XXI CONGRESSO NAZIONALE AIRO

Genova, 19-22 novembre 2011
Porto Antico di Genova
Centro Congressi

Associazione Italiana Radioterapia Oncologica

TUMORI DELL'AREA SELLARE
TERAPIA MEDICA

Francesco Minuto
DIMI-Università di Genova

Farmacoterapia

Dopamino-agonisti, analoghi della somatostatina, antagonisti ormonali

Radioterapia

Convenzionale

Stereotassica

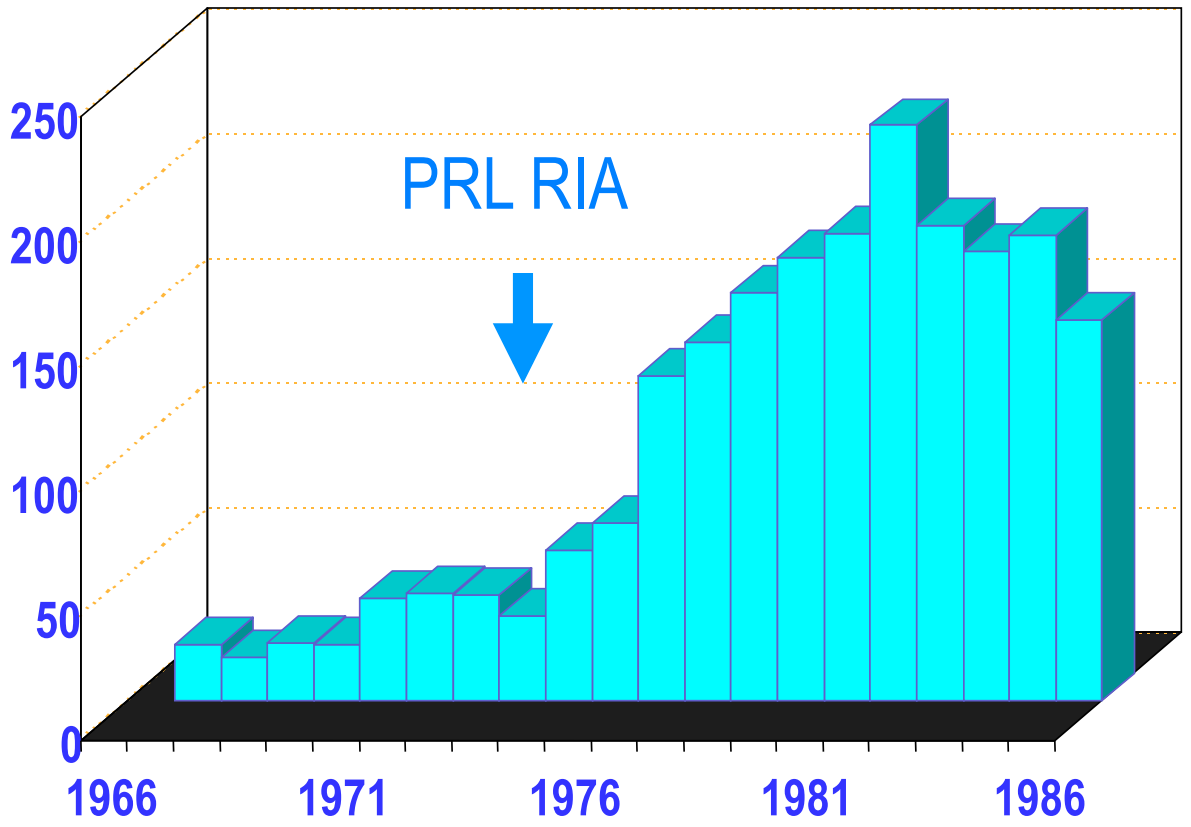
Chirurgia

Transcranica

Transfenoidale

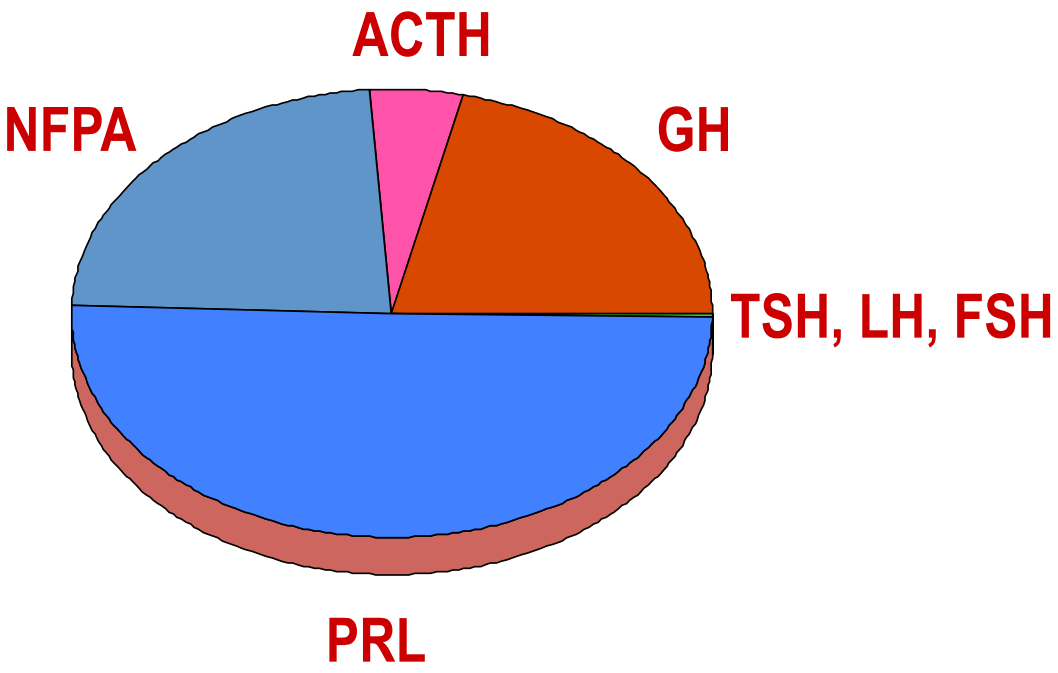
ADENOMI IPOFISARI

CASI/ANNO



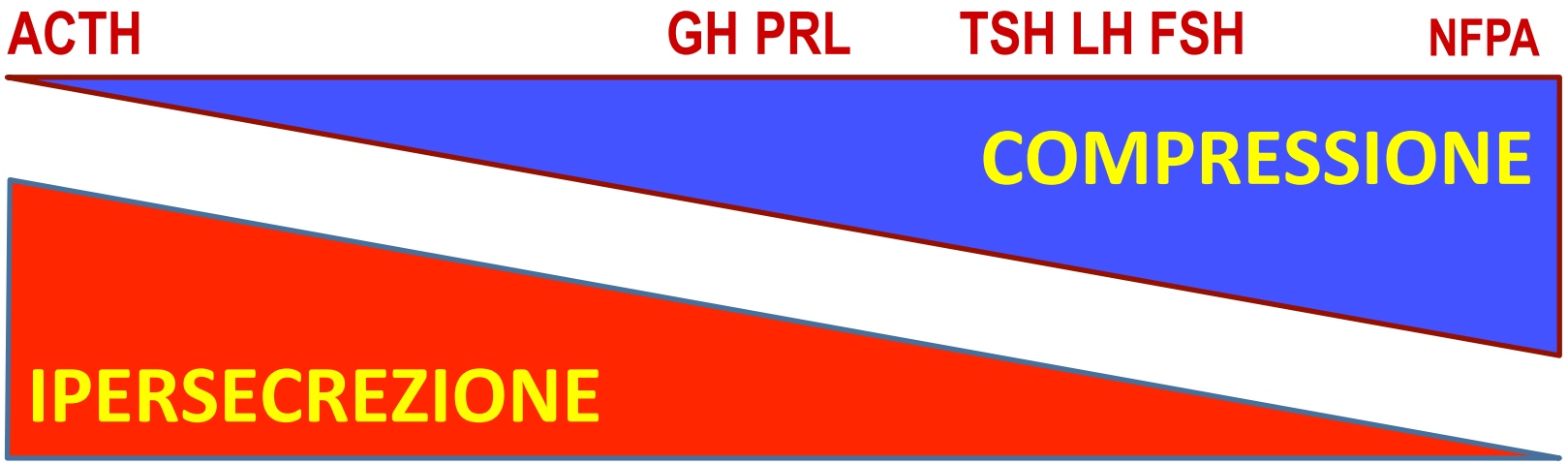
Ambrosi et al. 1991

FREQUENZA RELATIVA DEGLI ADENOMI IPOFISARI IN BASE ALLE CARATTERISTICHE FUNZIONALI



ADENOMI IPOFISARI

QUADRO CLINICO E STRATEGIA TERAPEUTICA



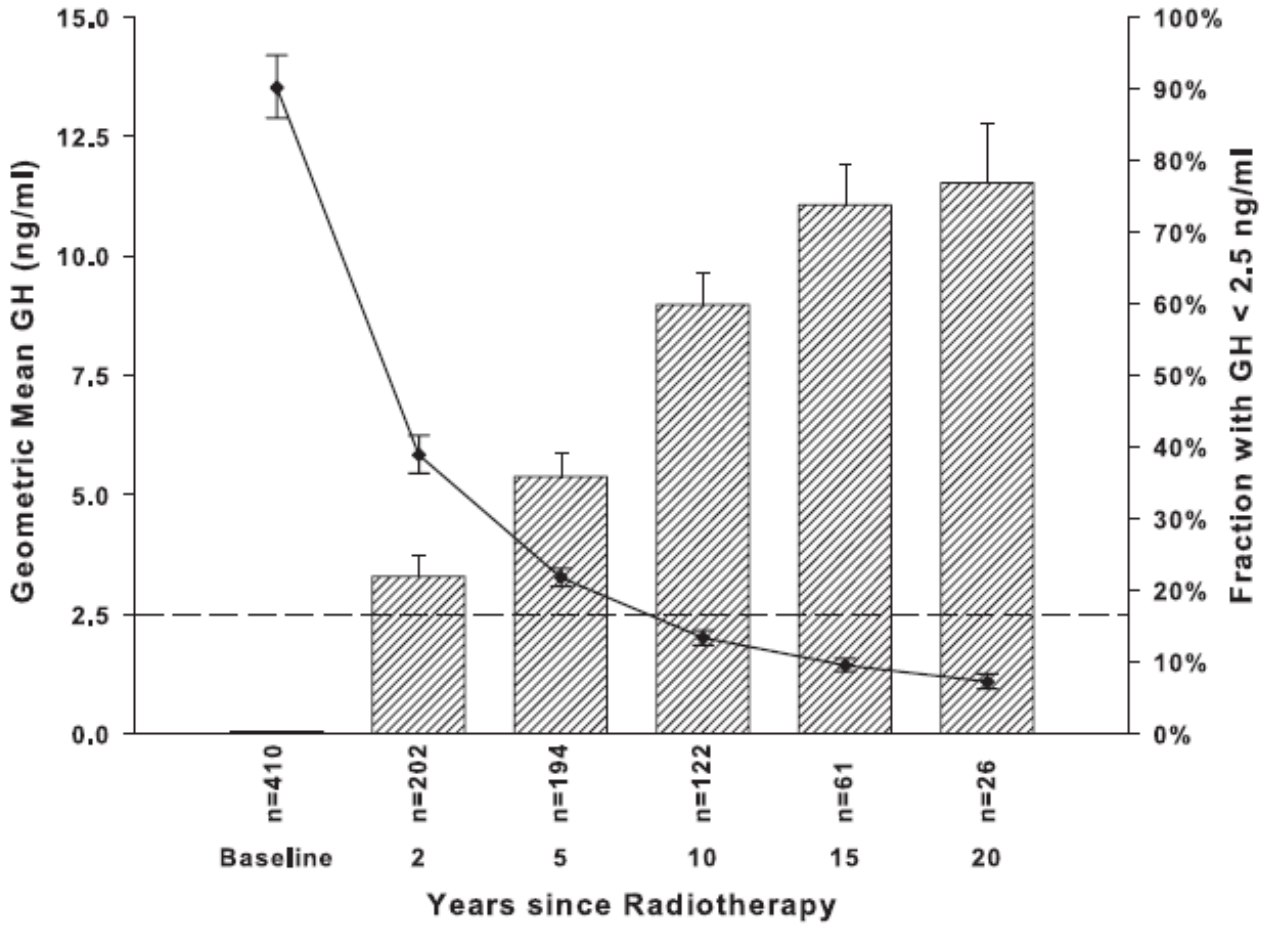
TERAPIA MEDICA

TERAPIA CHIRURGICA
RADIOTERAPIA

Conventional Pituitary Irradiation Is Effective in Lowering Serum Growth Hormone and Insulin-Like Growth Factor-I in Patients with Acromegaly

P. J. Jenkins, P. Bates, M. N. Carson, P. M. Stewart, and J. A. H. Wass, on behalf of the UK National Acromegaly Register Study Group*

J Clin Endocrinol Metab 91: 1239–1245, 2006



0021-972X/04/$15.00/0
Printed in U.S.A.

The Journal of Clinical Endocrinology & Metabolism 89(4):1613–1617

