GROWTH AND NUTRITION IMPROVEMENT WITH RECOMBINANT GROWTH HORMONE IN PATIENTS WITH SILVER-RUSSELL SYNDROME

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INTRODUCTION

- Silver-Russell syndrome (SRS) is an imprinting disorder characterized by intrauterine and postnatal growth retardation, feeding difficulties and several dysmorphic features.
- In 50-55% of patients, loss of methylation (LOM) in 11p15 region on the paternal allele is identified, whereas a maternal uniparental disomy of chromosome 7 (upd(7)mat) is present in the remaining 5-10%.
- Recombinant growth hormone (rGH) therapy under EMA indication for children born small for gestational age with no catch-up growth.

→ few data on growth impact during the first years of rGH therapy

- Malnutrition affects around 70% of them. Nutritional support can be necessary, especially before initiating rGH therapy
- Weight for height target is [75-85%] and/or BMI [12-14 kg/m²].
- Recommendation to start rGH therapy earlier than 4 years for its effects on body composition improvement appetite

→ few data on nutritional impact during the first years of rGH therapy.

AIM

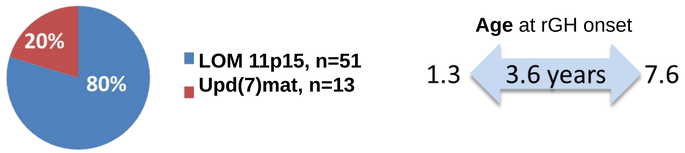
Assess rGH therapy impact on both growth and nutritional status in prepubertal patients with SRS during the first two years of treatment.

METHOD

- Molecularly proven SRS patients
- Before and during the first two years of rGH therapy
- Retrospective, monocentric analysis of growth and nutritional features
- In respect with French Ethical laws

RESULTS

64 prepubertal SRS patients



Age at rGH onset

1.3 — 3.6 years — 7.6

	All (n=64)	11p15 LOM (n=51)	upd(7)mat (n=13)	11p15 LOM vs upd(7)mat
NH-CSS ≥ 4	64/64 (100)	51/51 (100)	13/13 (100)	
SGA	61/64 (95.3)	50/51 (98.0)	11/13 (84.6)	0.10
Postnatal growth failure	61/64 (95.3)	48/51 (94.1)	13/13 (100)	1
Relative macrocephaly	58/64 (90.6)	46/51 (90.2)	12/13 (92.3)	0.77
Protruding forehead	59/63 (93.6)	47/50 (94.0)	12/13 (92.3)	1
Body asymmetry	41/62 (66.1)	40/50 (80.0)	1/12 (8.3)	*<0.0001*
Feeding difficulties	58/64 (90.6)	45/51 (88.2)	13/13 (100)	0.33

Table 1. Clinical characteristics of the Netchine-Harbison clinical scoring system (NH-CSS) in the cohort and comparison between 11p15 LOM and upd(7)mat groups. p values below 0.05 are indicated in italics.

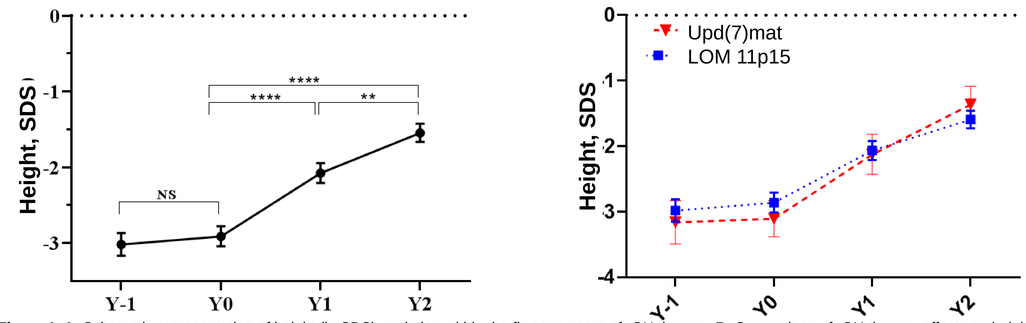


Figure 1. A. Schematic representation of height (in SDS) evolution within the first two years of rGH therapy. **B.** Comparison of rGH therapy effects on height regarding the molecular anomaly of SRS

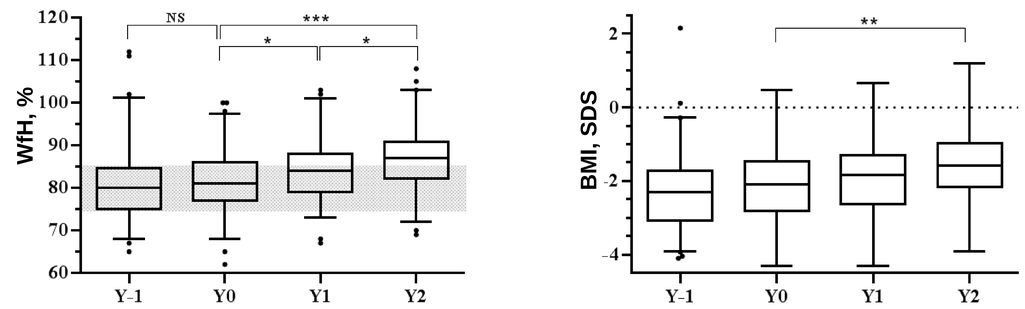


Figure 2. A. Schematic representation of weight for height (WfH) and **B.** body mass index (BMI) evolution within the first two years of rGH therapy.. The grey zone represents the targeted values for WfH for patients with SRS

CONCLUSIONS

- rGH therapy is effective in prepubertal SRS patients growth during the two first years of treatment at regular doses
- rGH therapy allowed a significant improvement of ideal weight for height/length in SRS patients
- Close management of nutritional parameters (Weight for height/length) is mandatory in these patients to prevent from long-term metabolic complications
- Knowledge on precise body composition before and during rGH therapy is lacking

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