Breast Cancer and Pregnancy

Navigating Diagnosis, Treatment, and Survivorship

Amanda Manorot MD

Erin Cobain, MD

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Agenda

Incidence of pregnancy associated breast cancer

Breast Imaging in pregnancy

Treatment differences

Delivery

Pediatric Outcomes

Breastfeeding

Fertility

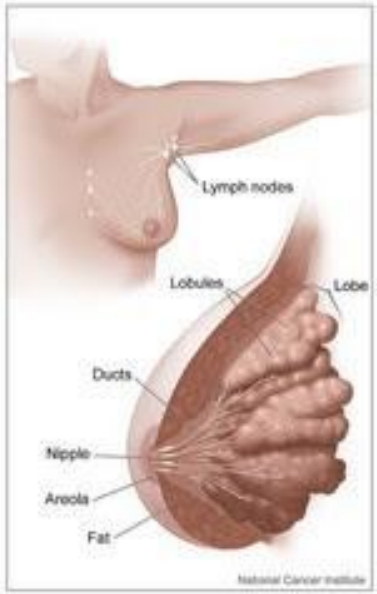
Pregnancy Associated Breast Cancer

Definition: Breast cancer diagnosed in pregnancy, 1 year postpartum or during lactation

Uncommon: 1 in every 3,000 pregnant women

Incidence: 15 to 35 per 100,000 deliveries

Majority diagnosed between the age of 32 to 38



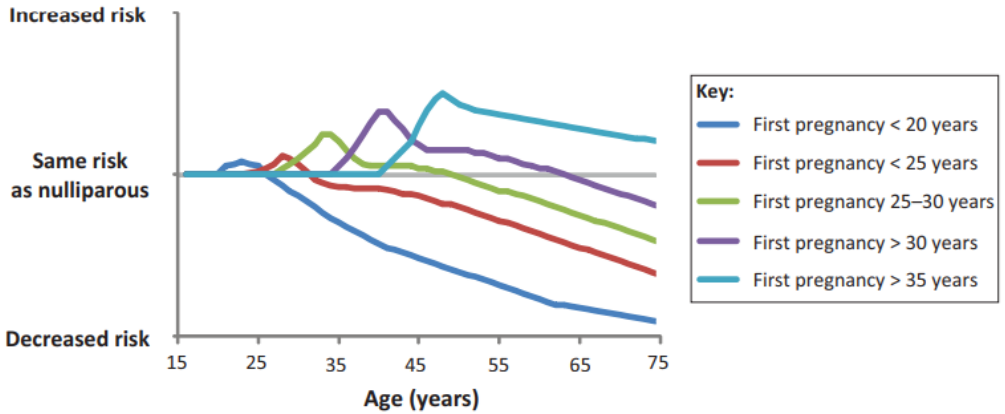
Pathological Features

Poorly differentiated, lymph node +, larger size, and more ER/PR negative

High levels of estrogen and progesterone found in pregnancy can bind receptor sites resulting in false positive assays

Invasive ductal carcinoma is most common

Does pregnancy increase breast cancer risk?



TRENDS in Molecular Medicine

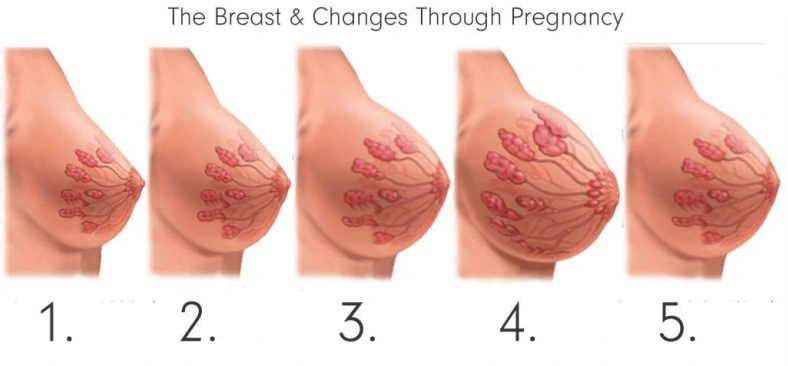
Challenges with diagnosis

Physiologic breast changes in pregnancy can make diagnosis more challenging

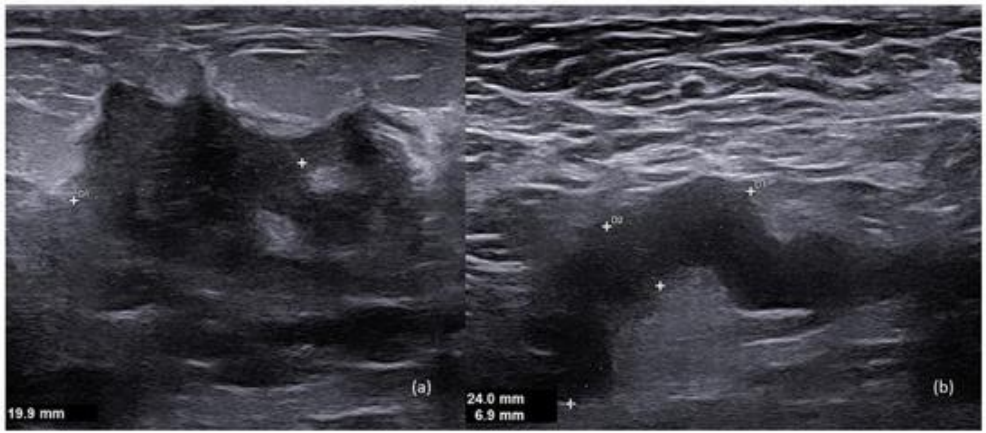
Average delay of 5 to 15 months from symptom onset to diagnosis reported.

