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## Background

Third generation aromatase inhibitors have been used to increase predicted adult height (PAH) in boys but in girls only in McCune-Albright syndrome.

## Objective and hypothesis

We overcame the theoretical concern of secondary hyperandrogenism by combining anastrozole to an LHRH analogue in a 6-year prospective study to test whether the combination therapy could significantly improve PAH compared to inhibition of puberty alone.

## Results

At 24m height for bone age (HFBA) improved significantly in group-A:  $-1.10 \pm 0.64$  ( $p < 0.001$ ) vs  $-1.05 \pm 0.19$  ( $p = 0.24$ ) in group-B. **PAH SDS in group-A improved already by 12m:  $0.73 \pm 0.35$  (+4.5 cm), at 18m:  $1.07 \pm 0.87$  (+6.64 cm) and even more at 24m:  $1.19 \pm 0.62$  (+7.39 cm) compared to group-B (at 24m):  $0.33 \pm 0.83$  (+2.05 cm,  $p = 0.01$ ).**

Group-A did not present clinical nor biochemical hyperandrogenism, had unchanged normal bone density z-scores for BA (DXA scans yearly) and normal lumbar spine face/profil X-rays (yearly).

## Method

Forty girls with idiopathic precocious or early puberty with PAH  $< -2$  SDS or  $> 1.5$  SDS lower than their target height (TH) were enrolled for 2 years. Twenty started on anastrozole 1 mg x 1/day p.o. + Leuprorelin/Triptorelin (group A) and 20 on LHRH analogue alone (group B).

Table 1. Patients' characteristics, mean ( $\pm$  SD)

Group	Age (yrs)	Height (SDS)	Height for BA (SDS)	BMI (SDS)	TH (SDS)	PAH (SDS)	Distance from TH (SDS)	Bone Age Advancement (yrs)
A: LHRHa+AI (n=20)	8.85 ( $\pm 1.83$ )	-0.16 ( $\pm 1.12$ )	-1.96 ( $\pm 0.65$ )	1.31 ( $\pm 0.69$ )	-0.30 ( $\pm 0.77$ )	-2.61 ( $\pm 1.07$ )	-2.30 ( $\pm 1.01$ )	2.15 ( $\pm 0.92$ )
B: LHRHa (n=20)	7.29 ( $\pm 2.04$ )	0.45 ( $\pm 0.82$ )	-1.33 ( $\pm 0.66$ )	1.2 ( $\pm 0.92$ )	-0.05 ( $\pm 0.49$ )	-1.91 ( $\pm 0.76$ )	-1.85 ( $\pm 0.65$ )	1.91 ( $\pm 0.69$ )
<i>p</i>	0.007	0.028	0.004	0.320	0.110	0.010	0.050	0.220

Table 2. Evolution (mean  $\pm$  SD) of height, height for bone age, BMI, height velocity and bone age advancement in group-A (LHRH analogue + anastrozole) and group-B (LHRH analogue alone). Gain in height for bone age, gain in bone age advancement and gain in predicted adult height are reported (*p*: vs visit 0; *p*: A vs B).

