# Latest results from the PATRO Adults study of Omnitrope® for the treatment of adult patients with growth hormone deficiency

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## Introduction

- Growth hormone deficiency (GHD) is a well-recognised condition amongst adults. All adults with severe GHD are eligible for GH replacement treatment, the main goals of which are to reverse the metabolic, functional and psychological abnormalities associated with adult GHD[1,2].
- Treatment of GHD in adults with GH replacement therapy has proved to be effective for improving body composition, exercise capacity, skeletal integrity, blood lipid profile and overall quality of life[2].
- The assessment of clinical practice guidelines is that the risks associated with GH therapy are low[2]. However, extended clinical studies are required to confirm the long-term safety of GH therapy in routine clinical practice, particularly with regard to the diabetogenic risk.
- Omnitrope® (somatropin) is a recombinant human GH (rhGH) approved by the European Medicines Agency in 2006, with approval granted on the basis of comparable quality, safety and efficacy to the reference product, Genotropin® (Pfizer).
- PATRO Adults is an ongoing observational, multicentre, open, longitudinal study of Omnitrope®, conducted in hospitals and specialised endocrinology clinics across Europe. The primary objective is to assess the safety and efficacy of Omnitrope® in adults treated in routine clinical practice[3].
- Here we present status and safety data from an interim analysis.

## Methods

- Eligible patients are male or female adults who are receiving treatment with Omnitrope® and who have provided informed consent.
- Patients who have received treatment with another rhGH product before starting Omnitrope® therapy are also eligible for inclusion.
- Efficacy assessments are based on analysis of:
  - Insulin-like growth factor (IGF) 1 levels within age- and gender-adjusted normal ranges
  - Anthropometric measures such as weight, waist circumference, total fat mass, lean body mass, total body water
  - Bone mineral density
  - Lipids
  - Cardiovascular risk factors (glucose metabolism, blood pressure, inflammatory markers)
  - Quality of life.
- All adverse events (AEs) are monitored and recorded.
- Particular emphasis is placed on: long-term safety; the recording of malignancies; the occurrence and clinical impact of anti-recombinant hGH antibodies; the incidence, severity and duration of hyperglycaemia; and the development of glucose intolerance or diabetes.
- Data is collected at each routine visit during treatment with Omnitrope®.
- For all patients included in the study, all available data (visits, laboratory data, findings from examinations, etc.) are recorded in a CRF.

## Results

- As of March 2016, 1043 patients were enrolled in the study (Table 1); of these, 562 (53.9%) had been previously treated with rhGH.
- Characteristics of enrolled patients are shown in Table 2.
- A total of 2025 AEs have been reported to date in 597 patients (Table 3); 317 of these (in 187 patients) were regarded as serious. Most AEs (1872/2025 [92.4%]) were mild to moderate in intensity, with few (227/2025 [11.2%]) resulting in any changes to Omnitrope® treatment.
- Table 4 shows treatment-related AEs that occurred with an incidence of >1.

**Table 1. Sites and subject enrollment by country**

| Country | Sites n | Enrolled subjects n (%) | Active subjects, n | Discontinued subjects, n |
|---|---|---|---|---|
| UK | 13 | 325 (31.2) | 279 | 46 |
| Sweden | 6 | 246 (23.6) | 231 | 15 |
| Germany | 29 | 280 (26.8) | 232 | 48 |
| Italy | 8 | 73 (7.0) | 55 | 18 |
| The Netherlands | 2 | 56 (5.4) | 31 | 25 |
| Spain | 2 | 34 (3.3) | 29 | 5 |
| France | 6 | 21 (2.0) | 19 | 2 |
| Czech Republic | 2 | 8 (0.8) | 8 | 0 |
| **Total** | **68** | **1043 (100.0)** | **884** | **159** |