Breast masses persisting for **>2 weeks** should be carefully evaluated

The majority (80%) of breast masses will be benign

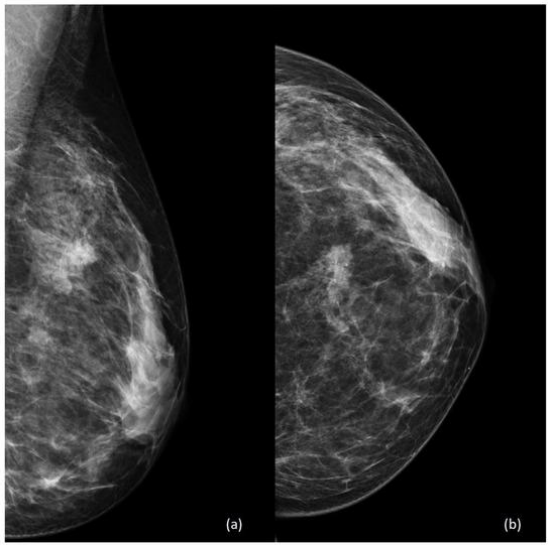


Imaging: ultrasound

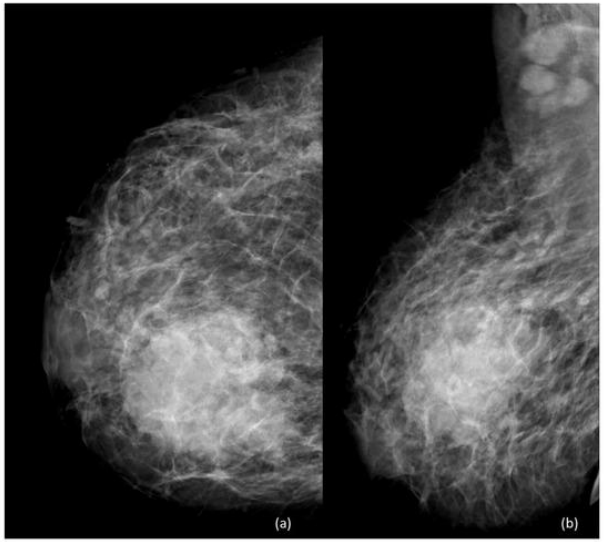


36 year old patient at 6 weeks gestation with invasive ductal carcinoma

Imaging: Mammogram

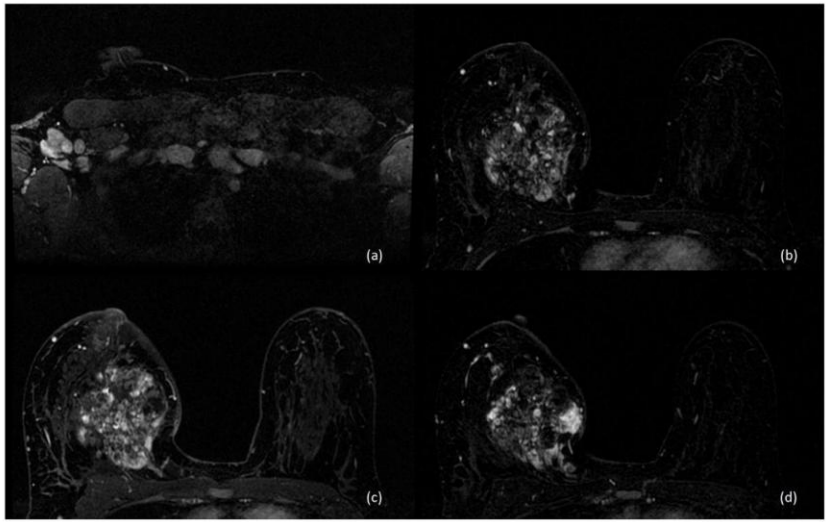


42 year old patient at 7 weeks gestation



36 year old breastfeeding patient at 6 months postpartum

Imaging: MRI



36 year old breastfeeding patient at 6 months postpartum

Further work up

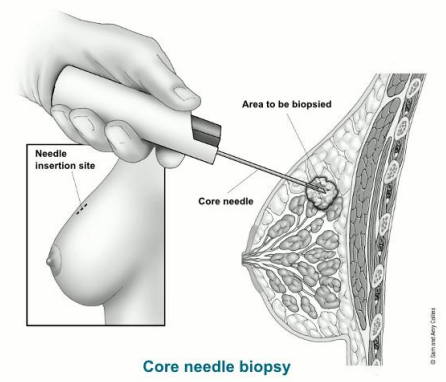
Core biopsy is safe at any gestational age.

- Recommended for any suspicious breast mass

Pathologist should be notified

Many women will meet guidelines for genetic testing due to age or hormone receptor negative status

Women with a genetic predisposition to breast cancer may be overrepresented among pregnant women with cancer



Staging studies

Chest Xray with fetal shielding = 0.001 mGy

US or MRI of the liver without contrast

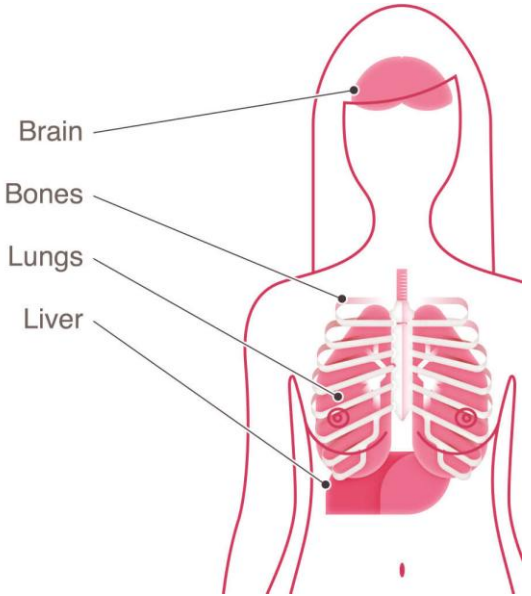
Brain MRI without contrast

Skeletal MRI without contrast

CT generally avoided with preference for MRI

Low dose bone scans with maternal hydration and urinary catheter

Alkaline phosphatase is elevated during pregnancy and is not indicative of bony disease



Treatment

Delay due to pregnancy leads to worse outcomes

Highly individualized treatment plans

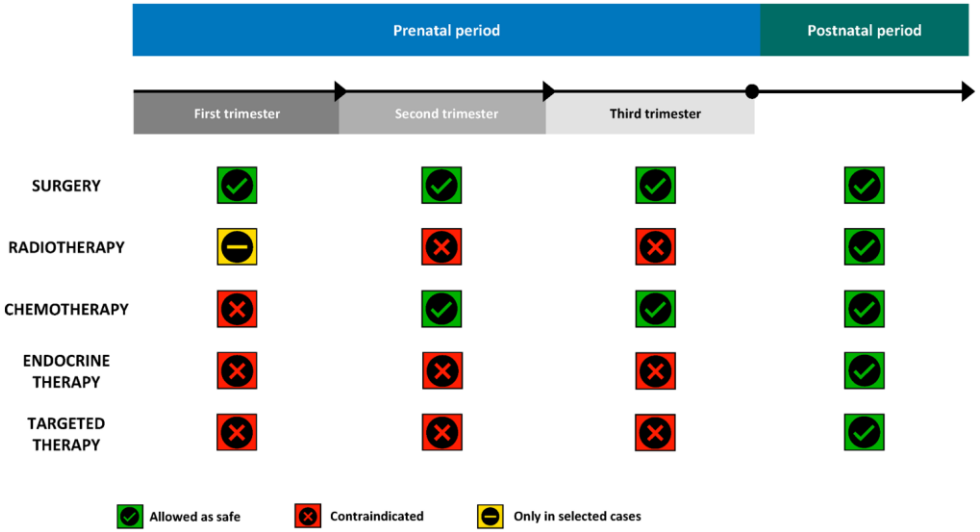
- Gestational age
- Stage of disease
- Patient and family preferences

