# Pregnancy post cancer treatment

**Dr Eleni Karapanagiotou**

**Guy's Cancer Centre**

# Outline:

- **Introduction – the issue**
- **The questions that may come up during the consultation**
  - Cancer patients
  - Breast cancer patients
- **Available evidence**
- **Conclusions**

# Survivorship data on cancer and fertility

- **Loss of reproductive potential after cancer treatment negatively impacts quality of life (QOL) in young survivors.**
- **Large-scale survivorship issue-according to 2006 SEER statistics-, approximately 120,000 women under age 50 develop cancer each year in the United States.**
- **As recently as 2009, only 34–72% of reproductive-age women treated for cancer recall having a discussion about the effects of cancer treatment on future fertility.**
- **Studies have shown that up to 75% of young women are interested in the opportunity to have children after a cancer diagnosis.**

**Loprinzi CL:Symptom management in premenopausal patients with breast cancer. Lancet Oncol. 2008; Tschudin S: Psychological aspects of fertility preservation in men and women affected by cancer and other life-threatening diseases. Hum Reprod Update. 2009; NCIFastStats. Statistics stratified by age. Surveillance Epidemiology and End Results(SEER). Schover LR. Patient attitudes toward fertility preservation. Pediatr Blood Cancer. 2009; 53:281–4**

# Breast cancer in the UK-survivorship

- **Breast cancer is the most common cancer in females, with a lifetime risk of one in nine in the UK**
- **the leading cause of death in women aged 35–54 years.**
- **Fifteen percent of cases are diagnosed before the age of 45 years, almost 5000 women of reproductive age in the UK annually.**
- **The prognosis of breast cancer is improving, with 5-year survival around 80% for the under 50s age group; however, the survival rate may be lower in very young women**

- **Royal College of Obstetricians and Gynaecologists- March 2011**

# Obstacles in cancer and fertility discussions

- **Health-care professionals do not ask the patient about intentions**
- **Patients do not think they can conceive after cancer treatment**
- **Lack of knowledge about the process – clinicians and patients**
- **Perceptions about disease recurrence**
- **Most patients have this discussion just before starting cancer treatment and therefore believe they have no time to pursue a fertility consultation without delaying planned treatments.**

# Pre-treatment fertility counselling and fertility preservation improve quality of life in reproductive age women with cancer

- retrospective survey study, using the California Cancer Registry
- sample reproductive age women with a history of leukaemia, Hodgkin's disease, non-Hodgkin lymphoma, breast cancer, or GI cancer
- 2532 patients aged 18-40 were contacted for participation in the study
- Post-treatment QOL was conceptualized to include satisfaction with treatment choices and satisfaction with life

Joseph M Letourneau ; Cancer. 2012

# Results and conclusions

- 1041 responded to questionnaires and 1491 did not respond
- 47–63% of respondents reported desiring to have children after treatment, with the highest rates among women with leukaemia (59%) and Hodgkin's (63%)
- Of the 918 patients who reported treatment with the potential to affect fertility, 560 (61%) were counselled about potential reproductive loss by a member of the oncology team 5% visited a fertility specialist, and 4% took action to preserve their fertility.
- Women counselled about their risk of infertility from cancer therapy by both an oncology team and a fertility specialist had significantly less regret about their decision to preserve fertility than those counselled only by an oncology team
- Receiving specialized counselling about reproductive loss and pursuing fertility preservation is associated with less regret and greater QOL for survivors, yet few patients are exposed to this potential benefit

Joseph M Letourneau ; Cancer. 2012

# The patient will ask:

- Is there an increased risk of recurrence of my cancer?
- Is there a risk for the baby?
- What are my chances of becoming  pregnant?
- When should I start trying?
- Do I need any investigations before attempting to become pregnant?
- Should I use my frozen embryos  (if has them) or try naturally?
- Should I see the ACU team?
- Will I be getting any psychological support?

