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# FERTILITY PRESERVATION IN BREAST CANCER PATIENTS: FOLLICULAR BIOMARKERS IN LETROZOLE ASSOCIATED OVARIAN HYPERSTIMULATION

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LABORATOIRE DE RECHERCHE EN REPRODUCTION HUMAINE

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## DISCLOSURE

- No conflict of interest

2

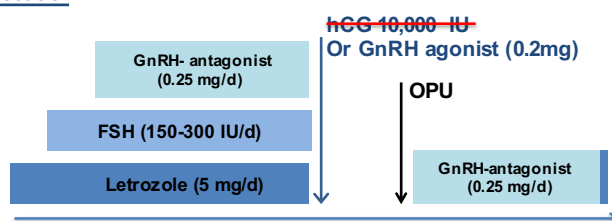
## BACKGROUND

- Breast cancer (BC) outcomes have greatly improved over the last decades, thanks to adjuvant therapies
- Chemotherapy and endocrine therapy may lead to infertility/POF
- Oocyte and/or embryo cryopreservation are one of the available options for fertility preservation
- Let-COH reproductive outcomes in breast cancer patients:
  - 40 FET → 45% LBR
  - 56 FET → 32.3% LBR

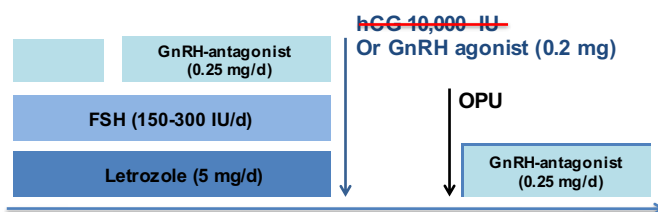
Oktay et al. 2015  
Pereira et al. 2016

## LETROZOLE ASSOCIATED COH PROTOCOLS


### Standard protocol



### Random start protocol



Goldrat et al. Human Reproduction 2015  
Cakmak et al. 2013

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### OBJECTIVES AND METHODS

**Objectives:**

- **Primary endpoint:** Oocyte maturation rate
- **Secondary endpoints** (follicular biomarkers related to oocyte quality)
  - Follicular Fluid (FF) steroid levels
  - Cumulus cell gene expression

<p style="text-align: center;"><b>Study group (Let-COH)</b></p> <ul style="list-style-type: none"> <li>• Breast cancer (ER pos/ER neg)</li> <li>• Age 18 - 41 years</li> <li>• Non metastatic disease</li> </ul> <p style="text-align: center;"><i>Exclusion criteria:</i></p> <ul style="list-style-type: none"> <li>• Basal FSH <math>\geq</math> 20IU/L</li> </ul>	<p style="text-align: center;"><b>Control group (Let-COH)</b></p> <ul style="list-style-type: none"> <li>• Male/ tubal/ idiopathic Infertility</li> <li>• Age 18 - 41 years</li> <li>• 1<sup>st</sup> or 2<sup>nd</sup> ICSI cycle</li> </ul> <p style="text-align: center;"><i>Exclusion criteria:</i></p> <ul style="list-style-type: none"> <li>• AMH &lt; 0.5 or &gt; 6.5 ng/ml</li> <li>• Severe endometriosis</li> </ul>
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- All patients were stimulated in an antagonist cycle (rFSH or HMG)
- Follicular biomarkers/ rFSH cycles analyzed
- Analysis according to ovulation trigger


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### objectives and methods

**Let-COH  
BC patients**

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**Control  
Infertile patients**



