The German ACROSTUDY: past and present
M Buchfelder, S Schlaffer, M Droste1, K Mann2, B Saller3, K Brübach3, G K Stalla4, C J Strasburger5 on behalf of the investigators of the German Pegvisomant Observational Study

Department of Neurosurgery, University of Erlangen-Nürnberg, Schwabachanlage 6, 91054 Erlangen, Germany, 1Endocrinologist, Oldenburg, Germany, 2Department of Medicine, Endocrinology, University of Essen-Duisburg, Essen, Germany, 3Endocrine Care Europe, Pfizer Inc., Nürnberg, Germany, 4Department of Endocrinology, Max-Planck Institute of Psychiatry, Munich, Germany and 5Division of Clinical Endocrinology, Department of Medicine, Charité Universitätsmedizin, Campus Mitte, Berlin, Germany

(Correspondence should be addressed to M Buchfelder; Email: michael.buchfelder@uk-erlangen.de)

Abstract
Pivotal studies have demonstrated that pharmacotherapy with pegvisomant (Somavert) is a highly effective treatment for acromegaly. Since clinical experience with the drug was very limited, the Pegvisomant Observational Study was launched in Germany immediately with the drug becoming commercially available to patients early in 2004. Its purpose was to record safety and efficacy data on as many patients as possible.

As of 12th August 2008 a total of 371 patients (185 males, 186 females) had been included in the study. They were on pegvisomant therapy for an average of 118 weeks. Median and mean doses of pegvisomant were 15 and 16.4 mg/day respectively. Treatment efficacy was monitored by IGF1 levels and the patients symptoms were evaluated by completion of a questionnaire (patient-assessed acromegaly symptom questionnaire). Safety data included liver function tests, fasting glucose, HbA1c measurements, and tumor size monitoring by repeated magnetic resonance imaging.

Normalization of IGF1 ranged from 55.7% of the 273 patients assessed after 6 months to 71.3% of 202 patients assessed after 24 months of treatment. It was 70.7% after 36 months (133 patients), 64.8% at 48 months (71 patients), and 58.4% after 60 months (24 patients). In 39 patients (10.9%) treatment was discontinued due to serious adverse events or adverse events with 25 (6.7%) of these patients having a potential causal relationship with the pegvisomant treatment. Liver function tests became abnormal in 20 patients and another three patients were recorded to have hepatobiliary disorders. Tumor size increase was reported in 20 patients, but only confirmed in nine patients by careful revision of all available images. Local injection site reactions were observed in 12 patients.

In conclusion, in this large group of pegvisomant-treated patients, long-term data for up to 5 years of treatment are now available. In 71.3% of patients with previously not sufficiently treatable acromegaly, IGF1 levels were normalized by pegvisomant therapy. Elevated transaminases usually normalized after discontinuation but in half of the affected patients also despite continuation of treatment without dose alteration. Tumor progression was a rare event. It did not exceed the expected rate in patients with acromegaly not treated with pegvisomant. As from this presently largest database of acromegalic patients treated with pegvisomant, long-term results are encouraging. The German data are now merged into the global ACROSTUDY and will constitute a major portion of the international ACROSTUDY project as a continuing global web-based observational study.

Introduction
Excessive GH secretion and consequently elevated insulin-like growth factor 1 (IGF1) plasma levels in acromegaly cause increased mortality and mobility (1). When microsurgery of the pituitary adenoma fails to achieve adequate disease control, medical therapy with dopamine agonists or somatostatin analogs are further treatment options (2). For the past 5 years, pegvisomant (Somavert), a pegylated recombinant analog of human GH which acts functionally as a GH receptor antagonist, has proven to be a highly efficient treatment option in patients with resistance to or intolerance of somatostatin analogs (3–5). However, when pegvisomant became commercially available in Germany, only <250 patients had been exposed to the drug during clinical trials (6). Thus, it seemed desirable to gain further clinical experience concerning long-term treatment effects and safety data in more patients with pegvisomant, representing a new class of drugs.
The German Pegvisomant Observational Study (GPOS), a non-interventional, surveillance study of patients treated with pegvisomant (7), was commenced as soon as pegvisomant sales were launched in this country. It was a preliminary, paper based, initial version of ACROSTUDY, which is now operated as a web-based international observational study on the drug, which was started later and into which the majority of the GPOS data have now been transferred. In this paper, we report on longitudinal data from the GPOS and its seventh, most recent interim analysis from August 2008. We discuss the implication of these data, which represented more than 80% of all prescriptions of pegvisomant in Germany for the medical treatment of acromegaly.