doi: 10.1210/jc.2003-031584

Growth Hormone and Pituitary Radiotherapy, But Not Serum Insulin-Like Growth Factor-I Concentrations, Predict Excess Mortality in Patients with Acromegaly

J. AYUK, R. N. CLAYTON, G. HOLDER, M. C. SHEPPARD, P. M. STEWART, AND A. S. BATES

Division of Medical Sciences (J.A., M.C.S., P.M.S.), University of Birmingham, Queen Elizabeth Hospital, Birmingham B15 2TH, United Kingdom; Department of Postgraduate Medicine (R.N.C.), University of Keele, Hartshill, Stoke-on-Trent, ST4 7QB, United Kingdom; Department of Diabetes and Endocrinology (A.S.B.), Birmingham Heartlands and Solihull National Health Service (NHS) Trust, B9 5SS, United Kingdom; and Regional Endocrine Laboratory (G.H.), Department of Clinical Biochemistry, University Hospital Birmingham NHS Trust, B29 6JD, United Kingdom

TABLE 2. All-cause and cause-specific mortality in patients with acromegaly treated with radiotherapy

Cause	Observed deaths	Expected deaths	SMR (95% CI)	*P*
All-cause	59	37.4	1.58 (1.22–2.04)	0.005
Cerebrovascular	16	3.6	4.42 (2.71–7.22)	0.005
Cardiovascular	20	12.5	1.60 (1.03–2.48)	0.096
Respiratory	7	4.0	1.75 (0.84–3.68)	0.261
Malignancy	12	12.0	1.00 (0.57–1.76)	1.000

