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Prospective assesment of the follicular growth and the oocyte cohort after controlled ovarian hyperstimulation (COH) for fertility preservation in 90 young cancer patients versus 180 matched controls

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Oocyte freezing for fertility preservation

Mature oocyte freezing :

- **No longer experimental and Standard technique for FP**
    ASRM Practice Committee, Fertil. Steril. 2013
    ASCO Practice Committee, JCO 2013
- **Similar results / fresh oocytes**
- **Safe**

Ovarian response and oocyte quality in cancer patients:
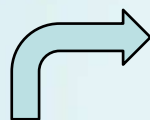
- **Little data**
- **Challenging question +++**

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COH outcomes in cancer patients

- - Few comparative studies
- - All retrospective
- - Historical control group
- - Various stimulation protocols

⟹ Conflicting results

Less mature oocyte Meta II despite same number of total oocytes

Friedler et Al. 2012 (meta-analysis); Domingo et Al. 2012; Garcia-Velasco et Al. 2013

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Aim of the study

(1) To investigate the pattern of the ovarian response under COH in cancer patients

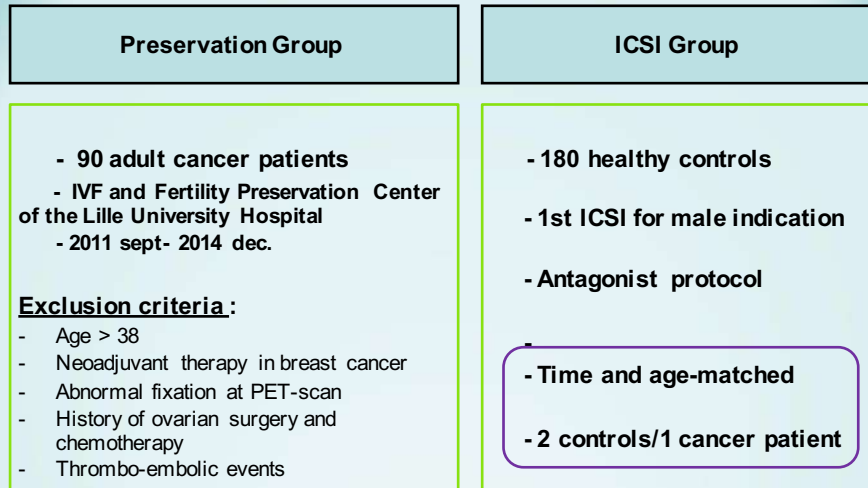(2) To analyze the quality of the oocyte cohort in terms of oocyte number and maturity

Prospective comparative study

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Materials and Methods (1): Patients
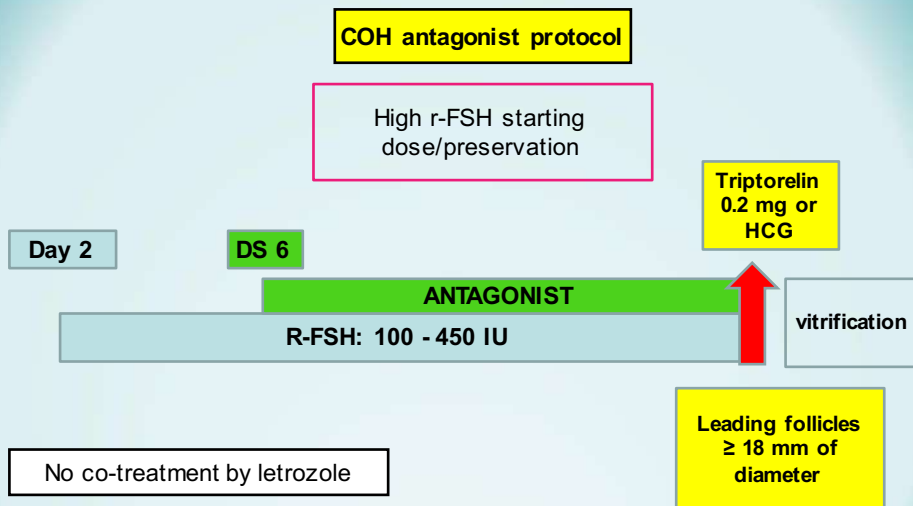
Preservation Group	ICSI Group
- 90 adult cancer patients - IVF and Fertility Preservation Center of the Lille University Hospital - 2011 sept- 2014 dec. **Exclusion criteria :** - Age > 38 - Neoadjuvant therapy in breast cancer - Abnormal fixation at PET-scan - History of ovarian surgery and chemotherapy - Thrombo-embolic events	- 180 healthy controls - 1st ICSI for male indication - Antagonist protocol - Time and age-matched - 2 controls/1 cancer patient

