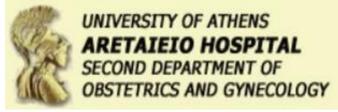


# Anastrozole is safe as monotherapy in early maturing girls with compromised growth, further improving gain in predicted adult height by the initial combination therapy of an LHRH analogue and an aromatase inhibitor. Results from the "GAIL" study

P1-P201



Eleni Dermitzaki<sup>1</sup>, Kleathis Kleanthous<sup>2</sup>, Maria Papagianni<sup>3</sup>, Achilleas Attilakos<sup>2</sup>, George Mastorakos<sup>4</sup>, Anastasios Papadimitriou<sup>2</sup>, Dimitrios T Papadimitriou<sup>1</sup>



<sup>1</sup>Division of Pediatric Endocrinology, Athens Medical Center, Athens, Greece

<sup>2</sup>Division of Pediatric Endocrinology, <sup>3</sup>rd Department of Pediatrics, Attikon University Hospital, Athens, Greece,

<sup>3</sup>rd Department of Pediatrics, Hippocraton General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece,

<sup>4</sup>Endocrine Unit, Second Department of Obstetrics and Gynecology, Aretaieion Hospital, Medical School, University of Athens, Athens, Greece

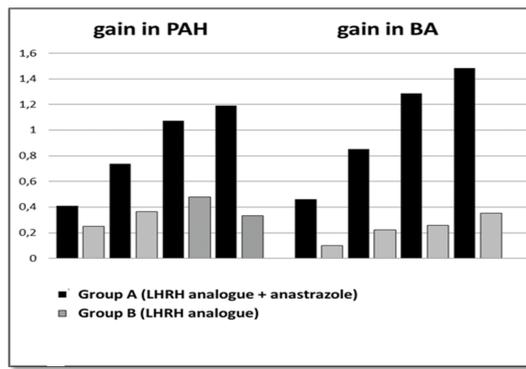
info@pedoendo.gr

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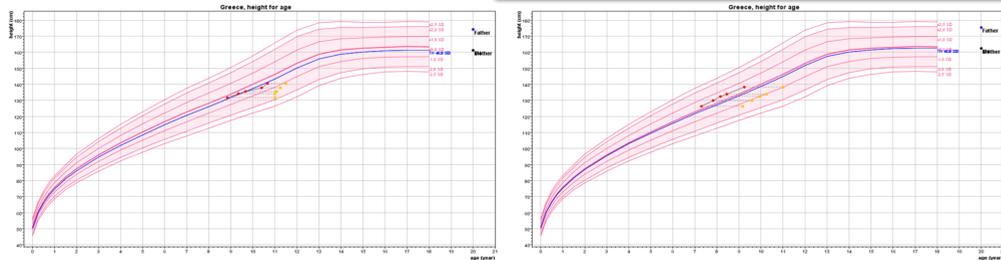
## Background

Third generation aromatase inhibitors (AI) have never been used as monotherapy, except for McCune-Albright syndrome and autonomous ovarian cysts, to increase predicted adult height in girls, mainly due to the theoretical concern of hyperandrogenism. Our previously published GAIL study has shown that the combination of anastrozole to an LHRH analogue for 24 months is safe and effective in ameliorating PAH in girls with early puberty +1.21 SDS (+7.51 cm) compared to inhibition of puberty alone +0.31 SDS (+1.92 cm, p = 0.001).

**Figure 1. Results from GAIL study. Gain in predicted adult height (PAH), and in bone age advancement (BAA) in group A (20 girls treated on anastrozole + LHRH analogue and group B (20 girls treated on LHRH analogue)**



[J Endocrinol Invest. 2016 Apr;39(4):439-46]



**Figure 2. A virtual growth curve for group-A: LHRHa + anastrozole ( left ) and group-B: LHRHa ( right ) using the mean age, height and bone age at each visit**

## Objective and hypothesis

Based on the knowledge that bone age advancement in boys is mediated mainly by paracrine and intracrine action of extragonadal estrogens, [J Clin Endocrinol Metab. 1999;84(12):4677-4694] we assessed the efficacy and safety of anastrozole monotherapy after completion of the combined treatment (Leuprorelin + Anastrozole) in further improving predicted adult height in early maturing girls with compromised growth who participated in the GAIL study ISRCTN11469487.