PROLATTINOMI

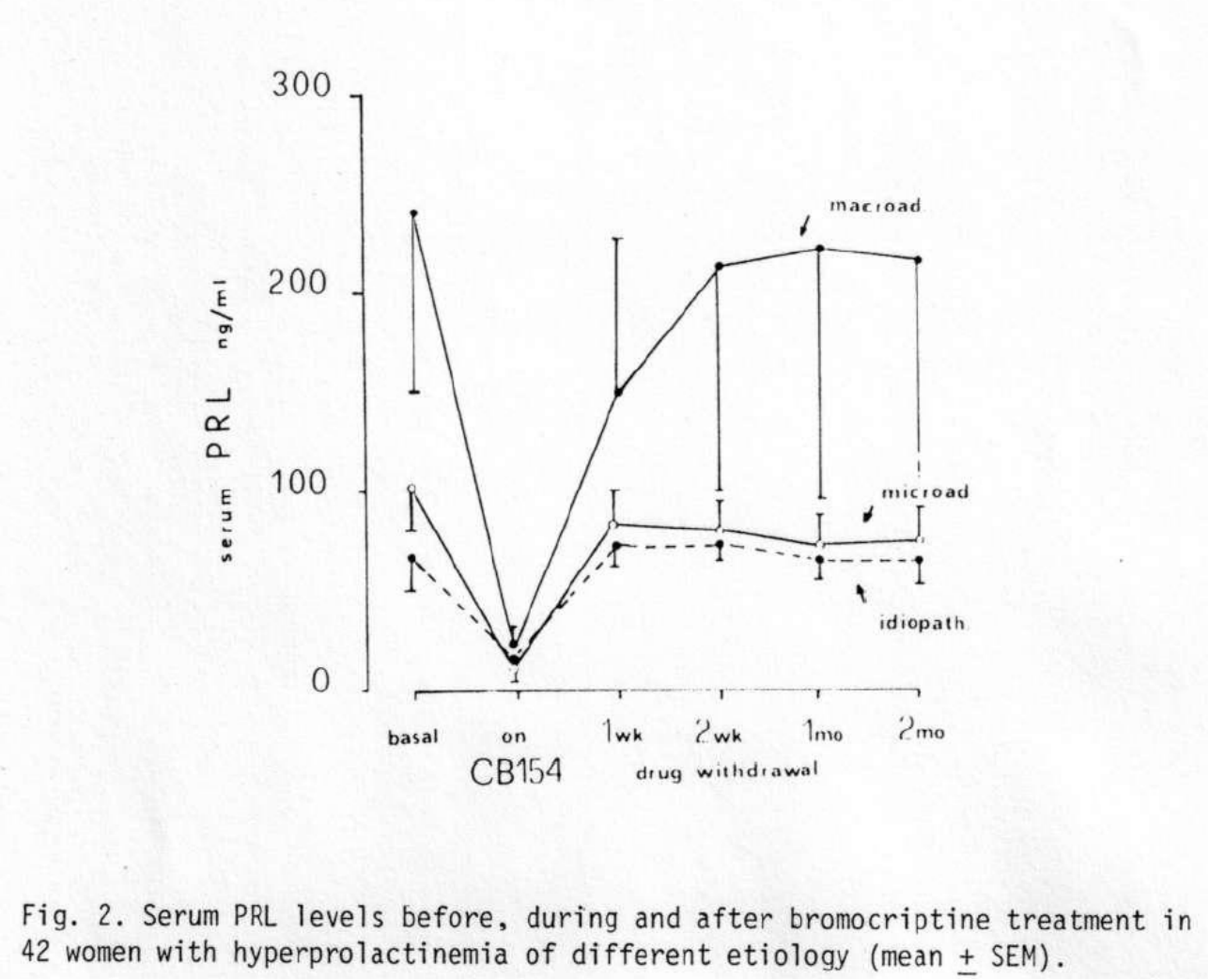
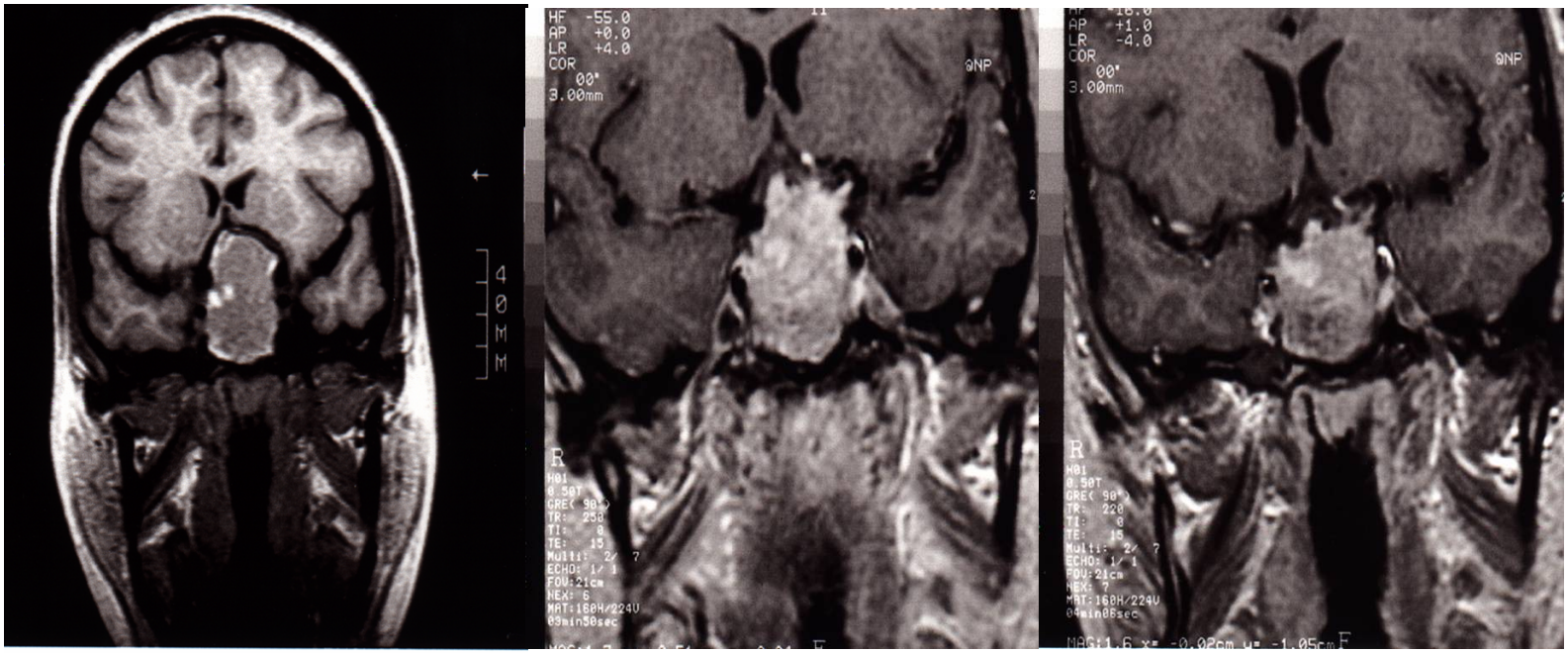


Fig. 2. Serum PRL levels before, during and after bromocriptine treatment in 42 women with hyperprolactinemia of different etiology (mean ± SEM).

Crosignani et al., 1985



basale	1 settimana	1 mese
1180 µg/l	550 µg/l	55 µg/l

JAMA. 1982 Jan 15;247(3):311-6.

Bromocriptine reduces pituitary tumor size and hypersection. Requiem for pituitary surgery?

Spark RF, Baker R, Bienfang DC, Bergland R.

