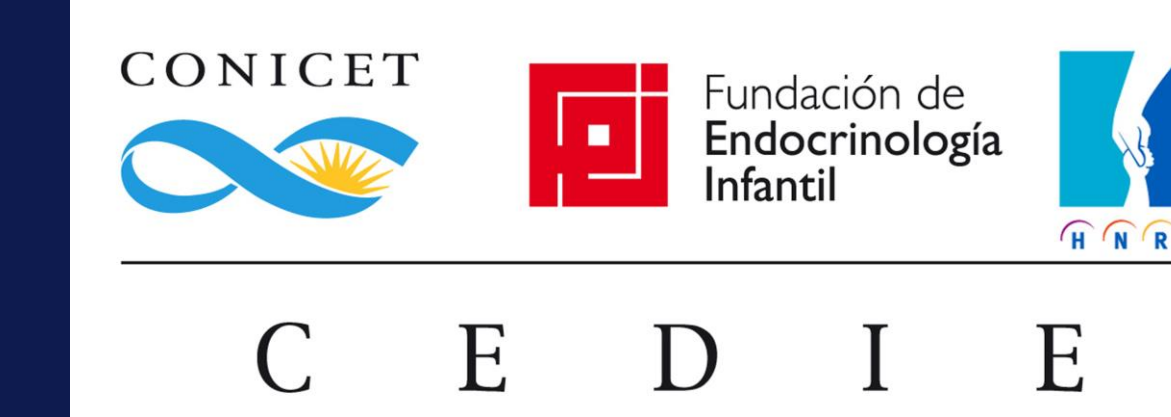


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## INTRODUCTION

Improvements in the treatment of acute lymphoblastic leukaemia (ALL) and non-Hodgkin lymphoma (NHL) have increased survival, with the consequent concern about the long-term effects that childhood chemotherapy may have on ovarian function. AMH is an indirect, reliable biomarker of the ovarian reserve, useful for the assessment of cancer therapy-related ovarian damage.

## AIM

To evaluate small ovarian follicle status in girls and adolescents with haematologic malignancies during and after treatment (Post Tx)

## METHOD

A prospective longitudinal cohort study including girls < 18 years-old with ALL or NHL (2013-2016).

**Hormonal evaluation:** baseline, every 3 months during chemotherapy, and annually up to 3 years after end of chemotherapy.

### Main outcome measure:

-Serum AMH level (EIA Immunotech-Beckman-Coulter)

### Secondary outcome measures:

-Serum FSH (IFMA)

Results were analysed according to age or pubertal stage and expressed as medians (range) or percentage, as appropriate

## RESULTS

**Table 1. Characteristics of included patients**

N= 23	
Median age at diagnosis, yr	7.3 (1-15.7)
Median total follow-up, yr	4.7 (3-5.1)
Median follow-up after treatment completion, yr	2.8 (2.5-3.1)
Pubertal, n (%)	8 (34.8)
Pre-Pubertal, n (%)	15 (65.2)

**Table 2. Immunophenotype of included patients**

Immunophenotype	n	%
<b>Acute lymphoblastic leukaemia</b>	19	82.6
Common ALL	16	84.2
Pro-B ALL	1	10
Pre-B ALL	2	15
<b>Non-Hodgkin lymphoma</b>	4	17.4

ALL Risk Stratification	n	%
Standard risk	3	15.8
Medium risk	10	52.6
High risk	6	31.6

