



# Efficacy of Growth Hormone Treatment in Patients with type 1 Diabetes mellitus and Growth Hormone Deficiency

Walter Bonfig<sup>1,2</sup>, Anders Lindberg<sup>3</sup>, Wayne Cutfield<sup>4</sup>, David Dunger<sup>5</sup>, Cecilia Camacho-Hübner<sup>6</sup>, Reinhard W. Holl<sup>7</sup>

<sup>1</sup> Department of Pediatrics, Klinikum Wels-Grieskirchen, Wels, Austria, <sup>2</sup> Department of Pediatrics, Technical University München, Munich, Germany  
<sup>3</sup> Pfizer Health AB, Sollentuna, Sweden, <sup>4</sup> Liggins Institute, University of Auckland, Auckland, New Zealand, <sup>5</sup> Department of Pediatrics, University of Cambridge, Cambridge, U.K., <sup>6</sup> Pfizer Inc, Endocrine Care, New York, USA, <sup>7</sup> Institute of Epidemiology and Medical Biometry, University of Ulm, Ulm, Germany

**Disclosures:** W Bonfig & RW Holl have nothing to disclose. W Cutfield received consultancy fees from Pfizer & is a member of the KIGS Steering Committee (SC). D Dunger was a former member of the KIGS SC. A Lindberg & C Camacho-Hübner are full-time employees of Pfizer.

**Background:** The combination of type 1 diabetes mellitus (T1DM) and growth hormone (GH) deficiency is uncommon. In a previous study we found in children with T1DM and GHD that with adequate adaptation of insulin dosage, metabolic control of T1DM did not worsen during GH treatment. However, decreased catch-up growth was observed and no data on GH dose was available (Bonfig et al, J Pediatr 2013).

**Objective:** To analyze first treatment year growth response and GH dosage in prepubertal patients with T1DM and GHD and to compare these data with a large control cohort within the KIGS® database.

**Patients & Methods:** In total 69 patients with T1DM and GHD treated with GH are documented in the KIGS® database. Of these, 24 patients were prepubertal and were included in this analysis. Of 30,570 control patients with GHD n=15,024 were prepubertal and served as controls. Multiple pituitary hormone deficiency was present in 6 (25%) patients with T1DM and GHD and in 2924 (19.5%) control patients. None of the T1DM and GHD patients were treated with glucocorticoids compared to 678 (4.5%) control patients.

For statistical analysis Wilcoxon rank sum test was performed using SAS software (version 9.2). Quality of diabetes control was not assessed in this analysis due to lack of longitudinal data on haemoglobin A1c in patients and controls in the KIGS® database.

## Results:

Patients with T1DM and GH deficiency have no difference in:

- age at start of GH treatment
- corrected height-SDS at start of treatment
- GH dosage at start of therapy
- first year growth response/growth velocity

They are different from the GHD controls in that they:

- have higher birth weight than controls
- are heavier at start of GH treatment
- have a higher mean/median GH dose after first treatment year

Height gain:

Median height SDS of children with T1DM and GHD improved from -2.62 (mean -2.58, SD 1.04) to -1.88 (mean -1.90, SD 1.11)

Safety:

- 10 adverse events (AEs) not related to GH treatment – all patients recovered
- 3 adverse events (AEs) related to T1DM (nephropathy, retinopathy and hypoglycemia & worsening metabolic T1DM control); only worsening of glycaemic control was attributed to GH treatment und GH dose was reduced by the caring physician.
- 1 serious adverse event (SAE): acute pancreatitis with hospital admission not related to GH treatment as reported by the KIGS investigator. The patient fully recovered.

**Conclusion:** In the “growth focused” KIGS® database prepubertal children with T1DM and GH deficiency are treated with adequate GH dosage and demonstrate regular catch-up growth.

Therefore taken together with previous data, GH treatment is not only metabolically safe, but also effective.

Preexisting T1DM should not be a reason to deprive children with GH deficiency from GH treatment and children with well controlled T1DM and GH deficiency suggesting growth pattern should undergo regular work-up of the GH/IGF-1 axis.

|                               | T1DM and GHD |        |              | GHD only |        |              | p     |
|-------------------------------|--------------|--------|--------------|----------|--------|--------------|-------|
|                               | n            | median | mean ± SD    | n        | median | mean±SD      |       |
| <b>Background</b>             |              |        |              |          |        |              |       |
| birth weight SDS              | 19           | 0.06   | -0.02 ± 1.15 | 13,582   | -0.80  | -0.81 ± 1.23 | 0.003 |
| mid parental height (MPH) SDS | 19           | -0.23  | -0.96 ± 1.32 | 14,127   | -1.40  | -1.36 ± 1.24 | 0.111 |
| max GH peak [µg/L]            | 22           | 6.93   | 6.80 ± 3.22  | 15,024   | 6.10   | 5.75 ± 2.75  | 0.208 |
| <b>Start of GH therapy</b>    |              |        |              |          |        |              |       |
| Chronological age [years]     | 24           | 10.20  | 9.39 ± 3.13  | 15,024   | 8.42   | 8.40 ± 3.46  | 0.144 |
| height SDS                    | 24           | -2.62  | -2.58 ± 1.04 | 15,024   | -3.01  | -3.13 ± 1.15 | 0.032 |
| height - MPH SDS              | 19           | -1.62  | -1.59 ± 1.38 | 14,127   | -1.61  | -1.76 ± 1.51 | 0.802 |
| weight SDS                    | 24           | -1.55  | -1.45 ± 1.22 | 15,024   | -2.18  | -2.25 ± 1.47 | 0.006 |
| BMI SDS                       | 24           | 0.04   | 0.13 ± 1.09  | 15,024   | -0.32  | -0.32 ± 1.27 | 0.084 |
| GH dose [mg/kg/week]          | 24           | 0.24   | 0.23 ± 0.08  | 15,024   | 0.20   | 0.22 ± 0.07  | 0.089 |
| <b>1-year on GH therapy</b>   |              |        |              |          |        |              |       |
| height velocity [cm/year]     | 24           | 7.54   | 8.16 ± 3.11  | 15,024   | 8.35   | 8.67 ± 2.54  | 0.375 |
| height SDS after              | 24           | -1.88  | -1.90 ± 1.11 | 15,024   | -2.30  | -2.36 ± 1.10 | 0.058 |
| delta height SDS              | 24           | 0.57   | 0.70 ± 0.55  | 15,024   | 0.69   | 0.78 ± 0.51  | 0.381 |
| weight SDS                    | 24           | -1.06  | -1.01 ± 1.27 | 14,935   | -1.69  | -1.73 ± 1.35 | 0.017 |
| BMI SDS                       | 24           | -0.05  | 0.11 ± 1.14  | 14,935   | -0.40  | -0.39 ± 1.21 | 0.077 |
| GH dose [mg/kg/week]          | 24           | 0.23   | 0.24 ± 0.08  | 15,024   | 0.20   | 0.21 ± 0.07  | 0.041 |

**Acknowledgments:** The authors express their thanks to all patients, parents and to all those KIGS investigators involved in providing data.

Walter.Bonfig@mri.tum.de

55<sup>th</sup> Annual Meeting of the European Society of Paediatric Endocrinology, 10-12 September 2016, Paris, France