Abstract

Twelve patients with pituitary tumor whose prior treatment included surgery and radiotherapy in four, surgery alone in four, radiotherapy alone in one, and none in three were studied. Nine had hyperprolactinemia, two had elevated serum growth hormones, and one had no pituitary hormone excess. Visual field defects were present in six. All had pituitary-gonadal insufficiency manifested as impotence or amenorrhea. All were tested with bromocriptine, 7.5 to 25 mg daily, and followed up for eight to 27 (mean 15) months. Serum prolactin levels decreased to normal in seven of nine patients. Serum growth hormone values were normalized in both acromegalics. When hormone levels were reduced to normal, pituitary tumor size decreased. Vision was restored to normal in five of six patients, including one patient with pituitary tumor but no pituitary hormone excess. Bromocriptine corrects the physiological defects associated with pituitary tumors that have been incompletely treated with surgery, radiotherapy, or both and may be a useful primary treatment for patients with pituitary tumors.

From BM SHERMAN & JA SCHLECHTE, 1986

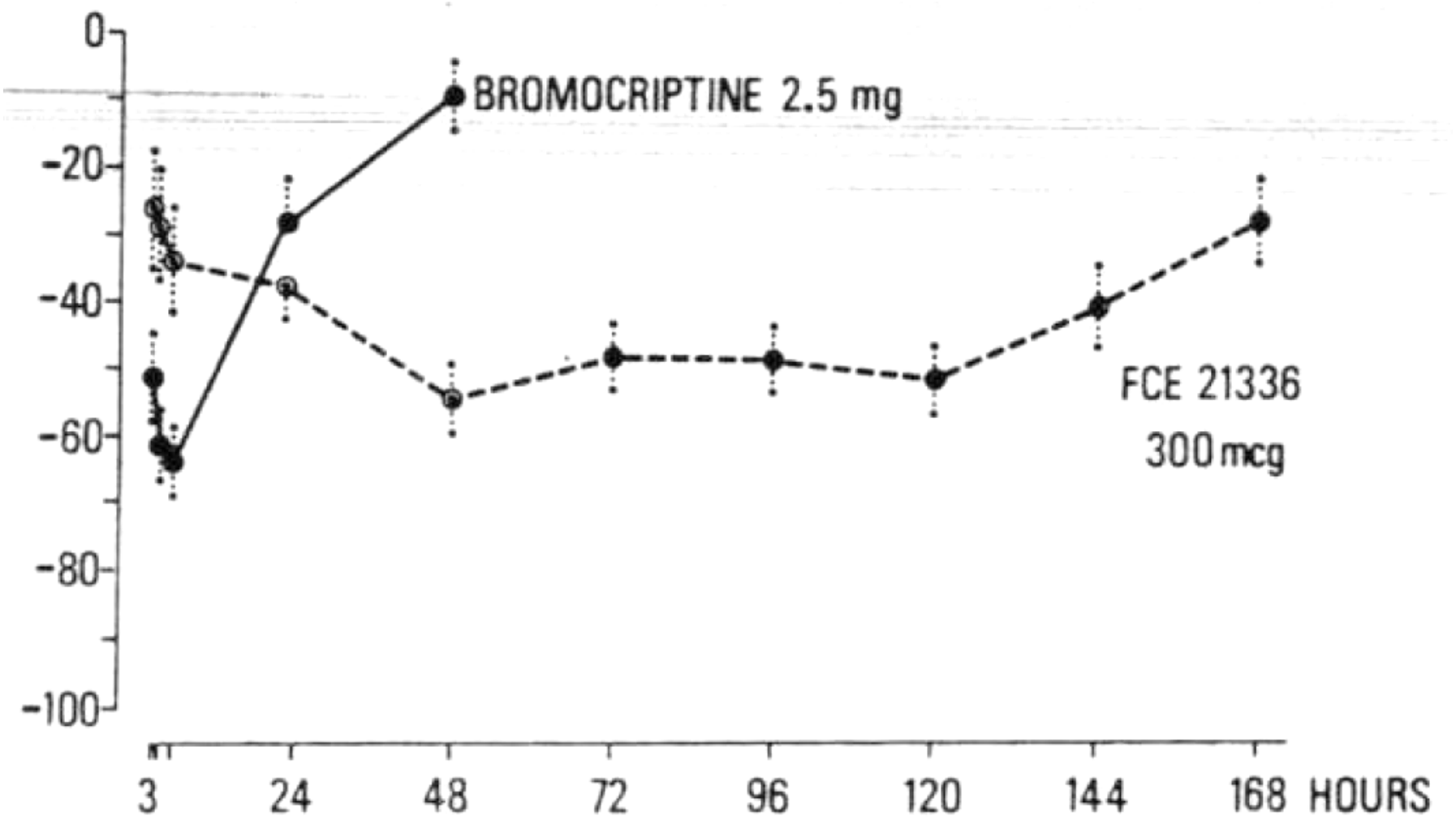
Alternative Approaches to Management of Hyperprolactinemia

Advantages		Disadvantages
	Surgery	
Potentially curative		Variable response
Reduces tumor mass		Complications Recurrence
Reduces PRL	**Bromocriptine**	Not curative
Reduces tumor mass		Cost
Restores fertility		Side effects Long-term consequences Compliance
	No therapy	
No surgery No medication		Risk of progression Subjective symptoms Osteopenia Need for follow-up

Long-lasting prolactin-lowering effect of cabergoline, a new dopamine agonist, in hyperprolactinemic patients

C Ferrari, C Barbieri, R Caldara, M Mucci, F Codecasa, A Paracchi, C Romano, M Boghen, and A Dubini

J Clin Endocrinol Metab 63: 941, 1986



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Withdrawal of Long-Term Cabergoline Therapy for Tumoral and Nontumoral Hyperprolactinemia

Annamaria Colao, M.D., Ph.D., Antonella Di Sarno, M.D., Ph.D.,
Paolo Cappabianca, M.D., Carolina Di Somma, M.D., Ph.D.,
Rosario Pivonello, M.D., Ph.D., and Gaetano Lombardi, M.D., Ph.D.

N Engl J Med. 2003 Nov 20;349(21):2023-33.

Diagnosis & Treatment of Hyperprolactinemia:
An Endocrine Society Clinical Practice Guideline

Journal of Clinical Endocrinology & Metabolism 96(2): 273–288, 2011

4.0. Management of prolactinoma

4.1. We recommend **dopamine agonist** therapy to lower prolactin levels, decrease tumor size, and restore gonadal function for patients harboring symptomatic prolactin-secreting microadenomas or macroadenomas(1|). We recommend using **cabergoline** in preference to other dopamine agonists because it has higher efficacy in normalizing prolactin levels, as well as a higher frequency of pituitary tumor shrinkage (1|).

4.2. We suggest that clinicians **not treat asymptomatic patients** harboring microprolactinomas with dopamine agonists (2|). We suggest treatment with a **dopamine agonist or oral contraceptive** in patients with amenorrhea caused by a microadenoma(2|).

4.3. We suggest that with careful clinical and biochemical follow-up, **therapy may be tapered** and perhaps discontinued in patients who have been treated with dopamine agonists for at least 2 yr, who no longer have elevated serum prolactin, and who have no visible tumor remnant on MRI (2|).

5.1. For **symptomatic patients who do not achieve normal prolactin levels** or show significant reduction in tumor size on standard doses of a dopamine agonist (resistant prolactinomas), we recommend that the dose be increased to maximal tolerable doses before referring the patient for surgery (1|

5.3. We suggest that clinicians offer **transsphenoidal surgery** to symptomatic patients with prolactinomas who cannot tolerate high doses of cabergoline or who are not responsive to dopamine agonist therapy. For patients who are intolerant of oral bromocriptine, intravaginal administration may be attempted. For **patients who fail surgical treatment** or who harbor aggressive or malignant prolactinomas, we suggest radiation therapy (2|).