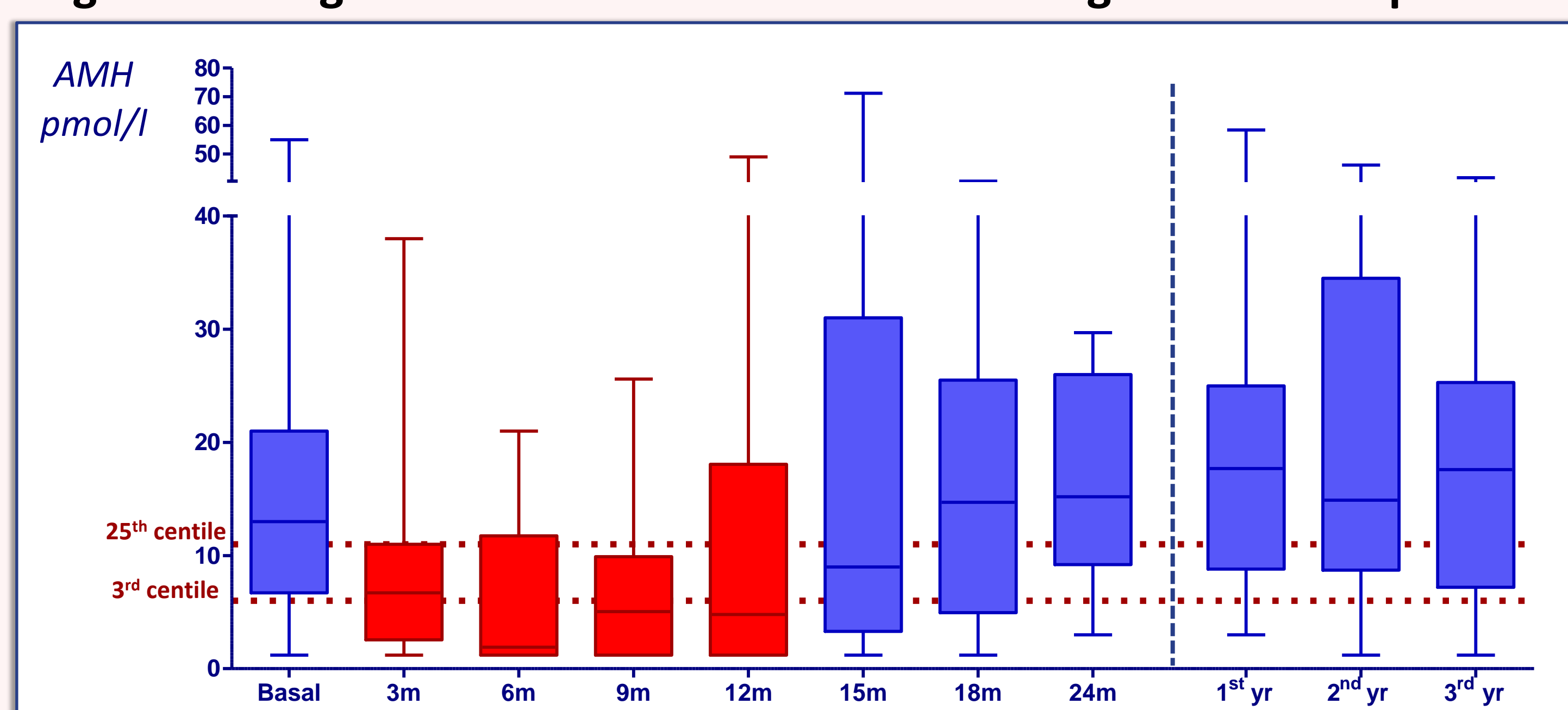
4/6 received cranial radiotherapy (1260 cGy)

- Girls who were pubertal at diagnosis received GnRHa (triptorelin) for 8.4 months (4.8-16).
- The interval between GnRHa suspension and restart of menses was 4.8 months (2.4-7.2).
- All the girls recovered regular menses.
- 8/15 prepubertal girls at diagnosis began puberty during the follow-up.