**Table 2. Patient characteristics at enrollment**

| Variable | Isolated GHD | Combined GHD | Other |
|---|---|---|---|
| **Gender** | | | |
| Male, n (%) | 55 (5.3) | 480 (46.0) | 8 (0.8) |
| Female, n (%) | 68 (6.5) | 423 (40.6) | 8 (0.8) |
| Total, n (%) | 123 (11.8) | 904 (86.7) | 16 (1.5) |
| **Mean (SD) age, years** | 45.4 (15.8) | 50.6 (15.0) | 43.1 (15.5) |
| **Mean (SD) BMI, kg/m²** | 30.2 (7.4) | 29.3 (6.0) | 30.6 (5.5) |

**Table 3. Summary of adverse events occurring in the safety population (N=1043)**

| | Subjects, n (%) | Adverse events, n |
|---|---|---|
| Any AE | 597 (57.2) | 2025 |
| **Relationship to study drug** | | |
| Not suspected | 562 (53.9) | 1903 |
| Suspected | 72 (6.9) | 116 |
| Missing | 6 (0.6) | 6 |
| **Intensity** | | |
| Mild | 469 (45.0) | 1351 |
| Moderate | 259 (24.8) | 521 |
| Severe | 59 (5.7) | 94 |
| Missing | 32 (3.1) | 59 |
| **Changes to Omnitrope® treatment** | | |
| Not changed | 539 (51.7) | 1784 |
| Increased | 21 (2.0) | 30 |
| Reduced | 47 (4.5) | 71 |
| Interrupted | 37 (3.5) | 60 |
| Permanently discontinued | 41 (3.9) | 66 |
| Missing | 10 (1.0) | 14 |
| **Serious adverse events** | | |
| No | 536 (51.4) | 1703 |
| Yes | 187 (17.9) | 317 |
| Missing | 5 (0.5) | 5 |

**Table 4. Treatment-related adverse events occurring with an incidence of >1, MedDRA preferred term and intensity (safety population, N=1043)**

| MedDRA preferred term | Intensity, n | | | Patients, n | Incidence* |
|---|---|---|---|---|---|
| | Mild | Moderate | Severe | | |
| Headache | 3 | 6 | 0 | 9 | 3.97 |
| Myalgia | 4 | 5 | 0 | 9 | 3.97 |
| Oedema peripheral | 7 | 1 | 0 | 8 | 3.52 |
| Arthralgia | 4 | 2 | 0 | 6 | 2.64 |
| Fatigue | 3 | 1 | 0 | 4 | 17.6 |
| Pain in extremity | 0 | 4 | 0 | 4 | 1.76 |
| Fluid retention | 3 | 1 | 0 | 4 | 1.76 |
| Paraesthesia | 2 | 1 | 0 | 3 | 1.32 |

*Defined as number of patients with the specified AE per 1000 patient-years. MedDRA, Medical Dictionary for Regulatory Activities

- Overall, 116 AEs in 72 patients were suspected as being treatment-related. These included 17 general disorders and administration-site conditions, 19 musculoskeletal and connective-tissue disorders, 19 nervous system disorders and 2 investigations (increased IGF levels).
- Twenty-two serious AEs in 14 patients were recorded as possibly related to study treatment, including one incidence of diabetes mellitus.
- Eight fatal cases were reported (two due to brain glioma, one due to lung neoplasm, two due to cerebrovascular accidents, one cardiac failure, one due to sepsis and one unknown cause). None of these cases was considered by investigators to be related to rhGH treatment.
- Of the 159 patients who have permanently discontinued treatment, 39 (3.7% of the total population) did so because of an AE. The most common reasons for other discontinuations were patients not wishing to continue with injections (n=32), patients lost to follow-up (n=9) and patients switched to another rhGH treatment (n=9).

## Conclusions

- Based on this interim analysis, Omnitrope® treatment in adults with GHD is well tolerated in a real-life clinical practice setting, both in rhGH-naive and previously treated patients.
- The ongoing PATRO Adults study will provide important data on the diabetogenic potential and overall safety of long-term GH replacement therapy in this population.
- In addition, this large, postmarketing surveillance study will extend the safety database for Omnitrope®, as well as contributing to the safety profile for all rhGH products.

## References

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