**Oocyte quality markers:**

- **HAS2**
- **PTGS2**
- **GREM1**

↔

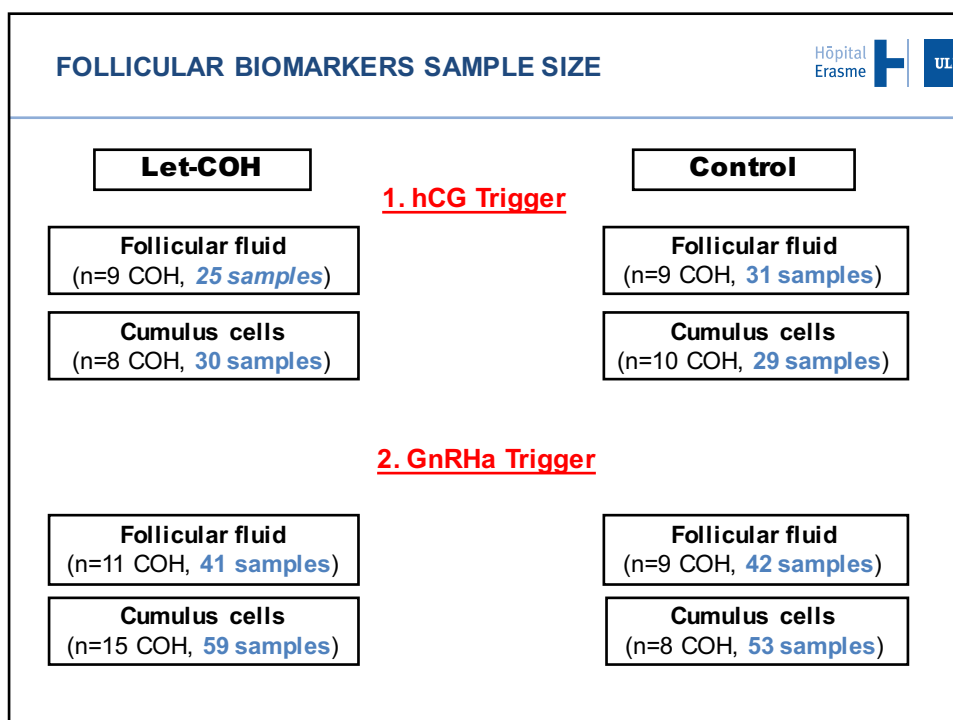
**Follicular steroid levels**

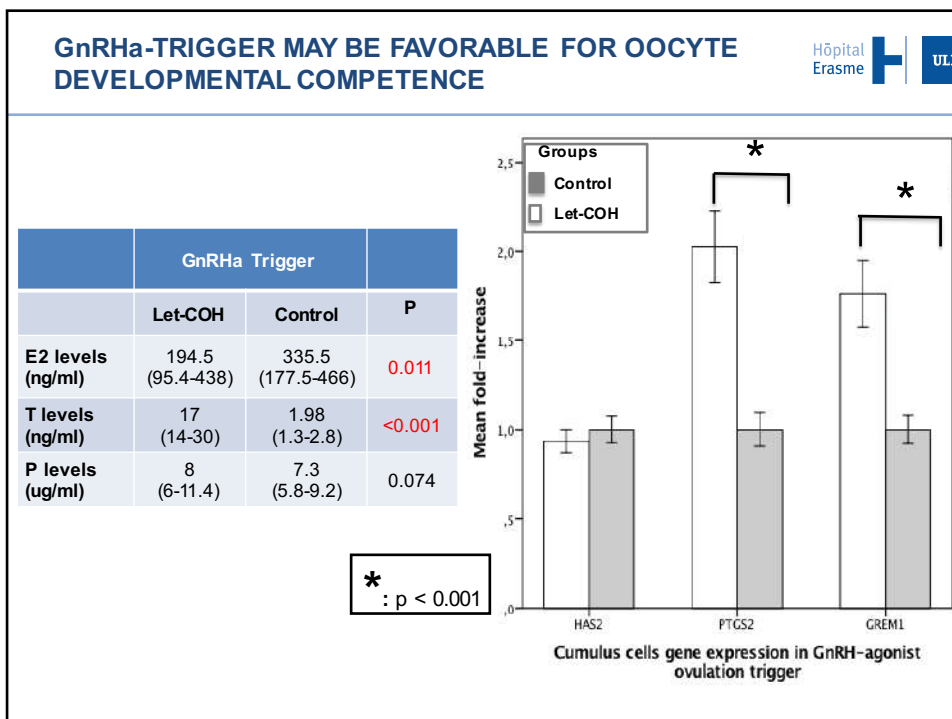
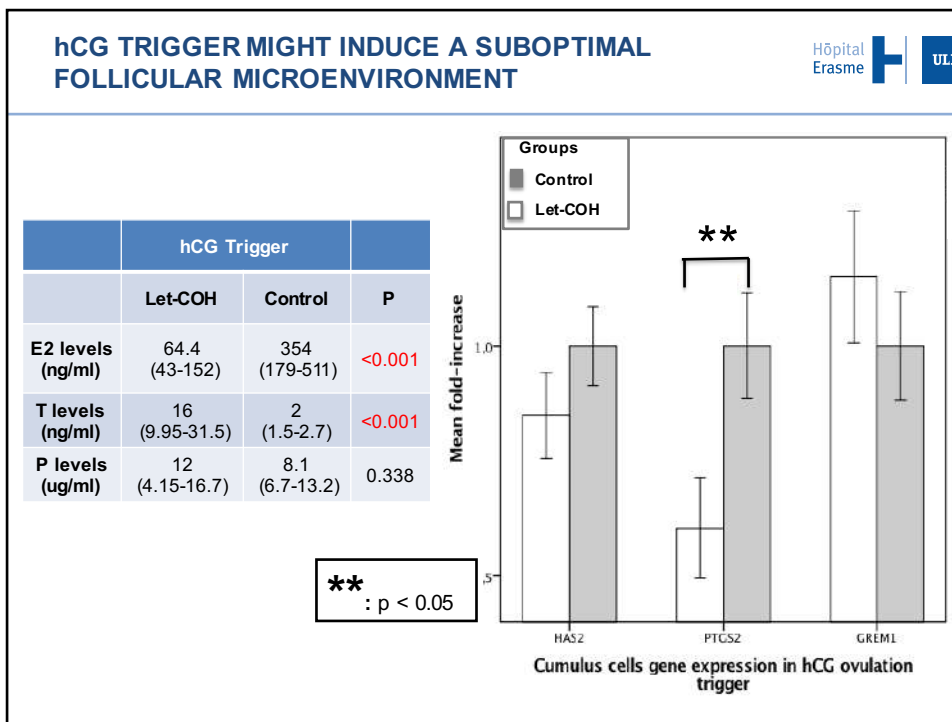
- **Estradiol**
- **Testosterone**
- **Progesterone**