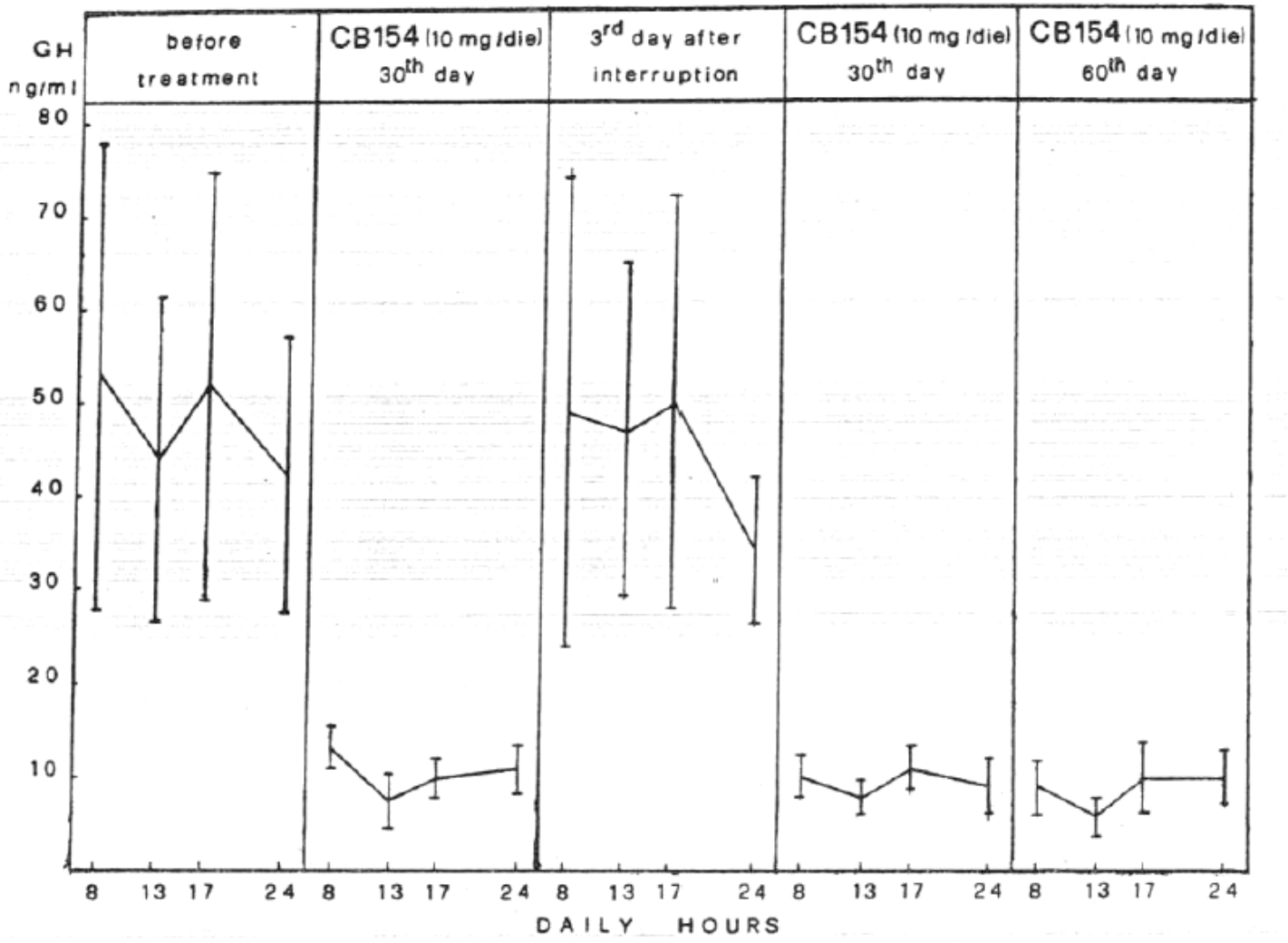
ACROMEGALIA

A. Verga, 1864

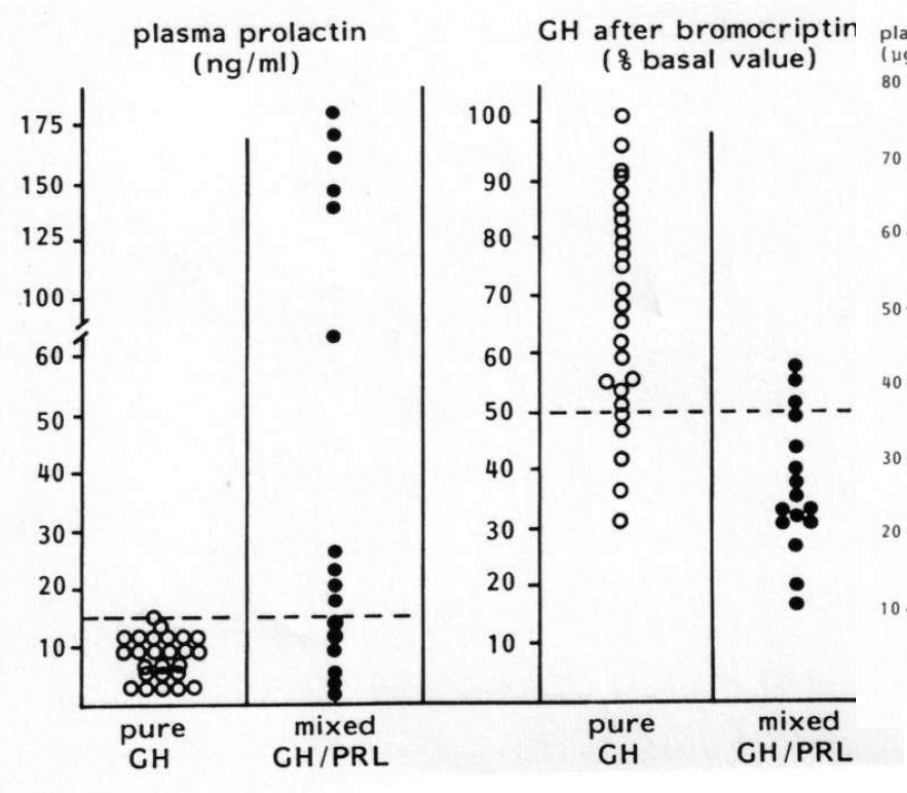
Stable Reduction of Plasma Growth Hormone (hGH) Levels During Chronic Administration of 2-Br-a-ergocryptine (CB-154) in Acromegalic Patients

