

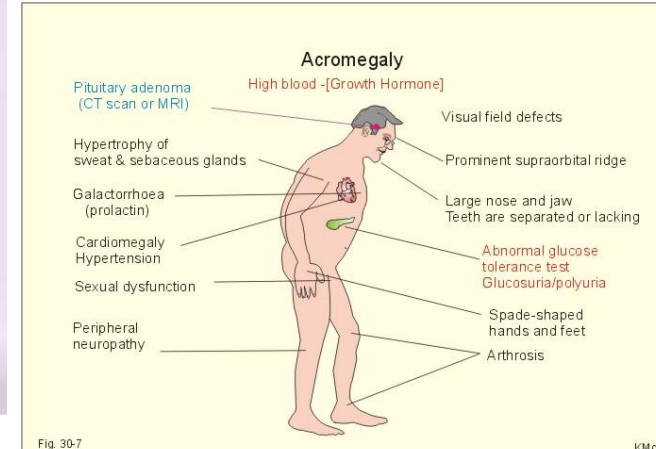
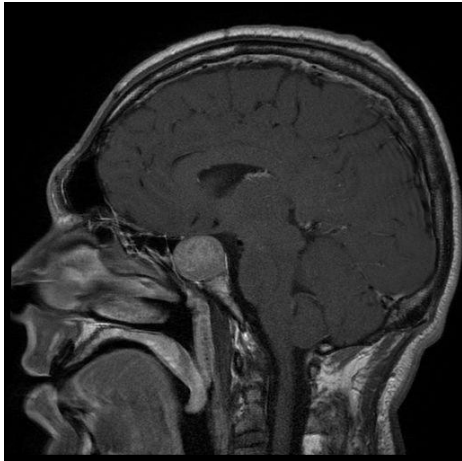
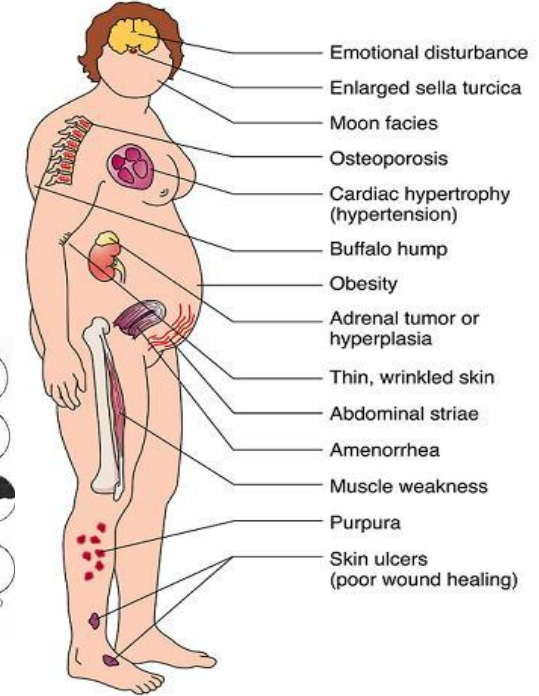
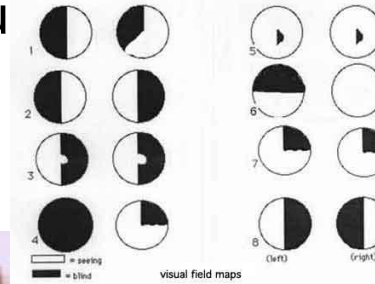
# Hipofiz Tümörleri Pasireotide

Prof. Dr. Erdiñç Ertürk  
Uludağ Üniversitesi Tıp Fakültesi  
Endokrinoloji Bilim Dalı

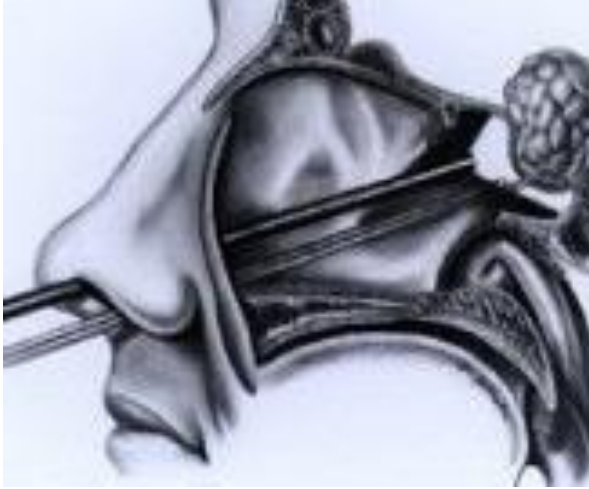
5. Hipofiz Sempozyumu  
22 Kasım 2008, Ankara

# Hipofiz adenomlarında belirtiler

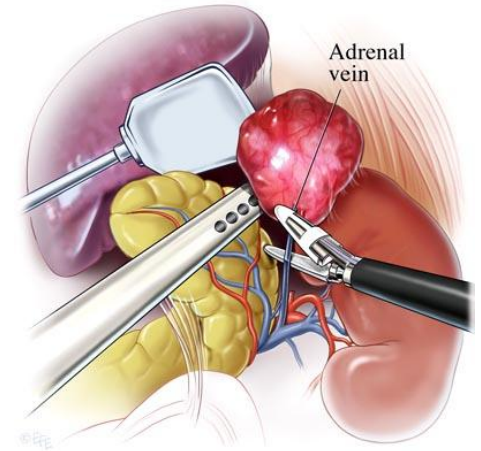
- Adenomun kitle etkisi
  - Hipopitüitarizm
  - Görme alanı daralması
  - Baş ağrısı vs
- Adenomun hormon hipersekresyonu
  - Prolaktinoma
  - Akromegali
  - Cushing
  - Hipertiroidi



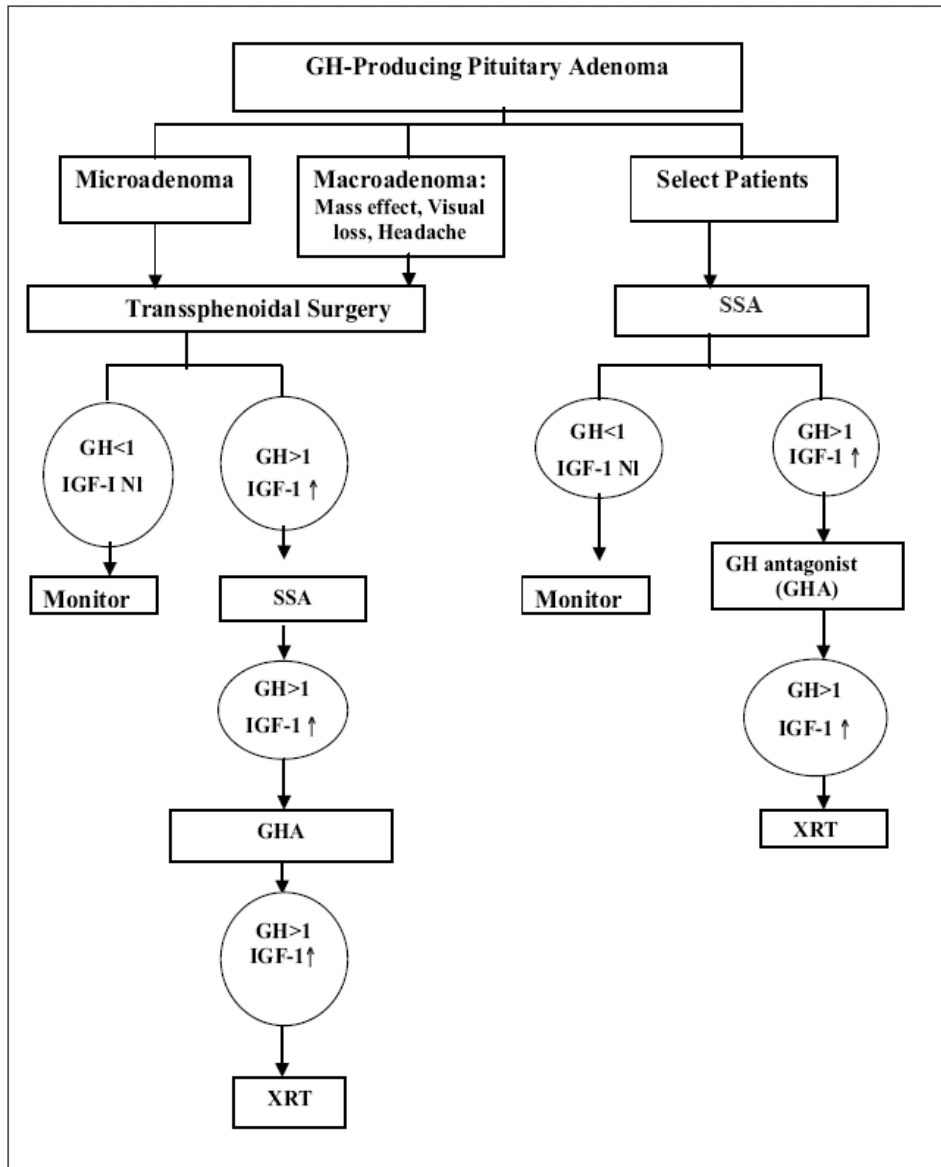
# Hipofiz adenomlarında tedavi seçenekleri



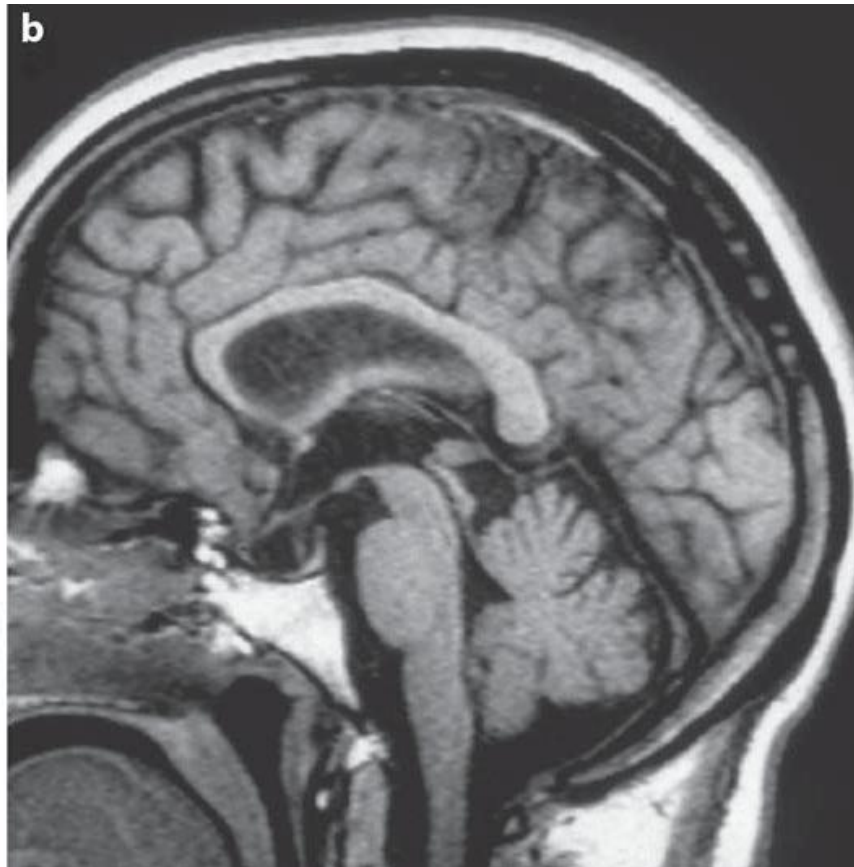
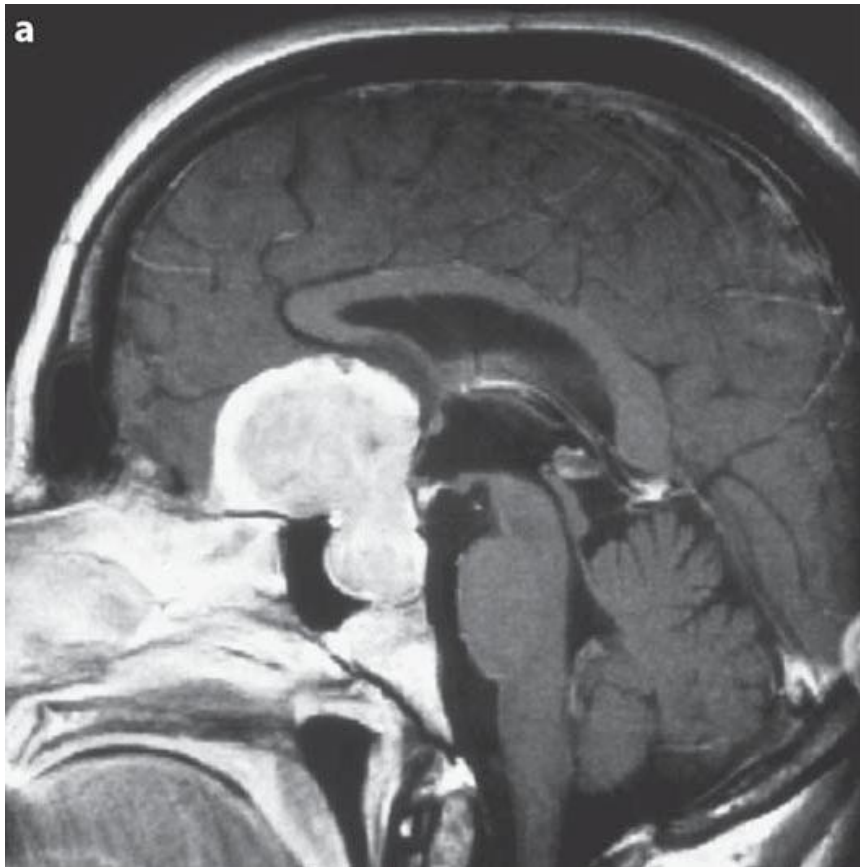
Cerrahi  
Radyoterapi  
Tıbbi tedavi  
Dopamin agonisti  
SS analog



# AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR THE DIAGNOSIS AND TREATMENT OF ACROMEGALY



# Akromegalide cerrahi tedavi



# Outcome of Surgery for Acromegaly Performed by Different Surgeons: Importance of Surgical Experience

*Table 4. Summary of published results of surgical outcome for acromegaly*

|                        | Definition of cure (ng/ml)                                  | No. of<br>(micro/macroadenomas) | Cure rate in<br>micros (%) | Cure rate in<br>macros (%) | Total cure<br>rate (%) |
|------------------------|-------------------------------------------------------------|---------------------------------|----------------------------|----------------------------|------------------------|
| Davis et al. [21]      | Basal GH<2<br>Nadir GH<2 during OGTT                        | 175 (90/85)                     | –                          | –                          | 52                     |
| Lissett et al. [10]    | Mean during OGTT<br>GH<2                                    | 73 (18/51)                      | 39                         | 12                         | 18                     |
| Fahlbusch et al. [9]   | Basal GH< 5                                                 | 396 (105/291)                   | 83                         | 70                         | 73                     |
| Sheaves et al. [3]     | Mean GH<2                                                   | 100 (53/47)                     | 61                         | 23                         | 42                     |
| Swearingen et al. [12] | Nadir GH<2 during OGTT<br>IGF-1 normalization               | 162 (33/129)                    | 91                         | 48                         | 57                     |
| Abosch et al. [4]      | Mean GH<5                                                   | 254 (??)                        | –                          | –                          | 76*                    |
| Ahmed et al. [18]      | Mean GH<2                                                   | 139 (79/60)                     | 91                         | 46                         | 67                     |
| Gittoes et al. [8]     | Basal GH<2<br>Nadir GH<0,8 during OGTT                      | 66 (22/44)                      | 86                         | 52                         | 64                     |
| Biermasz et al. [25]   | Basal GH<2<br>Nadir GH<2 during OGTT<br>IGF-1 normalization | 59 (??)                         | 67                         | 60                         | 61                     |
| Shimon et al. [7]      | MeanGH<2<br>Nadir GH<2 during OGTT<br>IGF-1 normalization   | 98 (46/52)                      | 84                         | 64                         | 74                     |
| Erturk et al.          | Basal GH<2<br>Nadir GH<2 during OGTT                        | 30 (11/19)                      | 63                         | 15                         | 33                     |

# Clinical, hormonal and magnetic resonance imaging (MRI) predictors of transsphenoidal surgery outcome in acromegaly

**Table 3** Univariate logistic regression analysis with IGF-I as criterion for cure.

|                                     | OR 95% CI         | P            |
|-------------------------------------|-------------------|--------------|
| Age                                 | 0.91 (0.86–0.96)  | <b>0.001</b> |
| Sex                                 |                   |              |
| •Male                               | 1                 |              |
| •Female                             | 1.24 (0.39–3.94)  | 0.56         |
| Adenoma size (MRI)                  |                   |              |
| • < 15 mm                           | 1                 |              |
| • > 15 mm                           | 7.04 (1.49–33.2)  | <b>0.013</b> |
| SSE (MRI)                           |                   |              |
| • < Optic chiasma                   | 1                 |              |
| • > Optic chiasma                   | 12 (2.14–67.6)    | <b>0.005</b> |
| ISE (MRI)                           |                   |              |
| •No (B)                             | 1                 |              |
| •Yes (A)                            | 5 (1.11–22.7)     | <b>0.04</b>  |
| ICE (MRI)                           |                   |              |
| •A + B1 + B2                        | 1                 |              |
| •C1 + C2 + D + E                    | 3.96 (0.91–17.16) | 0.06         |
| Invasive adenoma (MRI)              |                   |              |
| •A + B1 + B2 and < optic chiasma    | 1                 |              |
| •C1 + C2 + D + E or > optic chiasma | 7.2 (1.32–39)     | <b>0.02</b>  |
| Basal GH concentration              | 1.02 (1.00–1.03)  | <b>0.02</b>  |
| Nadir GH/OGGT                       | 1.02 (1.00–1.40)  | <b>0.03</b>  |
| IGF-I normalized for age and sex    | 1.02 (1.00–1.02)  | <b>0.01</b>  |

**Table 4** Univariate logistic regression analysis with basal GH as criterion for cure.

| Variable                            | OR 95% CI         | P            |
|-------------------------------------|-------------------|--------------|
| Age                                 | 0.94 (0.89–0.99)  | <b>0.03</b>  |
| Sex                                 |                   |              |
| •Male                               | 1                 |              |
| •Female                             | 5 (1.52–15.85)    | <b>0.008</b> |
| Adenoma size (MRI)                  |                   |              |
| • < 15 mm                           | 1                 |              |
| • > 15 mm                           | 5.26 (1.41–19.56) | <b>0.01</b>  |
| SSE (MRI)                           |                   |              |
| • < Optic chiasma                   | 1                 |              |
| • > Optic chiasma                   | 2.84 (0.82–9.82)  | 0.1          |
| ISE (MRI)                           |                   |              |
| •No (B)                             | 1                 |              |
| •Yes (A)                            | 2 (0.56–7.04)     | 0.28         |
| ICE (MRI)                           |                   |              |
| •A + B1 + B2                        | 1                 |              |
| •C1 + C2 + D + E                    | 5.5 (1.43–21.05)  | <b>0.01</b>  |
| Invasive adenoma (MRI)              |                   |              |
| •A + B1 + B2 and < optic chiasma    | 1                 |              |
| •C1 + C2 + D + E or > optic chiasma | 3.21 (0.86–12.06) | 0.08         |

# Gamma knife radiosurgery for acromegaly – long-term experience

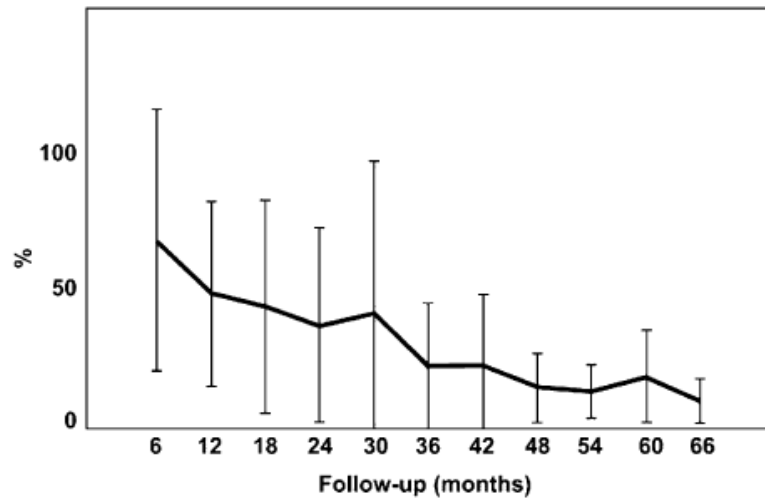


Fig. 1 Decrease in GH as percentage of baseline.

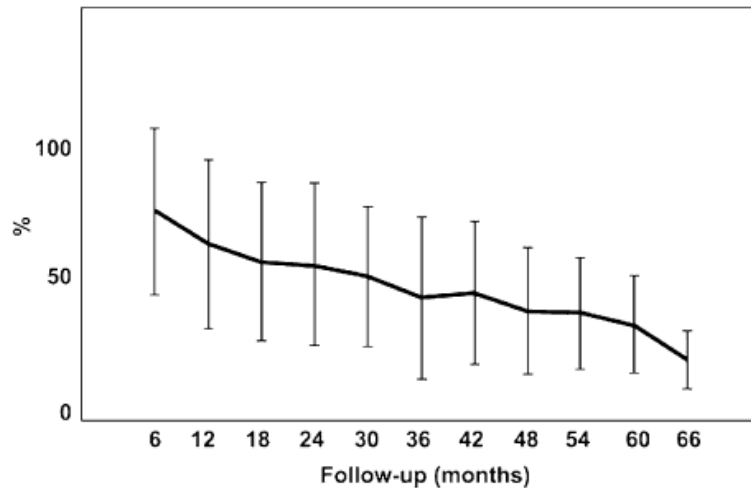
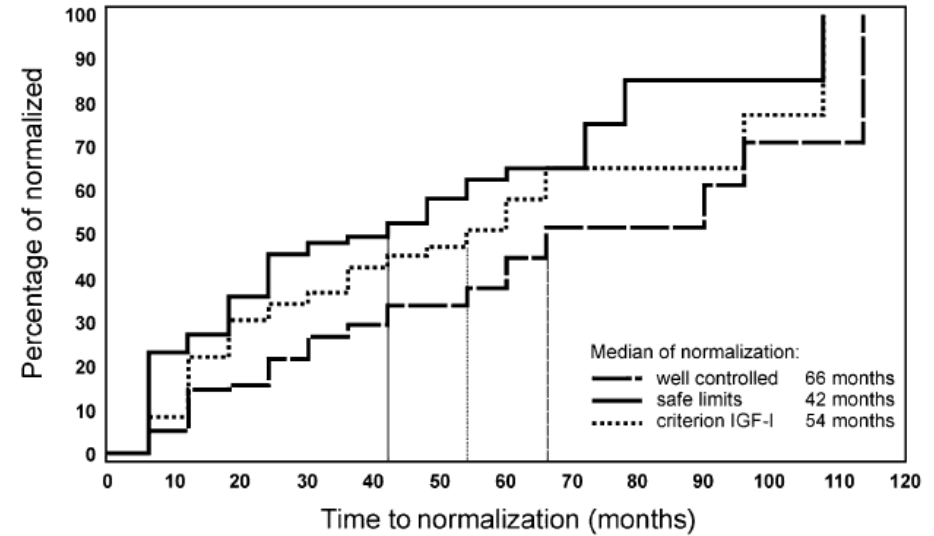


Fig. 2 Decrease in IGF-I as percentage of baseline.