# The patient with breast cancer will ask:

- When should I stop my endocrine therapy?
- How long should I try for?
- Is it safe to breast feed? (and how long?)
- When should I start back on my endocrine therapy and how long?
- Can I have more than one baby?

clinical practice guidelines

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# Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

F. A. Peccatori[1], H. A. Azim Jr[2], R. Orecchia[3], H. J. Hoekstra[4], N. Pavlidis[5], V. Kesic[6] & G. Pentheroudakis[5], on behalf of the ESMO Guidelines Working Group*

*[1]Fertility and Procreation Unit, Division of Gynaecologic Oncology, European Institute of Oncology, Milan, Italy; [2]Department of Medicine, BrEAST Data Centre, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; [3]Department of Radiotherapy, European Institute of Oncology, Milan, Italy; [4]Department of Surgical Oncology, University Medical Centre Groningen, Groningen, The Netherlands; [5]Department of Medical Oncology, University of Ioannina, Ioannina, Greece; [6]Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia;*

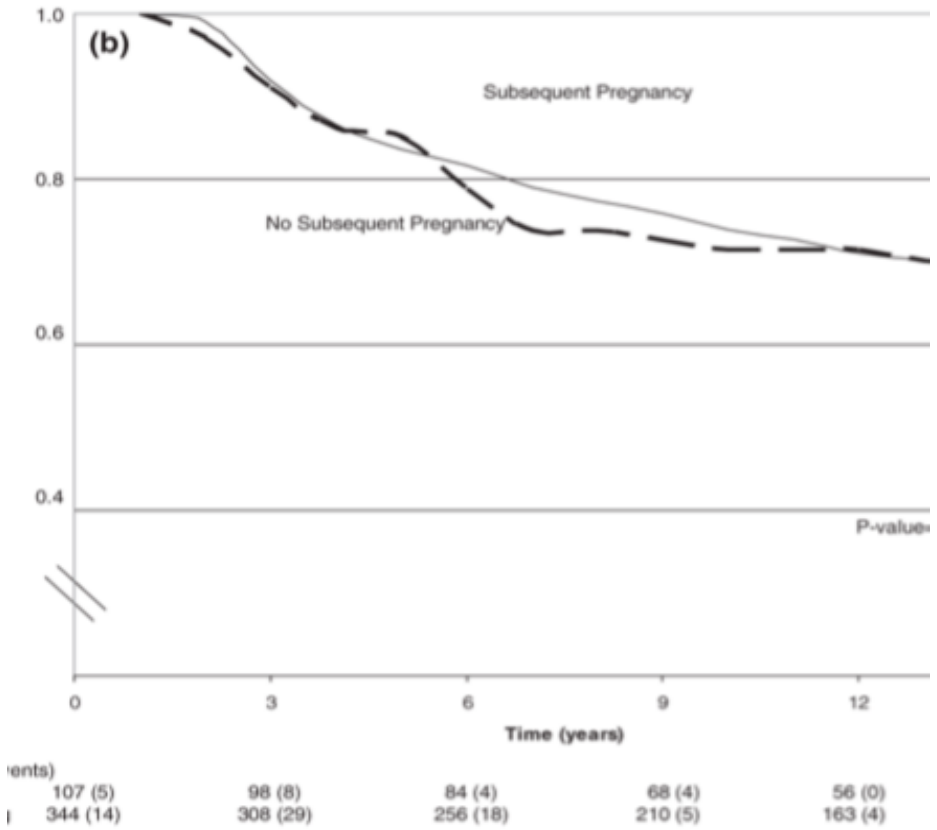
These Clinical Practice Guidelines are endorsed by the Japanese Society of Medical Oncology (JSMO)

# Pregnancy in cancer survivors: ESMO guidelines

- **Timing of pregnancy following cancer diagnosis should take into consideration the time of completion of therapy, risk of relapse, age and ovarian function of the patient.**
- **Pregnancy is not discouraged, even in women with history of an endocrine-sensitive breast cancer. Once pregnancy has occurred, induction of abortion has no impact on maternal prognosis and is strongly discouraged for such purposes.**
- **Patients considered for 5 years of ET in whom completion of the course could hinder their chances of future pregnancy it should be made clear that it is unknown whether early interruption could have detrimental effects on their breast cancer outcome. We strongly encourage the resumption of tamoxifen following delivery in these patients.**

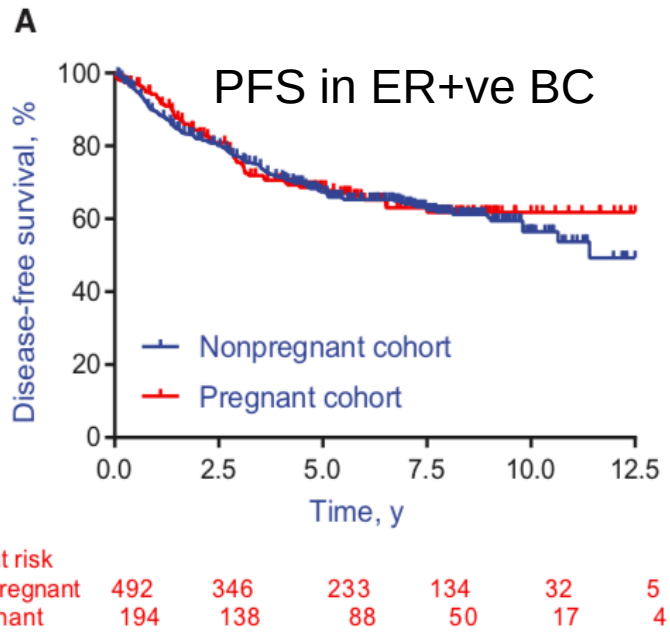
# Is there an increased risk of recurrence of my breast cancer?