Patients and methods

The German Pegvisomant Observational Study

GPOS was an observational, multi-center, surveillance study to monitor safety and efficacy of pegvisomant, which comprises a non-interventional data collection in accordance with the standard management of patients with acromegaly in everyday practice. It was started in January 2004 and used a protocol that is similar to the present protocol of ACROSTUDY, the Pfizer Inc. international database on pegvisomant treatment in acromegaly. Details of the study design and results of previous interim analyses (data close December 20th, 2005 and August 1st, 2006 respectively) have already been reported (7, 8). The study was approved by the Independent Ethics Committee of the Charité Universitätsmedizin, Berlin, Germany, and all patients gave their written informed consent. Documented visits in this observational study were at baseline, 6 and 12 months after start of pegvisomant, and yearly thereafter.

Patients

Until August 12th, 2008, 371 patients with acromegaly (185 men, 186 women, age 50.0±14.0 years, mean ± s.d.) were enrolled in the study, comprising 83% of all pegvisomant prescriptions in Germany and thus being a highly representative sample. Age at diagnosis of acromegaly was 41.4±12.9 years, indicating an average 8.6 years history of disease and previous treatment at the time of inclusion in the study. All 371 patients have received at least one dose of pegvisomant and were all included in the safety analysis. Mean treatment duration was 118.0±80.3 weeks, with a median treatment of 110.9 weeks. Total accumulated treatment experience thus was 771 patient years.

All but three patients had acromegaly due to a GH secreting pituitary adenoma. In three patients, autonomous GH hypersecretion was documented clinically and biochemically without morphological evidence for a pituitary tumor by magnetic resonance imaging (MRI). Two patients had multiple endocrine neoplasia type I (both female, 15 and 60 years old at baseline, macroadenomas) and one patient had a McCune–Albright Syndrome (male, 15 years old at baseline). In addition, there was one patient suffering from familial acromegaly (male, 33 years). Three hundred and twenty one patients (89.4%) had previous pituitary surgery, 135 had previous radiation therapy (42.2%), and 327 patients (89.1%) had previous medical therapy for acromegaly with either dopamine agonists (n=145, 41.1%) octreotide (n=315, 85.8%), lanreotide (n=36, 9.8%), and/or pegvisomant (n=28, 7.6% within clinical trials) before inclusion into the GPOS.

Laboratory analyses

Serum IGF1 levels were measured in the local laboratories and were interpreted according to the local, age-dependent reference ranges, as previously described (7). Central IGF1 determinations were offered and available for 146 patients at baseline. However, two different assays with different respective reference ranges were used (9, 10). Endogenous GH concentrations in the presence of pegvisomant were analyzed by a specific assay free of interference by the drug as described previously (11). Serum concentrations of pegvisomant were determined by an immunofluorometric sandwich type assay involving two MAbs named 10A7 and 6F1, raised against hGH and retaining high crossreactivity with pegvisomant. Liver function tests (AST, ALT, GGT) and routine biochemistry including glucose and HbA1c measurements were registered at every follow-up visit.

MRI evaluations

Baseline and follow-up MRI examinations were done at the treating physicians’ discretion. All MRI evaluations reported were performed and initially interpreted by local neuroradiologists or radiologists.