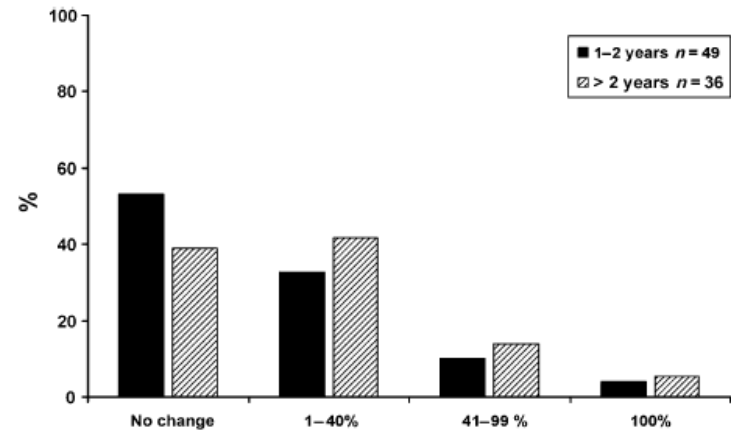
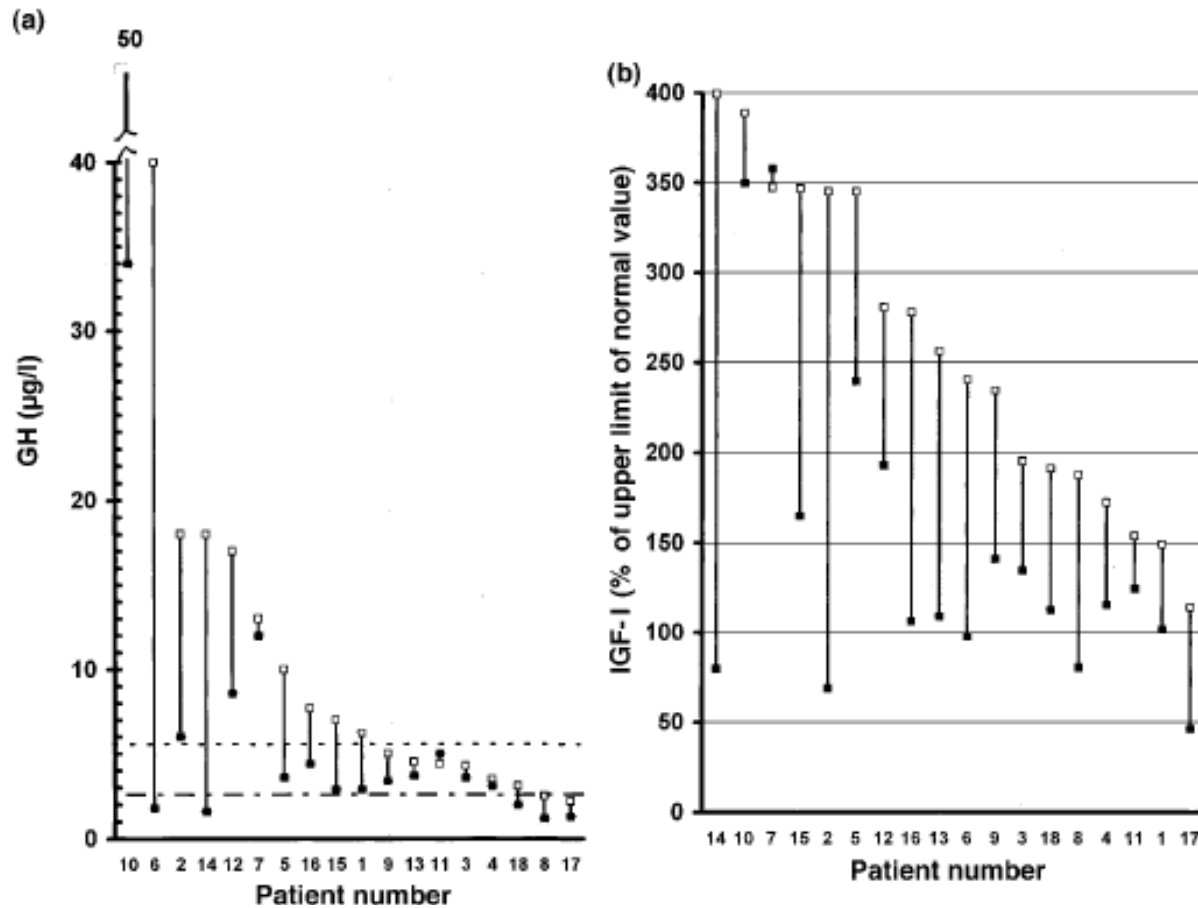
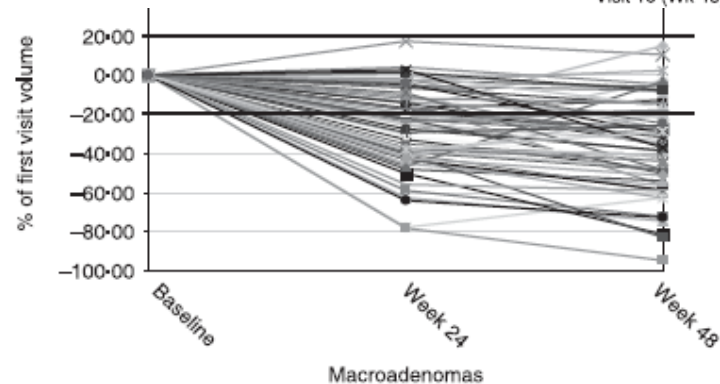
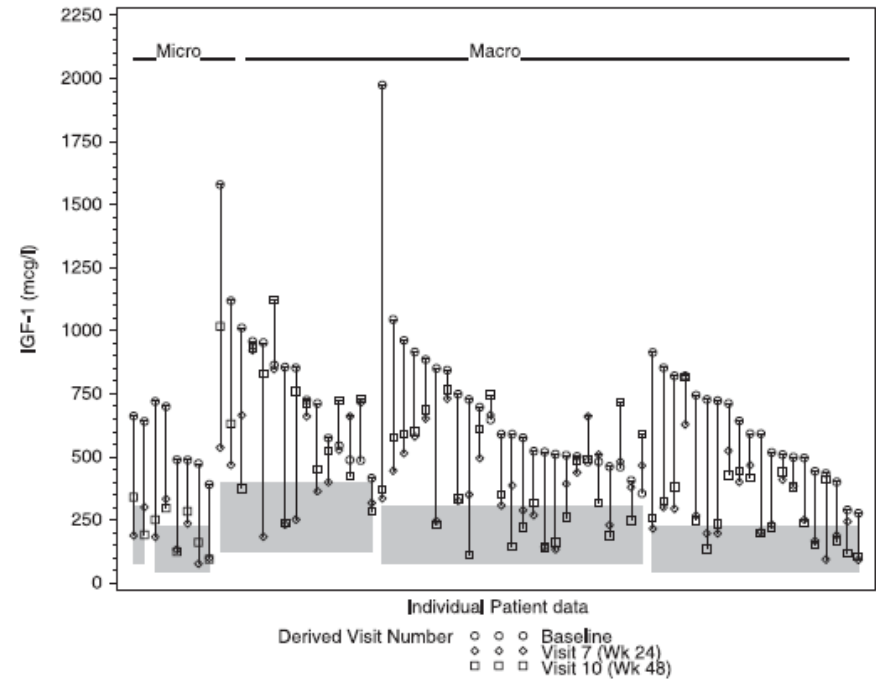
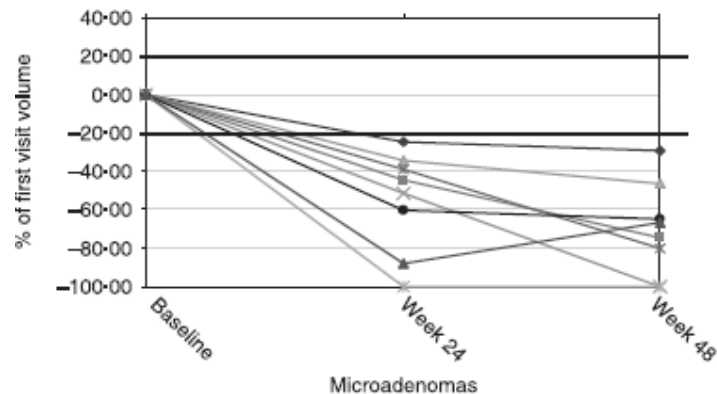
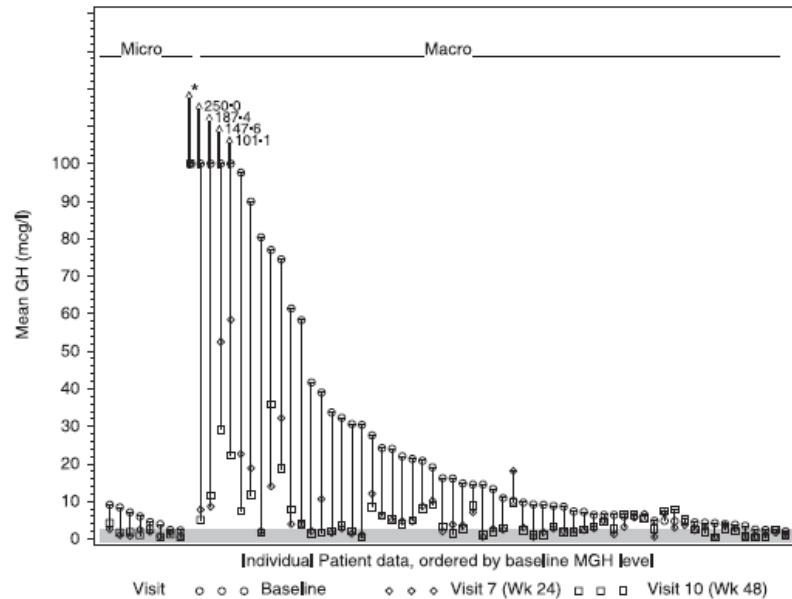


Fig. 4 Percentage shrinkage of adenoma (vertical parameter in MRI coronary projection).

# Cabergoline in acromegaly: a renewed role for dopamine agonist treatment?



# A prospective, multicentre study to investigate the efficacy, safety and tolerability of octreotide LAR<sup>®</sup> (long-acting repeatable octreotide) in the primary therapy of patients with acromegaly



# Long-Acting Somatostatin Analog Therapy of Acromegaly: A Meta-Analysis

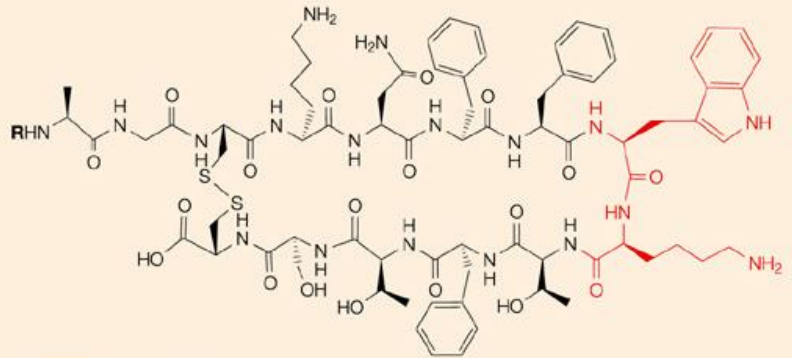
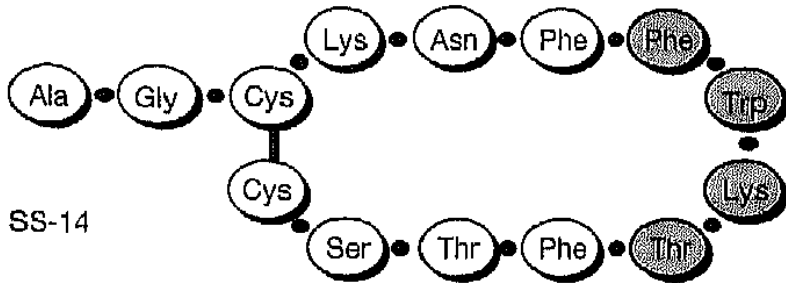
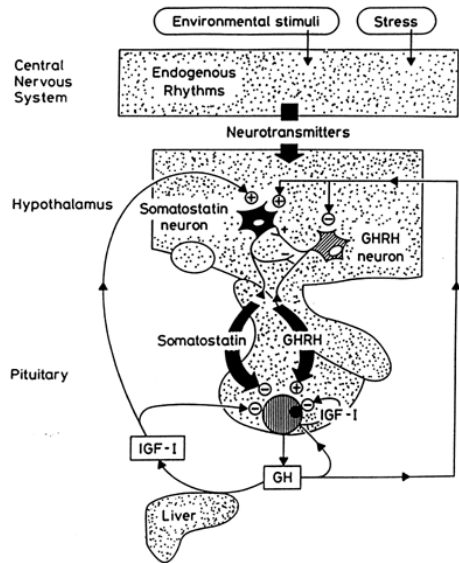
**TABLE 1.** Biochemical efficacy of somatostatin analog therapy for acromegaly

|                                                                   | % of subjects meeting efficacy criteria |                         | Mean GH levels |            | Mean IGF-I levels |            |
|-------------------------------------------------------------------|-----------------------------------------|-------------------------|----------------|------------|-------------------|------------|
|                                                                   | GH                                      | IGF-I normalization     | Pretherapy     | On therapy | Pretherapy        | On therapy |
| <b>Octreotide LAR</b>                                             |                                         |                         |                |            |                   |            |
| Unselected (n = 126)                                              | 54 ± 0.002 <sup>a</sup>                 | 63 ± 0.002 <sup>b</sup> | 15.8 ± 2.9     | 4.1 ± 0.8  | 601 ± 35          | 330 ± 75   |
| Preselected (n = 486)                                             | 58 ± 0.003                              | 68 ± 0.003              | 10.2 ± 2.3     | 2.3 ± 1.1  | 735 ± 48          | 313 ± 35   |
| All subjects (n = 612)                                            | 57 ± 0.05 <sup>c</sup>                  | 67 ± 0.05 <sup>d</sup>  | 12.6 ± 3.9     | 3.2 ± 1.53 | 644 ± 66          | 327 ± 30.5 |
| <b>Lanreotide SR</b>                                              |                                         |                         |                |            |                   |            |
| Unselected (n = 609)                                              | 48 ± 0.002                              | 42 ± 0.002              | 15.1 ± 6.0     | 5.3 ± 2.4  | 689 ± 95          | 432 ± 97   |
| Preselected (n = 305)                                             | 50 ± 0.005                              | 56 ± 0.003              | 19.7 ± 4.0     | 3.5 ± 0.5  | 735 ± 48          | 321 ± 24   |
| All subjects (n = 914)                                            | 48 ± 0.04                               | 47 ± 0.03               | 16.9 ± 3.2     | 5.9 ± 1.3  | 741 ± 51          | 442 ± 30   |
| <b>Octreotide (sc) (primary therapy only)</b>                     |                                         |                         |                |            |                   |            |
| All subjects (n = 266) (unselected, n = 252, preselected, n = 14) | 53 ± 0.05                               | 54 ± 0.05               | 40.8 ± 4.3     | 8.76 ± 1.0 | 693 ± 66          | 288 ± 41   |