Multidisciplinary care team

Some women will elect to terminate the pregnancy

Early termination does not improve outcomes

Cancer treatment can be safely managed in pregnancy



Surgical options

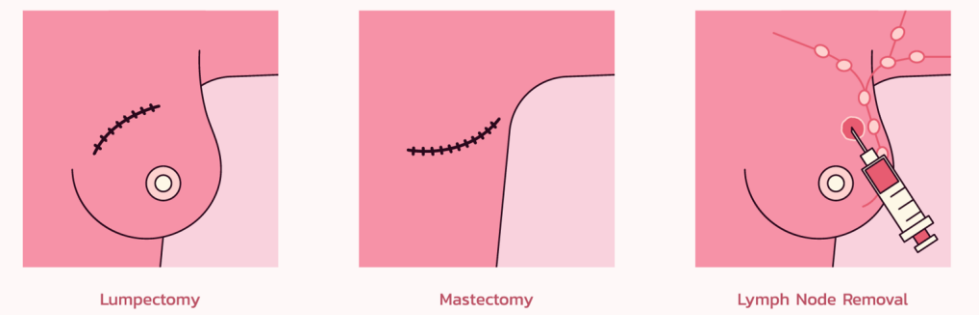
Mastectomy vs. Breast conserving surgery

Axillary lymph node dissection vs. Sentinel lymph node biopsy

Radiation delayed until postpartum if breast conserving surgery is chosen

Minimal fetal risk associated between options

Breast reconstruction is generally postponed to after delivery



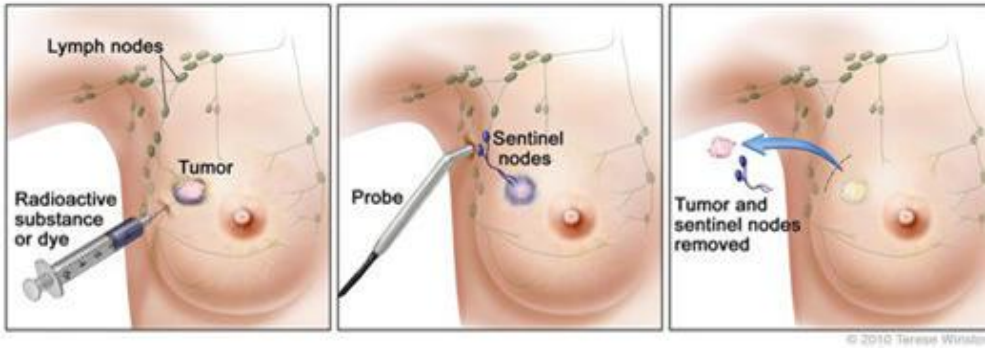
SLNB

If offered, limited current data should be discussed

Isosulfan blue dye and methylene blue is avoided

Small case series showed success with radiocolloid injection with no adverse effects

Same day injection of radioactive tracer is preferred to reduce time and dose of radiation exposure



Surgery during pregnancy

20 weeks left lateral tilt

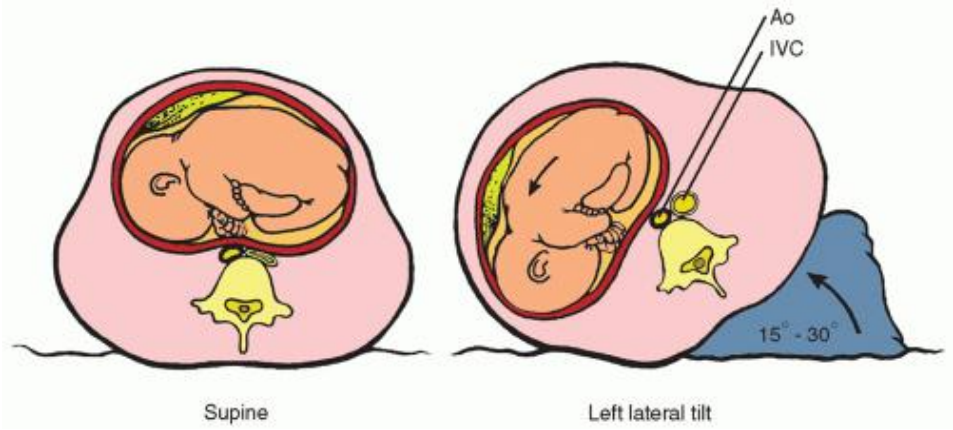
Anesthesia considerations

Risks of DVT or PE

Preterm labor and preterm birth

Discussion of continuous fetal monitoring after viability

Consultations with OB and Neonatology to discuss risks and consent for emergent cesarean delivery



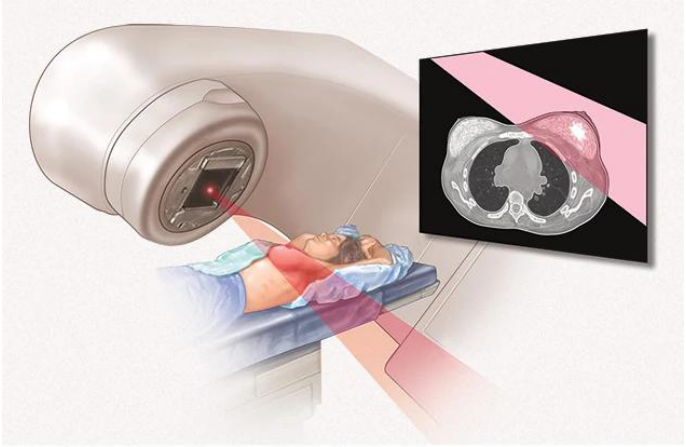
Radiation therapy

Generally avoided during pregnancy

- Pregnancy loss: miscarriage or stillbirth
- Malformations
- Growth disturbances
- Carcinogenic effects

Even with shielding, fetal exposure will increase as the fetus grows closer to the diaphragm

Typical radiation doses is 46 to 60 Gy



Absorbed radiation dose	**Effects on fetus**
1 mGy	Background
<50 mGy	Threshold of acceptable fetal exposure
60–200 mGy	Threshold of congenital fetal loss, congenital anomalies, intellectual effects
100 mGy at conception or >500 mGy after 25 weeks	Embryological/fetal death
50–500 mGy at 8-15 weeks	Growth restriction, intellectual effects
50–100 mGy (after first trimester)	0.3–1% childhood cancers
50–500 mGy (after first trimester)	1–6% childhood cancers
Absorbed radiation dose	**Imaging modality**
0.0005–0.001 mGy	Chest X-ray
0.001–0.001 mGy	Mammogram 2 views
0.1 mGy	Pelvis/Abdomen X-ray
0.01–1 mGy	Chest CT or pulmonary angiography
4–5 mGy	Bone scan Tc-99m
1.3–3.5 mGy	Abdominal CT
10–50 mGy	Pelvic CT
10–50 mGy	PET-CT whole body
Nil	MRI

