<td>17 (68%)</td>
</tr>
<tr>
<td>• Positive</td>
<td>92 (47%)</td>
<td>8 (32%)</td>
</tr>
<tr>
<td>Adjuvant chemotherapy received</td>
<td>118 (68%)</td>
<td>15 (60%)</td>
</tr>
<tr>
<td>Median duration of hormonal therapy in months (range)</td>
<td>48 (30-60)</td>
<td>33 (24-44)</td>
</tr>
</tbody>
</table>

#### Table 2

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Spontaneous pregnancy group, N = 247 (%)</th>
<th>ART pregnancy group, N = 84 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at conception (years)</td>
<td>35.3</td>
<td>36.5</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>33-38</td>
<td>34-43</td>
</tr>
<tr>
<td>Median time from diagnosis to conception (m/o)</td>
<td>42</td>
<td>48</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>24-63</td>
<td>36-84</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>miscarriage</td>
<td>31 (12.6%)</td>
<td>8 (33.3%)</td>
</tr>
<tr>
<td>induced abortion</td>
<td>24 (9.7%)</td>
<td>0</td>
</tr>
<tr>
<td>term pregnancy</td>
<td>191 (76.9%)</td>
<td>26 (76.5%)</td>
</tr>
<tr>
<td>other</td>
<td>3 (1.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Live birth</td>
<td>N = 190</td>
<td>N = 26</td>
</tr>
<tr>
<td>single</td>
<td>184 (99.8%)</td>
<td>24 (92.3%)</td>
</tr>
<tr>
<td>twin</td>
<td>6 (3.2%)</td>
<td>2 (7.7%)</td>
</tr>
</tbody>
</table>

Assisted reproductive technology (ART): 13 egg donation; 13 IVF; 11 ovulation induction (clomid)
### Safety of pregnancy with ART in BC survivors

#### Table 3
Long-term survival outcome.

<table>
<thead>
<tr>
<th></th>
<th>Spontaneous pregnancy group, N = 173 (%)</th>
<th>ART pregnancy group, N = 25 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval diagnosis-first clinical FU (mo)</td>
<td>107</td>
<td>112</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>81–131</td>
<td>85–123</td>
</tr>
<tr>
<td>Interval conception-last clinical FU (mo)</td>
<td>63</td>
<td>50</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>31–90</td>
<td>37–72</td>
</tr>
<tr>
<td>Cancer related events (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrence</td>
<td>8 (4.6)</td>
<td>0</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>10 (5.7)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Contralateral breast cancer</td>
<td>7 (4)</td>
<td>0</td>
</tr>
<tr>
<td>2nd primary cancer (non-breast)</td>
<td>3 (1.7)</td>
<td>0</td>
</tr>
<tr>
<td>Death (n)</td>
<td>11 (6.3)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

ART, assisted reproductive technology; FU, follow-up, mo, months.
How effective is ART after cancer treatment?

ORIGINAL ARTICLE

Assisted reproductive technology use and outcomes among women with a history of cancer¹

Barbara Luke¹, Morton B. Brown², Stacey A. Missmer³,⁴,⁵, Logan G. Spector⁶, Richard E. Leach¹, Melanie Williams⁷, Lori Koch⁸, Yolanda R. Smith⁹, Judy E. Stern¹⁰, G. David Ball¹¹, and Maria J. Schymura¹²

¹Department of Obstetrics, Gynecology, and Reproductive Biology, College of Human Medicine, Michigan State University, East Lansing, MI, USA
²Department of Obstetrics, Gynecology, and Reproductive Biology, Brigham and Women’s Hospital, Boston, MA, USA
³Department of Obstetrics, Gynecology, and Reproductive Biology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA
⁴Henry Ford Hospital and Henry Ford Medical School, Detroit, MI, USA
⁵Department of Obstetrics, Gynecology, and Reproductive Biology, University of California, San Diego, CA, USA
⁶Department of Obstetrics and Gynecology, Yale University, New Haven, CT, USA
⁷Department of Obstetrics and Gynecology, University of Arizona, Tucson, AZ, USA
⁸Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA
⁹Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI, USA
¹⁰Department of Obstetrics and Gynecology, Saint Louis University, St. Louis, MO, USA
¹¹Reproductive Endocrinology, Seattle, WA, USA
¹²Department of Obstetrics and Gynecology, New York State Department of Health, Albany, NY, USA

*Correspondence address. Tel: +1-517-353-1878; fax: +1-517-353-1864; E-mail: bluke@msu.edu

Blackwell Publishing Ltd. Published online 17 July, 2015. doi:10.1093/humrep/dev086

How effective is ART after cancer treatment?

- 441 women diagnosed with cancer, 53,426 controls
- 133 breast cancer patients
- Median age at ART treatment 34.8 and 35.1 y/o, respectively
- Results stratified by autologous oocyte or donor oocytes
How effective is ART after cancer treatment?