An MRI examination was documented at baseline in 252 patients (67.9%) and during follow-up in 245 patients (66.0%). If an increase in tumor volume was reported as a serious adverse event during the course of the study, all available MRI scans of this individual patient including those before pegvisomant treatment were re-evaluated in a reference centre, blinded for the previous interpretations of the MRI scans and for intervention data (i.e. previous treatments, start of pegvisomant treatment), as described previously (12). Apart from the mentioned MR studies, there were 44 patients who had a CT at baseline. In 10 of these patients, follow-up by CT was documented.
Results

Treatment with pegvisomant

The mean dose of pegvisomant at the time of the 7th interim analysis (data close 12th August 2008) was 16.4 ± 8.5 mg/day (median 15.0 mg/day). A daily dose of 10 mg pegvisomant or less was received by 132 patients (40%). Thirty patients received a dose above 30 mg/day. While 79.8% of the patients underwent a monotherapy with pegvisomant (mean dose ± S.D.: 13.9 ± 8.5 mg/day), 77 patients (20.2%) received either a combination with dopamine agonists (16 patients) or somatostatin analogs (61 patients). Forty of the latter patients received octreotide LAR (26 with 30 mg/month, 6 with 20 mg/month and 8 with 10 mg/month, mean dose 24.5 ± 8.2 mg/month), seven patients received lanreotide autogel (6 with 120 mg/month, 1 with 60 mg/month, mean dose 111.4 ± 22.7 mg/month), and seven patients received s.c. octreotide in doses between 50 µg and 500 µg/day (mean 233.3 ± 213.7 µg/day). Table 1 shows the mean and median doses of pegvisomant at the different interim analyses in relation to the rate of IGF1 normalizations.

Normalization of IGF1

Mean IGF1 as locally measured by different assays dropped from 460.2 ± 238.8 ng/ml at baseline to 239.6 ± 107.5 ng/ml at 60 months (Fig. 1). The normalization rate of IGF1 depended on the duration of treatment and on the dose of pegvisomant. It ranged from 55.7% of the 273 patients assessed after 6 months to 71.3% of the 202 patients assessed after 24 months of treatment. It was 70.7% after 36 months (133 patients), 64.8% at 48 months (71 patients), and 58.4% after 60 months (24 patients). Figure 2 shows the distribution of pegvisomant doses delivered to patients at 24 months dependent on whether they had a normalized, age-adjusted IGF1 or not. Of the patients who had a combination therapy of pegvisomant and other drugs, 42.1% had normal IGF1 levels after 6–12 months.

Clinical response

In a disease specific patient questionnaire, joint pain, soft tissue swelling, numbness or tingling of limbs and the general physical condition was significantly (P<0.05) improved after 6 months of treatment, while only soft tissue swelling and numbness were significantly improved after 24 months of treatment. Excessive sweating was significantly reduced at the 12 months follow-up visit.

Glucose metabolism in patients with diabetes

At baseline in 84 patients diabetes mellitus was documented. Of these, 68 patients (57.1%) were on therapy with oral antidiabetics or insulin. At the 6 months follow-up visit, 58 (49.4%) of the diabetic patients were still on antidiabetic medication, at the 12 months follow-up visit still 60 (43.8%). On pegvisomant therapy mean serum glucose of the

### Table 1 Evolution of the German ACROSTUDY: an overview of pertinent patient and treatment data from the interim analyses 1–7.

<table>
<thead>
<tr>
<th>No.</th>
<th>Date of interim analysis</th>
<th>Active centers</th>
<th>Total number of patients</th>
<th>Drop out</th>
<th>Pegvisomant mg/day (mean ± s.d.)</th>
<th>Pegvisomot mg/day (median)</th>
<th>Duration of treatment in patient years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>31.07.2004</td>
<td>40</td>
<td>102</td>
<td>4</td>
<td>16.0 ± 6.8</td>
<td>15.0</td>
<td>64.8 60.0 25.0</td>
</tr>
<tr>
<td>2.</td>
<td>15.12.2004</td>
<td>45</td>
<td>123</td>
<td>8</td>
<td>15.9 ± 6.8</td>
<td>15.0</td>
<td>60.0 56.7 24.7</td>
</tr>
<tr>
<td>3.</td>
<td>15.07.2005</td>
<td>62</td>
<td>184</td>
<td>18</td>
<td>16.8 ± 7.6</td>
<td>15.0</td>
<td>65.4 68.7 20.0</td>
</tr>
<tr>
<td>4.</td>
<td>20.12.2005</td>
<td>76</td>
<td>229</td>
<td>23</td>
<td>16.5 ± 7.7</td>
<td>15.0</td>
<td>64.0 70.9 23.4</td>
</tr>
<tr>
<td>5.</td>
<td>01.08.2006</td>
<td>85</td>
<td>263</td>
<td>36</td>
<td>16.4 ± 7.6</td>
<td>15.0</td>
<td>65.1 70.6 23.4</td>
</tr>
<tr>
<td>6.</td>
<td>15.07.2007</td>
<td>98</td>
<td>307</td>
<td>45</td>
<td>16.6 ± 7.4</td>
<td>15.0</td>
<td>62.2 68.5 23.3</td>
</tr>
<tr>
<td>7.</td>
<td>12.08.2008</td>
<td>101</td>
<td>371</td>
<td>73</td>
<td>16.4 ± 8.5</td>
<td>15.0</td>
<td>55.7 65.3 21.3</td>
</tr>
</tbody>
</table>