Chemotherapy in pregnancy

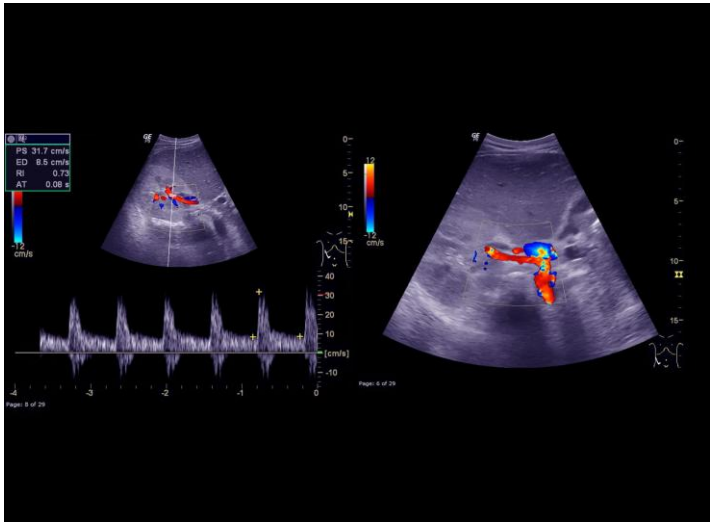
Given after the first trimester due to organogenesis

Fetal risks:

- Growth restriction
- Prematurity
- Low birth weight

Dosing similar to nonpregnant patients, adjusted for weight gain

Discontinued after 35 wks or within 3 weeks of a planned delivery



Delivery

Mode of delivery determined by routine OB indications

Vaginal delivery preferred

Delivery timing is individualized accounting for maternal and fetal outcomes. Often requires a multidisciplinary team approach

Ideal after fetal lung maturity is demonstrated (>34 wks)

Avoid iatrogenic preterm delivery with goal for planned delivery close to 37 wks

Pediatric Outcomes

Pediatric Outcome after Maternal Cancer Diagnosed during Pregnancy

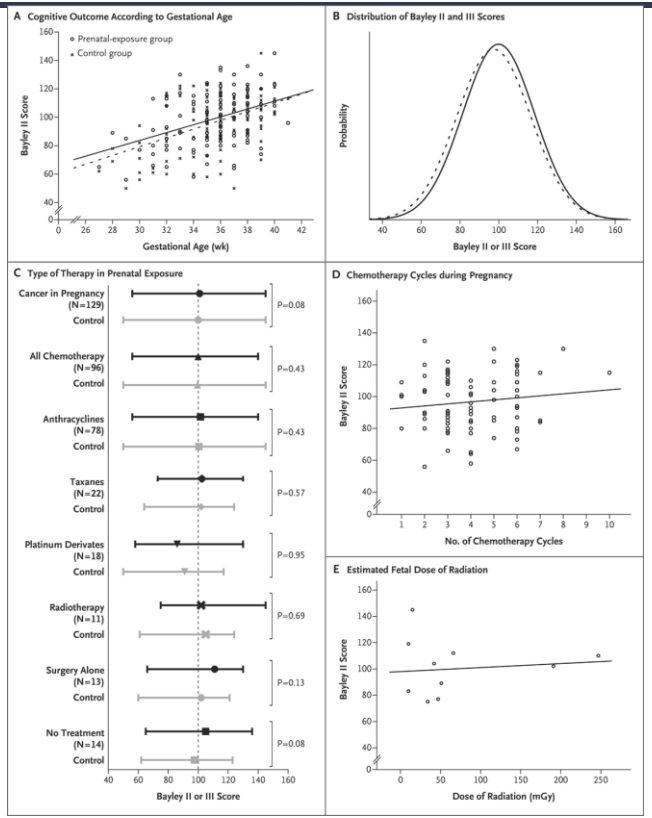
F. Amant, T. Vandenbroucke, M. Verheecke, M. Fumagalli, M.J. Halaska, I. Boere, S. Han, M.M. Gziri, F. Peccatori, L. Rob, C. Lok, P. Witteveen, J.-U. Voigt, G. Naulaers, L. Vallaeys, F. Van den Heuvel, L. Lagae, L. Mertens, L. Claes, and K. Van Calsteren, for the International Network on Cancer, Infertility, and Pregnancy (INCIP)

Early childhood development appears to be similar to children of similar gestational age where mothers did not undergo treatment for breast cancer

Cardiac, cognitive, and general development were matched at a median for 22 months

No documented fetal cardiac effects to children exposed to anthracyclines in the 2nd or 3rd trimester

No reported cases of childhood cancers after in utero exposure to chemotherapy



Breastfeeding

Recommended to avoid while receiving chemotherapy, anti-HER2 therapies, and endocrine therapy

Can breastfeed after treatment is completed

No evidence that breastfeeding affects prognosis

Increased risk of mastitis after radiation

Breastfeeding is discouraged prior to surgery to avoid engorgement and improve outcomes

Fertility after Breast Cancer

Fertility risks and often under discussed

Contraception planning for women who do not wish for additional pregnancy is also important as pregnancy is possible after cancer treatment

Timing:

- Typically advised to wait 2 years from time of diagnosis before attempting pregnancy
- 3 months after discontinuing tamoxifen
- 7 months after trastuzumab

Fertility

Among 130 women who attempted to become pregnant - 90 conceived (69.2%)

Live birth rate of 57.6%

Factors associated with pregnancy

- Younger age < 30 at diagnosis
- Nulliparity
- Partnered at diagnosis

Endocrine therapy was inversely associated

Original Article

Pregnancy After Breast Cancer: Results From a Prospective Cohort of Young Women With Breast Cancer

Philip D. Poorvu, MD[1]; Shari I. Gelber, MS, MSW[2]; Yue Zheng, MSc[2]; Kathryn J. Ruddy, MD, MPH[3]; Rulla M. Tamimi, ScD[4]; Jeffrey Peppercorn, MD, MPH[5]; Lidia Schapira, MD[6]; Virginia F. Borges, MD[7]; Steven E. Come, MD[8]; Matteo Lambertini, MD, PhD[9,10]; Shoshana M. Rosenberg, ScD, MPH[1,11]; and Ann H. Partridge, MD, MPH[1]

TABLE 2. Proportion of Survivors Achieving a Pregnancy (n = 108) and Associated Characteristics Among 1026 Eligible Women in the Cohort