**TABLE 2.** Tumor shrinkage on somatostatin analog therapy

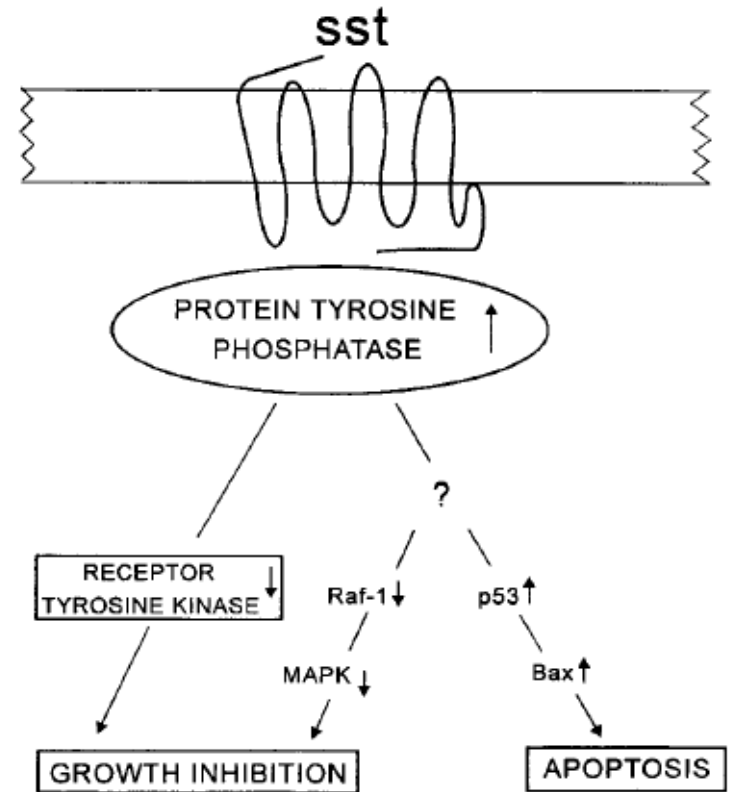
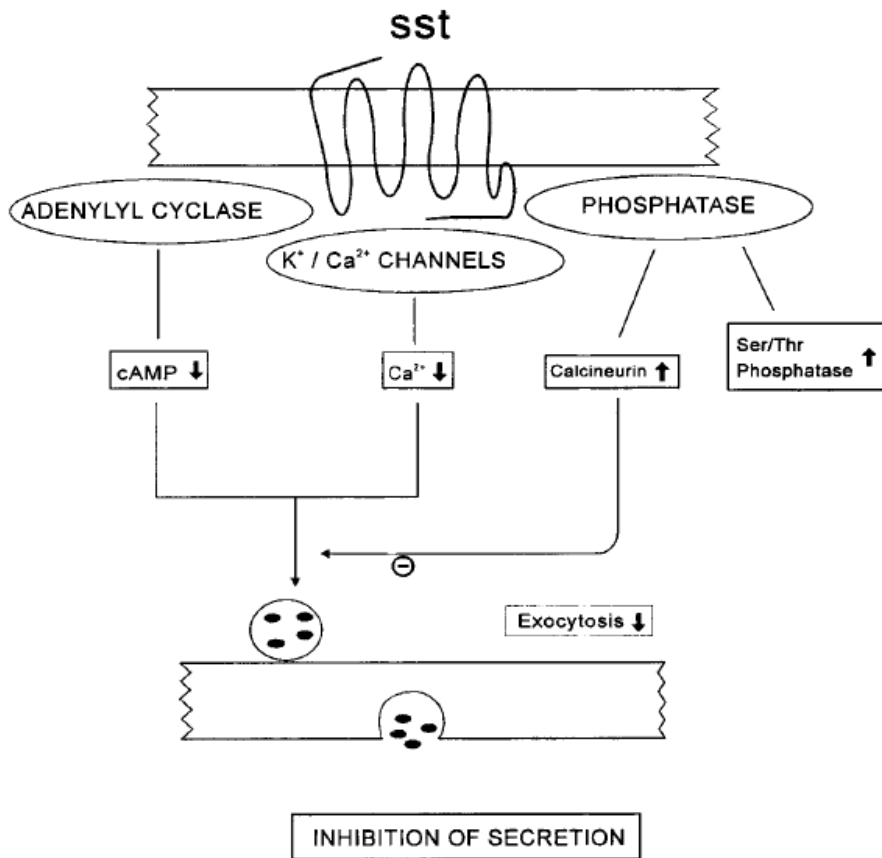
|                                              | Amount of tumor shrinkage |                     |                     |                              |
|----------------------------------------------|---------------------------|---------------------|---------------------|------------------------------|
|                                              | ≥ 10 & < 25%              | 25–50%              | > 50%               | > 10%                        |
| <b>Secondary somatostatin analog therapy</b> |                           |                     |                     |                              |
| <b>Octreotide LAR</b>                        |                           |                     |                     |                              |
| Unselected (n = 24)                          | 54                        | 4                   |                     | 58                           |
| Preselected (n = 108)                        | 10                        | 36                  |                     | 46                           |
| All subjects (n = 132)                       | 18.2<br>(3.65–29.45)      | 29.5<br>(19.9–34.9) | 0                   | 47 <sup>a</sup><br>(31.4–55) |
| <b>Lanreotide SR</b>                         |                           |                     |                     |                              |
| Unselected (n = 154)                         | 5.8                       | 7.8                 | 1.3                 | 14.9                         |
| Preselected (n = 94)                         |                           | 33                  |                     | 33                           |
| All subjects (n = 248)                       | 5.59<br>(1.99–9.19)       | 15.0<br>(8.2–21.8)  | 0.7<br>(0.1–2.5)    | 21<br>(16.7–26.5)            |
| <b>Primary somatostatin analog therapy</b>   |                           |                     |                     |                              |
| <b>Octreotide LAR</b>                        |                           |                     |                     |                              |
| Unselected (n = 23)                          | 17.4                      | 26                  | 43                  | 87                           |
| Preselected (n = 29)                         | 76                        | 13.7                |                     | 89                           |
| All subjects (n = 52)                        | 50<br>(30.2–69.8)         | 21.1<br>(2.8–39.4)  | 17.3<br>(4.65–25.9) | 88.5 <sup>b</sup><br>(76–95) |
| <b>Lanreotide SR</b>                         |                           |                     |                     |                              |
| Unselected (n = 37)                          | 16                        | 10.8                | 2.7                 | 32                           |
| Preselected (n = 34)                         | 32.3                      | 23.5                |                     | 55.8                         |
| All subjects (n = 71)                        | 30.9<br>(20.9–40.9)       | 18.3<br>(3.1–33.7)  | 1.4<br>(0–7.6)      | 50.7<br>(38–63.4)            |
| <b>Octreotide sc</b>                         |                           |                     |                     |                              |
| All subjects (n = 468) <sup>c</sup>          | 19.9<br>(13.9–24.4)       | 17.3<br>(9.3–25.3)  | 3.7<br>(2.1–5.9)    | 40.8<br>(32.5–49.3)          |