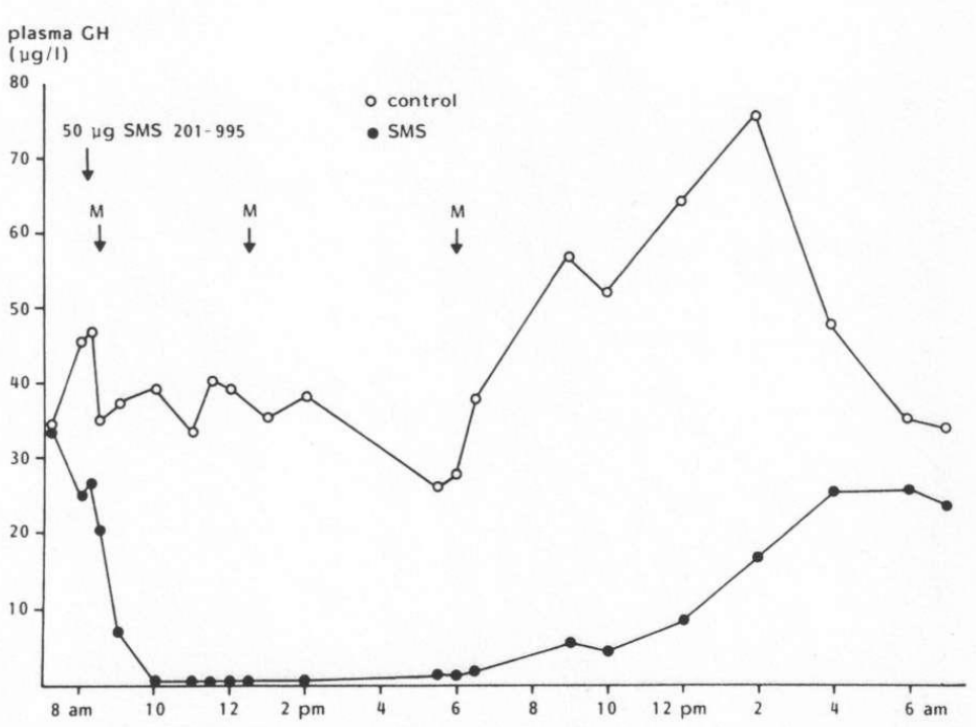
PG Chiodini, A Liuzzi, L Botalla, G Oppizzi, EE Muller, and F Silvestrini

J Clin Endocrinol Metab 40: 705,1975



LAMBERTS, 1985





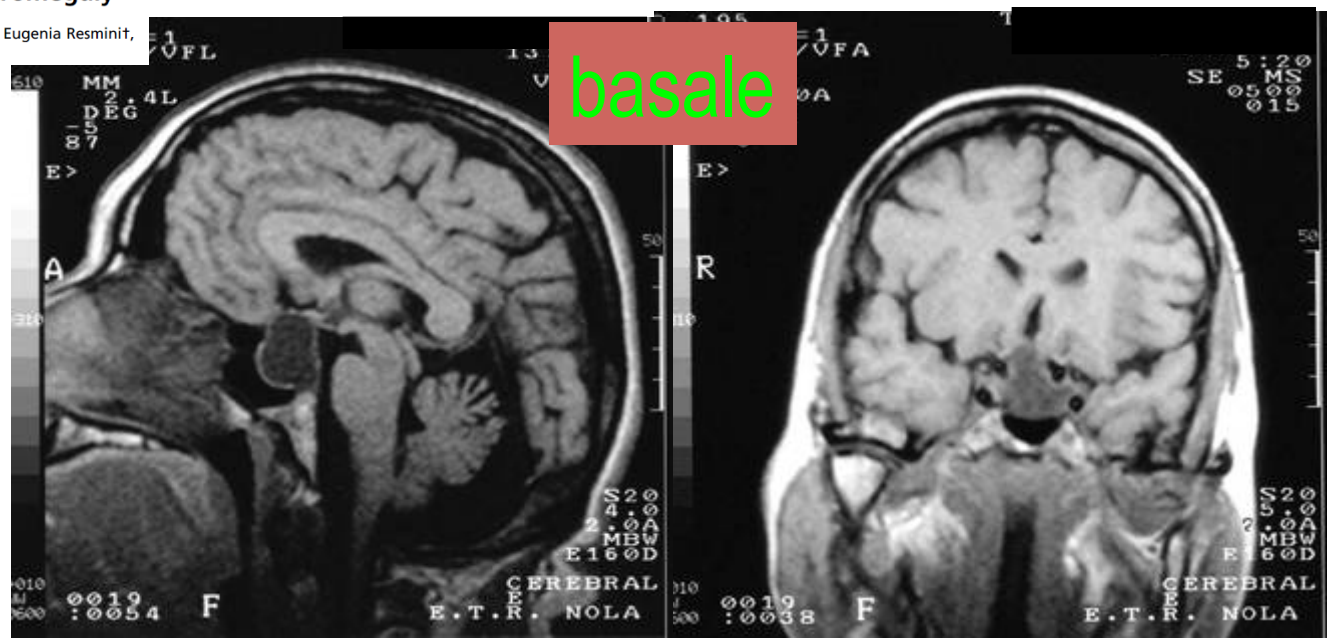
Clinical Endocrinology (2009) 71, 237–245 doi: 10.1111/j.1365-22

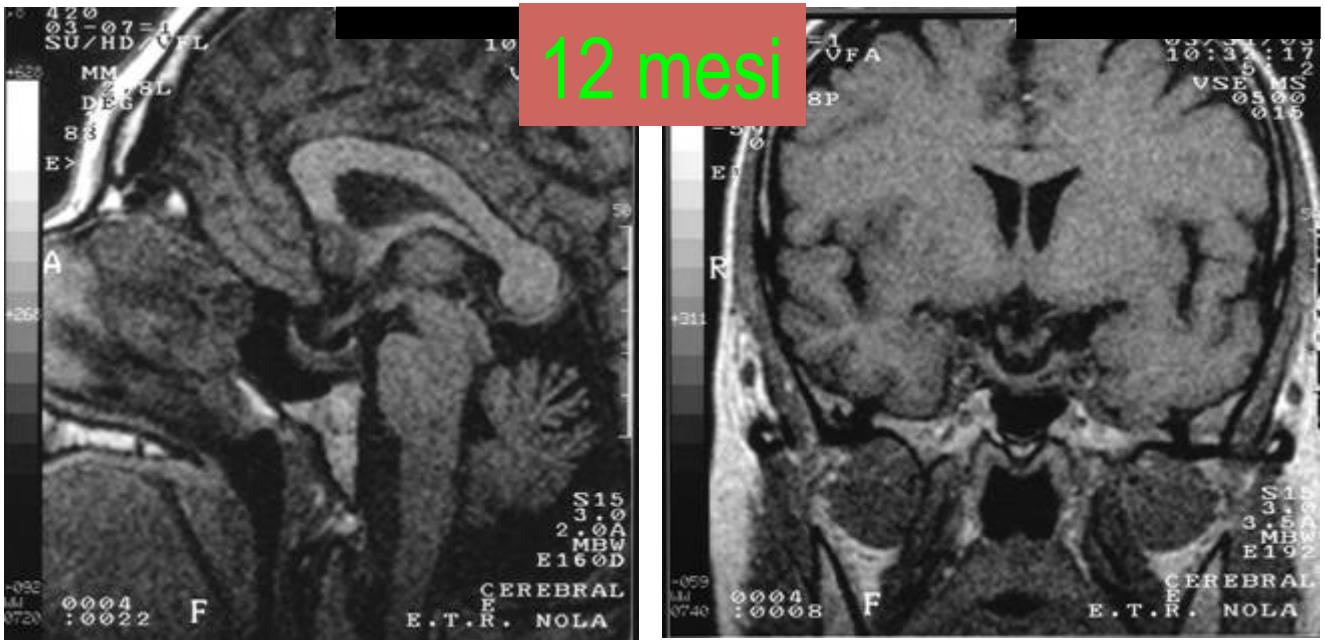
ORIGINAL ARTICLE

Significant tumour shrinkage after 12 months of lanreotide Autogel-120 mg treatment given first-line in acromegaly