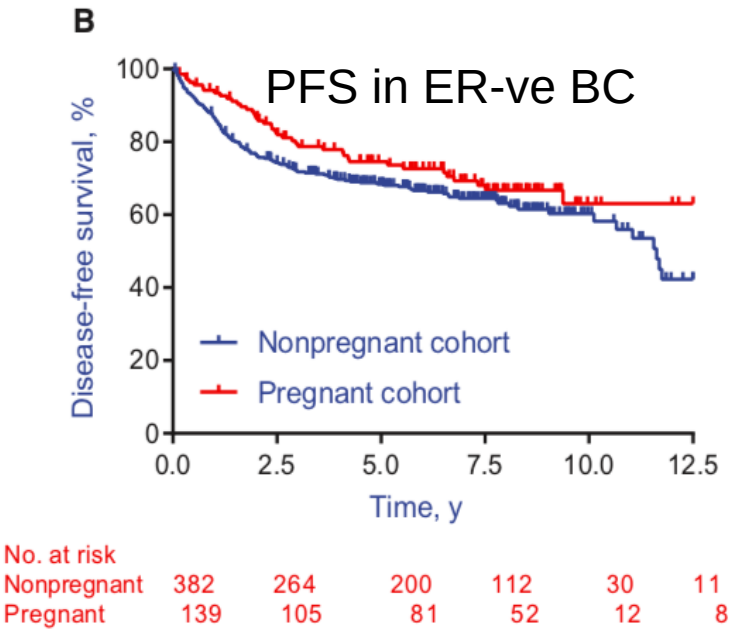
## A pregnancy following breast cancer does not have a negative impact on prognosis




Ives A: Pregnancy after breast cancer: population based study. BMJ 2007; Kroman N: Pregnancy after treatment of breast cancer—a population-based study on behalf of Danish Breast Cancer Cooperative Group. Acta Oncol 2008; Azim HA Jr: Safety of pregnancy following breast cancer diagnosis: a meta-analysis of 14 studies. Eur J Cancer 2011; MooHyun LEE: Outcomes of pregnancy after breast cancer in Korean Women; A large cohort study. Cancer Resarch and Treatment 2019

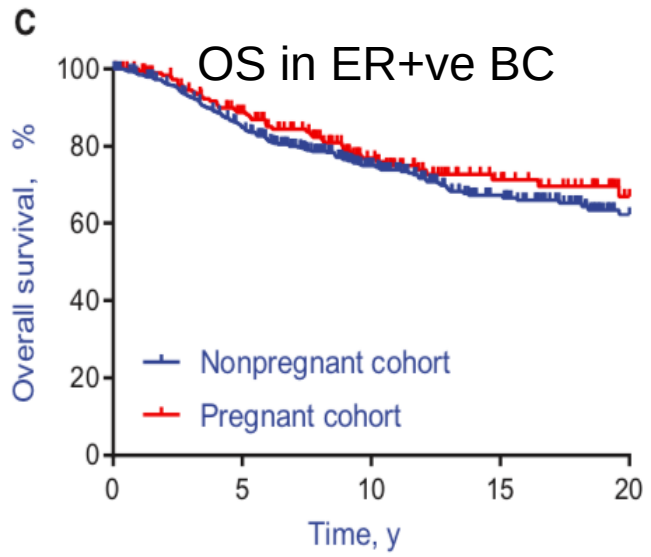
# No difference in PFS between pregnant and non-pregnant women

