

# Aromatase inhibitors in girls: Anastrozole combined to the LHRH analogue leuprorelin in Girls with early or precocious puberty and a compromised growth potential

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| <b>Submission date</b><br>13/12/2014   | <b>Recruitment status</b><br>No longer recruiting              | <input type="checkbox"/> Prospectively registered    |
| <b>Registration date</b><br>13/01/2015 | <b>Overall study status</b><br>Completed                       | <input type="checkbox"/> Protocol                    |
| <b>Last Edited</b><br>17/04/2024       | <b>Condition category</b><br>Nutritional, Metabolic, Endocrine | <input type="checkbox"/> Statistical analysis plan   |
|  |  | <input checked="" type="checkbox"/> Results          |
|  |  | <input type="checkbox"/> Individual participant data |

## Plain English summary of protocol

Background and study aims:

The pituitary gland is a pea-sized structure in the brain that makes, amongst other things, a chemical called the growth hormone. Growth hormone deficiency occurs when this gland does not produce enough growth hormone. This deficiency can develop at any age. In children, it results in slow growth compared to children of the same age with the affected child looking smaller and younger than their peers. Treatment with aromatase inhibitors have been shown to be successful in increasing predicted adult height (PAH) in boys, but, in girls, it has only shown to be successful for those that have McCune-Albright syndrome (a genetic disorder). Luteinising hormone is another hormone produced in the pituitary gland. It stimulates the production of the sex hormones, including oestrogen. Oestrogen promotes the maturation of the skeletal bones, which leads to a slow in growth. Blocking the production of luteinising hormone using a drug called leuprorelin slows down bone maturation and therefore potentially increases the amount of time available for growth. We want to investigate whether anastrozole (a aromatase inhibitor) combined with leuprorelin for up to 2 years (or until the age of 11 years) is a safe and effective treatment for improving PAH in girls with precocious (very early) or early puberty with a compromised (less than usual) growth potential, compared to leuprorelin alone.

Who can participate?

Girls with idiopathic precocious (breast development occurring before 7.5 years) or early puberty (breast development occurring between 7.5-9 years), that have not had hormone therapy before and a compromised growth potential .

What does the study involve?

Participants are randomly allocated into one of two groups. Those in group 1 receive a combination of leuprorelin and anastrozole for 2 years or until they reach the age of 11 years. Those in group 2 are given only leuprorelin for 2 years or until they reach the age of 11 years. After completing the initial phase of treatment , girls on the combined treatment are then randomised to receive anastrozole or no treatment at all and followed up every 6 months until

bone age reaches 14 years or they reach near adult height. Girls on leuprorelin only are followed up every 6 months with no relevant treatment until bone age reaches 14 years or near adult height is achieved. Follow-up includes clinical examination, hormonal and biochemical measurements, pelvic ultrasound and a bone age X-ray. DXA scans and X-rays of the lumbar spine are assessed yearly.

What are the possible benefits and risks of participating?

Parents are informed that anastrozole treatment is an off-label treatment and will be asked to sign a written informed consent. Anastrozole is safe for humans. While widely used off-label in boys, in girls it has been given mainly as a treatment for McCune-Albright syndrome. In a previous trial, 5 girls received the combined treatment. There were no side effects in any of the girls.

Where is the study run from?

1. Pediatric Endocrine Unit, Attikon University Hospital, Athens (Greece)
2. Department of Pediatric-Adolescent Endocrinology and Diabetes, Athens Medical Center, Athens (Greece)

When is the study starting and how long is it expected to run for?

January 2008 to December 2017

Who is funding the study?

Investigator initiated and funded (Greece)

Who is the main contact?

Dr Dimitrios T. Papadimitriou

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## Contact information

**Type(s)**

Scientific

**Contact name**

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## Additional identifiers

**Protocol serial number**

9804

# Study information

## Scientific Title

The aromatase inhibitor anastrozole combined to the LHRH analogue leuprorelin vs leuprorelin alone in ameliorating predicted adult height In girls with early or precocious puberty with a compromised growth potential

## Acronym

GAIL (Girls treated with an Aromatase Inhibitor plus Leuprorelin)

## Study objectives

Whether the combination of an aromatase inhibitor (anastrozole) with an LHRH analogue (leuprorelin) can significantly improve predicted adult height in girls with idiopathic precocious or early puberty and a compromised growth potential compared to inhibition of puberty alone.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Attikon University Hospital Ethics Committee, 2008, ref: 36/2008 13/3/08.

