

# The ZOMATRIP study

## Four year combination therapy of GH and GnRHa in girls with a short predicted adult height during early puberty

### Adult height outcome

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## Conclusion

A 4 year combination treatment of GH and triptorelin in girls with a final height prediction below -2.5 SDS was safe and significantly increased height (mean 12.0 ± 2.6 cm) above the predicted adult height. This outcome must be weighed against the marked financial and psychological burden of the treatment.

## Background

A combination of growth hormone and a GnRH agonist is sometimes used to improve adult height in children with a poor height prediction but there are few studies to support this practice

## Study Design

Open label, 6 study centers in Belgium

### Participants:

#### inclusion criteria:

- female
- early puberty (breast stage M2-M3)
- bone age < 12.0 y
- adult height prediction < 151.0 cm (-2.5 SDS)
- normal body proportions (SH/H within 2SDS (Gerver)
- informed consent

#### exclusion criteria:

- syndromic short stature
- adopted children
- disease or chronic use of medication that interferes with growth

### Intervention:

4 year combination therapy of GH (Zomacton) transjections 50 µg/kg/day & Triptorelin (Decapeptyl SR) IM injections 3.75 mg/month

### Methods

standard anthropometric measurements every 6 months during the intervention period, then every year until final height

height SDS calculations based on Flemish growth curves (Roelants 2009)

patient diary for compliance, adverse events and medication use

lab tests for safety and efficacy/compliance every year

bone age readings :Greulich and Pyle method

height predictions: Bayley-Pinneau method

adult height definition: height at bone age ≥ 16 years

## Results

### Participants

24 girls age 8-13 y were recruited of which 18 girls completed the 4 year treatment phase and 16 girls completed the study per protocol (PP). Reasons to drop out were: doping concerns in sports (1), no wish to postpone puberty any further after 2.5 or 3 years (3), poor compliance (1), premature stop of GH injections (1) and loss of follow-up after the treatment phase.

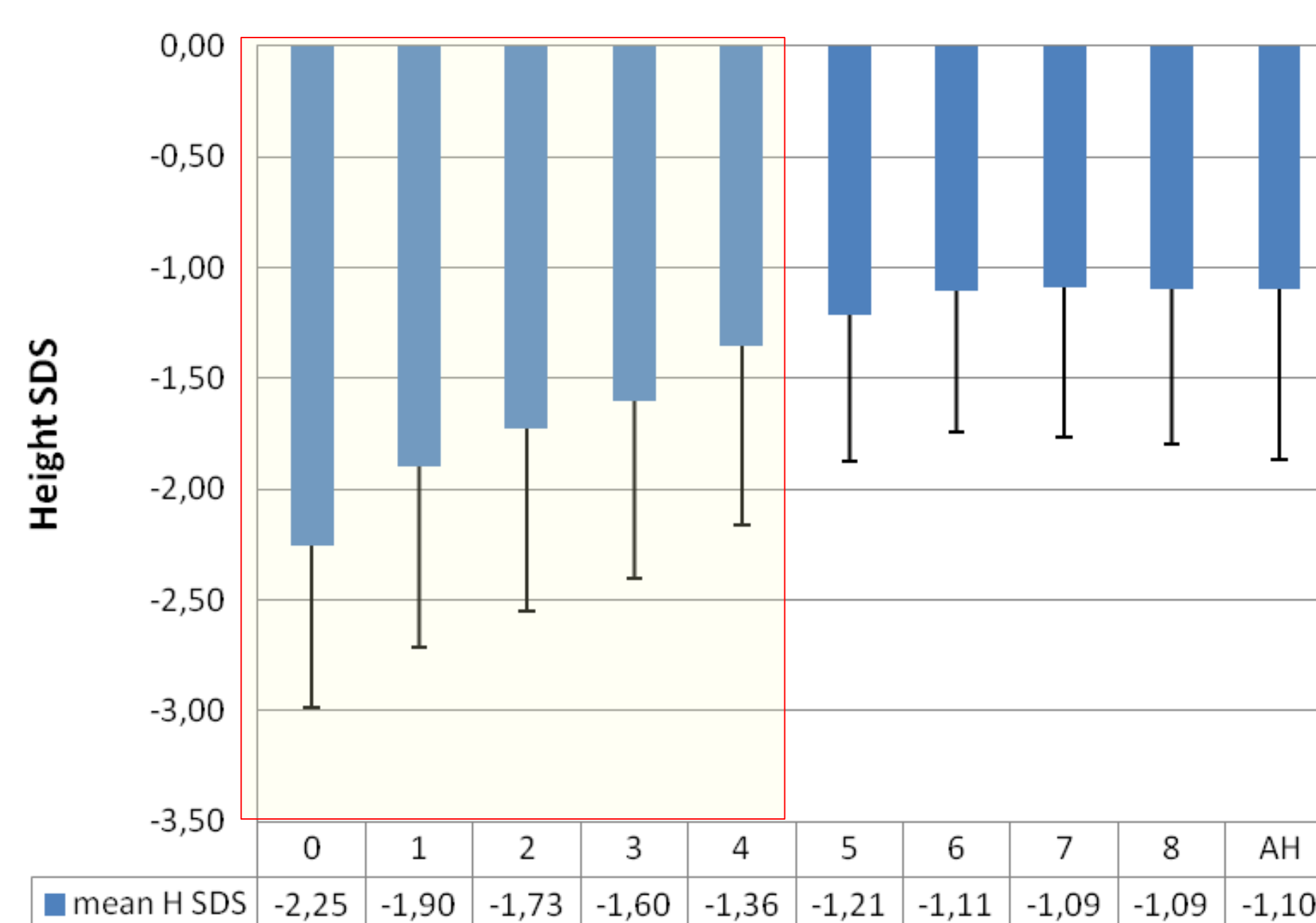
Table 1 Parameters at the start of treatment