**Table 3. AMH levels (median and range), number of patients with AMH < 3<sup>rd</sup> centile**

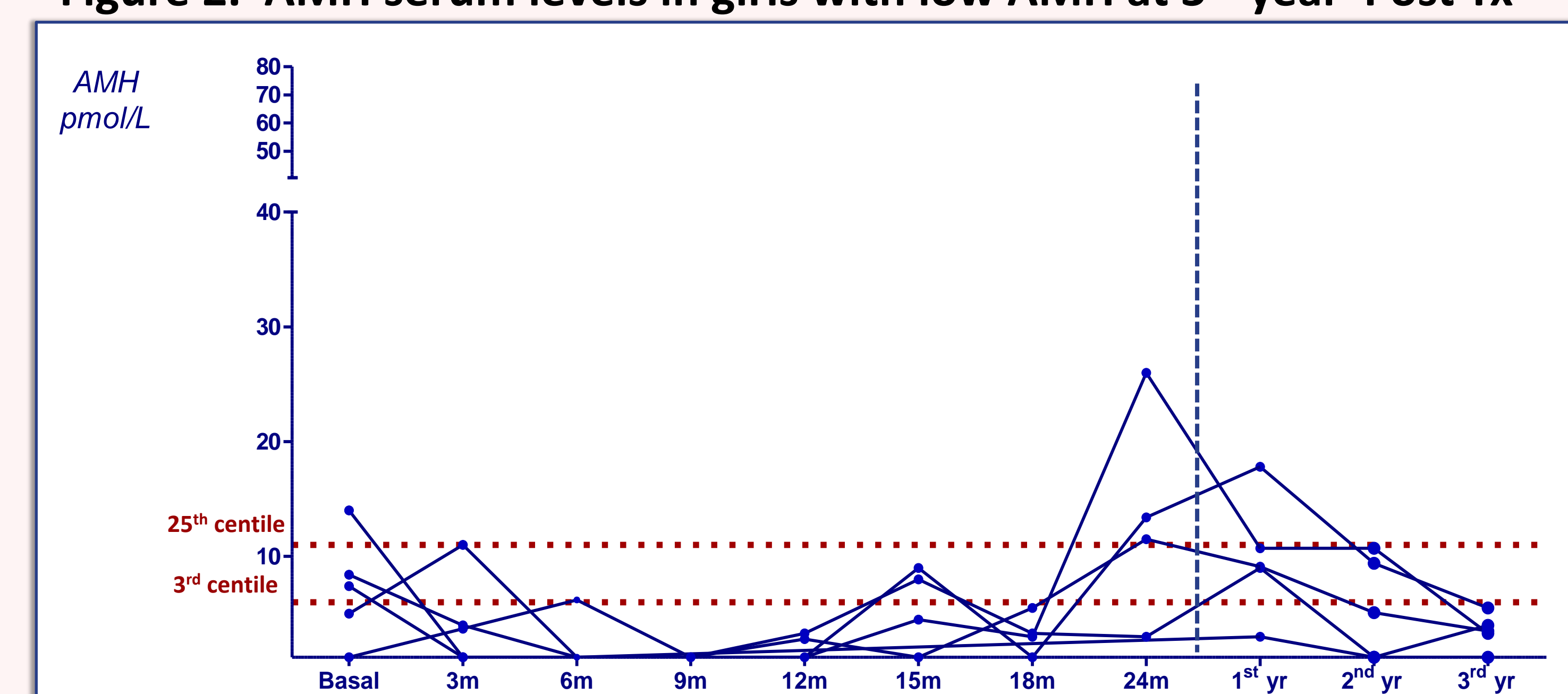
	basal	3m	6m	9m	12m	15m	18m	24m	1 <sup>st</sup> yr postTx	2 <sup>nd</sup> yr postTx	3 <sup>rd</sup> yr postTx
<b>AMH pmol/L</b>											
Median (range)	13 (1.2-55)	6.7 (1.2-38)	1.9 (1.2-21)	5,1 (1.2-25.6)	4.8 (1.2-49)	9.0 (1.2-71.2)	14.7 (1.2-40.5)	15.2 (3.0-29.7)	17.7 (3.0-58.4)	14.9 (1.2-46.2)	17.6 (1.2-41.7)
< 3 <sup>rd</sup> centile n (%)	4 (17.4)	8 (34.8)	14 (63.3)	12 (60.0)	10 (50.0)	5 (26.3)	5 (27.7)	2 (10.5)	3 (13.0)	3 (13.0)	5 (21.73)

**Figure 1. Progression of AMH serum levels during the follow-up**



- AMH was low (<3<sup>rd</sup> centile) in 20 patients (86.9%) at some point during treatment. In 4 girls AMH was low since diagnosis, all were prepubertal. In the others, a marked decrease of AMH was observed during first year of treatment (Figure 1).
- 15/20 (75%) patients recovered normal serum AMH. (Table 3)

**Figure 2. AMH serum levels in girls with low AMH at 3<sup>rd</sup> year Post Tx**



- 4/5 girls who did not recover AMH had basal AMH <25<sup>th</sup> centile before treatment (Figure 2) and a diagnosis of high-risk ALL or NHL, receiving more aggressive chemotherapy.

**Table 4. FSH levels (median and range) and number of patients with FSH > 97<sup>th</sup> centile in pubertal girls**

	basal	3m	6m	9m	12m	15m	18m	24m	1 <sup>st</sup> yr postTx	2 <sup>nd</sup> yr postTx	3 <sup>rd</sup> yr postTx
<b>FSH UI/L</b>											
Pubertal, n	8	8	8	7	8	7	7	10	15	15	16
Median (range)	5 (1-9)	2.3 (0.8-9.8)	5.2 (0.8-16.9)	2.3 (0.2-30.9)	3.5 (0.4-14.8)	4.4 (0.9-11.0)	3.8 (1.2-5.5)	5.2 (1.2-12.3)	4.4 (0.6-15.2)	4.3 (2.1-7.9)	5.9 (1.5-22.2)
> 97 <sup>th</sup> centile n (%)	1 (12.5)	1 (12.5)	2 (25)	1 (14.3)	1 (12.5)	1 (12.5)	0	2 (20)	1 (6.7)	0	2 (12.5)

- Increased FSH was seen in 5/16 (31,2%) girls.

## CONCLUSIONS

These preliminary results suggest that most girls with ALL or NHL suffered a transient dysfunction of the ovarian follicles during chemotherapy, with long term recovery in most of them. Most of the girls with persistently low AMH had received more aggressive chemotherapy.

