SHORT-TERM (3 MONTHS) COMPARED TO LONG-TERM RESPONSE TO SOMATOSTATIN ANALOGUES IN ACROMEGALY

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INTRODUCTION. In acromegaly, the reported therapeutical efficacy of somatostatin analogs (SSA), *i.e.* normalization of GH and IGF-1, is 50 – 70% (44 – 34% in unselected patients). This specific treatment is financially supported by the Romanian National House of Health Insurance for patients with acromegaly.

AIM OF STUDY: to retrospectively evaluate whether random GH and IGF-I levels achieved after 3 months of SSA treatment are predictive for the efficacy of SSA (lanreotide, octreotide) after longer treatment with the same dose.

METHOD: A retrospective review of 71 patients with acromegaly admitted in the Department of Neuroendocrinology, "C.I. Parhon" Institute, Bucharest (2006 – 2012) and treated for at least 6 months with SSA according to the Protocol of the Romanian National House of Health Insurance for patients with acromegaly. In 40 of them data on random serum GH and IGF-1 were available at baseline, after 3 months and at the last evaluation on the same SSA dose. Two patients have been evaluated on 2 different doses of SSA. In the other 31 patients not included in this study, the dosage has been either increased after 3 months – in 21 patients, or evaluated after > 3 months – in 10 patients).

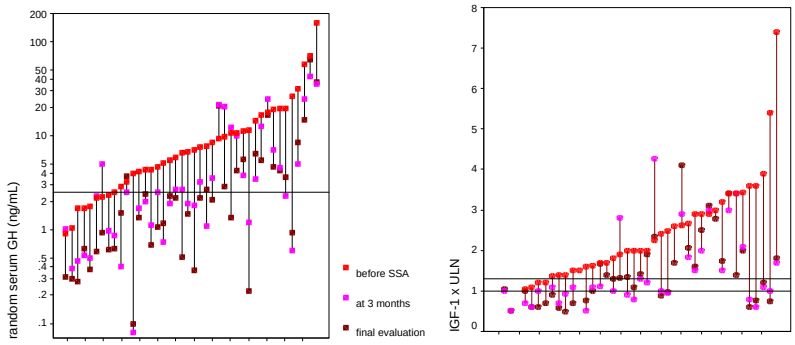
MATERIALS: Serum GH (usually in Parhon Institute): IRMA assay - MAIA Clone (Radim, Italy) – sandwich method with monoclonal a.b. - Sensibility 0.2 ng/ml. Serum IGF-1 (various laboratories, commercial kits). Follow-up protocol: random serum GH (mean of 4 blood samples extracted at 4 hours interval) and IGF-1 were measured at baseline and after 3, (6), 12 and >12 months after therapy initiation. Optimal response to SSA included random GH ≤ 2.5 ng/mL and normal age-adjusted IGF-1 level.

RESULTS

PATIENTS CHARACTERISTICS (n = 40 patients)	
Sex (F: M)	28:12
Age at diagnosis, mean ± SD, (range)	42 ± 11.6 years (22 – 62 years)
Previous pituitary surgery	35 (29 SS, 4 FS, 2 SS+FS)
Previous radiotherapy or radiosurgery	26 (10 HVR, 2 NVR, 12 GK, 1 HVR+GK, 1 HVR+NVR)
Tumor size at treatment initiation	25 macro, 15 micro

SOMATOSTATIN ANALOG TREATMENT CHARACTERISTICS (n = 40 patients)	
Treatment type / no patients	
Somatuline PR (n = 22 patients)	30 mg/14 days = 15 30 mg/10 days = 4 30 mg/7 days = 3
Sandostatin LAR (n =18 patients)	20 mg/28 days = 10 30 mg/28 days = 10
Treatment duration (until last follow-up on the same SSA dosage), mean ± SD	15 ± 10 months (range 5 - 44 months)

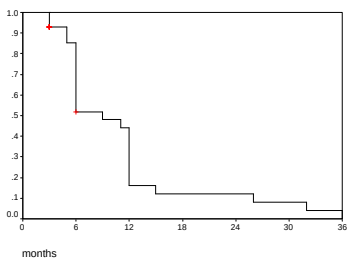
Short vs longer-term response to SSA



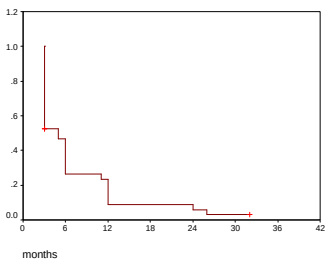
	Before SSA	3 months	last evaluation
mean ± SD random GH (ng/ml)	14.9 ± 27*	6.5 ± 9.8	5.7 ± 0.6*
mean ± SD IGF1 (x ULN)	2.4 ± 1.3*	1.5 ± 0.9	1.4 ± 2.3*

*P < 0.05

GH normalization rate

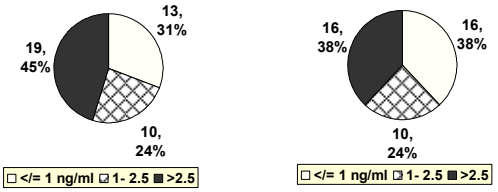


IGF1 normalization rate



A random GH ≤ 2.5 ng/mL at 3 months has a 86.9% positive predictive value for normal GH at final evaluation and a 72.7% negative predictive value.
Normal IGF-1 (x ULN) ≤1 at 3 months has a 85% positive predictive value for normal IGF-1 at final evaluation and a 83% negative predictive value.

Random GH response to SSA (3 months vs. final evaluation)



Concordant values between the two points of evaluation were found in 33/42 patients (78.5%).

IGF-1 response to SSA

Normal serum IGF-1 was recorded at 3 months in 20/35 patients (57.1%) and at the last evaluation in 17/35 patients (48.5%), concordant values in 32/35 patients (91.4%).

Discordances between short and long-term response

Normal values at 3 months and elevated at the last evaluation were found:
- for GH in 3/42 patients (7.1%)
- for IGF1 in 3/35 patients (8.5%, 2 of them up to 1.3 x ULN).

3 patients with IGF-1 < 1.3 x ULN at 3 months had higher final values.

Normalization only at the last evaluation was recorded in 6/42 patients (14%) only for GH.

Discordances GH - IGF1 (12/42 = 28.5%)

Normal GH with high IGF-1 : 7 patients
High GH, normal IGF-1 : 5 patients

CONCLUSION

- In our series, the response to somatostatin analogues evaluated at 3 months was concordant with the response after longer treatment with the same dose in 78.5% of patients for GH and 91.4% for IGF-1.
- When discordances between IGF-1 and random GH occur at 3 months, we suggest a re-evaluation on the same SSA dose. If the discordance persists, a dosage increase should be considered.