Variable	Pregnancy Within 5 Y of Diagnosis, No. (%)	Multivariable Analysis	
		OR [95% CI]	*P*
Age at diagnosis, y			
≤30	22 (23.4)	6.63 (3.18-13.83)	<.0001
31-35	51 (20.8)	5.86 (3.37-10.17)	<.0001
36-40	35 (5.1)		
Parity at diagnosis			
0	62 (15.7)	2.66 (1.56-4.53)	.001
≥1	46 (7.3)		
Partnered at diagnosis			
Yes	87 (11.7)	4.63 (2.31-9.25)	.0002
No	16 (7.1)		
Missing	5 (8.8)		
Stage			
0	17 (19.5)	1.70 (0.78-3.71)	.17
I	34 (9.6)	Ref	
II	48 (11.2)	1.05 (0.62-1.78)	.85
III	9 (6.5)	0.41 (0.18-0.95)	.04
Oral endocrine therapy			
Yes	48 (7.1)	0.35 (0.20-0.59)	.001
No	60 (16.9)		

Abbreviations: OR, odds ratio; Ref, reference category.

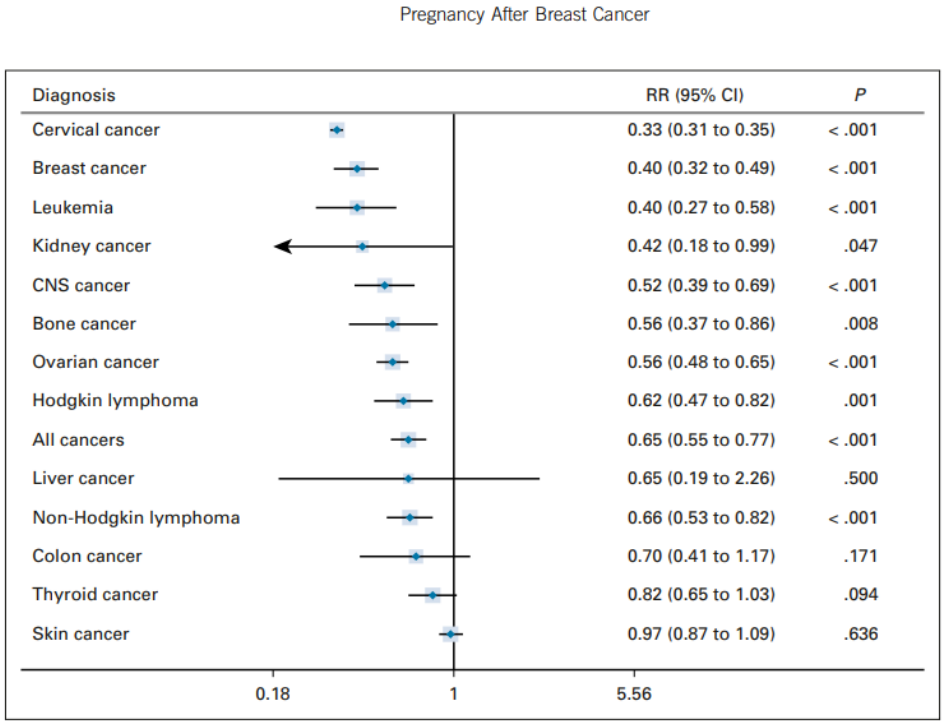
Fertility

Pregnancy After Breast Cancer: A Systematic Review and Meta-Analysis

Authors: Matteo Lambertini, MD, PhD, Eva Blondeaux, MD, Marco Bruzzone, MSc, Marta Perachino, MD, Richard A. Anderson, MD, Evandro de Azambuja, MD, PhD, Philip D. Poorvu, MD, ... SHOW ALL ... , and Fedro A. Peccatori, MD, PhD AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 39, Number 29 • https://doi-org.proxy.lib.umich.edu/10.1200/JCO.21.00535

- Breast cancer survivors have a 60% reduced likelihood of subsequent pregnancy compared to the general population
- Proper and timely referral to fertility specialists
- Strengthen oncofertility programs
- Patients should be adequately counseled prior to treatment



Psychosocial impact

2025 systematic review by Rahimi et al. found heightened levels of distress, depression and anxiety.

- Causing fetal abnormalities due to chemotherapy
- Fear of not being able to properly care for the child
- Fear of not breastfeeding
- Worry about the child's normal development
- Guilt of not being able to comfort or bond emotionally
- Confronting mortality

Intense fear of recurrence

Body image disruption

Concern for the child vs. self

Relationship challenges

Impact on motherhood

Isolation

Financial toxicity

Resources

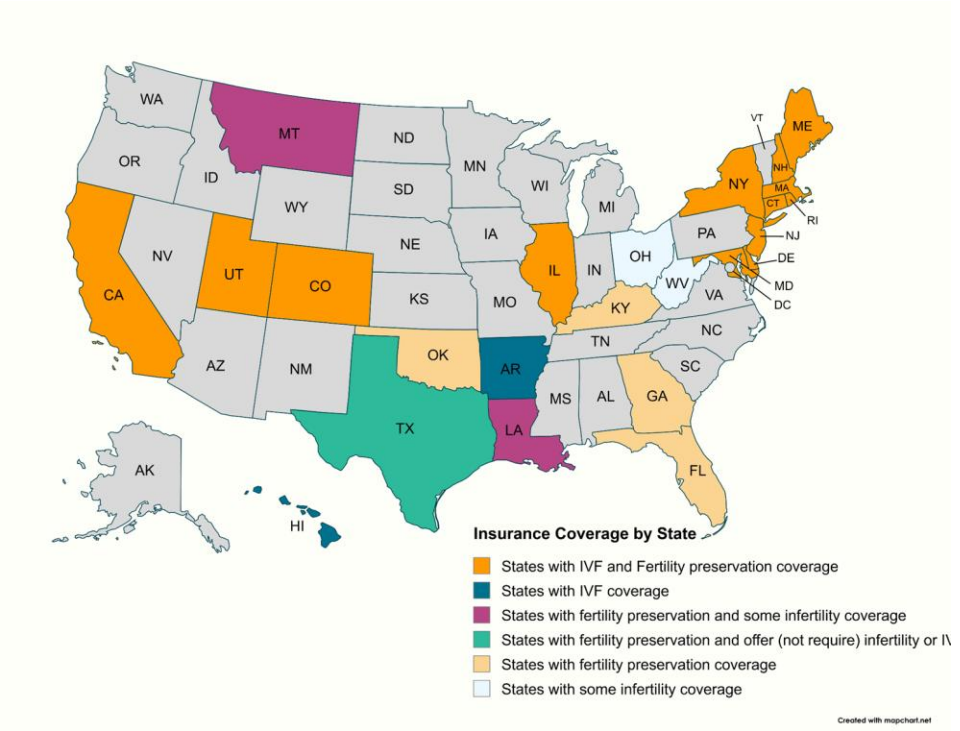
[Hope for Two - The Pregnant with Cancer Network]