# Somatostatin (SRIF)

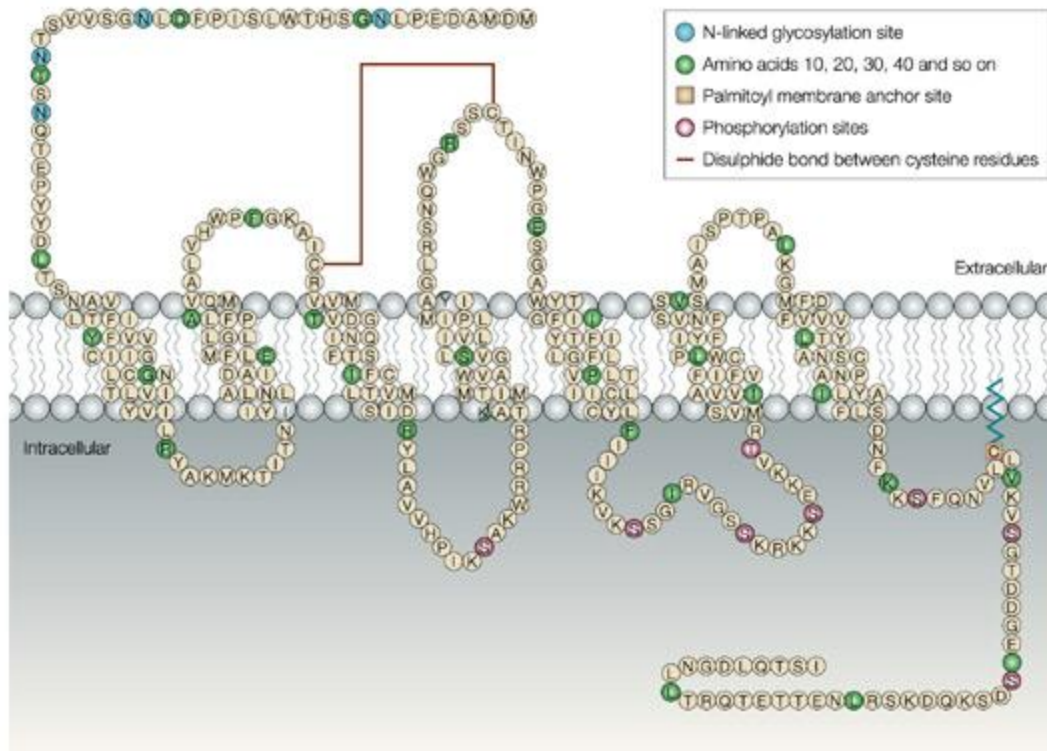


- 2 (SRIF-28) R = H-Ser-Ala-Asn-Ser-Asn-Pro-Ala-Met-Ala-Pro-Arg-Glu-Arg-Lys-

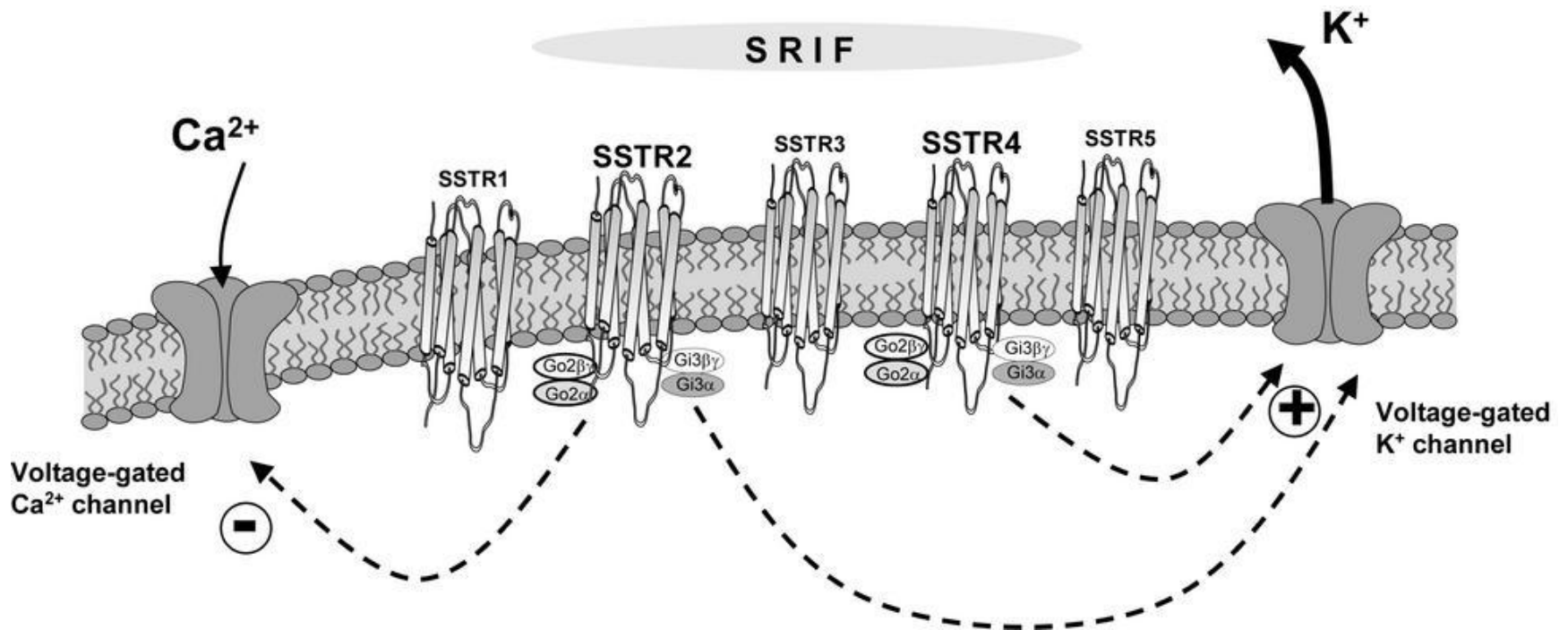
# Somatostatin etkisi



# Somatostatin reseptörü



# Somatostatin reseptör alt tipleri (sst<sub>1-5</sub>)



# SS reseptör alt tiplerinin özellikleri

**Table 1. Characteristics of the cloned subtypes of human somatostatin receptors<sup>a</sup>**

|                                           | <i>sst<sub>1</sub></i>                              | <i>sst<sub>2A</sub></i>                      | <i>sst<sub>3</sub></i>    | <i>sst<sub>4</sub></i>                   | <i>sst<sub>5</sub></i>    |
|-------------------------------------------|-----------------------------------------------------|----------------------------------------------|---------------------------|------------------------------------------|---------------------------|
| Chromosomal localization                  | 14q13                                               | 17q24                                        | 22q13.1                   | 20p11.2                                  | 16p13.3                   |
| Amino acids                               | 391                                                 | 369                                          | 418                       | 388                                      | 363                       |
| mRNA (kb)                                 | 4.8                                                 | 8.5 (?)                                      | 5.0                       | 4.0                                      | 4.0                       |
| G-protein coupling                        | +                                                   | +                                            | +                         | +                                        | +                         |
| Effector coupling                         |                                                     |                                              |                           |                                          |                           |
| Adenylyl cyclase activity                 | ↓                                                   | ↓                                            | ↓                         | ↓                                        | ↓                         |
| Tyrosine phosphatase activity             | ↑                                                   | ↑                                            | ↑                         | ↑                                        |                           |
| Ca <sup>2+</sup> channels                 |                                                     | ↓                                            |                           |                                          |                           |
| Na <sup>+</sup> /H <sup>+</sup> exchanger | ↑                                                   |                                              |                           |                                          |                           |
| Phospholipase C/IP <sub>3</sub> activity  |                                                     | ↑                                            |                           |                                          | ↓↑                        |
| Phospholipase A2 activity                 |                                                     |                                              |                           | ↑                                        |                           |
| MAP kinase activity                       |                                                     |                                              | ↓                         | ↑                                        | ↓                         |
| Tissue distribution <sup>b</sup>          | Brain, pituitary, stomach, liver, pancreas, kidneys | Brain, pituitary, stomach, pancreas, kidneys | Brain, pituitary, stomach | Brain, stomach, pancreas, lungs, stomach | Brain, pituitary, stomach |

# Somatostatin Receptors in Pituitary Function, Diagnosis and Therapy

**Table 2.** Expression of somatostatin receptor subtypes in normal human pituitary and pituitary adenomas

| Adenoma          | Somatostatin receptor subtype mRNA expression, number/total (%) |                  |                  |                  |                  | Reference                 |
|------------------|-----------------------------------------------------------------|------------------|------------------|------------------|------------------|---------------------------|
|                  | sst <sub>1</sub>                                                | sst <sub>2</sub> | sst <sub>3</sub> | sst <sub>4</sub> | sst <sub>5</sub> |                           |
| GH-secreting     | 24/51 (65)                                                      | 94/108 (96)      | 23/66 (49)       | 2/70 (4)         | 82/109 (83)      | 14, 20, 21, 24–28, 31, 46 |
| NFA              | 17/46 (37)                                                      | 33/46 (72)       | 23/45 (51)       | 3/40 (8)         | 14/40 (35)       | 14, 21, 24–27, 61         |
| Prolactinoma     | 33/37 (89)                                                      | 27/37 (73)       | 11/35 (31)       | 4/33 (12)        | 24/33 (73)       | 14, 21, 24–27, 47, 61     |
| Corticotroph     | 5/10 (50)                                                       | 6/10 (60)        | 3/9 (33)         | 1/8 (13)         | 6/8 (75)         | 14, 24–27                 |
| TSH-secreting    | 3/3 (100)                                                       | 3/3 (100)        | 1/3 (33)         | 2/3 (67)         | 2/3 (67)         | 14, 21                    |
| Normal pituitary | 5/5 (100)                                                       | 5/5 (100)        | 1/5 (20)         | 0/5 (0)          | 5/5 (100)        | 14, 27                    |

NFA = Clinically non-functioning pituitary adenoma.

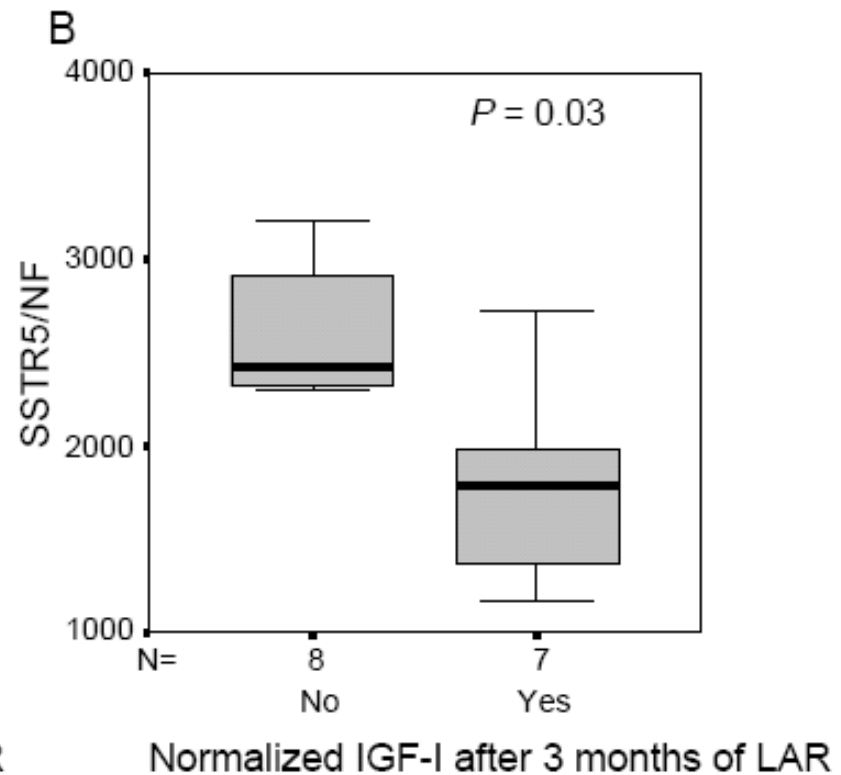
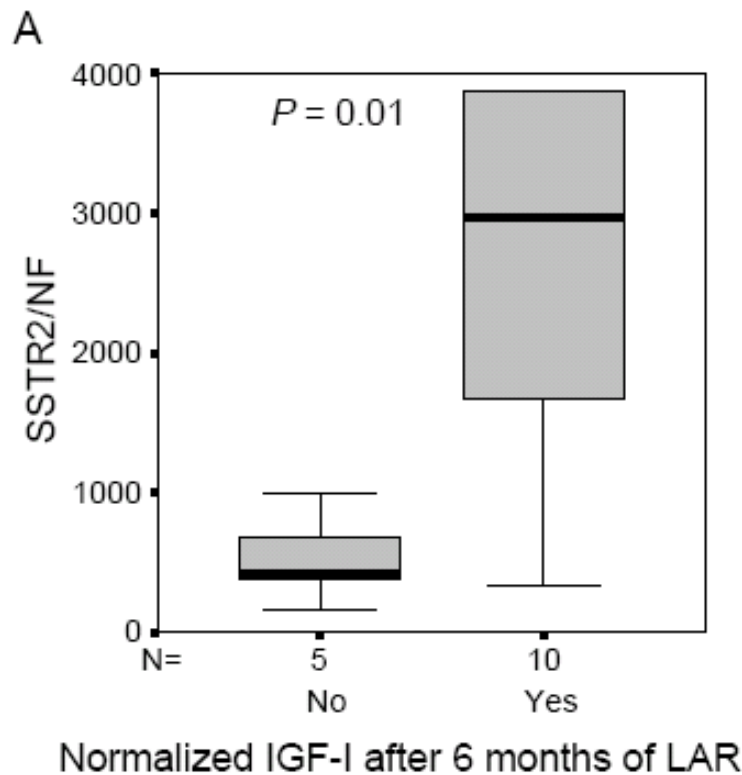
# Quantitative analysis of somatostatin receptor subtype (SSTR1–5) gene expression levels in somatotropinomas and non-functioning pituitary adenomas

**Table 5** Correlations between the mRNA content for each SSTR subtypes and growth hormone (GH) levels at diagnosis and percent decrease in GH and insulin-like growth factor-I (IGF-I) levels after 3 and 6 months of therapy with octreotide LAR.

|          | After 3 months with octreotide LAR |                         |                            | After 6 months with octreotide LAR |                            |
|----------|------------------------------------|-------------------------|----------------------------|------------------------------------|----------------------------|
|          | GH at diagnosis<br>(n=20)          | % GH decrease<br>(n=15) | % IGF-I decrease<br>(n=15) | % GH decrease<br>(n=15)            | % IGF-I decrease<br>(n=15) |
| SSTR1    |                                    |                         |                            |                                    |                            |
| <i>r</i> | −0.76                              | 0.02                    | 0.02                       | 0.11                               | 0.23                       |
| <i>P</i> | 0.75                               | 0.94                    | 0.9                        | 0.7                                | 0.41                       |
| SSTR2    |                                    |                         |                            |                                    |                            |
| <i>r</i> | 0.18                               | 0.51                    | 0.26                       | 0.66                               | 0.56                       |
| <i>P</i> | 0.45                               | 0.05*                   | 0.35                       | 0.008*                             | 0.03*                      |
| SSTR3    |                                    |                         |                            |                                    |                            |
| <i>r</i> | 0.14                               | −0.05                   | 0.11                       | 0.14                               | 0.05                       |
| <i>P</i> | 0.57                               | 0.87                    | 0.69                       | 0.61                               | 0.87                       |
| SSTR4    |                                    |                         |                            |                                    |                            |
| <i>r</i> | −0.37                              | −0.41                   | −0.17                      | −0.29                              | −0.02                      |
| <i>P</i> | 0.12                               | 0.12                    | 0.55                       | 0.29                               | 0.95                       |
| SSTR5    |                                    |                         |                            |                                    |                            |
| <i>r</i> | −0.36                              | −0.41                   | −0.67                      | −0.26                              | −0.31                      |
| <i>P</i> | 0.12                               | 0.13                    | 0.007*                     | 0.35                               | 0.25                       |

Statistical significance was determined by Spearman's correlation test. \*Significant *P* Value.

