Early treatment with rhGH in patients with Prader-Willi syndrome results in improved height with no respiratory adverse effects.

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Background

Prader-Willi syndrome (PWS) is a complex genetic disorder caused by lack of expression of paternally inherited imprinted genes on Chr15q11-q13.

Treatment with rhGH has beneficial effects on growth, body composition and development. The ideal age for starting GH is not clear, although there has been a trend towards starting at younger ages and the dose titration and monitoring of treatment remain controversial.

Unexpected death in infants and children with PWS have been reported in patients with or without rhGH treatment (complicated course of a relatively mild respiratory tract infection, sleep apnea, adenoid/tonsil hypertrophy, hypoventilation orrelated to obesity).

There is suggestion of a high risk period during the first months of GH treatment, with the advice to start at a low dose of rhGH and increasing during the first weeks and months to reach a standard replacement dose (1.0 mg/m^2/d or 0.035 mg/kg/d).
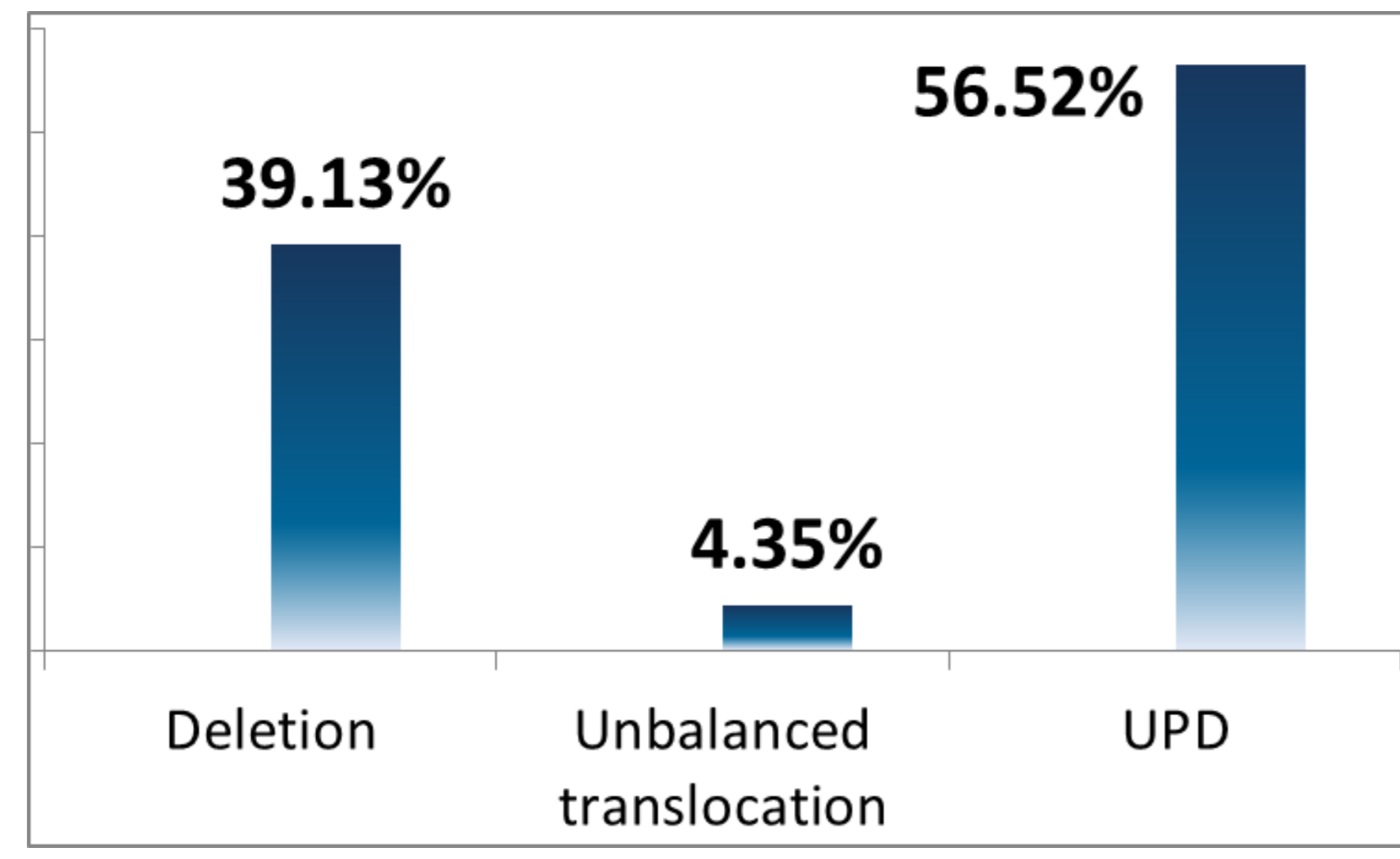
Aim