[Young Survival Coalition]

[Cancer and Pregnancy Registry]

[Livestrong Fertility]

[Suman B Koman]



Lactation support

Find an IBCLC Lactation Consultant | USLCA - United States Lactation Consultant Association

Get Support from WIC | WIC Breastfeeding Support

Breastfeeding | Office on Women's Health

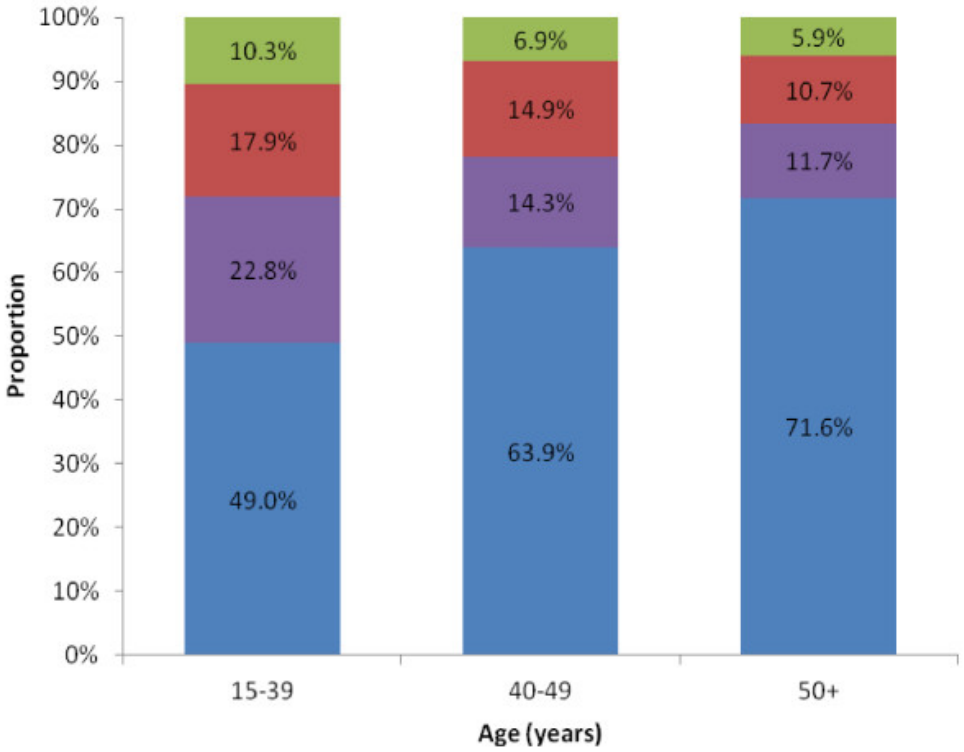
Get Breastfeeding Help - La Leche League International

Postpartum Support International - PSI

Other useful websites for reliable information or support:

- American Academy of Pediatrics – www.healthychildren.org/English/ages-stages/baby/breastfeeding/Pages/default.aspx
- KellyMom – www.kellymom.com
- New Mom Health – www.newmomhealth.com
- Academy of Breastfeeding Medicine protocols – www.bfmed.org/protocols

Breast Cancer Subtypes by Age



HER2+
ER/PR+,HER2+
TNBC
ER/PR+,HER2-

Require Chemotherapy Treatment

- even more TNBC in young African American women
- more luminal B than A, more basal type in young women

Slide adapted form Adrienne Waks, MD

Keegan et al, BCR 2012; Carey et al, JAMA 2006; Sweeney et al, Cancer Epi Bio Prev 2014

A Few Thoughts Regarding Systemic Therapy for Breast Cancer During Pregnancy

Chemotherapy Agents, particularly **Adriamycin** and **Cytoxan**, can be administered safely during the second and third trimesters.

Taxane-based chemotherapy (**Paclitaxel**) may be administered during second and third trimesters of pregnancy, but data is more limited and Taxane is often avoided if possible.

Immunotherapy (**Pembrolizumab**) cannot be administered during pregnancy.

HER2-directed therapy, such as **Trastuzumab and Pertuzumab**, cannot be administered during pregnancy.

Endocrine therapy, such as **aromatase inhibitors, tamoxifen or ovarian function suppression** cannot be administered during pregnancy.

Systemic treatment during pregnancy often deviates from standard of care, however, this does not necessarily compromise treatment outcomes.

Impact of Systemic Therapy for Breast Cancer on Future Fertility

Risk of Treatment-Related Amenorrhea

Table 4. Rates of 2-year treatment-related amenorrhea following common adjuvant chemotherapy regimens and overall by age.

Regimen	Age at diagnosis (years)			
	≤30	31–35	36–40	Overall
AC (+/−H, +/−P)	1/4 (25.0%)	1/14 (7.1%)	3/120 (2.5%)	5/138 (3.6%)
AC-T(+/−H, +/−P)	5/60 (8.3%)	19/97 (19.6%)	43/172 (25%)	67/329 (20.4%)
TC (+/−H, +/−P)	2/17 (11.8%)	2/17 (11.8%)	5/24 (20.8%)	9/58 (15.5%)
TH	0/5 (0%)	1/3 (33.3%)	2/19 (10.5%)	3/27 (11.1%)
TCH (+/−P)	0/1 (0%)	1/14 (7.1%)	3/17 (17.6%)	4/32 (12.5%)
All regimens	10/93 (10.8%)	27/160 (16.9%)	65/286 (22.7%)	102/539 (18.9%)

Slide adapted from Adrienne Waks, MD

Poorvu et al, JNCI Cancer Spectrum, 2018; Poorvu et al, NPJ Breast, 2021

The POSITIVE Trial: Can endocrine therapy safely be interrupted for pregnancy?