## Study design

Prospective Phase IIa and IIb study, performed in two cooperating centers.

## Primary study design

Interventional

## Study type(s)

Treatment

## Health condition(s) or problem(s) studied

Compromised predicted adult height in girls with early or precocious puberty

## Interventions

An initial phase IIa trial with 5 girls on the combined treatment for 1 year was performed. Girls with idiopathic precocious (<7.5yrs) or early (7.5-9yrs) puberty, all with a PAH lower than -2 or more than 1.5 SDS lower than their target height (TH) are randomized on leuprorelin 0.3 mg/kg /month plus anastrozole 1 mg/day p.o. (group-A) or on leuprorelin only (group-B) for 2 yrs or until the age of 11 yrs. After completion of this initial phase, girls on the combined treatment will be randomized to anastrozole monotherapy 1 mg/day p.o. or no treatment and followed every 6 months until bone age reaches reaches 14 years or near adult height is achieved (height velocity < 2 cm/year). The girls on leuprorelin only will be followed every 6 months without any relevant hormonal treatment until bone age reaches 14 years or near adult height is achieved.

## Intervention Type

Drug

## Phase

Phase II

**Drug/device/biological/vaccine name(s)**

1. Anastrozole 2. Leuprorelin

**Primary outcome(s)**

1. Predicted adult height calculated according to the Bayley Pinneau tables with a bone age calculated according to the atlas of Greulich and Pyle, at 6-12-18-24 months.
2. Height velocity
3. Height for bone age
4. Bone age advancement
5. BMI

Participants are followed until bone age reaches 14 or near adult height is achieved.

**Key secondary outcome(s)**

1. Potential hyperandrogenism (clinical or biochemical)
2. Ovarian cyst formation (pelvic ultrasound)
3. Bone mineral density (evaluated yearly by DXA)
4. Radiological evaluation of the lumbar spine (yearly)
5. Reports of peculiar behavior

**Completion date**

31/12/2017

**Eligibility****Key inclusion criteria**

1. Idiopathic precocious (breast development < 7.5 yrs) or early puberty (breast development 7.5-9 yrs)
2. Previously naïve to any hormonal therapy
3. PAH lower than -2 SDS or -1.5 SDS lower than their target height (mid parental height -6.5 cm)

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Child

**Sex**

Female

**Total final enrolment**

40

**Key exclusion criteria**

1. Organic precocious puberty
2. Syndromic, systemic or hereditary conditions that either impair growth or associate with PP
3. Bone diseases related to short stature (i.e. hypochondroplasia)

**Date of first enrolment**

01/01/2008

**Date of final enrolment**

31/12/2014

## Locations

**Countries of recruitment**

Greece

**Study participating centre**

**Attikon University Hospital, 3rd Department of Pediatrics, Pediatric Endocrine Unit**

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Haidari

Athens

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**Study participating centre**

**Athens Medical Center, Department of Pediatric-Adolescent Endocrinology and Diabetes**

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## Sponsor information

**Organisation**

Attikon University Hospital

**Organisation**

Athens Medical Center

## Funder(s)

**Funder type**

Other

## Funder Name

Investigator initiated and funded

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request

### IPD sharing plan summary

Available on request

### Study outputs

| Output type                        | Details   | Date created | Date added | Peer reviewed? | Patient-facing? |
|------------------------------------|---|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a>    | results   | 01/04/2016   |            | Yes            | No              |
| <a href="#">Results article</a>    |   | 08/05/2020   | 08/02/2023 | Yes            | No              |
| <a href="#">Other publications</a> | results from the second phase of the GAIL study | 02/04/2024   | 17/04/2024 | Yes            | No              |