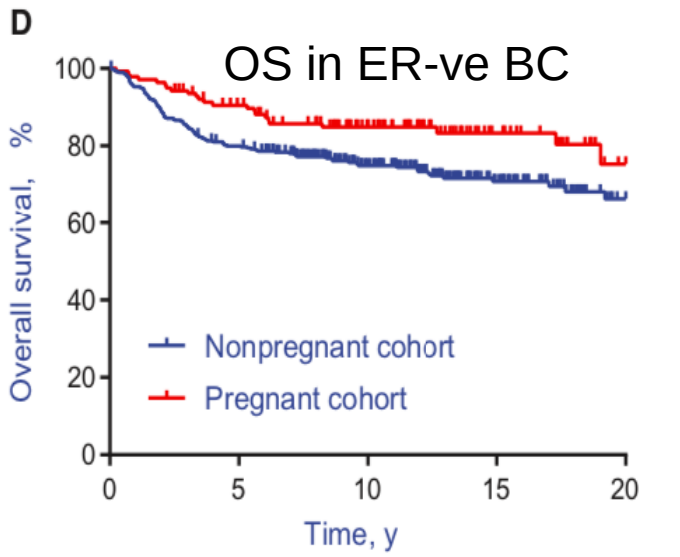



Lambertini and Azim Jr; JNCI J Natl Cancer Inst 2018

# No difference in OS between pregnant and non-pregnant women




Lambertini and Azim Jr; JNCI J Natl Cancer Inst 2018

# Is there a risk for the baby?

**Neonatal outcomes in men or women with prior history of cancer were highly comparable with those of the general population**

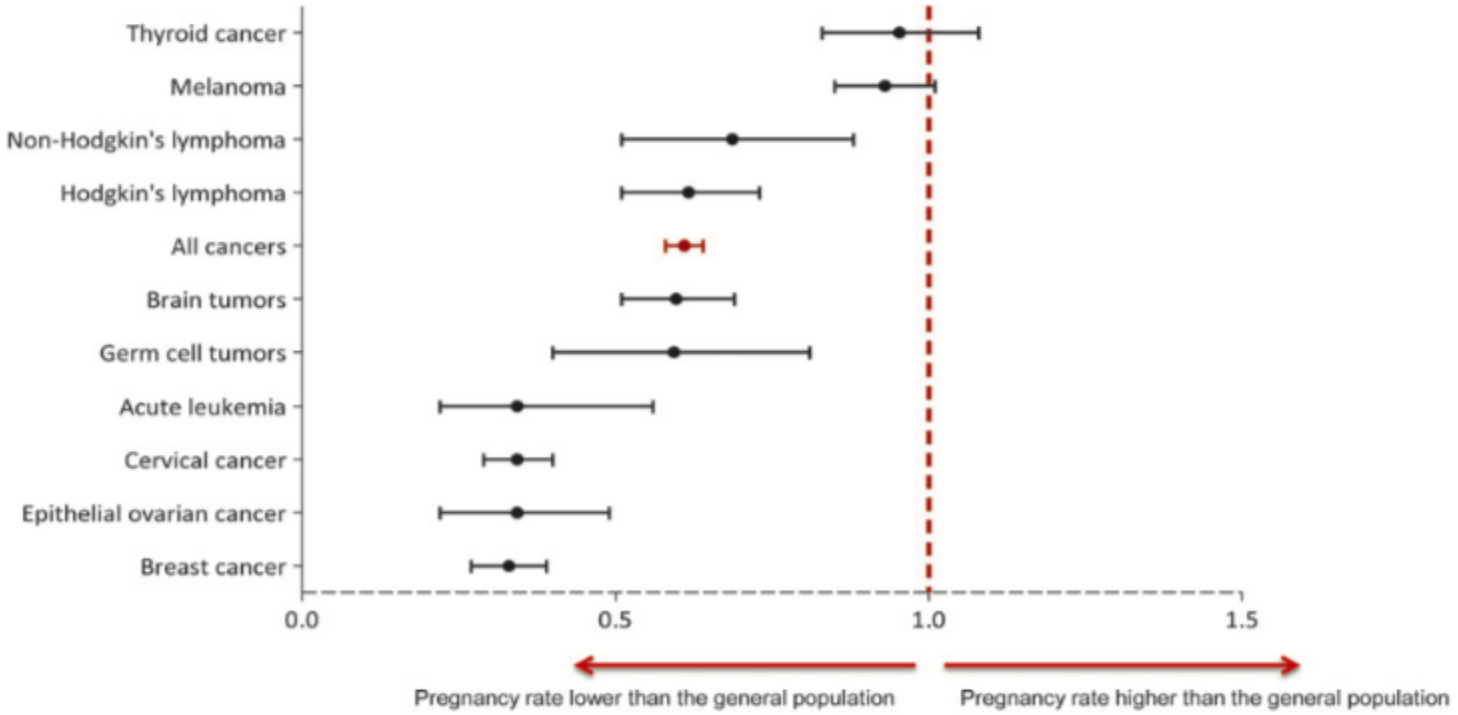
**Blatt J. Pregnancy outcome in long-term survivors of childhood cancer. Med Pediatr Oncol. 1999;33:29–33.**