Premenopausal women wishing to become pregnant

Age ≤42 years at study entry

At least 18 months and no more than 30 months of prior endocrine therapy for stage I-III HR+ BC

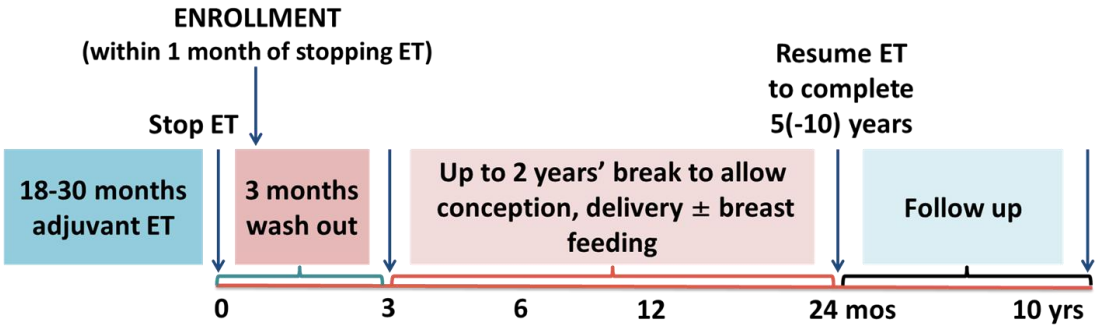
Prior chemotherapy ± fertility preservation allowed

No clinical evidence of recurrence

Partridge AH, et al. SABCS 2022. GS4-09.

The POSITIVE Trial: Treatment Approach

- Planned endocrine therapy (ET) interruption (within 1 month of trial enrollment)
- Up to 2 years to attempt pregnancy, conceive, deliver, and breastfeed, including 3-months washout period
- If no pregnancy by 1 year, fertility assessment strongly recommended
- ET resumption strongly recommended after pregnancy to complete planned 5-10 yrs
- Long-term follow-up



Slide adapted from Adrienne Waks, MD

Partridge AH, et al. SABCS 2022. GS4-09.

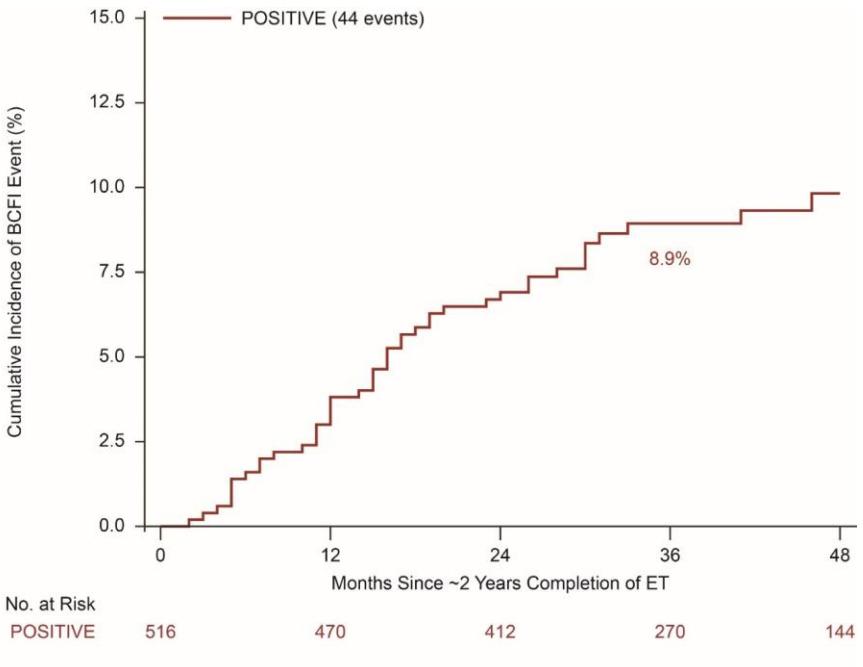
The POSITIVE Trial: Pregnancy Outcomes

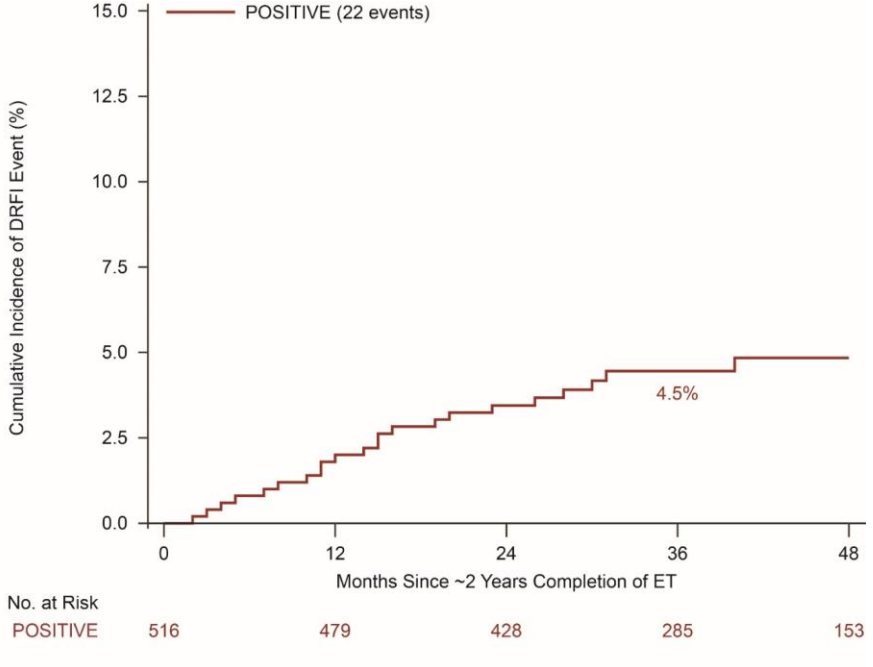
	N	% of 497	% of 368
Secondary endpoint population	497	100%	
At least one on trial pregnancy	368	**74%**	100%
At least one live birth (full-term or preterm)	317	**64%**	**86%**
At least one miscarriage	93	19%	25%
At least one elective abortion	16	3%	4%
At least one stillbirth/neonatal death	1/1	0.2% / 0.2%	0.3% / 0.3%

Note: 110 women had more than one pregnancy, and may contribute information to more than one row