Annamaria Colao*, Renata S. Auriemma*, Alberto Reborat, Mariano Galdiero*, Eugenia Resminit, Francesco Minutot, Gaetano Lombardi*, Rosario Pivonello* and Diego Feronet

T.M.
F, 66 anni





ATG 120 mg
ogni 8 settimane

Clinical Endocrinology (2009) 70, 757–768 doi: 10.1111/j.1365-226

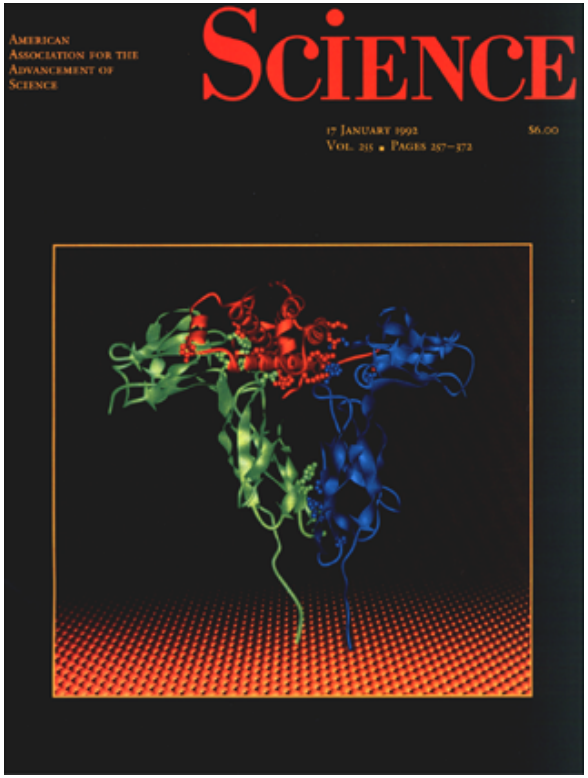
ORIGINAL ARTICLE

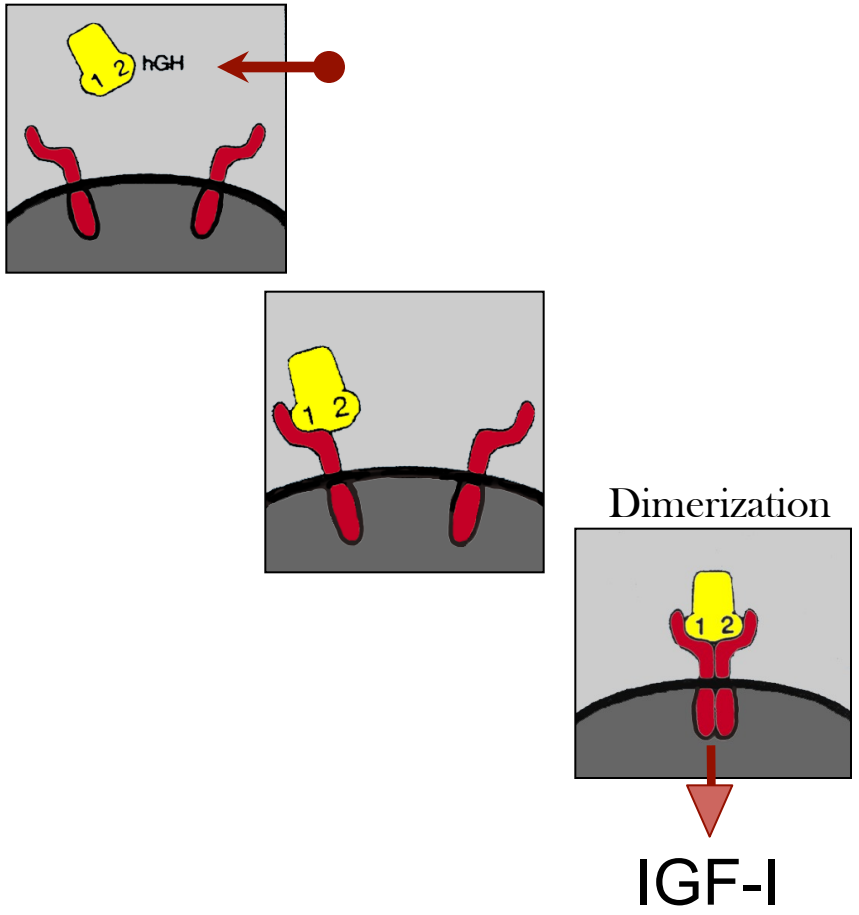
Octreotide LAR *vs.* surgery in newly diagnosed patients with acromegaly: a randomized, open-label, multicentre study

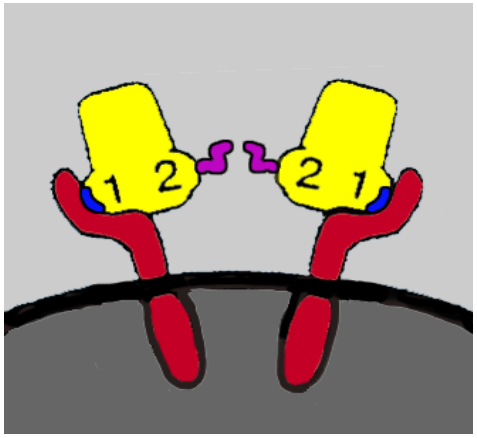
Annamaria Colao*, Paolo Cappabiancat, Philippe Caront, Ernesto De Menis§, Andrew J. Farrall¶, Monica R. Gadelha**, Abdel Hmissitt, Aled Rees‡‡, Martin Reincke§§, Mitra Safaritt, Guy T'Sjoen¶¶, Hakim Bouterfatt and Ross C. Cuneo***

- Questo primo studio randomizzato in pazienti non selezionati indica che il risultato a 48 settimane di terapia con octreotide LAR in 1° linea non si differenzia significativamente da quello ottenuto con la chirurgia.
- Poichè una risposta completa con la chirurgia in pazienti con macroadenomi è difficile da ottenere, la terapia di 1° linea con octreotide LAR può essere considerata un'alternativa percorribile nella maggior parte dei pazienti, grazie anche al minimo tasso di complicazioni.

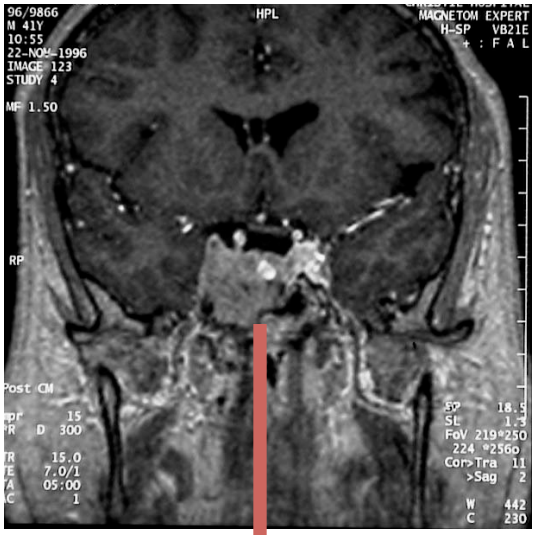
Mechanism of hGH binding and signal transduction