# What are the chances of becoming pregnant?
# Pregnancy rates in cancer survivors

- **pregnancy rates are 40% lower among female cancer survivors compared with the general population adjusting for women's age, education level and previous parity.**
- **women diagnosed with melanoma or thyroid cancer have pregnancy rates highly comparable with the general population**
- **women diagnosed with breast cancer have the lowest chance of subsequent pregnancy, which is nearly 70% lower compared to the general population.**

**Stensheim H Pregnancy after adolescent and adult cancer: a population-based matched cohort study. Int J Cancer 2011**

# Data from a population-based study from Norway including16,105 female cancer survivors and 85,500 controls




Stensheim H  Pregnancy after adolescent and adult cancer: a population-based matched cohort study. Int J Cancer 2011

# Why breast cancer survivors have low chance of subsequent pregnancy

- **gonadotoxic chemotherapy**
- **prolonged treatment periods with tamoxifen**
- **Misconception that pregnancy could stimulate cancer recurrence**

# Planned and unplanned pregnancies in breast cancer survivors – single centre.

- **175 women completed a questionnaire**
- **42% (72/175) had completed their family, 41% (72/175) reported that they would like to have children and 4% (7/175) did not wish to have children.**
- **27 respondents had actively tried to conceive-13 (48%) had a live birth.**
- 12 unintended pregnancies; the majority of which were terminated (58% (7/12)) with only 3 live births.
- Among those who did not wish to conceive, only 32% (36/111) reported using contraception.

**Kopeika J and J Mansi: Cancer 2019**

# When should the patient start trying: Timing of subsequent pregnancy

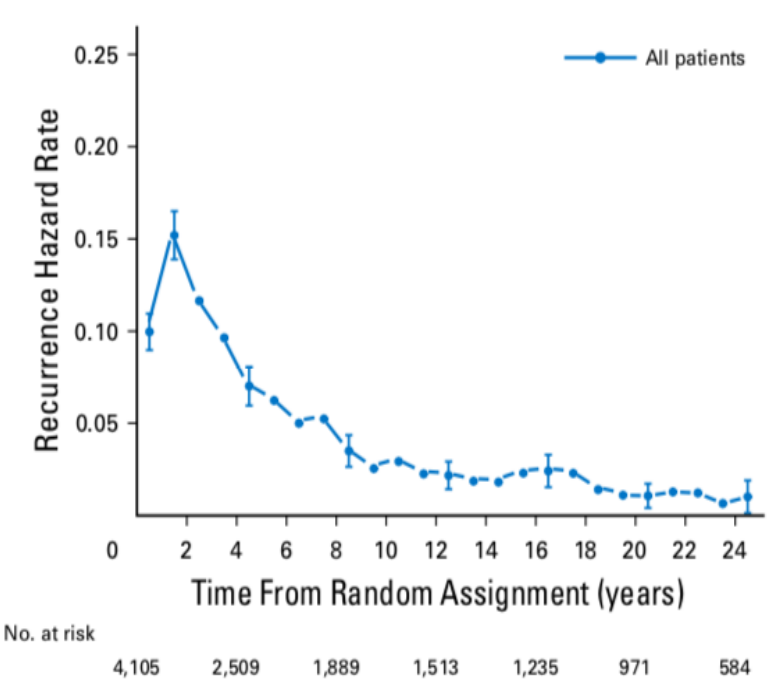
- **Very challenging question**
- **no particular time-point is considered optimal to allow patients to become pregnant following cancer diagnosis.**
- **Timing should consider:**
  - cancer type
  - time of completion of therapy
  - risk of relapse
  - age and ovarian function
- **Most research is in breast cancer**