## Methods

Group A1 (10 girls), after completion of the combined therapy with anastrozole and leuprorelin for 24 months or until age 11, were randomized to receive anastrozole 1 mg/day as monotherapy until bone age of 14 yrs with a 6-month follow-up. Each visit comprised of physical examination, laboratory tests, bone age X-ray, pelvic ultrasound. DEXA scans were performed yearly.

	BMI	TH	PAH
Group A1	1,18	160,98	152,36
Group A2	1,16	161,33	153,92
p	0,12	0,31	0,31

## Results

There was **significant gain in PAH by 30 months (p=0,04)**. This was mainly achieved due to the **reduction in the advancement rate of the bone age**, extending the growth period in combination with the increase in girls' height velocity SD (statistically significant at 12,18,24 and 30 months). Testosterone levels rose slightly in 3 girls, but none developed clinical hyperandrogenism. One girl presented ovarian stromal hyperplasia and one hyperlipidemia. Overall, hematocrit, lipid and biochemical profiles did not change significantly during treatment. DEXA scans showed normal BMD z scores for bone age without significant interpatient changes. Anastrozole monotherapy until bone age 14 yrs further improved adult height or near adult height by +3.85 cm (+0,62 SDS) p=0.001

**Table 2. Evolution of PAH, BAA, BMI and HV in group-A1**

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
PAH <sub>cm</sub>	152,38	154	155,17	155,4	155,9	156,36
p		0,18	0,059	0,06	0,04	0,03
BAA	0,14	-0,24	-0,21	-0,22	-0,23	-0,29
p		0,12	0,16	0,12	0,16	0,11
BMI	1,14	1,03	0,9	0,96	0,91	0,97
p		0,35	0,20	0,29	0,23	0,31
HV	-3,44	-3,39	-0,73	-0,42	0,94	2,58
p		0,47	0,002	<0,001	<0,001	<0,001

**Table 3. Evolution (average±SD) of testosterone levels in group-A1**

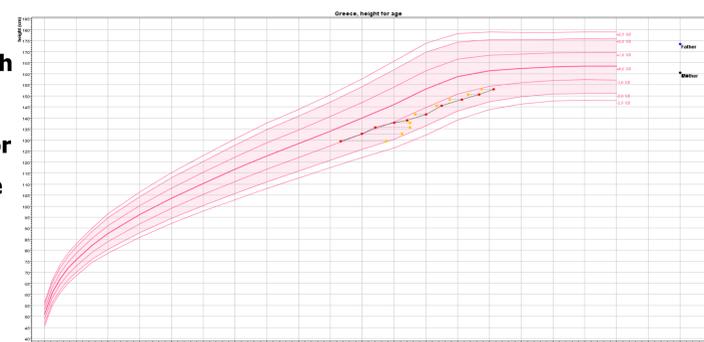
	VISIT 1	VISIT 2	VISIT 3	VISIT 4	VISIT 5	VISIT 6
TESTO	0,23 ±0,14	0,3±0,17	0,38±0,2	0,33±0,14	0,37±0,19	0,32±0,04
p		0,18	0,06	0,08	0,06	0,15

**Table 4.**

**Near Adult Height and distance from Target Height in subgroups A1, A2 and group B**

	PAH inclusion	PAH at 2 yrs	NAH cm	NAH-PAH (at 2 yrs)	NAH-PAH (inclusion)	TH-NAH
GROUP A1	146,5	152,36	156,21	3,85	9,7	4,7
p			0,01		0,001	
GROUP A2	148,1	153,92	155,58	1,66	7,4	5,7
p			0,26		0,006	
p (A1 vs A2)				0,043	0,13	
GROUP B	151,08	153,0	154,7	1,7	3,6	8,7
p			0,08		0,004	
p (A1 vs B)				0,03	0,002	0,01
p (A2 vs B)				0,47	0,02	0,05

**Figure 3. A virtual growth curve for group-A1: LHRHa + anastrozole for 2 years and anastrozole monotherapy until BA 14yrs**



## Conclusion.

**Girls who received anastrozole monotherapy until bone age 14, after the completion of the combined therapy with LHRH analogue + anastrozole, further improved their near adult height by 2,3 cm.**

**Aromatase inhibitors seem to be safe and effective in ameliorating PAH or near adult height in girls with accelerated bone age and compromised growth potential. Our results imply the possible use of aromatase inhibitors in the treatment of short stature in girls, even as monotherapy.**