To study retrospectively children who presented in our multidisciplinary PWS clinic and assess their response to rhGH treatment in terms of auxology, IGF1 concentration and potential complications.

Patients

47 • Male 27; Female 20

5 • Lost to follow-up

2 • Refused treatment with rhGH

40
• Male: Female 1:1
• Treated with rhGH and under follow-up

Genetic background in this cohort of patients with PWS

39.13% Deletion
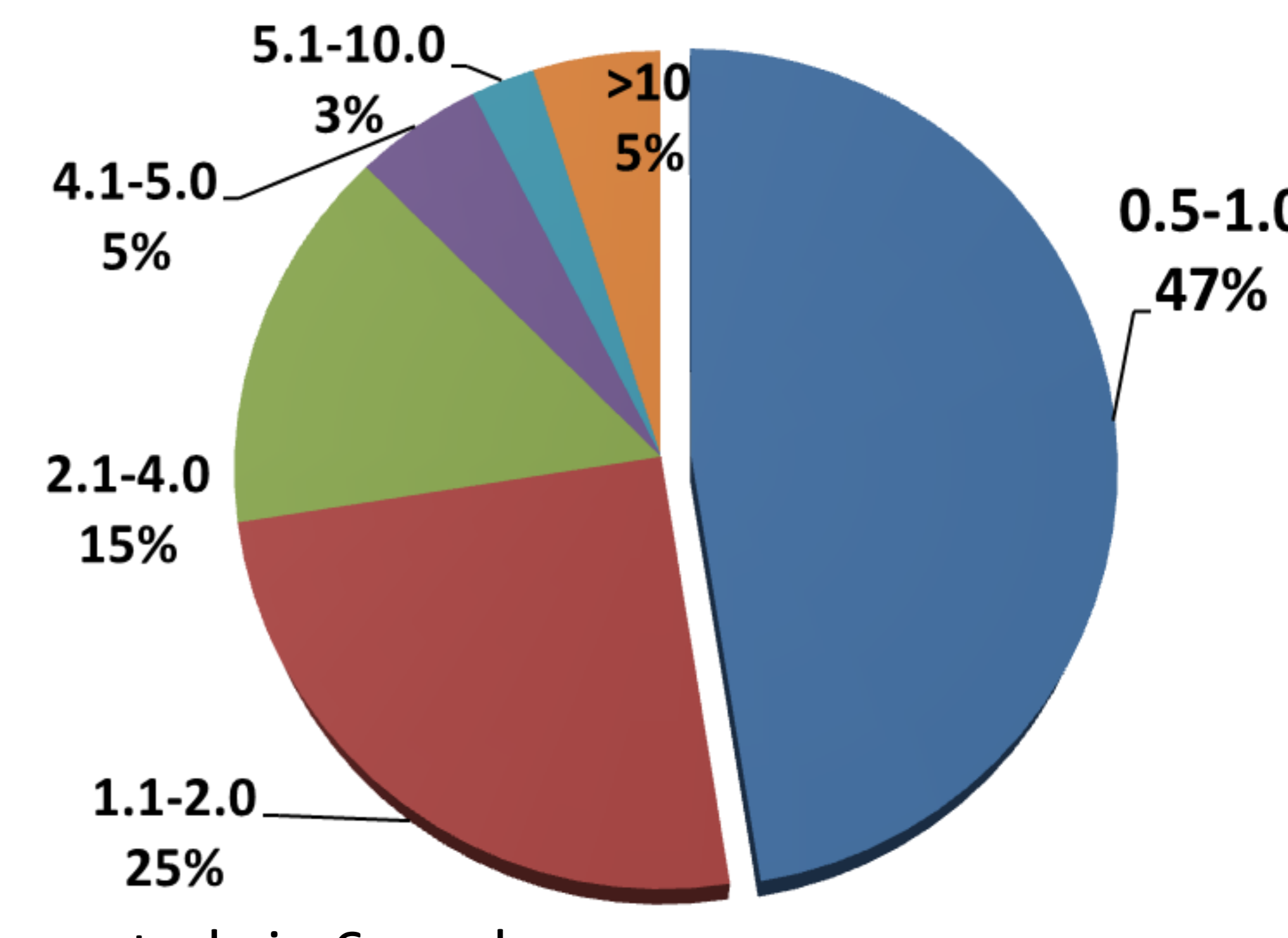4.35% Unbalanced translocation
56.52% UPD