# Quantitative analysis of somatostatin receptor subtype (SSTR1–5) gene expression levels in somatotropinomas and non-functioning pituitary adenomas



# Somatostatin Receptors

Yogesh C. Patel and Coimbatore B. Srikant

|                     | <i>IC</i> <sub>50</sub> (nM) <sup>b</sup> |                          |                         |                         |                         |
|---------------------|-------------------------------------------|--------------------------|-------------------------|-------------------------|-------------------------|
|                     | <i>sst</i> <sub>1</sub>                   | <i>sst</i> <sub>2A</sub> | <i>sst</i> <sub>3</sub> | <i>sst</i> <sub>4</sub> | <i>sst</i> <sub>5</sub> |
| SRIF-14             | 0.1–2.26                                  | 0.2–1.3                  | 0.3–1.6                 | 0.3–1.8                 | 0.2–0.9                 |
| SRIF-28             | 0.1–2.2                                   | 0.2–4.1                  | 0.3–6.1                 | 0.3–7.9                 | 0.05–0.4                |
| Octreotide          | 290–1140                                  | 0.4–2.1                  | 4.4–34.5                | > 1000                  | 5.6–32                  |
| Lanreotide          | 500–2330                                  | 0.5–1.8                  | 43–107                  | 66–2100                 | 0.6–14                  |
| Vapreotide          | > 1000                                    | 5.4                      | 31                      | 45                      | 0.7                     |
| Seglitide           | > 1000                                    | 0.1–1.5                  | 27–36                   | 127– > 1000             | 2–23                    |
| BIM 23052           | 6.3–100                                   | 10–13.5                  | 2.1–5.6                 | 16–141                  | 1.2–7.3                 |
| BIM 23056           | 110– > 1000                               | 132– > 1000              | 10.8–177                | 17–234                  | 5.7–14.1                |
| BIM 23268           | 18.4                                      | 15.1                     | 61.6                    | 16.3                    | 0.37                    |
| L 362855            | > 1000                                    | 1                        | 6.2                     | 63– > 1000              | 0.1–0.016               |
| CH 275 <sup>c</sup> | 3.2–4.3                                   | >1000                    | >1000                   | 4.3–874                 | >1000                   |

# SOM230

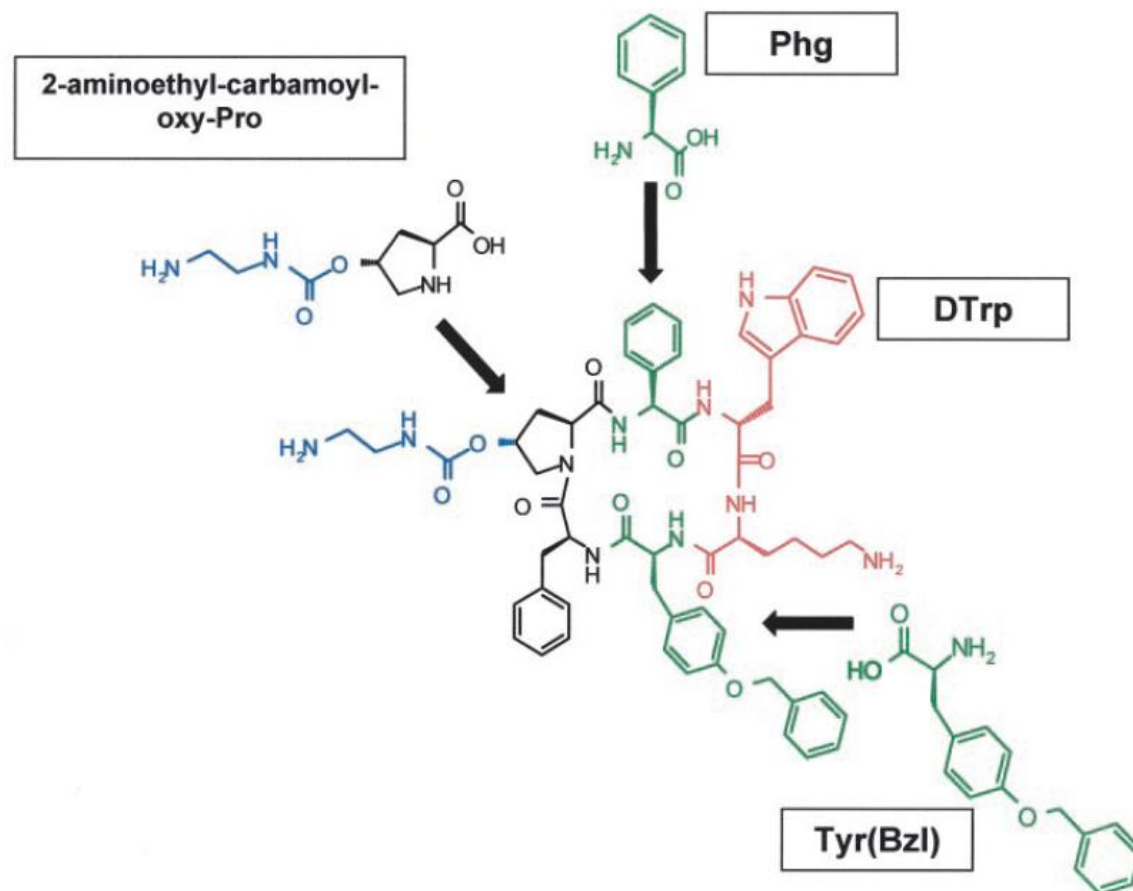
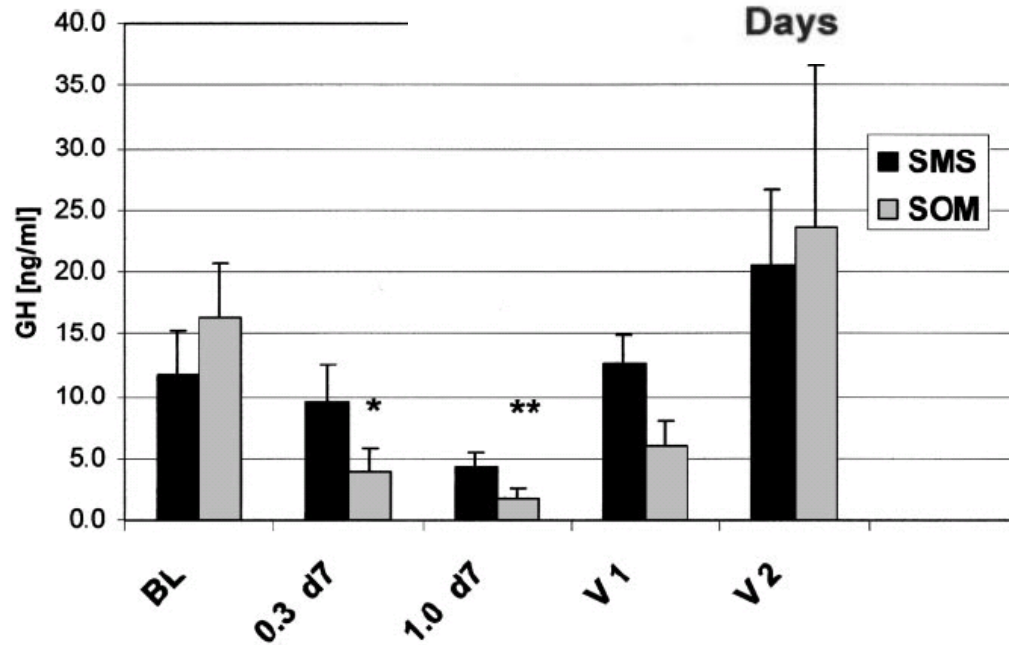
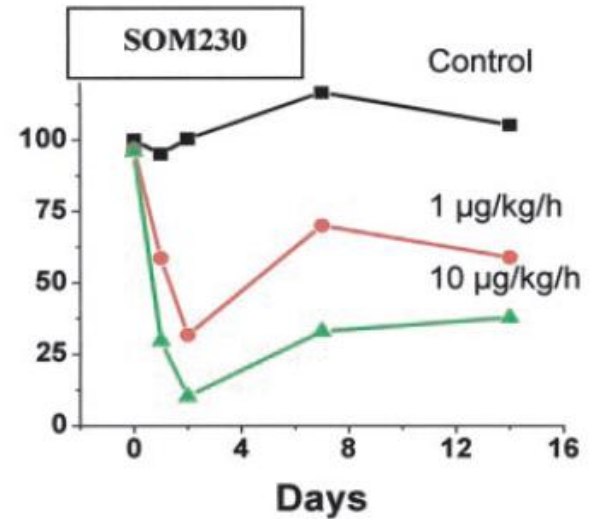
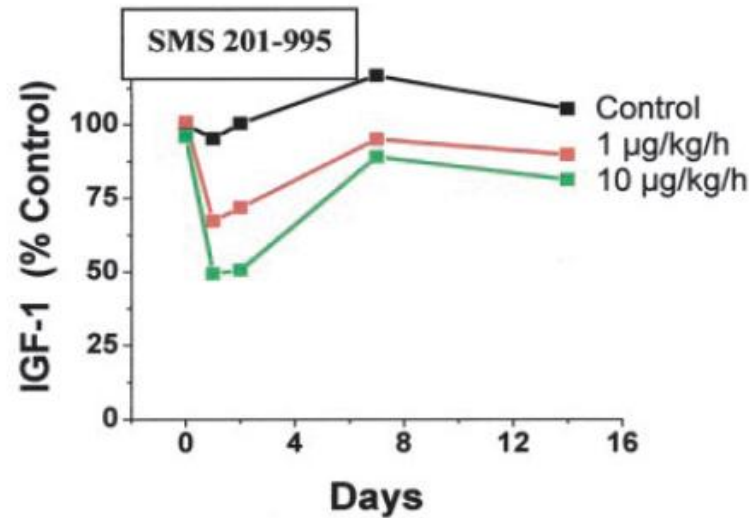
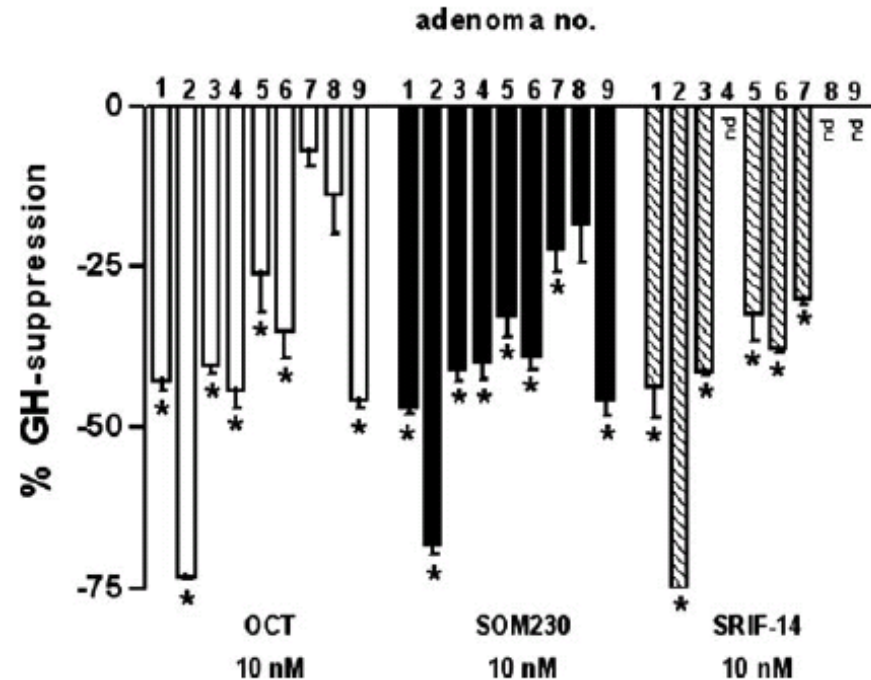
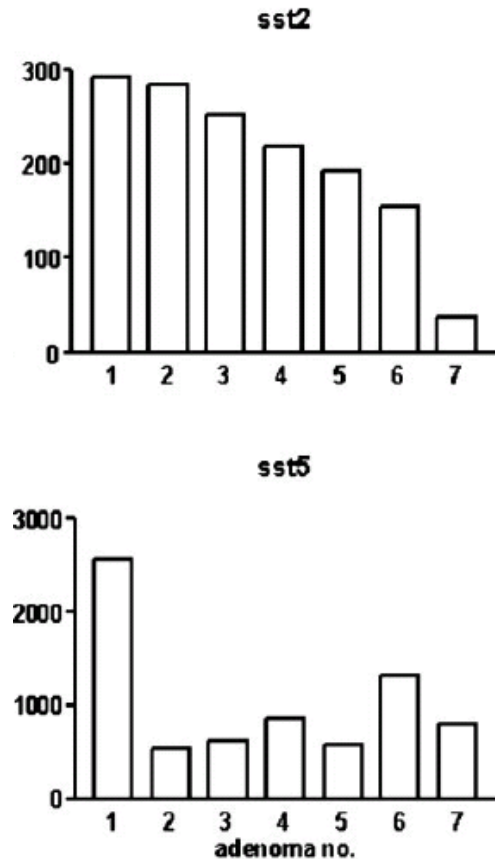


FIG. 1. The cyclohexapeptide analog SOM230 was synthesized on solid phase using an Fmoc/tBu strategy before cyclization in solution. SOM230 contains the special amino acid derivatives, 2-aminoethyl-carbamoyl-oxy-Pro, Phg, Tyr(Bzl), and DTrp (D-tryptophan), which strongly contribute to its unique binding to human sst1, sst2, sst3, and sst5.