Girls per protocol n=16	median	range
Birth length (cm)	47.0	45-50.5
Birth weight (g)	2820	2390-3500
Gestational age (wk)	39	35-41
Mother's height (cm)	158.8	150-168
(SDS)	-1.53	-2.79 - +0.24
Father's height (cm)	170.0	162.0-181.1
(SDS)	-1.65	-2.80 - 0.0
Age at start (year)	11.2	(8.0-13.2)
Height at start (cm)	132.4	(119.0-135.2)
(SDS)	-2.48	-3.62 -0.99
Bone age (year)	10.5	(9.0 - 12)
Predicted adult height (cm)	147.9	(142.5-150.2)
(SDS)	-3.21	-4.10 - -2.72

### Height evolution

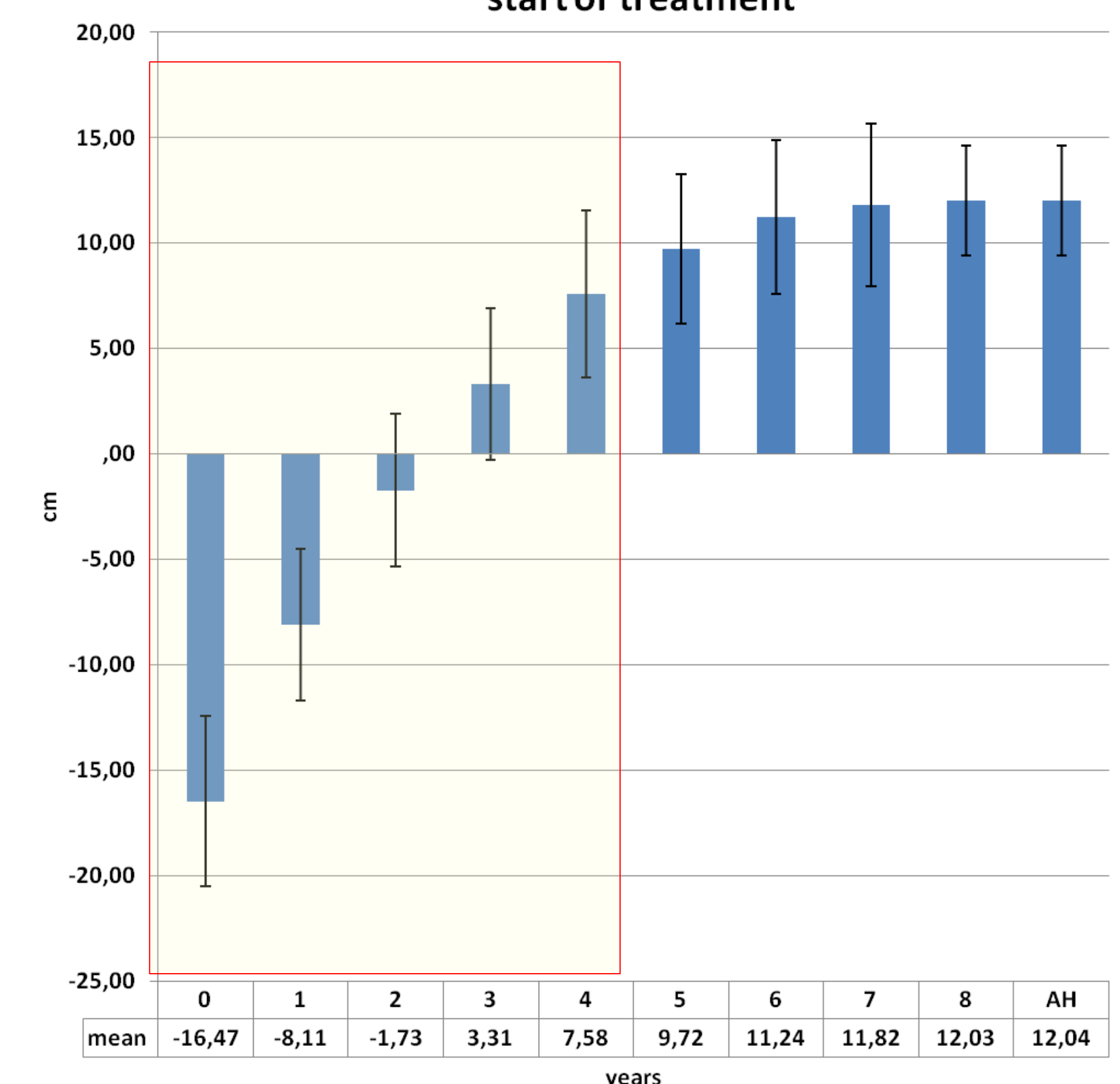
In the PP group, height (mean ± SD) increased from 131.3 ± 4.1 cm to 155.3 ± 4.7 cm and an adult height of 159.8 ± 4.8 cm. Mean height SDS rose from -2.25 ± 0.73 at the start of treatment to -1.36 ± 0.81 at the end of the treatment period and further increased to -1.10 ± 0.76 at adult height. (Fig.1).

Figure 1 mean height SDS



Height surpassed initial predicted height by 7.6 ± 3.9 cm at the end of the 4 y treatment phase and 12.0 ± 2.6 cm at final height (Fig. 2).

Figure 2 Height minus predicted adult height at the start of treatment



### Bone age

Bone age increased by 2.4 ± 0.5 yrs from 10.4 ± 0.6 yrs to 12.8 ± 0.6 yrs during the 4 y treatment phase. Bone age progression accelerated afterwards to about 1.3 years per calendar year