Group	Height (SDS)		Height for Bone Age (SDS)		Gain in Height for Bone Age (SDS)		BMI (SDS)		Height Velocity (SDS)		Bone Age Advancement (yrs)		Gain in Bone Age (yrs)		Predicted Adult Height (SDS)		Gain in Predicted Adult Height (SDS)	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Visit 0 n(A)=20 n(B)=20	-0.16 ( $\pm 0.12$ )	0.45 ( $\pm 0.82$ )	-1.96 ( $\pm 0.65$ )	-1.33 ( $\pm 0.66$ )	-	-	1.31 ( $\pm 0.69$ )	1.2 ( $\pm 0.92$ )	-	-	2.15 ( $\pm 0.92$ )	1.91 ( $\pm 0.69$ )	-	-	-2.61 ( $\pm 1.07$ )	-1.91 ( $\pm 0.76$ )	-	-
<i>p</i>	0.028		0.004		-	-	0.32		-	-	0.22		-	-	0.01		-	-
6 months n(A)=20 n(B)=20	-0.24 ( $\pm 1.12$ )	0.48 ( $\pm 0.76$ )	-1.61 ( $\pm 0.71$ )	-1.16 ( $\pm 0.50$ )	0.35 ( $\pm 0.27$ )	0.17 ( $\pm 0.39$ )	1.20 ( $\pm 0.88$ )	1.25 ( $\pm 0.81$ )	-0.02 ( $\pm 1.24$ )	1.42 ( $\pm 2.28$ )	1.66 ( $\pm 1.13$ )	1.80 ( $\pm 0.75$ )	0.45 ( $\pm 0.17$ )	0.10 ( $\pm 0.49$ )	-2.20 ( $\pm 1.02$ )	1.66 ( $\pm 0.63$ )	0.41 ( $\pm 0.21$ )	0.24 ( $\pm 0.54$ )
<i>p, p</i>	0.40	0.11	<0.001	0.03	0.04		0.16	0.14	0.009		<0.001	0.18	0.002		<0.001	0.027	0.11	
12 months n(A)=18 n(B)=19	-0.33 ( $\pm 1.17$ )	0.57 ( $\pm 0.72$ )	-1.38 ( $\pm 0.78$ )	-1.01 ( $\pm 0.46$ )	0.65 ( $\pm 0.56$ )	0.29 ( $\pm 0.51$ )	1.08 ( $\pm 1.43$ )	1.20 ( $\pm 0.82$ )	-1.33 ( $\pm 1.63$ )	0.49 ( $\pm 2.49$ )	1.41 ( $\pm 0.99$ )	1.76 ( $\pm 0.67$ )	0.85 ( $\pm 0.26$ )	0.22 ( $\pm 0.54$ )	-1.98 ( $\pm 1.00$ )	-1.49 ( $\pm 0.64$ )	0.73 ( $\pm 0.35$ )	0.36 ( $\pm 0.66$ )
<i>p, p</i>	-	-	<0.001	0.01	0.02		0.27	0.31	0.007		<0.001	0.047	<0.001		<0.001	0.01	0.02	
18 months n(A)=14 n(B)=13	-0.72 ( $\pm 1.20$ )	0.49 ( $\pm 0.52$ )	-1.31 ( $\pm 0.67$ )	-1.12 ( $\pm 0.41$ )	0.67 ( $\pm 0.26$ )	0.24 ( $\pm 0.62$ )	1.06 ( $\pm 0.59$ )	1.21 ( $\pm 0.75$ )	-0.53 ( $\pm 2.19$ )	0.58 ( $\pm 1.17$ )	0.67 ( $\pm 1.05$ )	1.78 ( $\pm 0.59$ )	1.22 ( $\pm 0.25$ )	0.25 ( $\pm 0.61$ )	-1.74 ( $\pm 0.90$ )	-1.49 ( $\pm 0.59$ )	0.99 ( $\pm 0.37$ )	0.42 ( $\pm 0.75$ )
<i>p, p</i>	-	-	<0.001	0.008	0.016		0.82	0.36	0.06		<0.001	0.07	<0.001		<0.001	0.03	0.01	
24 months n(A)=10 n(B)=11	-0.65 ( $\pm 1.35$ )	0.38 ( $\pm 0.39$ )	-1.15 ( $\pm 0.67$ )	-1.05 ( $\pm 0.19$ )	0.76 ( $\pm 0.28$ )	0.22 ( $\pm 0.71$ )	1.36 ( $\pm 0.70$ )	1.16 ( $\pm 0.50$ )	0.41 ( $\pm 2.84$ )	-0.72 ( $\pm 0.85$ )	0.72 ( $\pm 1.07$ )	1.72 ( $\pm 0.53$ )	1.34 ( $\pm 0.36$ )	0.35 ( $\pm 0.53$ )	-1.55 ( $\pm 0.77$ )	-1.43 ( $\pm 0.40$ )	1.03 ( $\pm 0.42$ )	0.33 ( $\pm 0.83$ )
<i>p, p</i>	-	-	<0.001	0.24	0.001		0.62	0.11	0.18		<0.001	0.08	<0.001		<0.001	0.18	0.03	