*No data available at this point of time.

![Figure 1](https://www.eje-online.org)
diabetic patients decreased from 141.4 ± 61.0 to 102.0 ± 24.1 mg/dl at the 24 months follow-up visit, while HbA1c decreased from 7.0 ± 1.4 to 6.5 ± 1.3% during the same time interval (Table 2).

Liver function

In a total of 20 patients liver enzymes elevated more than three times above the upper limit of normal were recorded during pegvisomant treatment. In 15 of these (75%) ALT elevation was the dominant finding, in one patient AST was more abnormal, while in four patients the elevation of GGT were predominant. In seven patients treatment with pegvisomant was permanently discontinued for liver enzyme elevations and in six of them, normalization of the enzymes was documented. Of the two patients in whom pegvisomant was temporarily withdrawn, one recovery was documented on later continuation. The other patient was put onto a combination therapy with somatostatin analogs. In 11 patients, pegvisomant was continued despite the elevated liver enzymes that were noticed. Spontaneous normalization was documented in ten and one had elevated GGT levels already at the baseline visit. Among the patients affected by liver enzyme elevations, gallstones were detected in abdominal ultrasound examinations in seven. All of these patients with elevated transaminases and thus obviously also those with gallstones had previously had exposure to somatostatin analogs.

Other adverse effects

In 39 patients (10.5%) treatment discontinuations followed the recording of a serious adverse effect or adverse effect. In 25 (6.7%) of these the investigators suspected a causal relationship with pegvisomant therapy. Apart from liver enzyme elevations and apparent tumor size increase, as mentioned above, hepatobiliary disorders were recorded in three patients and other causes (muscle spasm, myalgia, pregnancy, cholecystectomy, hypophysectomy) in five other patients. A total of 12 patients reported some degree of local or diffuse lipohypertrophy, predominantly at the injection sites.

Pituitary tumor size

The size of the pituitary tumor or residual adenoma at baseline before pegvisomant treatment was classified to be larger than 10 mm in diameter in 222 out of the 371 patients (59.8%) and smaller than 10 mm in diameter in 44 patients (11.8%). No visible tumor was found in 25 patients (6.7%), 9 patients (2.4%) had a visible tumor without data on tumor size, and in 67 patients (18.0%) no data about baseline pituitary imaging were available. An increase in pituitary tumor volume was reported by the responsible investigator as an adverse event in 20/311 patients (6.4%). In 11 of these cases (55.0%), increases in tumor volume could not be verified at meticulous re-evaluation. In nine patients (45.0%), an increase in tumor volume was confirmed at re-evaluation (four males, five females, age at start of