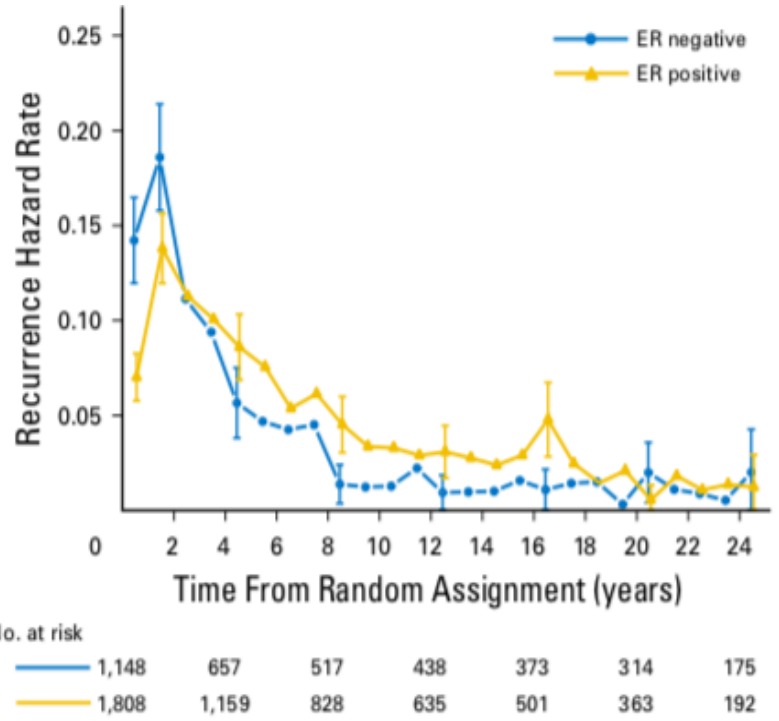
# Timing of pregnancy after breast cancer

- **2 small studies partly answer the question**
- **A small Australian study included 62 BC ladies and concluded that localised disease with good prognosis conception six months after treatment is unlikely to reduce survival**
- **An American study included 107 BC showed a small, nonsignificant adverse effect among women who conceived within 12 months of diagnosis**
- **ESMO/RCOG guidelines: in breast cancer patients, it is reasonable to postpone pregnancy for 2 years following diagnosis [IV, C] to allow resumption of adequate ovarian function, and to overcome the time frame associated with a relatively high risk of recurrence.**

**Ives A,:Pregnancy after breast cancer: Population based study. BMJ. 2007; Kranick JA:. Is pregnancy after breast cancer safe? Breast J. 2010 Kranick JA: Is pregnancy after breast cancer safe? Breast J. 2010**