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Materials and Methods (2): protocol

COH antagonist protocol

High r-FSH starting dose/preservation

Triptorelin 0.2 mg or HCG

Day 2   DS 6

ANTAGONIST

R-FSH: 100 - 450 IU

vitrification

Leading follicles ≥ 18 mm of diameter

No co-treatment by letrozole

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3

Results: Indications Preservation Group

Pie chart showing:
- Breast cancer; 54%
- Haematological malignancies; 28%
- Solid tumors; 18%
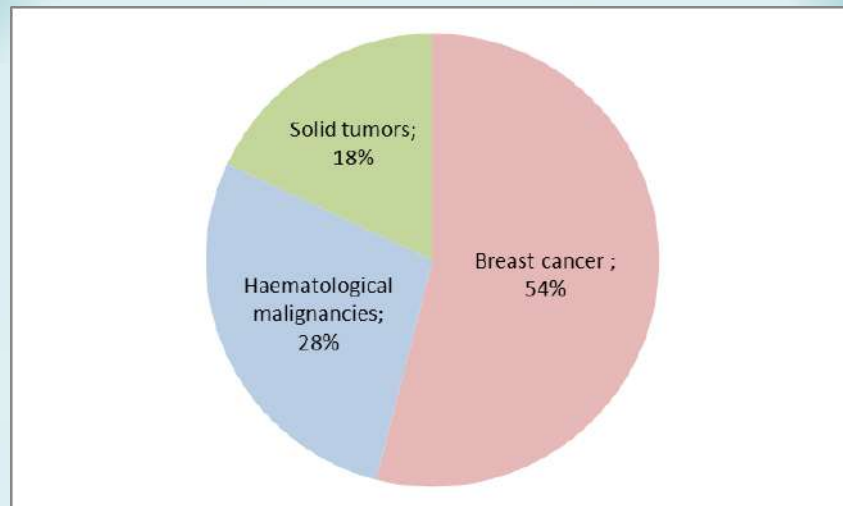
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Results (1) : COH outcomes

TABLE 1			
Population characteristics and COH outcomes (mean ± SD)			
	Cancer patients (n=90)	**Controls** (n=180)	p-value (<0.05)
Age	29 ± 5	29 ± 5	NS
BMI	23.1 ± 4.3	23.9 ± 4.3	NS
AMH (pmol/L.)	34.5 ± 42.2	44 ± 26.1	**<0.05**
Total AFC	23.9 ± 17.5	33.6 ± 16.6	**<0.0001**
Oral contraceptive pill	50%	0%	
r-FSH starting dose (IU)	303.2 ± 93.5	183.6 ± 95.2	<0.0001
r-FSH cumulative dose (IU)	3260 ± 1258	2026 ± 1111	<0.0001
Duration of COH (days)	**10.5 ± 1.7**	**11 ± 1.7**	**NS**
E2 levels at triggering day (pg/mL)	**1618** ± 1336	**2056** ± 915.2	**<0.001**
Number of follicles 11-14 mm	5.3 ± 4.8	5 ± 3.6	NS
Number of follicles ≥ 15 mm	**9.2 ± 6.2**	**9.3 ± 4.4**	**NS**

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Results (2): Oocyte cohort

| TABLE 2			
Oocyte cohort (mean ± SD)			
	Cancer patients (n=90)	Controls (n=180)	p-value
Total oocytes	**11.1 ± 7.8**	**11.1 ± 5**	**NS**
Number of mature MII oocytes	**6.2 ± 4.7**	**8.8 ± 4.2**	**<0.0001**
Number of immature oocytes (MI + GV)	1.2 ± 1.4	1 ± 1.2	NS
Number of atretic oocytes	**32%**	**11%**	**<0.001**
Number of MII oocytes/ total oocytes	**56%**	**78%**	**<0.0001**
Number of MII oocytes/ follicles ≥ 15 mm	75%	100%	<0.0001
< 8 Metaphase II oocytes obtained	63%	42%	<0.001
Low ovarian response i.e. ≤ 4 total oocytes	23.3%	7.8 %	<0.001