McKenzie et al. 2004; Cillo et al. 2007; Anderson et al. 2009; Gebhardt et al. 2011; Barberi et al. 2012

MATURATION RATES ARE COMPARABLE BETWEEN BREAST CANCER AND INFERTILE PATIENTS						
hCG TRIGGER		P	GnRHa TRIGGER		P	
Let-COH	Control		Let-COH	Control		
<b>Patients (n)</b>	21	38	29	32		
<b>Age</b>	33 (27-35)	32.5 (28-34)	0.947	32.5 (29-35)	32 (30.34.7)	0.710
<b>BMI (kg/m<sup>2</sup>)</b>	21.7 (19.7-23.4)	21.8 (20.4-28.8)	0.166	22 (19.4-26.6)	22.3 (19.8-23.8)	0.894
<b>AMH (ng/ml)</b>	1 (0.54-4.3)	2.3 (1.3-3.2)	0.115	2.2 (1.4-4)	4 (2.9-5.9)	0.003
<b>Gn doses (IU)</b>	1812 (947-2700)	1568 (1350-2006)	0.363	2400 (1912-3600)	1350 (1200-1518)	<0.001
<b>E2 level at trigger (pg/ml)</b>	174 (84-454)	465 (998-2004)	<0.001	317 (168-469)	2387 (1864-2826)	<0.001
<b>Oocytes retrieved (n)</b>	6.5 (3-9.7)	6 (5-9)	0.541	8 (4.5-14)	11 (8.2-15.7)	0.042
<b>Mature oocytes (n)</b>	5 (2-7.7)	5 (4-8)	0.433	6 (3-11)	8.5 (5-14.5)	0.037
<b>Maturation rate (%)</b>	82.9 (67.3-100)	85.7 (75-100)	0.521	85.7 (66.6-100)	89.1 (75.4-98.6)	0.816

7





**CONCLUSIONS**

Let-COH is an effective fertility preservation procedure for breast cancer patients

- **Oocyte maturation rates are comparable to healthy infertile women**
- **GnRHa trigger appears to improve follicular microenvironment surrounding the mature oocyte**

11

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