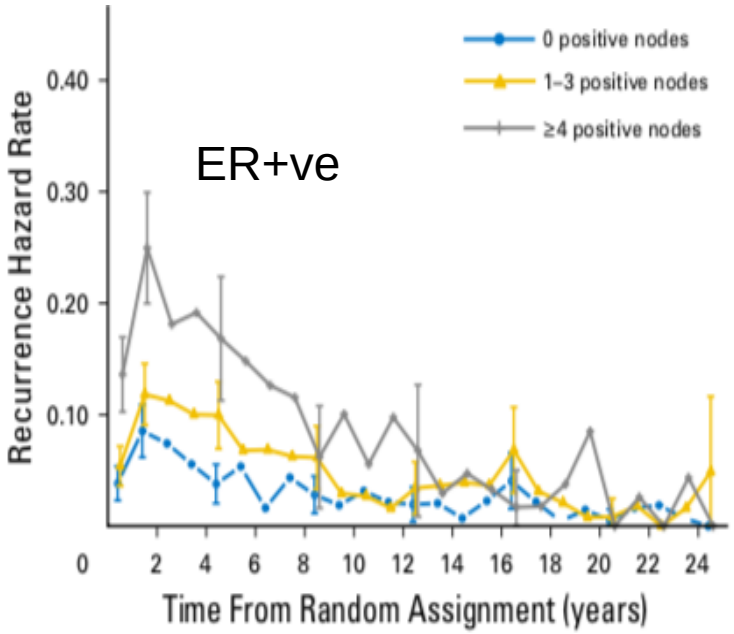
# Recurrence rates in breast cancer

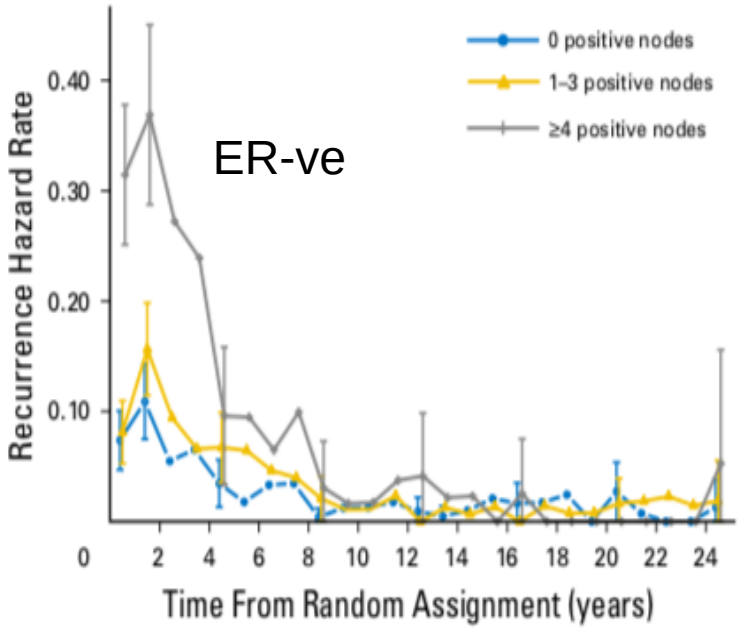



Colleoni M and Goldhirsch A: Annual Hazard Rates of Recurrence for Breast Cancer During 24 Years of Follow-Up: Results From the International Breast Cancer Study Group Trials I to V, JCO 2016

# Recurrence rates according to LNs involved

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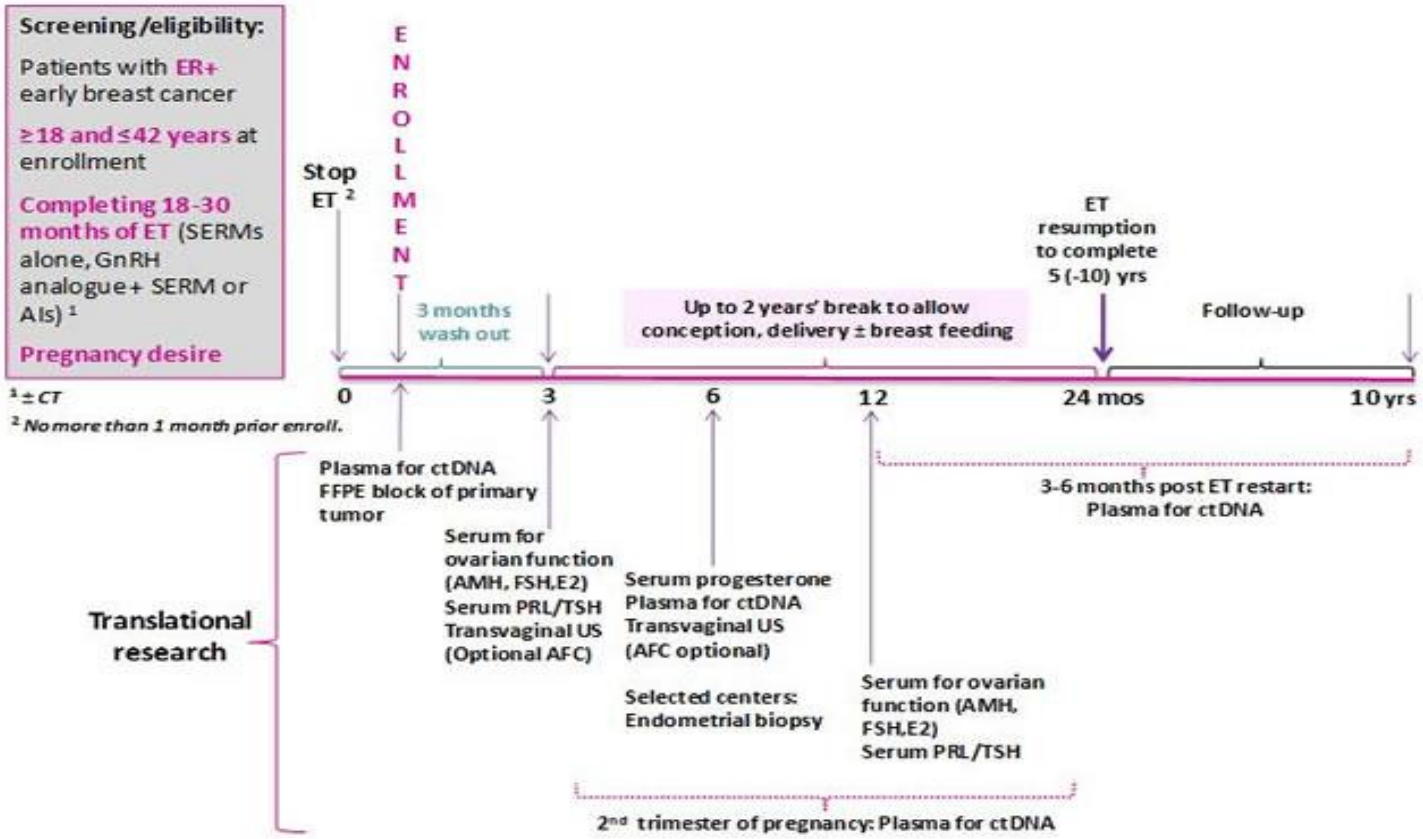
# IBCSG 48-14 POSITIVE: aim

