LONG-TERM EFFICACY AND SAFETY OF RHGH IN CHILDREN WITH SHOX DEFICIENCY: PRELIMINARY DATA OF A NATIONAL ITALIAN SURVEY.

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ESPE 2021 The 59th Annual Meeting Online 22-26 September 2021

INTRODUCTION

The phenotypic spectrum of short stature homeobox-containing gene deficiency disorders (SHOX-D) ranges from non-specific short stature to Leri-Weill dyschondrosteosis. **Current guidelines support recombinant human Growth Hormone (rhGH) in SHOX-D children[1,2], but long-term data are still lacking[3].** Moreover, no correlation has been established yet between the severity of phenotype, including the response to rhGH, and the underlying SHOX pathogenic variant[4].

AIMS

1) **To evaluate long-term efficacy and safety of rhGH**
2) To identify potential predictive factors influencing response to rhGH

METHODS

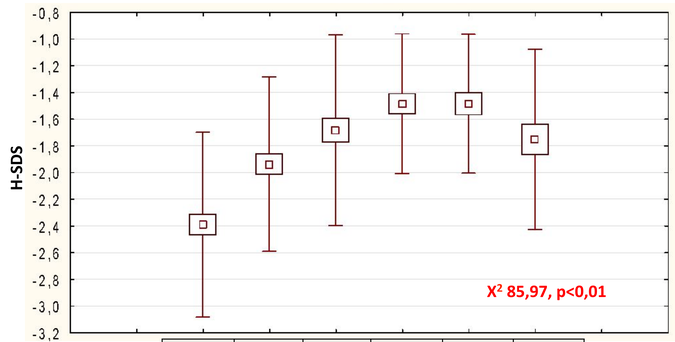
	We collected
What?	▪ Anamnestic (age, gender, ethnicity) and genetic data (genotype) ▪ Family data (parental height, sitting height and arm span) ▪ Anthropometric data [height SDS (H-SDS), BMI-SDS, arm span/height ratio (AS/H), sitting height/height ratio (S/H), pubertal stage, growth velocity (GV)-SDS, target height (TH)]. ▪Clinical data (Rappold score, bowing of tibia, high-arched palate, muscular hypertrophy) ▪ Biochemical data (IGF-1, TSH, FT4, glucose metabolism) ▪ Instrumental data (bone age, bone abnormalities) ▪ Therapeutic data (rhGH dose, side effects)
Who?	Children and adolescents with a genetic confirmation of SHOX-D treated on rhGH. Exclusion criteria: chronic disease, other already defined genetic or endocrine disease, treatment with drugs that affect growth, malnutrition and psychosocial disorders.
When?	Data were collected at the beginning of rhGH (T0), yearly during the first 4 years of rhGH (T1, T2, T3, T4) and at final height (T5), when available.

RESULTS

(a) Baseline (T0) features in enrolled patients (n.86):

Parameter	Mean value ± SDS
Female/Caucasian (%)	52/94
Prepubertal stage (%)	79
Age (years)	8.64±3.13
Bone age (years)	7.83±3.05
H-SDS	- 2,39±0,69
TH-SDS/ Parental disproportions (%)	-1.30±0.98 / 48
BMI-SDS	-0.05±1.00
AS-H ratio	0.97±0.08
S-H ratio	0.56±0.02
GV-SDS	-1.27±1.84
Rappold score	7.41±4.83
rhGH initial dose (mg/kg/week)	0,25±0,04

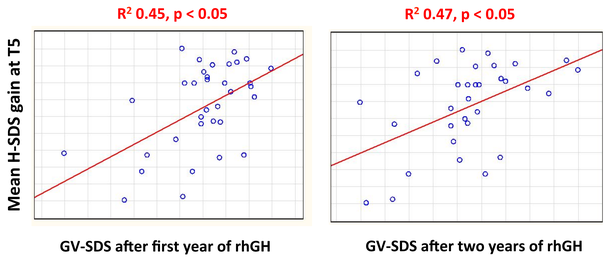
(b) Longitudinal data (mean rhGH duration 5.94±2.16 years):



	T0	T1	T2	T3	T4	T5
Num.	86	86	64	48	40	36
H-SDS	-2.39±0.69	-2.01±0.43	-1.73±0.47	-1.51±0.46	-1.43±0.46	-1.64±0.59

GV SDS (T0 -1.27±1.84, T1 2.39±1.37, T2 1.44±1.91, T3 0.95±1.87, T4 0.77±2.41, X2 56.65, p <0.01) and S/H ratio (T0 0.56±0.02, T1 0.55±0.02, T2 0.54±0.01, T3 0.54±0.01, T4 0.53±0.01, T5 0.54±0.01, X2 15.77, p <0.01) improved significantly along rhGH.
Mean H-SDS gain was: T4 vs. T0 +1.18±0.49 and T5 vs. T0 +0.68±0.89

(c) Correlations between mean H-SDS gain at T5 and GV-SDS in the first two years of treatment:



(d) No adverse effects were reported a part from transient impaired glucose metabolism (2/86 cases) and transient headache (1 case).

(e) No differences in clinical and therapeutic data were detected between patients carrying mutations involving enhancers (51/86) and ones with no-sense and missense mutations in SHOX gene, both at the beginning of rhGH and along follow-up.

CONCLUSIONS

Our preliminary data confirm the efficacy and safety of rhGH in SHOX-D children. Besides wide phenotypic spectrum, all SHOX-D genotypes seem to adequately respond to rhGH

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