Results

➢ All patients (n=40) had detailed sleep studies before starting rhGH.

➢ 15% (n=6) had evidence of sleep apnoea, requiring non invasive ventilation before rhGH Tx

1. Age at start of treatment

Mean age at start of treatment 2.1 ± 2.6 years (range 0.58-12.8).

47% (n=19) started treatment before the age of 1yr (0.58-0.97 yrs).

Pie chart:
- 0.5-1.0 47%
- 1.1-2.0 25%
- 2.1-4.0 15%
- 4.1-5.0 5%
- 5.1-10.0 3%
- >10 5%

2. Starting dose of rhGH

➢ Mean starting dose of rhGH 0.025mg/kg/d (0.5mg/m^2/day; range 0.36-0.64 mg/m^2/d)
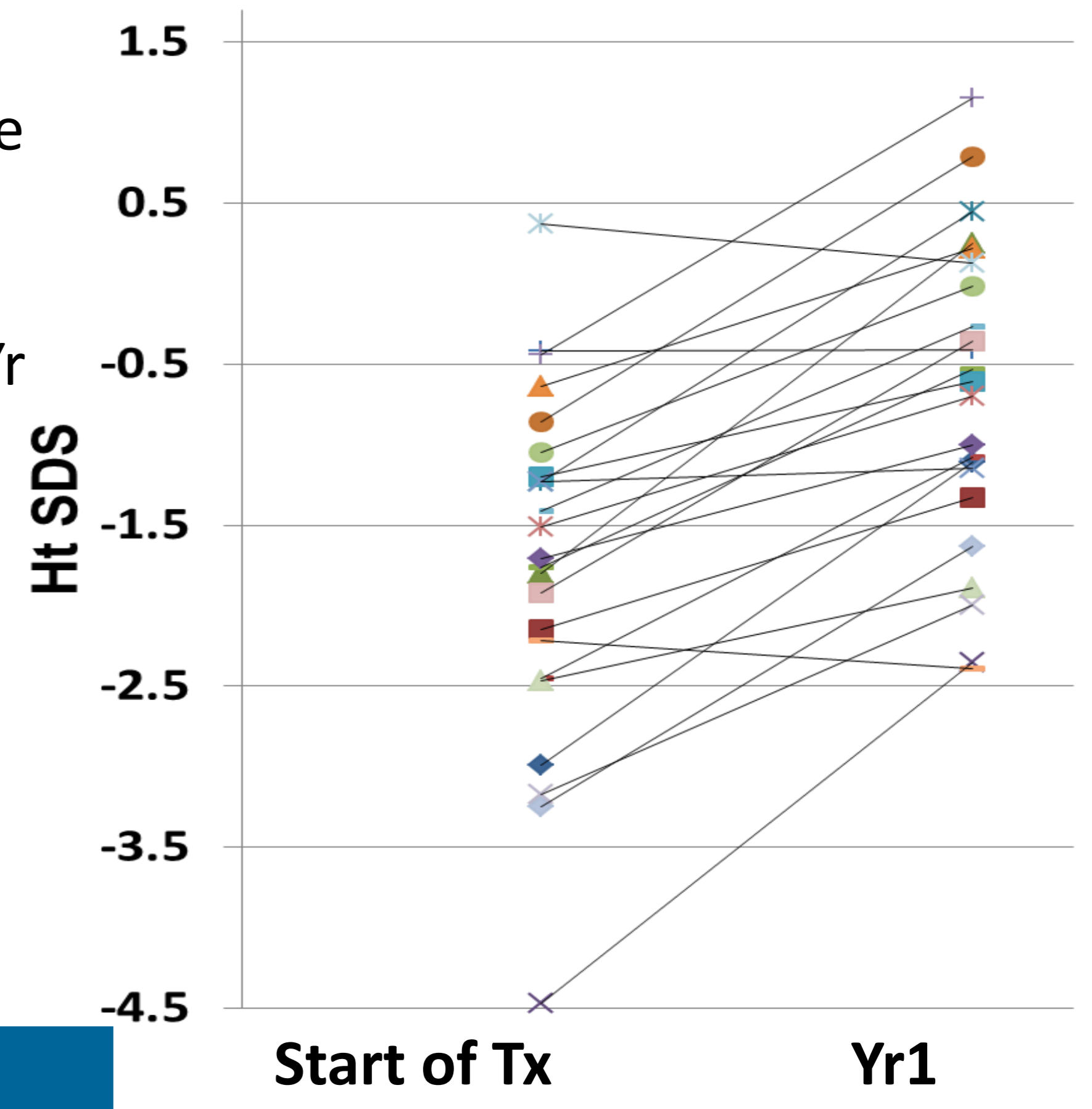➢ Increased to 1mg/m^2/day following a 2nd sleep study in 6 weeks.

3. Auxology

	Pre Treatment		Year 1	
	Mean	*Range*	*Mean*	*Range*
Ht SDS	-1.65 ± 1.1	-4.5 to 0.37	-0.28 ± 0.94	-2.4 to +2.3
Wt SDS	-1.43 ± 1.8	-5.5 to 3.3	-0.24 ± 1.8	-4.0 to 3.7
BMI SDS	-0.46 ± 1.6	-3 to 4	0.08 ± 2	-3.0 to 4.6
rhGH	*Starting dose*		*Year 1 dose*	
mg/m^2/d	0.5 ± 0.1	0.36 to 0.64	0.78 ± 0.2	0.3 to 1.2

Mean change in Ht of 1.37 SDS.

No correlation between genotype and response to treatment.

60% of patients had IGF1 > than +2.0 SDS at 1Yr and the dose of rhGH remained unchanged.

➢ No patient had worsening of the respiratory status
➢ 2/6 patients with previous sleep apnoea discontinued ventilatory support after starting Tx

Graph: Ht SDS, Start of Tx → Yr1

Conclusions

In patients with PWS early treatment with rhGH results in improved height in the 1st year with no adverse effect on respiratory function.
Only one patient had a brief pause in treatment during spinal surgery.
We recommend dose titration using auxology and IGF1 concentration

References

1. Goldstone AP et al. Recommendations for the Diagnosis and Management of Prader-Willi Syndrome. JCEM 2009; 93(11): 4183-4197
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