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Results (3)

➡ **Comparison Breast cancer vs Haematological malignancies**

NO DIFFERENCE except

Younger age
↑ **Duration of COH (11 vs 10 days)**

Haematological malignancies
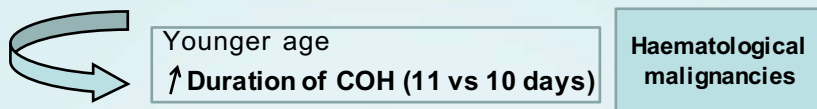
➡ **Multivariate analysis**

BMI, age, r-FSH doses, E2, cancer } **Maturation rate**

Cancer disease was the most significant

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What do we learn?

- The results of this prospective study confirm those of the retrospective previous reports

- Lower number MII oocytes in cancer group and
- High atretic oocyte rate :
  - Fragility, defect of maturation?
  - Impairment of the oocyte-follicle dialog due to the cancer disease?

- Influence of the triggering mode?

- Efficiency of the preservation procedure?

OOCYTE ACCUMULATION or COMBINATION OF DIFFERENT FERTILITY PRESERVATION TECHNIQUES

Thank you for your attention

What do we learn ?

same pattern of the follicular growth in both groups
despite **higher FSH dose and lower AMH levels in cancergroup**

We retrieved same number of total oocytes in both groups
Less meta ll oocytes

Despite Higher rate of atretic oocytes

- **Fragility, defect of maturation? Influence of the mode of triggering?**
- **impairment of the oocyte-follicle dialog due to alteration**
- **of the follicular microenvirenment?**

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Conclusion

➡ **Cancer may adversely affect the quality of the follicle-oocyte dialog.**

...... inflammation / apoptotic processes ?
...... hormonal modifications ?
...... DNA , chromosomic damages ?

➡ **Further studies are needed in order to define the real potential quality of these oocytes after reutilization**

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Results (4): Breast cancer vs Haematological malignancies

TABLE 4			
Population characteristics and COH outcomes in breast cancer versus hematological malignancies (mean ± SD)			
	Breast Cancer (n=49)	Hematological malignancies (n=25)	p-value 95% CI
Age	**30.8 ± 3.3**	**26 ± 6.5**	**<0.01**
AMH (pmol/L.)	34,2 ± 37,4	22,4 ± 12,4	NS
R-FSH starting dose (UI)	293,6 ± 97,6	321 ± 62	NS
R-FSH cumulative dose (UI)	**3101 ± 1307**	**3692 ± 1024**	**<0.05**
Duration of COH (days)	**10.3 ± 1,5**	**11.3 ± 2**	**<0.05**
Estradiol level E2 at triggering day (pg/mL)	1752 ± 1432	1313 ± 822,6	NS
Number of follicles ≥15 mm	8,7 ± 4.4	8,2 ± 4.9	NS
Total oocytes	11,1 ± 6.9	11 ± 7,6	NS
Number of mature MII oocytes	6,2 ± 4,5	7 ± 5.3	NS
Low ovarian response : ≤ 4 total oocytes	22.4% (11)	20% (5)	NS

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Multivariate analysis

TABLE 3 – Effect of cancer on maturation rate in multivariate analysis			
	β	95% IC	p-value
Cancer (yes Versus no)	-18.65	-24.99 to -12.31	<0.0001
Age*	2.74	0.24 to 5.23	0.032
BMI*	-1.87	-4.36 to 0.63	0.14
AMH*	-3.30	-6.66 to 0.07	0.055
Duration of stimulation*	2.49	-0.26 to 5.24	0.076
E2 peak at triggering*	0.08	-2.67 to 2.83	0.95
Total dose of r-FSH*	-2.91	-6.77 to 0.94	0.14

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