Table 2 Glucose and HbA1c levels in diabetic patients.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (mean ± s.d.)</th>
<th>6 months FU (mean ± s.d.)</th>
<th>12 months FU (mean ± s.d.)</th>
<th>24 months FU (mean ± s.d.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose fasting (mg/dl)</td>
<td>141.4 ± 61</td>
<td>125.8 ± 55.6</td>
<td>111.6 ± 45.6</td>
<td>102.0 ± 24.1</td>
</tr>
<tr>
<td>n=58</td>
<td></td>
<td>n=51</td>
<td>n=50</td>
<td>n=28</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.0 ± 1.4</td>
<td>6.5 ± 1.2</td>
<td>6.5 ± 1.2</td>
<td>6.5 ± 1.3</td>
</tr>
<tr>
<td>n=71</td>
<td></td>
<td>n=65</td>
<td>n=67</td>
<td>n=41</td>
</tr>
</tbody>
</table>

*Indicates a significant reduction (P < 0.05) versus baseline.
between elevated IGF1 and mortality. However, since an ignorance of pharmacodynamics and of the relationship reached in terms of IGF1 suppression or simply patient satisfaction already achieved under what was considerations, the occurrence of side effects, adequate maximal IGF1 suppression. This might be due to cost always titrate the dose as it would be required for independently from study protocols do obviously not be achieved in almost every patients treated, if studies suggest that with the drug IGF1 normalization to-treat acromegaly. Results from pharmacodynamic levels(4, 5, 13) , the GPOS found much lower normal-

of patients treated with this drug achieved normal IGF1 (4, 5). However, while in the clinical studies up to 97% pivotal studies had demonstrated its safety and efficacy experience with its clinical use was very limited. The drug became commercially available in Germany, medical treatment options for acromegaly. When the ant and highly efficient drug added 5 years ago to The GH receptor antagonist pegvisomant is an import-
definition. The successful conduct of the study is the nationwide reflection of clinical practice under field conditions, which frequently differ from clinical studies. Over the years between 2004 and 2008, an increasing use of combination therapies was recognized (14, 15).

Another strength of this observational study was the careful observation of side effects. Both liver function studies and tumor size monitoring were performed in a more accurate fashion as they could be carried out on a broader international level. The successful conduct of the study was facilitated by the frequent feedback to the investigators which for the first 2.5 years of the study was performed by interim analyses of the database every 6 months and reported to the treating physicians in investigator meetings. Increases in serum levels of liver enzymes were detected in a few individual patients during initial clinical studies. However, the fact that a spontaneous normalization of these occurs also on continuation of pegvisomant therapy was found in the huge cohort of the GPOS and reported separately in a previous paper (16). The overall prevalence was 23/371 (6%).

Moreover, since it was feared that along with lowering of IGF1 levels progression of the GH secreting adenoma could occur, annual serial MRI investigations were recommended. When an increase in tumor volume was suspected and reported to health authorities as an adverse event, a careful re-evaluation of all pertinent images of the individual patient was performed that included a review of the investigation prior to pegvisomant exposure. Surprisingly, these re-evaluation did not confirm the initial suspicion in the majority of patients. We recently reported the re-evaluation details based on the 6th interim analyses of the German ACROSTUDY, which was based on 18 patients with suspected tumor progression. In ten patients the tumor appeared stable upon careful re-assessment while eight tumors had expanded (12). In the most recent interim analysis, reported herein, two patients with suspected tumor progression are

pegvisomant therapy 52.0±16.6 years (mean±s.d.). None of these patients was on combination treatment with somatostatin analogs. Two of them had a rebound of tumor size after previous shrinkage and subsequent discontinuation of somatostatin analogs, reaching their original volumes. In three patients there was documented tumor growth on other medication before pegvisomant therapy was commenced (Fig. 3) and in three others there was a slight, clinically insignifi-
cant size increase during pegvisomant. In one patient there was tumor growth on a previously stable adenoma only while the patient was on pegvisomant. As a consequence of alert by the local neuroradiologist, in four patients treatment with pegvisomant was discontinued. In one patient therapy was re-instituted after re-evaluation of the images.

