

# Primary Medical Therapy of Acromegaly with Somatostatin Analogues: Analysis of the German Acromegaly Register

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for the Participants of the German Acromegaly Register

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## Introduction:

Primary medical therapy has been discussed as an alternative to surgery in selected patients with acromegaly. To evaluate this treatment option, we screened the newly established German Acromegaly Register for patients treated primarily with somatostatin analogues (SA). The German Acromegaly Register is an initiative of the Pituitary Working Group of the German Endocrine Society. The aim of the German Acromegaly Register is to collect data on patients suffering from Acromegaly in Germany, both retrospectively and prospectively.

## Methods:

The Register uses the UK electronic database to assure comparison between these two countries with different health care systems. All German health care providers are invited to participate. To assure correct and uniform data entry, two trained nurses visit all centers for data acquisition. GH and IGF-1 levels are those reported by case notes. Due to variations in assays and reference ranges, normalization of IGF-1 is assessed using local criteria. Sponsorship is provided by an unrestricted grant from Novartis Oncology, Germany.

Results are expressed as mean±SEM. GraphPad Prism 4.0 (GraphPad Software Inc., San Diego, USA) was used for statistical analyses. The Mann-Whitney test and the Kruskal-Wallis test, followed by Dunn's multiple comparison test, were performed where appropriate.

## Results:

At the time of this analysis, retrospective data from 1000 patients had been entered into the database, with a mean age (+/-SEM) at diagnosis of 44.3±/0.4 years. Initial random GH levels of patients with biochemical data available were 29.7±/2.1 ng/ml, with 92.3% of GH levels >2.5 ng/ml and 96.1% of IGF-1 levels elevated. Radiological evaluation revealed micro- and macroadenomas in 21.2% and 63.6% of patients, respectively.

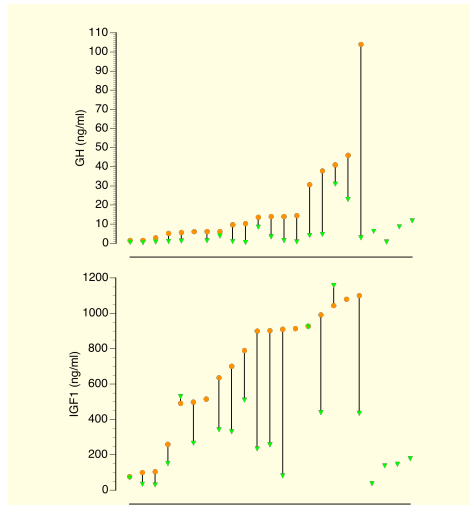


Fig.1 Pre- (orange circles) and post- (green triangles) treatment GH (upper panel) and IGF-1 (lower panel) levels in patients treated with SA as primary treatment

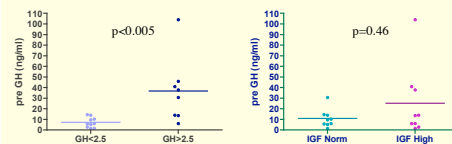


Fig.2 Pre-treatment GH levels in patients with SA as primary treatment: with post-treatment GH levels < or > 2.5 ng/ml (left panel) or with post-treatment IGF-1 levels normalized or elevated (right panel)

Forty-two patients received SA with the intention of primary treatment (Group 1). Biochemical data after 6-18 months were considered for re-evaluation, which was available for 23 patients (Fig.1). Random GH<2.5 ng/ml were found in 50% of patients, and normal IGF-1 in 54.5%. GH and IGF-1 were reduced to 27.0±/5.2% and 56.0±/7.8% of initial values, respectively.