# SOM230: A New Somatostatin Peptidomimetic with Potent Inhibitory Effects on the Growth Hormone/Insulin-Like Growth Factor-I Axis in Rats, Primates, and Dogs



# The Novel Somatostatin Analog SOM230 Is a Potent Inhibitor of Hormone Release by Growth Hormone- and Prolactin-Secreting Pituitary Adenomas *in Vitro*



# A Single-Dose Comparison of the Acute Effects between the New Somatostatin Analog SOM230 and Octreotide in Acromegalic Patients

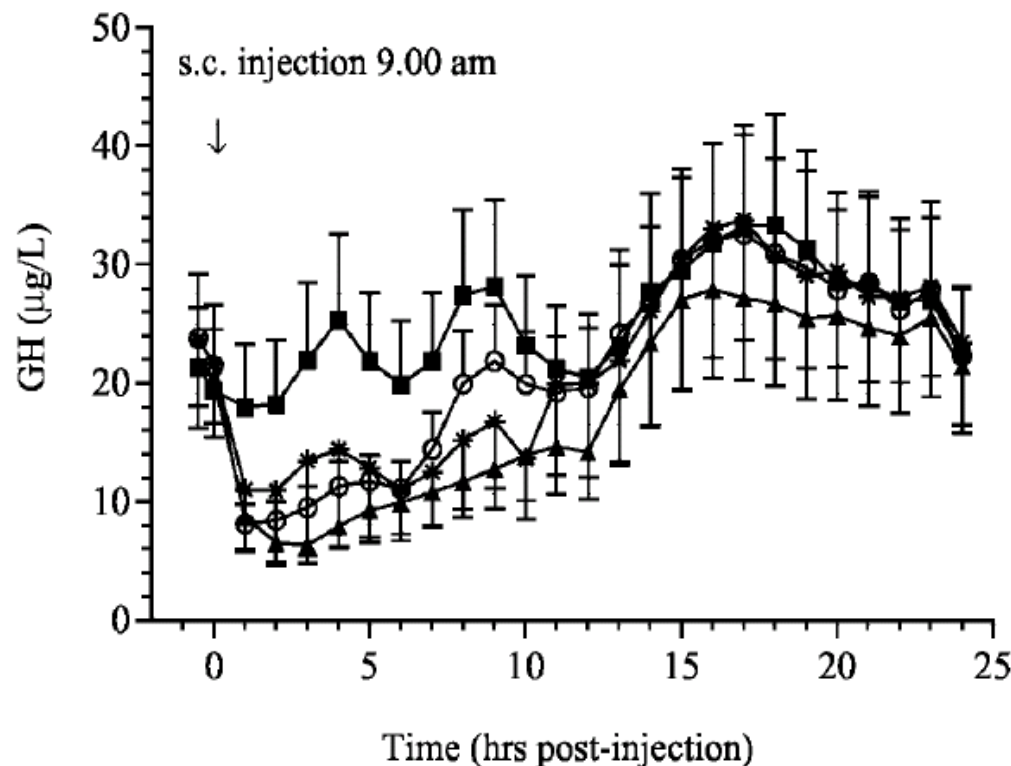


FIG. 1. Twenty-four-hour GH concentration curves on the CD (■—■) and treatment days after sc injection of 100 μg OCT (\*—\*), 250 μg SOM230 (▲—▲), and 100 μg SOM230 (○—○). Data are expressed as mean ± SEM (n = 12).

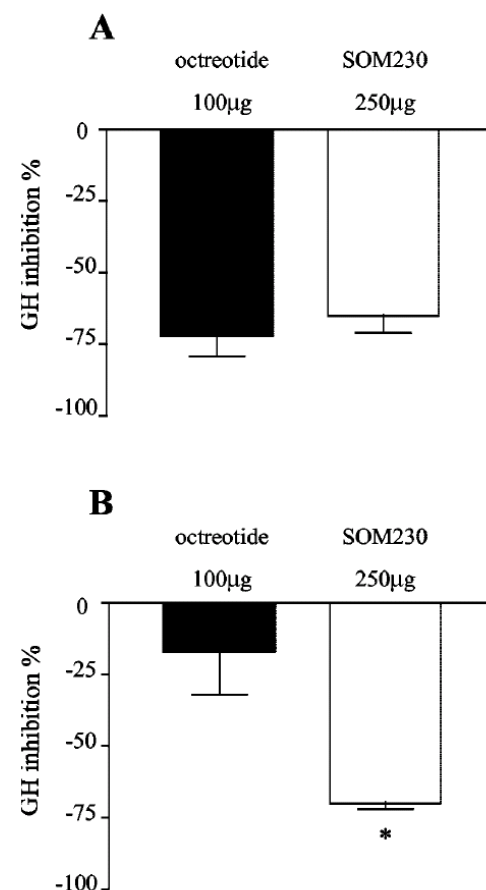


FIG. 3. GH suppression 2–8 h after sc injection. The bars represent mean ± SEM percentual GH suppression induced by 100 μg octreotide (■) and 250 μg SOM230 (□), compared with the CD. A, Group showing equal response to OCT and SOM230 (n = 8). B, Group showing higher sensitivity to SOM230 (n = 3; \*,  $P < 0.05$ ).

# Functional Activity of the Multiligand Analog SOM230 at Human Recombinant Somatostatin Receptor Subtypes Supports Its Usefulness in Neuroendocrine Tumors

| Compound          | sst <sub>1</sub> | sst <sub>2</sub> | sst <sub>3</sub> | sst <sub>4</sub> | sst <sub>5</sub> |
|-------------------|------------------|------------------|------------------|------------------|------------------|
| SRIF-14           | 0.93±0.12        | 0.15±0.22        | 0.56±0.17        | 1.50±0.40        | 0.29±0.04        |
| Octreotide        | 280±20           | 0.38±0.08        | 7.10±1.40        | >1,000           | 6.30±1.00        |
| SOM230            | 9.30±0.10        | 1.00±0.10        | 1.50±0.30        | >1,000           | 0.16±0.01        |
| Octreotide/SOM230 | 30               | 0.4              | 5                | –                | 39               |

Data are mean IC<sub>50</sub> values (nmol/l) from 3–7 experiments (adapted from Bruns et al. [7]).

| Compound          | sst <sub>1</sub> | sst <sub>2</sub> | sst <sub>3</sub> | sst <sub>4</sub> | sst <sub>5</sub> |
|-------------------|------------------|------------------|------------------|------------------|------------------|
| SRIF-14           | 1.80±1.20        | 0.24±0.06        | 0.30±0.13        | 0.39±0.15        | 0.32±0.23        |
| Octreotide        | >1,000           | 0.06±0.02        | 7.40±3.50        | >1,000           | 87±66            |
| SOM230            | 32±13            | 0.39±0.09        | 0.70±0.22        | >1,000           | 0.55±0.12        |
| Octreotide/SOM230 | >30              | 0.15             | 11               | –                | 158              |

Data are mean EC<sub>50</sub> values (nmol/l) from 3–5 experiments.

## Pasireotide (SOM230) effectively reduces pituitary tumor volume in patients with active acromegaly: preliminary 6-month results from a phase II extension study

Results: Thirty patients entered the extension study. Of 26 patients who received pasireotide for at least 6 months, 65% achieved GH  $\leq 2.5$   $\mu\text{g/l}$  and/or normalized IGF-I, 62% had normalized IGF-I and 42% achieved GH  $\leq 2.5$   $\mu\text{g/l}$ . Nineteen patients had both baseline and per-protocol follow-up MRI scans at 6 months. Mean tumor volume reduction at 6 months was 18.1 $\pm$ 4.6% s.e.m. for all 19 patients. In 10 of the 19 patients (53%), tumor volumes decreased by a mean of 33.4 $\pm$ 4.2% (20% measurement error threshold).

# <http://clinicaltrials.gov/ct2/results?term=pasireotide>

Active, not recruiting [Study of Pasireotide Long Acting Release \(LAR\) Injection in Patients With Acromegaly and Patients With Carcinoid Disease](#)  
Conditions: Carcinoid Tumor; Acromegaly Intervention: Drug: Pasireotide

Active, not recruiting [An Extension Study to Assess the Long-Term Safety and Efficacy of Pasireotide in Patients With Acromegaly](#)  
Condition: Acromegaly Intervention: Drug: Pasireotide

Recruiting [Safety and Efficacy of Pasireotide Long Acting Release \(LAR\) vs. Octreotide LAR in Patients With Active Acromegaly](#)  
Condition: Acromegaly Intervention: Drug: Pasireotide

Active, not recruiting [Study Comparing SOM230 Subcutaneously and Sandostatin Subcutaneously in Acromegalic Patients](#)  
Condition: Acromegaly Interventions: Drug: SOM230

# Hipofiz adenomlarında belirtiler

- Adenomun kitle etkisi
  - Hipopitüitarizm
  - Görme alanı daralması
  - Baş ağrısı vd
- Adenomun hormon hipersekresyonu
  - Prolaktinoma
  - Akromegali
  - Cushing
  - Hipertiroidi

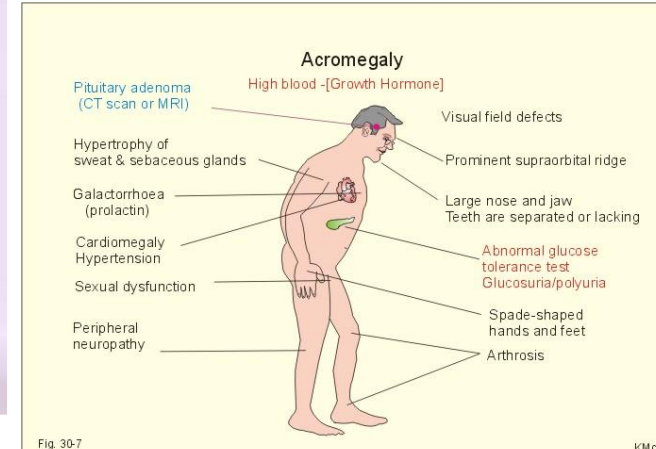
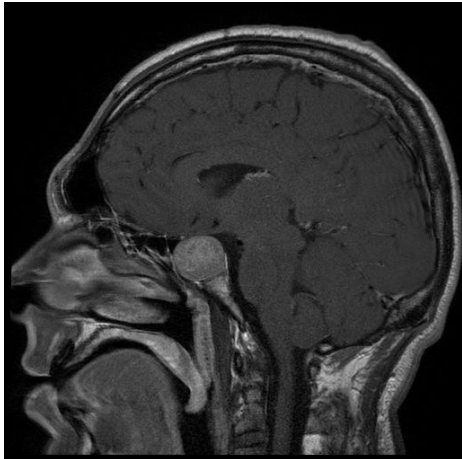
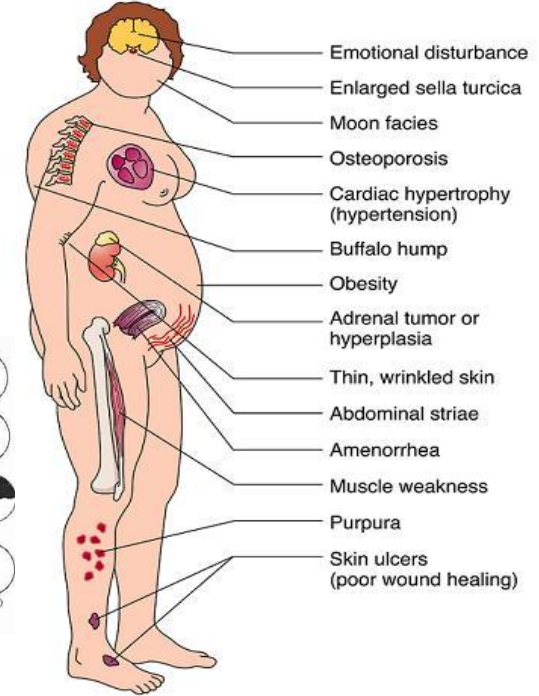
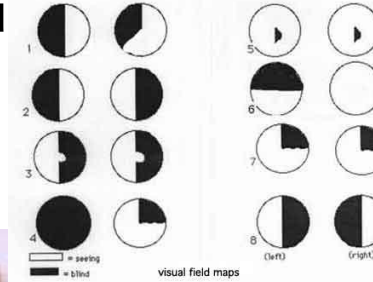


Fig. 30-7

# **Treatment of Adrenocorticotropin-Dependent Cushing's Syndrome: A Consensus Statement**

**Part I: Criteria for Cure and Remission of ACTH-Dependent Cushing's Syndrome**

**Part II: Surgical Treatment of Cushing's Disease**

**Part III: Persistent Disease after Transsphenoidal Surgery**

**Part IV: Medical Therapy of Cushing's Disease**

**Part V: Management of Ectopic ACTH Syndrome, Nelson's Syndrome, Special Patient Populations, and the Patient after Successful Surgical Treatment**