Discussion

The GH receptor antagonist pegvisomant is an important and highly efficient drug added 5 years ago to medical treatment options for acromegaly. When the drug became commercially available in Germany, experience with its clinical use was very limited. The pivotal studies had demonstrated its safety and efficacy (4, 5). However, while in the clinical studies up to 97% of patients treated with this drug achieved normal IGF1 levels (4, 5, 13), the GPOS found much lower normalization rates (7, 8) reaching a maximum of 71.3% at 24 months. It reflects the reality of patient care in difficult-to-treat acromegaly. Results from pharmacodynamic studies suggest that with the drug IGF1 normalization could be achieved in almost every patients treated, if only the dose was adequately adapted. Physicians acting independently from study protocols do obviously not always titrate the dose as it would be required for maximal IGF1 suppression. This might be due to cost considerations, the occurrence of side effects, adequate patient satisfaction already achieved under what was reached in terms of IGF1 suppression or simply ignorance of pharmacodynamics and of the relationship between elevated IGF1 and mortality. However, since a remarkable 83% of those acromegalic patients treated with pegvisomant in this country are monitored and documented in this German Database, one strength of the study is the nationwide reflection of clinical practice under field conditions, which frequently differ from clinical studies. Over the years between 2004 and 2008, an increasing use of combination therapies was recognized (14, 15).

Figure 3 Steady increase in tumor volume documented by serial analysis of MR images in a 31-year-old male patient. For an intra- and suprasellar pituitary adenoma (A) he underwent transcranial (B) and transsphenoidal surgery and bromocriptine treatment (C). Thereafter, radiosurgery was performed for the parasellar residual tumor (D). While the irradiated tumor portion regressed during cabergoline and somatostatin analog therapy (E), on the contralateral side intrasellar tumor became visible, which progressed during pegvisomant treatment (F) and finally required a third operation.

Steady increase in tumor volume
added to our previous paper (12), of which growth in one was not confirmed. Thus, 11 of the 20 patients with suspected growth turned out to have stable tumor sizes upon blinded analysis of serial MRI images. Since many patients underwent treatments with somatostatin analogs prior to pegvisomant, a re-expansion of the tumor to their prior size following somatostatin analog induced shrinkage (17) and subsequent discontinuation does not surprise, but should not be called ‘tumor growth’. Serial MR analyses of the entire patient history revealed that in three patients the adenomas had increased in size already during previous medical treatments, such as dopamine agonists or somatostatin analogs. Only a small minority of patients (n = 3) showed some size increase only on pegvisomant. All progressions were relatively minor size increases that could not be recognized clinically. Other reports of tumor size increase (5, 13, 15, 18–20) did not pay tribute to potential tumor size increase before pegvisomant therapy and also did not evaluate for potential somatostatin induced tumor shrinkage and subsequent rebound, although in an individual patient such a course is described (13). In this cohort and in the medical literature, except for one patient, whose tumor progression occurred during combination therapy with pegvisomant and somatostatin analogs (19), all hitherto reported tumor size increases were observed during monotherapy with pegvisomant (20). Although some concern remains that the standards of radiology that have falsely suspected tumor expansion, could for the same reason have failed to detect enlargement in other patients, documented tumor progressions clearly do not exceed the rate expected during other medical treatments for acromegaly (21).

In those patients with diabetes mellitus as a concomitant disease, HbA1c and fasting glucose were significantly improved during the study. Moreover, the number of patients requiring insulin or oral antidiabetics was reduced. These data support previous findings that the GH receptor antagonist reduces insulin resistance by inhibiting the effects of excess GH. In contrast to somatostatin analogs pegvisomant does not inhibit pancreatic insulin secretion (18, 22).

Although the study provided a huge amount of data on patients treated with pegvisomant, data were not available for every patient at each and any follow-up visit. This weakness is most visible in the patient’s self-assessed acromegaly symptoms questionnaire. While the total score was significantly improved at 12 months (8), it lacked a significance level at 24 months, probably due to the limited numbers of patients returning the score sheet.

Conclusions
The present study summarizes the experience in the largest cohort of patients to date observed during pegvisomant therapy. Representing a major logistic success, 83% of all patients treated with the GH receptor antagonist in Germany could be enrolled and documented into this observational study. The database provides information about treatment strategies in real countrywide medical practice and provides important safety and efficiency data. It is only reasonable that the data obtained in this German database are merged into the even more ambitious, web-based global database called ACROSTUDY (6) that will not only generate more data on safety and efficacy of pegvisomant treatment, but will also enable the comparison of treatment modalities between different countries.