Partridge AH, et al. SABCS 2022; NEJM 2023

Breast Cancer Outcomes in POSITIVE Trial

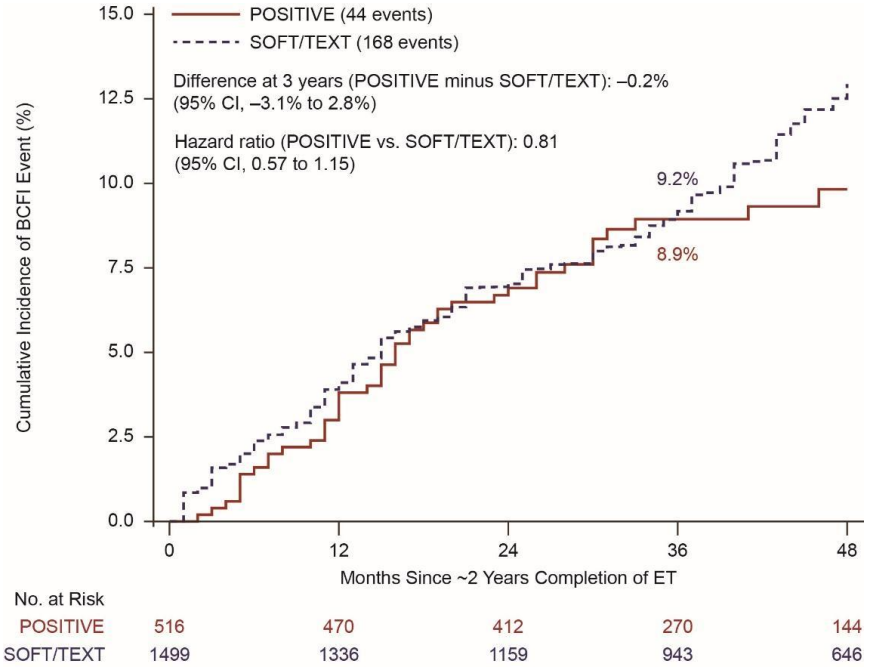


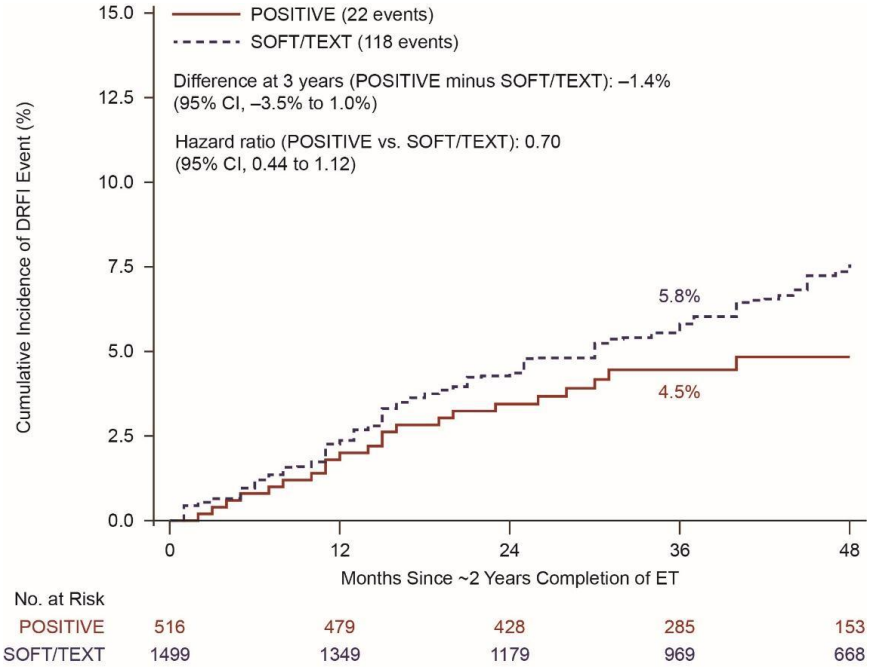


1638 patient-years of follow-up (41 months median follow-up)

Partridge AH, et al. SABCS 2022; NEJM 2023

Breast Cancer Outcomes in POSITIVE Trial Compared to SOFT/TEXT Trials

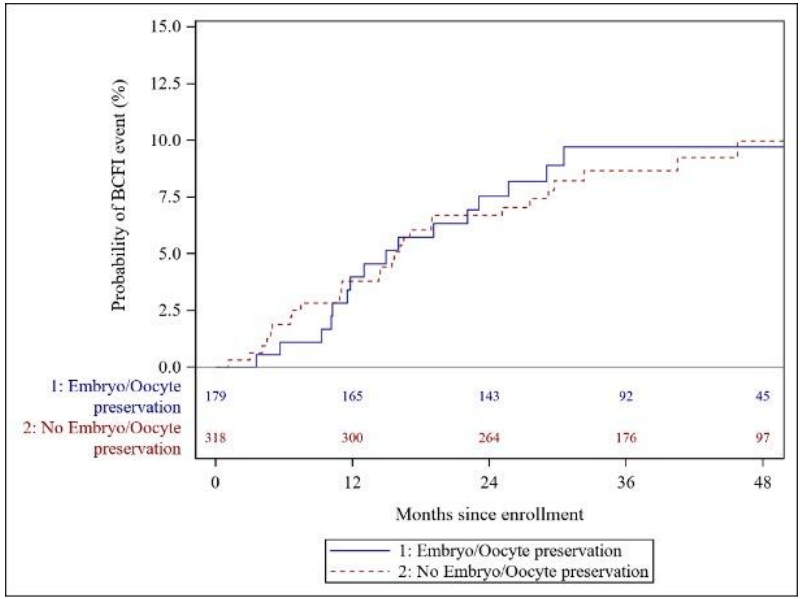




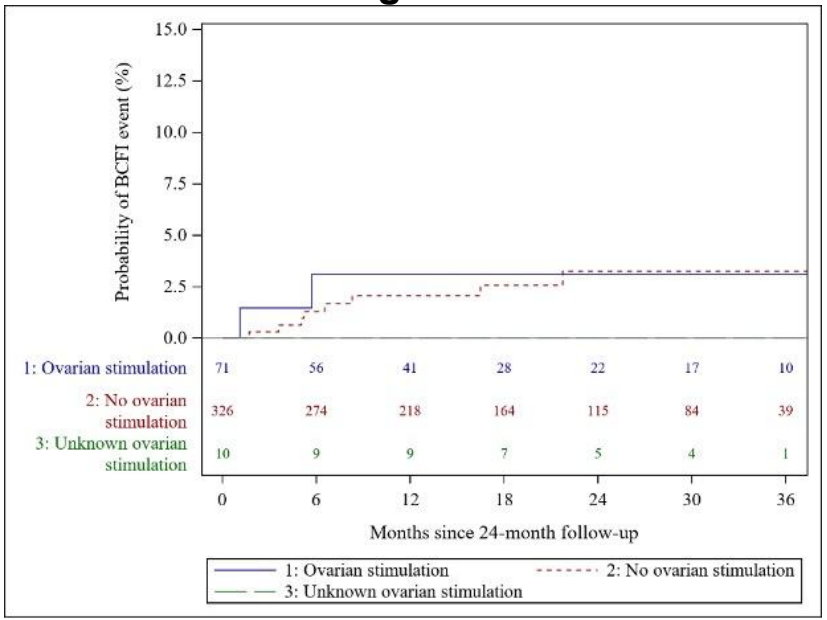
Partridge AH, et al. SABCS 2022; NEJM 2023

Ovarian stimulation is safe, does not compromise breast cancer outcome in POSITIVE Trial

Embryo/oocyte cryopreservation - at breast cancer diagnosis



As part of ART following breast cancer diagnosis



Azim, et al. SABCS 2023; JCO 2024

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