- **To assess the risk of BC relapse associated with temporary interruption of ET to permit pregnancy and to evaluate pregnancy success and offspring outcome.**
- **A true risk of BC recurrence of 2% per year is assumed for patients who do not interrupt ET.**
- **500 participants**
- **Study start date DEC 2014-estimated primary completion date June 2020- estimated completion date Dec 2026**

# IBCSG 48-14 POSITIVE: design



# Do I need any investigations before attempting to become pregnant?

- **No clear recommendations in either ESMO/ASCO-NCCN/RCOG guidelines**
- **Standard breast cancer surveillance procedures**
- **At GSTT we request CT staging and bone scan before women try to conceive (based on previous experience of recurrence occurring during pregnancy in patients with a past history of breast cancer)**

# When to stop endocrine therapy before conceiving?

**TAMOXIFEN**

- **high frequency of severe congenital abnormalities**
- **The half-life of tamoxifen and its metabolites is long**
- **washout period of 3 months before conceiving**

Braems G: Use of Tamoxifen Before and During Pregnancy; The Oncologist 2011

# Is it safe to breastfeed?

**Table 1.** Characteristics of pregnancies among patients in the pregnant cohort (n = 333)

| Characteristics | All patients (n = 333) No. (%) | ER-positive patients (n = 194) No. (%) | ER-negative patients (n = 139) No. (%) | P* |
|---|---|---|---|---|
| Breastfeeding status§ | | | | |
| Yes | 25 (13.3) | 21 (19.1) | 4 (5.1) | .05 |
| No | 39 (20.7) | 23 (20.9) | 16 (20.5) | |
| Unknown | 124 (66.0) | 66 (60.0) | 58 (74.4) | |

- **As compared with matched women from the nonpregnant cohort, no difference in DFS was observed in patients who breastfed their newborns or in those who did not**
- **No data on duration of breastfeeding-discussion with the involved parties**

Lambertini and Azim Jr; JNCI J Natl Cancer Inst 2018

# How long should I breastfeed

- **Depends on the type of cancer and risk**
- **The American Academy of Paediatrics consider breastfeeding absolutely possible and safe as long as patients are not on chemotherapy, biological agents, ET**
- **The American Academy of Paediatrics has issued guidelines on most chemotherapeutic agents and biological agents**

# How long should an ER+ve BC survivor to be on adjuvant ET?

- **ESMO guidelines: strongly encourage the resumption of tamoxifen following delivery in ER+ve BC survivors**
- **POSITIVE study allows 2 year interruption of ET and resume of ET until subject completes 5-10 years of ET as required**
- **Several studies on adjuvant ET in BC show established benefit with a total of 5-10 years depending on the risk factors of BC.**

# Recommendations

- **Best to discuss fertility issues at time of diagnosis**
- **After treatment, ensure cancer survivor is aware that can explore pregnancy**
- **Link with ACU if possible to discuss likelihood of conception**
- **Data clear in breast cancer survivors:**
  - safe pending on timing
  - may need ACU support
  - can interrupt endocrine therapy provided they resume after
  - can breast feed

# Recommendations: additional comments.

- **All oncologic health care providers should be prepared to discuss infertility as a potential risk of therapy. This discussion should take place as soon as possible once a cancer diagnosis is made**
- **Encourage patients to participate in registries and clinical studies, as available, to define further the safety and efficacy of these interventions and strategies.**
- **Refer patients to psychosocial providers when they are distressed about potential infertility**

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| Levels of evidence | |
|---|---|
| I | Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity |
| II | Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity |
| III | Prospective cohort studies |
| IV | Retrospective cohort studies or case–control studies |
| V | Studies without control group, case reports, experts opinions |

| Grades of recommendation | |
|---|---|
| A | Strong evidence for efficacy with a substantial clinical benefit, strongly recommended |
| B | Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended |
| C | Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, …), optional |
| D | Moderate evidence against efficacy or for adverse outcome, generally not recommended |
| E | Strong evidence against efficacy or for adverse outcome, never recommended |