Declaration of interest
Sven Schlafer declares no potential conflicting interests. Michael Buchfelder, Michael Droste, Klaus Mann, Günter-Karl Stalla and Christian J Strasburger are members of the National German AcroStudy Board. Christian J Strasburger is also a member of the International ACROSTUDY Board. Katja Brütbach and Bernhard Saller are currently employed by Pfizer. ACROSTUDY™ is supported by Pfizer Inc. This paper forms part of a European Journal of Endocrinology supplement, supported by Pfizer Inc.

Funding
The German Pegvisomant Observational Study (GPOS) is sponsored by Pfizer Pharma GmbH, Karlsruhe, Germany.

Acknowledgements
The manuscript was written on behalf of the investigators of the German Pegvisomant Observational Study by the members of its scientific board. The authors thank all the investigators and study nurses of the individual centers for contributing data to this study: Dr M Droste, Endocrinologist, Oldenburg; Prof. Dr G K Stalla, Max-Planck-Institute of Psychiatric, Munich; Prof. Dr B Al lolio, University of Würzburg: Würzburg; Dr M Faust, University of Cologne, Cologne; Dr M Brendel, University of Giessen, Giessen; Dr R Finke, Dr H Tuchtel, Endocrinologists, Berlin; Dr M Bidingmaier, Medizinische Klinik-Innenstadt, Ludwig-Maximilians University, Munich; Dr M Engelbach, Dr R Santen, Endocrinologists, Frankfurt am Main; Prof. Dr R Hampel, University of Rostock, Rostock; Prof. Dr K Mann; University of Essen-Duisburg, Essen; Prof. Dr P H Kann, Philippus-University, Marburg; Prof. Dr B Boehm, University of Ulm, Ulm; Prof. Dr C Kasperk, Ruprecht-Karls-University, Heidelberg; Dr C Kerber Helios Klinikum, Schwerin; PD Dr H Wallaschofski, University of Greifswald, Greifswald; Prof. Dr H Moenig, University of Kiel, Kiel; Prof. Dr M Stumvoll, University of Leipzig-Leipzig; PD Dr J Schopohl, Medizinische Klinik-Innenstadt, Ludwig-Maximilians University, Munich; Dr B Völz, Klinikum Görlitz, Görlitz; Dr K Würl, Endocrinologist, Dresden; Dr J Ittner, Endocrinologist, Augsburg; Dr K Reschke, Otto-von-Guericke University, Magdeburg; Dr J Jacobit, Endokrinologikum, Hamburg; Prof. Dr G Ramadori, Georg-August-University, Göttingen; Dr A Schindler, Endocrinologist, Greifswald; Prof. Dr S Zeuzem, Saarland University Hospital, Homburg; Prof. Dr K Badenhoop, Johann Wolfgang Goethe-University, Frankfurt; Prof. Dr F U Beil, University Clinic Eppendorf, Hamburg; Prof. Dr A F Pfleger, Charité-Universitätsmedizin, Berlin, Campus Benjamin Franklin; Dr C Vogel, Chemnitz; Prof. Dr I C Hofbauer, Technical University, Dresden; Prof. Dr J J Strasburger, Division of Clinical Endocrinology, Department of Medicine, Charité-Universitätsmedizin, Campus Mitte, Berlin; Prof. Dr U Tuschy, Helios Klinikum, Erfurt; PD Dr U Plößker, Campus Virchow-Klinikum, Charité-Universitätsmedizin, Berlin; Dr B Seiditz.
Endocrinologist, Berlin; Dr F Demtröder, Endocrinologist, Dortmund; Prof.