<table>
<thead>
<tr>
<th>Cancer status and diagnosis</th>
<th>Women using only autologous oocytes</th>
<th>Women who ever used donor oocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n, women</td>
<td>%</td>
</tr>
<tr>
<td>No cancer</td>
<td>48,138</td>
<td>55.0</td>
</tr>
<tr>
<td>All cancers</td>
<td>393</td>
<td>28.8</td>
</tr>
<tr>
<td>Probability of conception</td>
<td></td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>Probability of a live birth</td>
<td></td>
<td>p = 0.67</td>
</tr>
</tbody>
</table>

Assisted reproductive technology use and outcomes among women with a history of cancer

25/12/2017
How effective is ART after cancer treatment?

<table>
<thead>
<tr>
<th>Cancer status and diagnosis</th>
<th>Women using only autologous oocytes</th>
<th>Women who ever used donor oocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n, women</td>
<td>%</td>
</tr>
<tr>
<td>No cancer</td>
<td>48138</td>
<td>55.0</td>
</tr>
<tr>
<td>All cancers</td>
<td>393</td>
<td>28.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P &lt; 0.0001</em></td>
</tr>
<tr>
<td>No cancer</td>
<td>26492</td>
<td>86.7</td>
</tr>
<tr>
<td>All cancers</td>
<td>113</td>
<td>85.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P = 0.78</em></td>
</tr>
<tr>
<td>No cancer</td>
<td>48138</td>
<td>47.7</td>
</tr>
<tr>
<td>All cancers</td>
<td>393</td>
<td>24.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P &lt; 0.0001</em></td>
</tr>
</tbody>
</table>
SAFETY AND FEASIBILITY OF ART PREGNANCY IN BC SURVIVORS

✓ Pregnancy with assisted reproductive technology (ART) in breast cancer (BC) survivors is still rare

✓ No apparent increase in BC relapse or mortality after ART pregnancy

✓ IVF/ICSI with autologous oocytes after BC treatment is quite ineffective

✓ Egg donation can be considered in BC survivors with outcome that are not different from non-cancer patients

PREGNANCY OUTCOMES IN BC SURVIVORS
Pregnancy outcomes

Pregnancy Outcomes After a Breast Cancer Diagnosis: A Systematic Review and Meta-analysis
Brigitte Gerdé,1 Elizabeth Sullivan,2 Angela Ives,3 Chris Isabel Saunders,4 Hazel Ward,5 Annette Anzaldua6

Clinical Breast Cancer, 2017 article in press

16 studies identified (7 population based, 9 cohort/control)
2,523 pregnancies after BC and 22,964 controls
Mean time to pregnancy 29 months (11-63), mean time to first birth 40 months (10-228)
Pregnancy outcomes

COHORT and CASE/CONTROL studies

- Of 1,287 women who received systemic treatment after surgery (median age 33y), 14% became pregnant
- 12% experienced a miscarriage, 21% terminated pregnancy
- 72% had a live birth

MATCHED POPULATION BASED studies

- Of 711 women, only 3% subsequently conceived
- Women with ER positive tumors were 4 times less likely to become pregnant compared to ER negative tumors
Pregnancy outcomes

Prevalence of preterm, low birthweight, and small for gestational age delivery after breast cancer diagnosis: a population-based study

Kilita Vernet-Black, Hazel B. Nathanielsz, Egegne Efo, and Diane Louise Rockley

Breast Cancer Research

North Carolina Cancer and birth registries (1990-2009)

512 births from mothers with previous breast cancer

Average age at diagnosis 31.8 y, mean time to delivery 3.3 y

Data were adjusted for multiple variables, including ethnicity and compared to general population (1,911,757 women)

Prevalence ratios (PR) were estimated for:

- Preterm birth (PTB)
- Low birth weight (LBW)
- Small for gestational age (SGA)
Pregnancy outcomes

RESULTS

✓ Increased prevalence rate of PTB, LBW and SGA for women with breast cancer history

  PTB: 21.1% vs 10.8% PR 1.67 (95% CI 1.42-1.97)
  LBW: 14.8% vs 8.8% PR 1.50 (95% CI 1.23-1.84)
  SGA: 13.3% vs 11.2% PR 1.30 (95% CI 1.05-1.61)

✓ Risk was higher if BC patients received chemotherapy (2x) or births occurred within 2 years (2.5x)

✓ Data coherent with Australian, Swedish and Norwegian studies

PREGNANCY OUTCOME IN BC SURVIVORS

✓ Pregnancy in breast cancer survivors is still a rare event (3-15%).
  • Prospective studies of women seeking pregnancy needed

✓ Possibly increased risk of miscarriage and terminations.
  • Prospective studies and healthcare education needed

✓ Possibly increased prevalence of PTB, LBW and SGA.
  • Careful monitoring and prospective studies needed
BREAST CANCER DURING PREGNANCY: A NEED FOR ACTION

Breast Cancer during Pregnancy

Long and Winding Road of Cancer and Pregnancy: A Need for Action

Pedro A. Faccin, European Institute of Oncology, Milan, Italy

Cancer treatment in a pregnant woman is still a matter of debate, because life-saving therapies for the mother raise concerns about potential detrimental effects on the developing fetus. Recent data support the administration of chemotherapy from the second trimester onward in order to achieve optimal outcomes, with no evidence of increased risk for congenital malformations. The aim of this Editorial is to contribute to the discussion on the optimal management of pregnant patients with breast cancer, with the goal of improving outcomes for both mother and fetus.
Thank you!