### Adult height prediction after 4 years of treatment

At the end of the treatment period, final height prediction (162.4 ± 5.5 cm) was 14.8 ± 4.2 cm above the predicted value at the start of treatment (147.6 ± 2.0 cm). Due to the bone age acceleration, adult height was 2.6 cm lower than predicted at the end of the treatment period.

### Adverse events

The clinical adverse events consisted of injection site reactions (pain, bruising, scarring) and common health problems for this age group.

There were 3 serious adverse events (SAE):

- pyelonephritis needing IV antibiotics
- fracture of metatarsals in ballet dancer (possibly related to the intervention)
- depression, 2 years after the stop of treatment

### Laboratory measurements

Mean serum IGF-1 levels peaked from 326 ± 128 ng/ml at start to 714 ± 228 ng/ml after 2 years of treatment. One year post treatment IGF-I decreased again to 521 ± 164 ng/ml

Fasting insulin levels increased 2.5 fold but fasting glucose and HbA1c levels remained within the normal range. Fasting insulin normalized again after the stop of treatment. One obese patient had an impaired glucose tolerance at the start, which remained stable throughout the study.

### References

Roelants M, Hauspie R and Hoppenbrouwers K (2009) References for growth and pubertal development from birth to 21 years in Flanders Belgium. Ann Human Biol 36:680-694.