Figure 1. Gain in height for bone age (HFBA, SDS), gain in bone age advancement (BAA, years) and gain in predicted adult height (PAH, SDS) in group-A and group-B

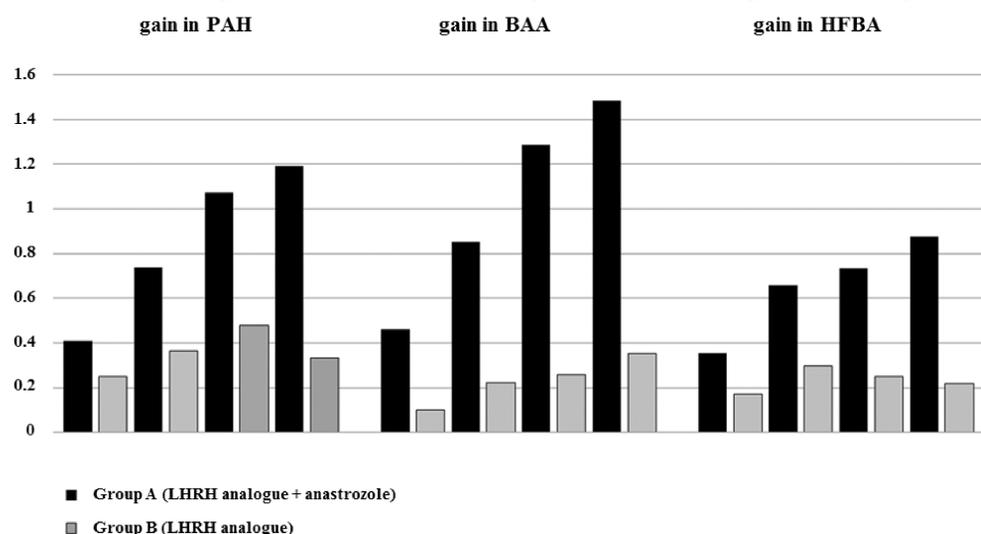
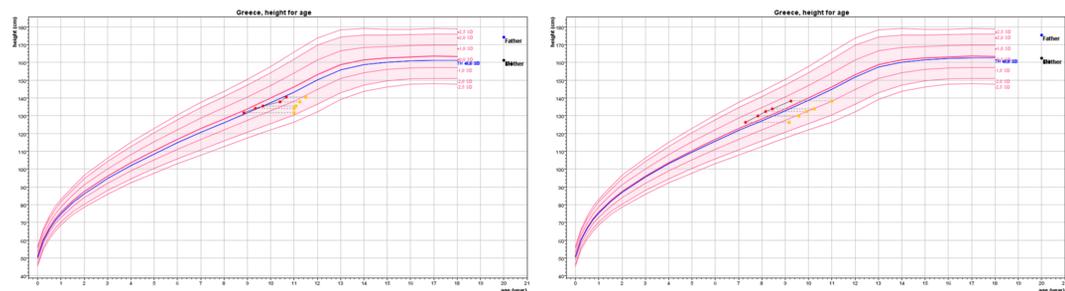


Figure 2. A virtual growth curve for group-A: LHRHa + anastrozole (left) and group-B: LHRHa (right) using the mean age, height and bone age at each visit



## Conclusion

Inhibition of puberty with co-administration of anastrozole for up to 2 years is safe and effective in improving PAH in girls with precocious/puberty with compromised growth potential.