Dr Schmiegl, Ruhr-University, Bochum; Dr R Gellner, University of Muenster, Muenster; Prof. Dr K J Gräff, Endocrinologikum, Berlin; Dr U Schröder; Endocrinologikum, Hannover; Prof. Dr F Ball, Endocrinologikum, Lübeck; Dr K Ventzke, Endocrinologikum, Bremen; Prof. Dr J Hensen, Nordstadt-Hospital, Hannover; Dr H Lux, Endocrinologikum, Nürnberg; Dr H Ehrhardt, Dr A Alexopoulos, Endocrinologists, Ulm; PD Dr C Spitzweg, Klinikum Grosshadern, Ludwig-Maximilians-University, Munich; Dr D Schnabel, Charité, Campus Virchow-Klinikum, OHC Kinderklinik, Berlin; Dr A Dost, University of Jena, Jena; Prof. Dr M M Weber, Johannes Gutenberg University, Mainz; Dr K Viemer, Carl Thieme Hospital, Cottbus; Dr W Omran, Endocrinologist, Mainz; Dr R Keuser, Endocrinologist, Koblenz; Dr K Salzgeber, Endocrinologikum, Ulm; Dr R Gutkeunst, Endocrinologikum, Lübeck; Dr C Terkamp, Medizinische Hochschule, Hannover; Dr S Gaissmaier, Endocrinologikum, Munich; Dr T Eversmann, Endocrinologikum, Munich; Prof. Dr J Seufert, University of Freiburg, Freiburg; Dr C Jaurusch-Hancke, Deutsche Klinik für Diagnostik, Wiesbaden; Prof. Dr M Ritter, Ibbenbuehren Hospital, Ibbenbuehren; Dr C Undechs, Endocrinologin, Jena; Dr E Jochem, Krankenhaus der Barmherzigen Brüder, Trier; Prof. Dr Schürmeyer Mutterhaus der Borromäerinnen, Trier; PD Dr T Schleiffer, St Wilhelms-Hospital, Wilhelmshaven; Prof. Dr W Karges, RWTH, University of Aachen, Aachen; Dr J Meuser, Dietrich-Bonhoeffer-Klinikum, Neubrandenburg; Dr J Wildbrett, Endocrinologist, Dresden, Dresden; Dr J Krug, Städtisches Klinikum ‘St Georg’, Leipzig, Prof. Dr M Buchfelder, University of Erlangen-Nürnberg, Erlangen; Prof. Dr D Klingmüller, University of Bonn, Bonn; PD Dr U Schmitz, Medizinische Universitäts-Poliklinik, Bonn; PD Dr B Perras, University of Schleswig-Holstein, Lübeck; Prof. Dr R Zick, St Bonifatius Hospital, Lingen; Prof. Dr E Leicht, Endocrinologist, Homburg, PD Dr B Manfras, Endocrinologikum, Ulm; Prof. Dr F Schuppert, Bad Oeynhausen Hospital, Bad Oeynhausen; Prof. Dr O A Müller, Rotkreuzkrankenhaus, Munich; Dr E Stahlmer, Endocrinologist, Hamburg; Dr U Kajdan; Endocrinologist, Kirchhain; Prof. Dr Gallwitz, University of Tübingen, Tübingen; Dr H Rochlütz, Endocrinologist, Waldkraiburg; Dr C Heckmann, Endocrinologist, Wuppertal; Dr E Haak, Endocrinologist, Bad Mergentheim, Dr R Weber, Hospital Rosenheim, Rosenheim; PD Dr med. B L Herrmann, Institut of Cardiodiabetes, Bochum; PD Dr S Schneider, University Hospital Bergmannsheil, Bochum; Prof. Dr W A Scherbaum, University Hospital, Düsseldorf, PD Dr U Deuk, Endocrinologist, Köln; Dr B Jacobs, Marienhospital Osnabrück, Osnabrück; Dr med. B Gerbert, Endocrinologikum, Dresden; PD Dr M Wolf, Hospital Bietigheim-Bissingen, Bietigheim-Bissingen; Dr T West, Dr J Lippe, Endocrinologists, Düsseldorf; Dr H Biering, Endocrinologikum, Berlin.

References

8 Strasburger CJ, Buchfelder M, Droste M, Mann K, Stalla GK, Saller B & German Pegvisomant Investigators. Experience from the German Pegvisomant Observational Study. Hormone Research 2007 68 70–73.

Received 21 July 2009
Accepted 4 August 2009