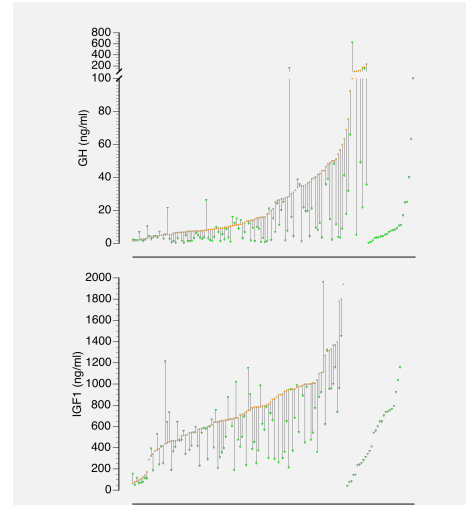


Fig.3 Pre- (orange circles) and post- (green triangles) treatment GH (upper panel) and IGF-1 (lower panel) levels in patients treated with SA prior to other treatments

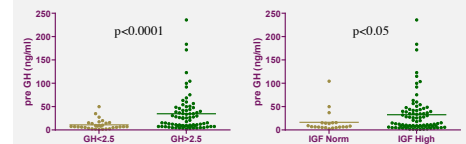


Fig.4 Pre-treatment GH levels in patients with SA prior to other treatments: with post-treatment GH levels < or > 2.5 ng/ml (left panel) or with post-treatment IGF-1 levels normalized or elevated (right panel)

Another 196 patients received SA prior to other forms of therapy (Group 2), with biochemical data available for re-evaluation in 144 patients treated for 9.0±/1.8 months (Fig.3). In this subgroup, random GH<2.5 ng/ml was obtained in 26.0% of patients, and normal IGF-1 in 17.1%. GH and IGF-1 were reduced to 72.2±/9.5% and 81.7±/4.4% of initial values, respectively.

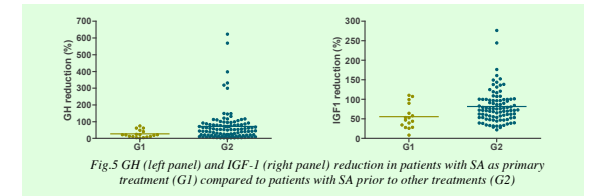


Fig.5 GH (left panel) and IGF-1 (right panel) reduction in patients with SA as primary treatment (G1) compared to patients with SA prior to other treatments (G2)

## Discussion:

- Patients with favorable biochemical response (GH<2.5 ng/ml or normalized IGF-1 levels) had significantly lower pre-treatment random GH (Fig.2,4).
- Compared with patients in Group 2, patients in Group 1 had significantly better response rates regarding GH reduction (Fig.5, p<0.01), IGF1 reduction (Fig.5, p<0.05), and IGF1 normalization (p<0.05).
- Due to the retrospective nature, the reasons for patient's assignment to either treatment group are difficult to elucidate. Pre-treatment random GH did not differ significantly between both groups (19.5±/5.7 ng/ml compared with 29.0±/3.5 ng/ml, p=0.19).
- The better response rate in Group 1 may be explained by the lower rate of macroadenomas (43.5% compared with 83.3%, p<0.05). However, biochemical response parameters did not differ between micro- and macroadenomas in separate analysis for each group (G1: %GH p=0.41, %IGF-1 p=0.92, G2: %GH p=0.86, %IGF-1 p=0.81).

## Summary:

- Primary medical treatment with SA clearly presents an alternative to other treatment options in some patients.
- Prospective studies are necessary to define patients, which may specifically benefit from either medical or surgical treatment.

## Participants of the German Acromegaly Register:

Biering H, Blosssey HC, Blum H, Bogner U, Caspar-Bell G, Demtröder F, Diederich S, Droste M, Faust M, Finke R, Gräf KJ, Gerbert B, Grußendorf M, Hampel R, Herrmann R, Herrmann BL, Höfken K, Hüfner M, Jacobbeit J, Joekenhövel F, Knippert A, Koch C, Krone W, Lehnert H, Löbner C, Mann K, Meuser J, Meyer A, Mönig HI, Müller UA, Paschke R, Petersenn S, Pfeiffer A, Plöckinger U, Raue F, Reincke M, Reschke K, Rühl H, Schopohl J, Schories M, Schröder H, Schröder HE, Schröder U, Schulte HM, Strasburger CJ, Tuschy U, von Werder K, Weber MM, Würl K