The PATRO Adults study of Omnitrope® for the treatment of adult patients with growth hormone deficiency: latest results

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Paolo Beck-Peccoz[1], Charlotte Höybye[2], Robert D. Murray[3], Suat Simsek[4], Alfonso Leal-Cerro[5], Markus Zabransky[6], Günter Stalla[7]

[1]Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Cà Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Department of Endocrinology, Metabolism and Diabetology, Karolinska University Hospital, Stockholm, Sweden; [3]Department of Endocrinology, Leeds Centre for Diabetes and Endocrinology, St James's University Hospital, Leeds, UK; [4]Medisch Centrum Alkmaar, The Netherlands; [5]Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío, Seville, Spain; [6]Sandoz International GmbH, Holzkirchen, Germany; [7]Max Planck Institute of Psychiatry, Department of Internal Medicine, Endocrinology and Clinical Chemistry, Munich, Germany

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 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 being 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 diabetes during treatment with Omnitrope®.
- 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 30 Jan 2015, 855 patients were enrolled in the study (Table 1); 456 (53%) patients had been previously treated with rhGH.
- Characteristics of enrolled patients are shown in Table 2.
- A total of 1179 AEs have been reported to date in 363 patients (Table 3); 109 of these (in 68 patients) were regarded as serious. Most AEs (1079/1179; 91.5%) were mild to moderate in intensity, with few resulting in any changes to Omnitrope® treatment.

Table 1. Sites and subject enrollment by country

Country	No. of sites (n=64)	No. of enrolled subjects n (%)	No. of active subjects	No. of discontinued subjects
UK	13	274 (32.0)	247	27
Sweden	6	221 (25.8)	212	9
Germany	28	188 (22.0)	174	14
Italy	8	67 (7.8)	54	13
The Netherlands	2	53 (6.2)	35	18
Spain	2	32 (3.7)	31	1
France	3	15 (1.8)	13	2
Czech Republic	2	5 (0.6)	5	0
Total	**64**	**855 (100.0)**	**771**	**84**

Table 2. Patient characteristics at enrollment

Variable	Isolated GHD	Combined GHD	Other	N/A
Gender				
Male, n (%)	44 (5.1)	396 (46.3)	3 (0.4)	8 (0.9)
Female, n (%)	53 (6.2)	343 (40.1)	4 (0.5)	4 (0.5)
Total (%)	97 (11.3)	739 (86.4)	7 (0.8)	12 (1.4)
Mean (SD) age, years	45.8 (15.8)	51.0 (15.1)	34.7 (13.2)	42.4 (16.2)
Mean (SD) BMI, kg/m²	30.2 (7.5)	29.5 (6.2)	26.3 (5.5)	39.0 (n/a)

Table 3. Summary of AEs

	No. of subjects (%) n=855	No. of AEs
Any AE	363 (42.5)	1179
Relationship to study drug		
Not suspected	335 (39.2)	1062
Suspected	66 (7.7)	107
Missing	5 (0.6)	10
Intensity		
Mild	293 (34.3)	784
Moderate	154 (18.0)	295
Severe	36 (4.2)	61
Missing	18 (2.1)	39
Outcome		
Resolved completely	187 (21.9)	381
Resolved with sequelae	47 (5.5)	68
Ongoing	264 (30.9)	688
Fatal	3 (0.4)	3
Missing	24 (2.8)	39
Changes to Omnitrope® treatment		
Not changed	318 (37.2)	985
Increased	19 (2.2)	28
Reduced	46 (5.4)	71
Interrupted	28 (3.3)	51
Permanently discontinued	21 (2.5)	34
Missing	7 (0.8)	10
Serious AEs		
No	343 (40.1)	1063
Yes	68 (8.0)	109
Missing	5 (0.6)	7

- Table 4 shows drug-related AEs that occurred with an incidence of >2.

Table 4. Drug-related AEs occurring with an incidence of >2, by MedDRA preferred term and intensity (N=855)

MedDRA preferred term	Maximum intensity No. of patients			Total No. of patients	Incidence* (subject years =1337.2)
	Mild	Moderate	Severe		
Insulin-like growth factor increased	10	2	0	12	8.97
Headache	4	5	0	9	6.73
Myalgia	2	5	0	7	5.23
Oedema peripheral	6	1	0	7	5.23
Arthralgia	4	2	0	6	4.49
Fatigue	3	1	0	4	2.99
Pain in extremity	0	3	0	3	2.24

*defined as the number of patients with the AE per 1000 patient-years

- Overall, 107 AEs in 66 patients were suspected as being drug related. Three fatal cases were reported (one due to brain cell glioma, one due to lung neoplasm and one due to unknown causes). None of these cases was considered by the investigators as possibly related to rhGH treatment.
- Of the 84 patients who have permanently discontinued treatment, 18 (2.1%) did so due to an AE.

Conclusions

- On the basis of this interim analysis, Omnitrope® treatment in adults with GHD is well tolerated in a real-life clinical practice setting, both in previously 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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