# Long-term remission rates after pituitary surgery for Cushing's disease: the need for long-term surveillance

| Reference,<br>location of<br>study              | Median<br>follow-up<br>time (months) | Immediate<br>postoperative<br>remission (%) | Later<br>relapse<br>rate (%) | Overall<br>remission<br>rate (%) |
|-------------------------------------------------|--------------------------------------|---------------------------------------------|------------------------------|----------------------------------|
| Atkinson <i>et al.</i>                          | 115                                  | 71.4 (45/63)                                | 22.2 (10/45)                 | 55.6 (35/63)                     |
| Rees <i>et al.</i>                              | 72                                   | 77 (41/53)                                  | 5 (2/41)                     | 74 (39/53)                       |
| Yap <i>et al.</i>                               | 92                                   | 68.5 (61/89)                                | 11.5 (7/61)                  | 60.1 (54/89)                     |
| Chee <i>et al.</i>                              | 88                                   | 78.7 (48/61)                                | 14.6 (7/48)                  | 67.2 (41/61)                     |
| Van Aken <i>et al.</i>                          | 35                                   | 58.6 (17/29)                                | 17.6 (3/17)                  | 48.3 (14/29)                     |
| Bochicchio <i>et al.</i>                        | 46                                   | 76.3 (510/668)                              | 12.7 (65/510)                | 66.6 (445/668)                   |
| Ram <i>et al.</i> (1994) <sup>62</sup> NIH, USA | 34                                   | 71 (12/17)                                  | 25 (3/12)                    | 52.9 (9/17)                      |
| Viganti <i>et al.</i>                           | 38.5                                 | 83.3 (30/36)                                | 20 (6/30)                    | 66.7 (24/36)                     |
| Toms <i>et al.</i>                              | 24                                   | 100 (11/11)                                 | 36.4 (4/11)                  | 63.6 (7/11)                      |
| Arnott <i>et al.</i>                            | 22                                   | 86 (24/28)                                  | 12.5 (3/24)                  | 75 (21/28)                       |
| Burke <i>et al.</i>                             | 56                                   | 81.5 (44/54)                                | 4.5 (2/44)                   | 77.8 (42/54)                     |
| Tindall <i>et al.</i>                           | 57                                   | 84.9 (45/53)                                | 2.1 (1/46)                   | 83 (44/53)                       |
| Pieters <i>et al.</i>                           | 54                                   | 59 (160/270)                                | 25 (4/16)                    | 44 (12/27)                       |
| Guilhaume <i>et al.</i>                         | 24                                   | 70 (42/60)                                  | 14.3 (6/42)                  | 60 (36/60)                       |
| Mampalam <i>et al.</i>                          | 46                                   | 79.2 (171/216)                              | 5.3 (9/171)                  | 75 (162/216)                     |

# Treatment options for Cushing disease after unsuccessful transsphenoidal surgery

- Reoperasyon
- Radyoterapi
- Bilateral adrenalectomi
- Tıbbi tedavi

## *Medical therapy for Cushing disease*

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### **drugs that inhibit steroidogenesis**

ketoconazole  
mitotane  
metyrapone  
trilostane  
aminoglutethimide  
etomidate

### **drugs that modulate ACTH release**

#### *dopamine agonists*

bromocriptine  
cabergoline

#### *somatostatin agonists*

octreotide

#### *GABA agonists*

valproic acid

#### *serotonin antagonists*

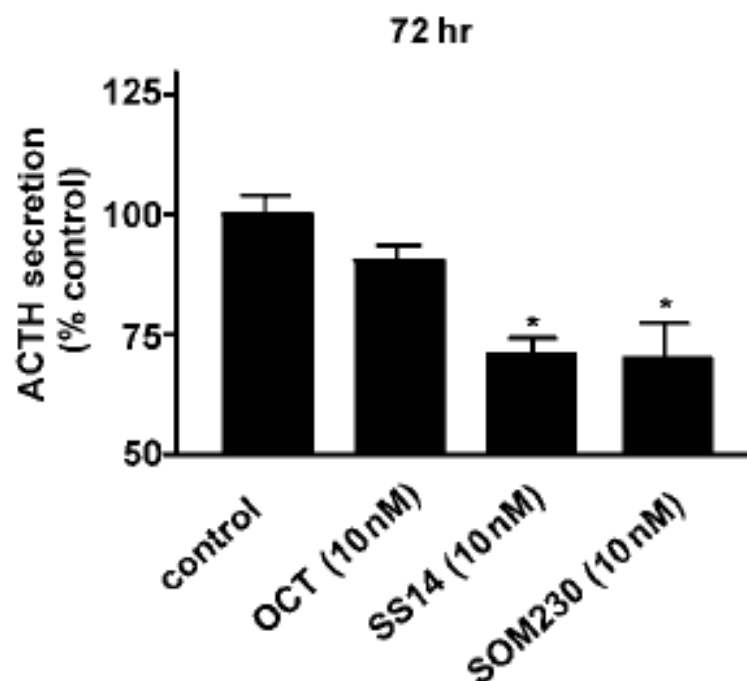
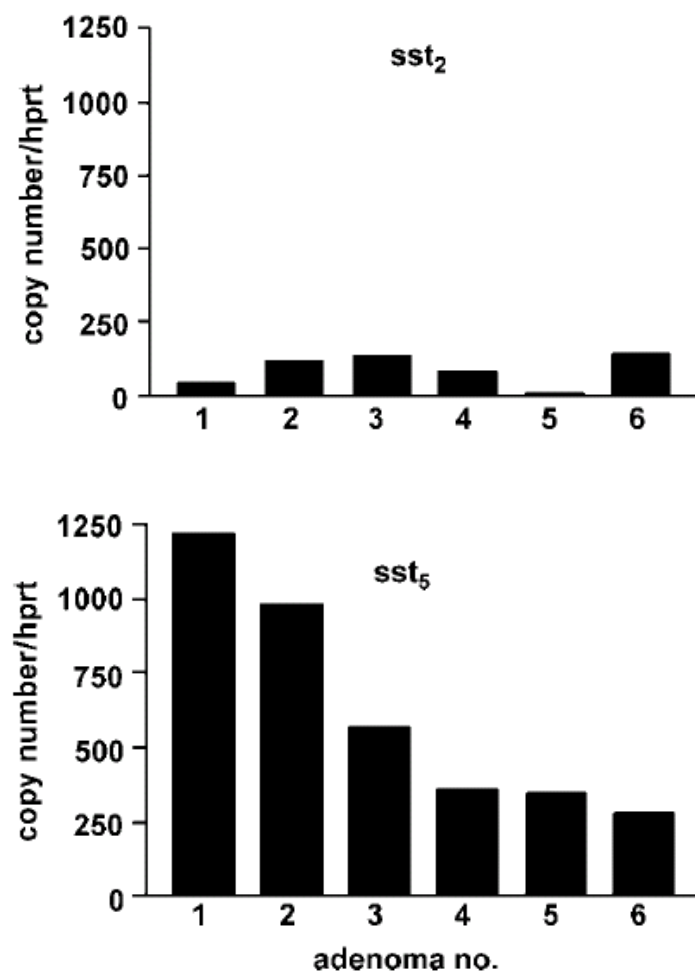
cyproheptadine  
ketanserin  
ritanserin

### **cortisol-receptor antagonists**

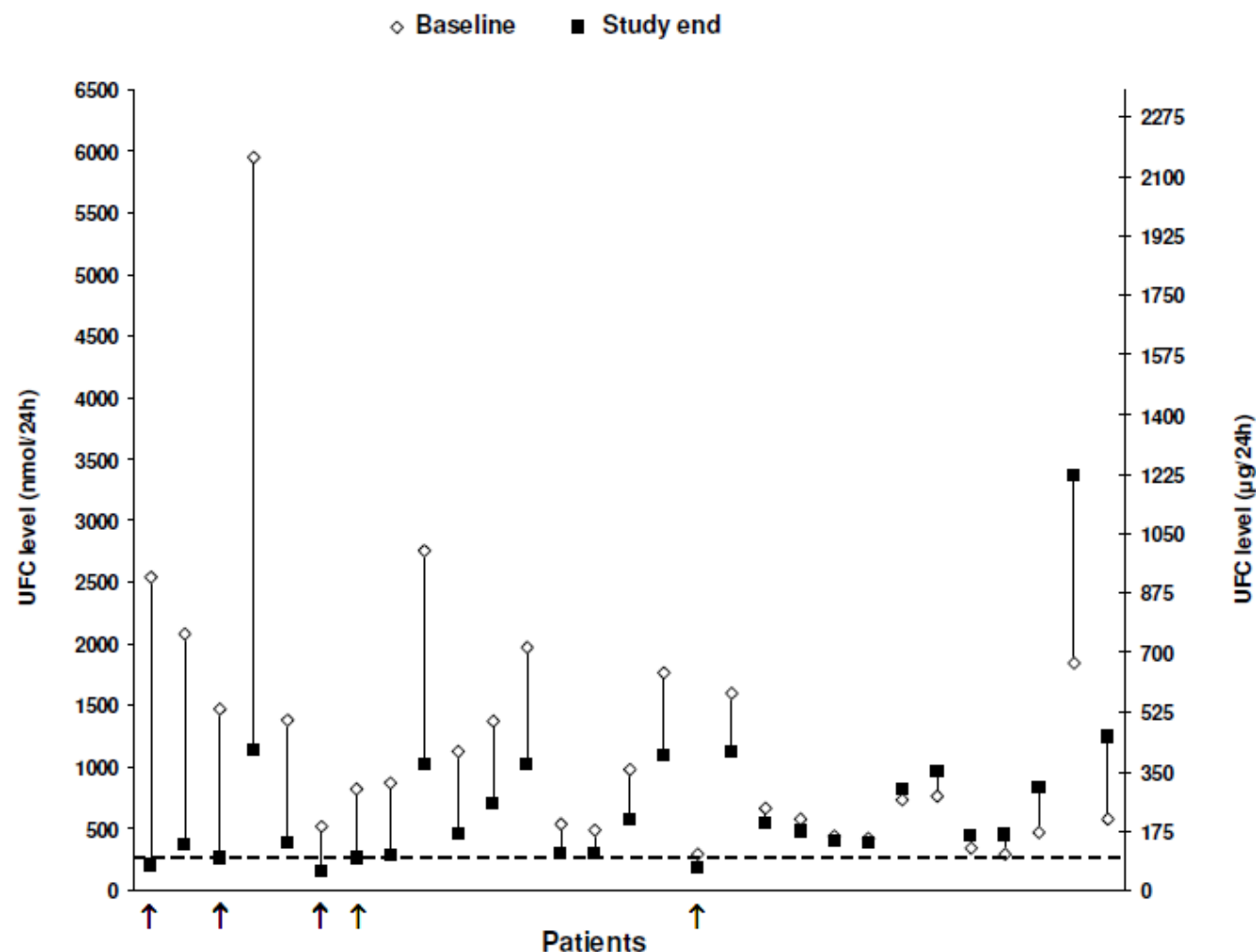
mifepristone (RU-486)

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# The multi-ligand somatostatin analogue SOM230 inhibits ACTH secretion by cultured human corticotroph adenomas via somatostatin receptor type 5



# Treatment of pituitary dependent Cushing's disease with the multi-receptor ligand somatostatin analog pasireotide (SOM230): A multicenter, phase II trial



# <http://clinicaltrials.gov/ct2/results?term=pasireotide>

Recruiting [Safety and Efficacy of Different Dose Levels of Pasireotide in Patients With de Novo, Persistent or Recurrent Cushing's Disease](#)  
Condition:Cushing's Disease Intervention:Drug: Pasireotide

Active, not recruiting [Extension Study to Assess the Safety and Efficacy of Pasireotide in Patients With Cushing's Disease](#)  
Condition:Cushing Disease Intervention:Drug: Pasireotide

Active, not recruiting [A Study to Assess SOM230 in Patients With Pituitary Cushing's Disease](#)  
Condition:Cushing's Syndrome Intervention:Drug: SOM230

Recruiting [Pharmacokinetics and Safety of Single Subcutaneous Pasireotide \(SOM230\) in Subjects With Varying Degrees of Hepatic Function](#)  
Conditions:Hepatic Cirrhosis; Alcoholism Intervention:Drug: Pasireotide

Recruiting [Safety and Efficacy of Pasireotide Long Acting Release vs. Octreotide Long Acting Release in Patients With Metastatic Carcinoid Disease](#)  
Condition:Carcinoid Disease Interventions:Drug: Pasireotide; Drug: Octreotide

Active, not recruiting [Study Evaluating SOM230 in Patients With Metastatic Carcinoid Tumors](#)  
Condition:Carcinoid Tumors Interventions:Drug: SOM230

Active, not recruiting [Study of Pasireotide Long Acting Release \(LAR\) Injection in Patients With Acromegaly and Patients With Carcinoid Disease](#)  
Conditions:Carcinoid Tumor; Acromegaly Intervention:Drug: Pasireotide

Active, not recruiting [An Extension Study to Assess the Long-Term Safety and Efficacy of Pasireotide in Patients With Acromegaly](#)  
Condition:Acromegaly Intervention:Drug: Pasireotide

Recruiting [Safety and Efficacy of Pasireotide Long Acting Release \(LAR\) vs. Octreotide LAR in Patients With Active Acromegaly](#)  
Condition:Acromegaly Intervention:Drug: Pasireotide

Active, not recruiting [Study Comparing SOM230 Subcutaneously and Sandostatin Subcutaneously in Acromegalic Patients](#)  
Condition:Acromegaly Interventions:Drug: SOM230