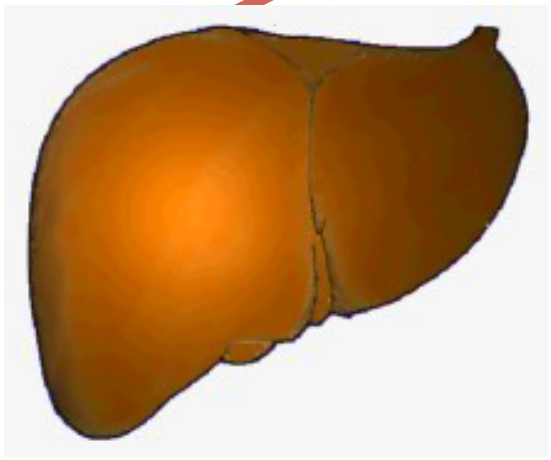


Pegvisomant



- 191 amino acid GH analogue
- 9 amino acid substitutions
- 4 - 5 PEG moieties
- molecular weight 42 - 46000 D
- half-life >70 hours
- subcutaneous administration

GH

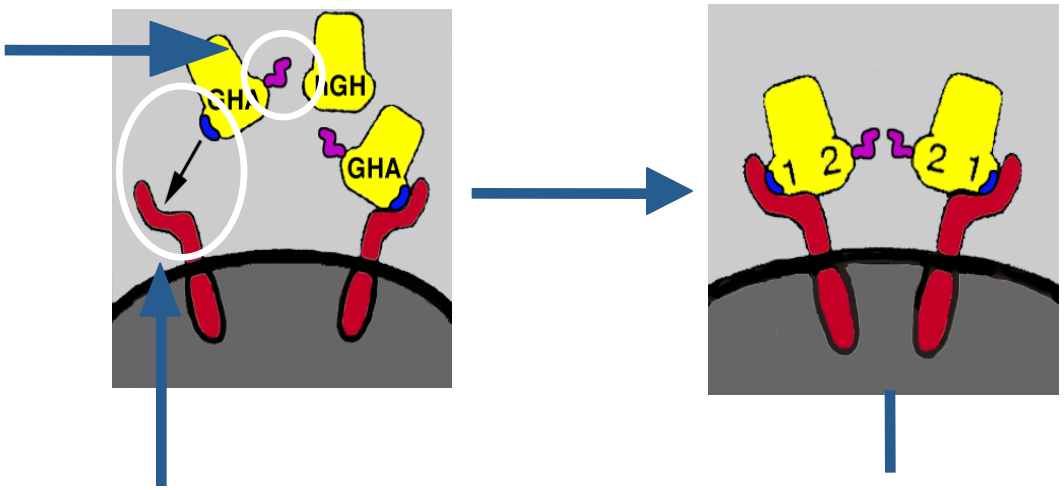


serum GH cannot be used as a disease marker

Goal of therapy - to lower IGF-I into the age-related reference range

Growth hormone receptor antagonist design

Site-2 binding disrupted by substituting an amino acid with a long side-chain in the G120 position



Site-1 binding to GH receptor enhanced, preventing hGH from binding to the receptor ..... greatly increasing the potency of the GHA

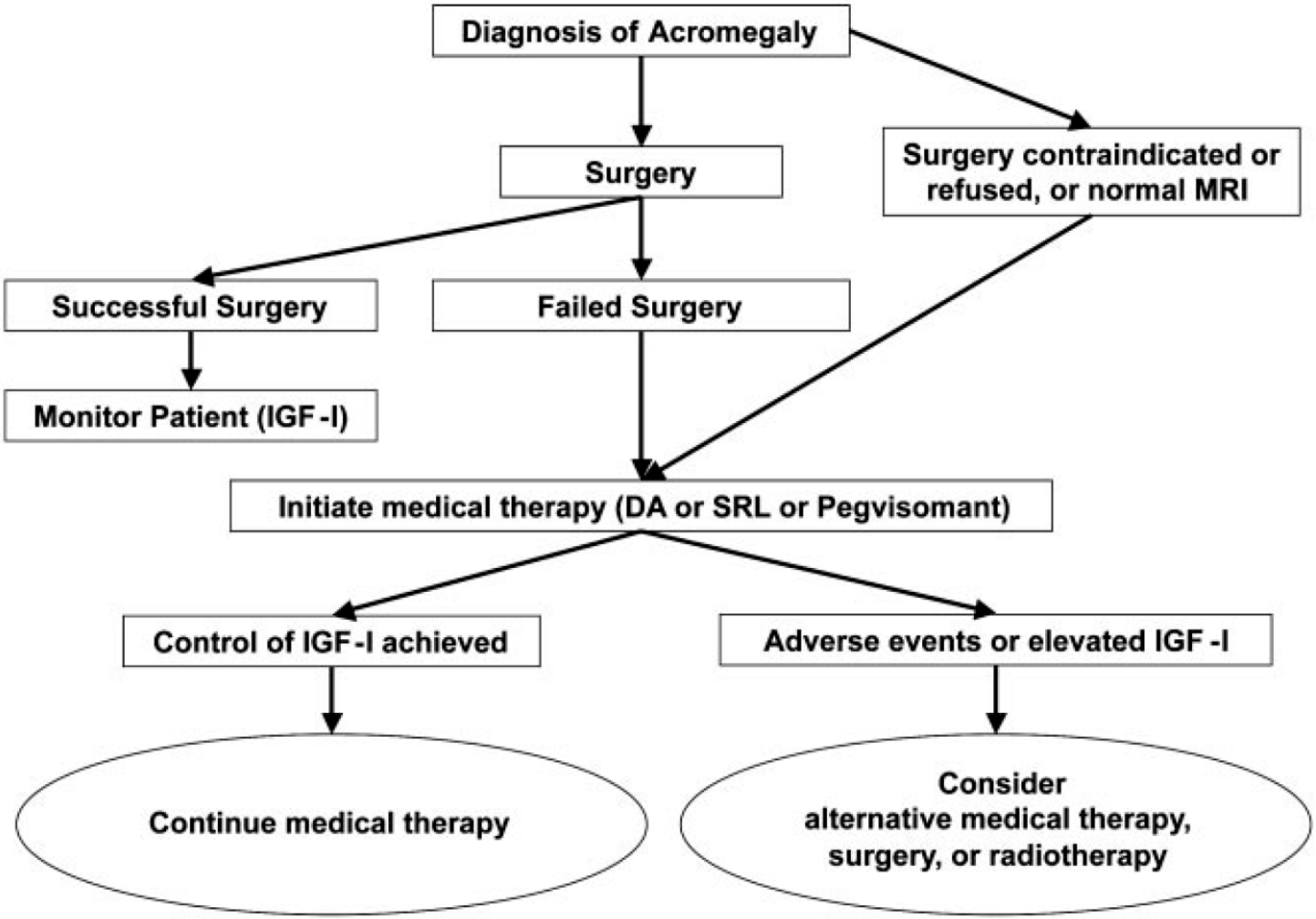
Dimerization is prevented; signal transduction and IGF-I production do not occur

Optimizing Control of Acromegaly: Integrating a Growth Hormone Receptor Antagonist into the Treatment Algorithm

The Journal of Clinical Endocrinology & Metabolism 88(10):4759–4767

doi: 10.1210/jc.2003-030518

DAVID R. CLEMMONS, KAZUO CHIHARA, PAMELA U. FREDA, KEN K. Y. HO, ANNE KLIBANSKI, SHLOMO MELMED, STEPHEN M. SHALET, CHRISTIAN J. STRASBURGER, PETER J. TRAINER, AND MICHAEL O. THORNER



Guidelines for Acromegaly Management: An Update

S. Melmed, A. Colao, A. Barkan, M. Molitch, A. B. Grossman, D. Kleinberg, D. Clemmons, P. Chanson, E. Laws, J. Schlechte, M. L. Vance, K. Ho, and A. Giustina

J Clin Endocrinol Metab 94: 1509–1517, 2009

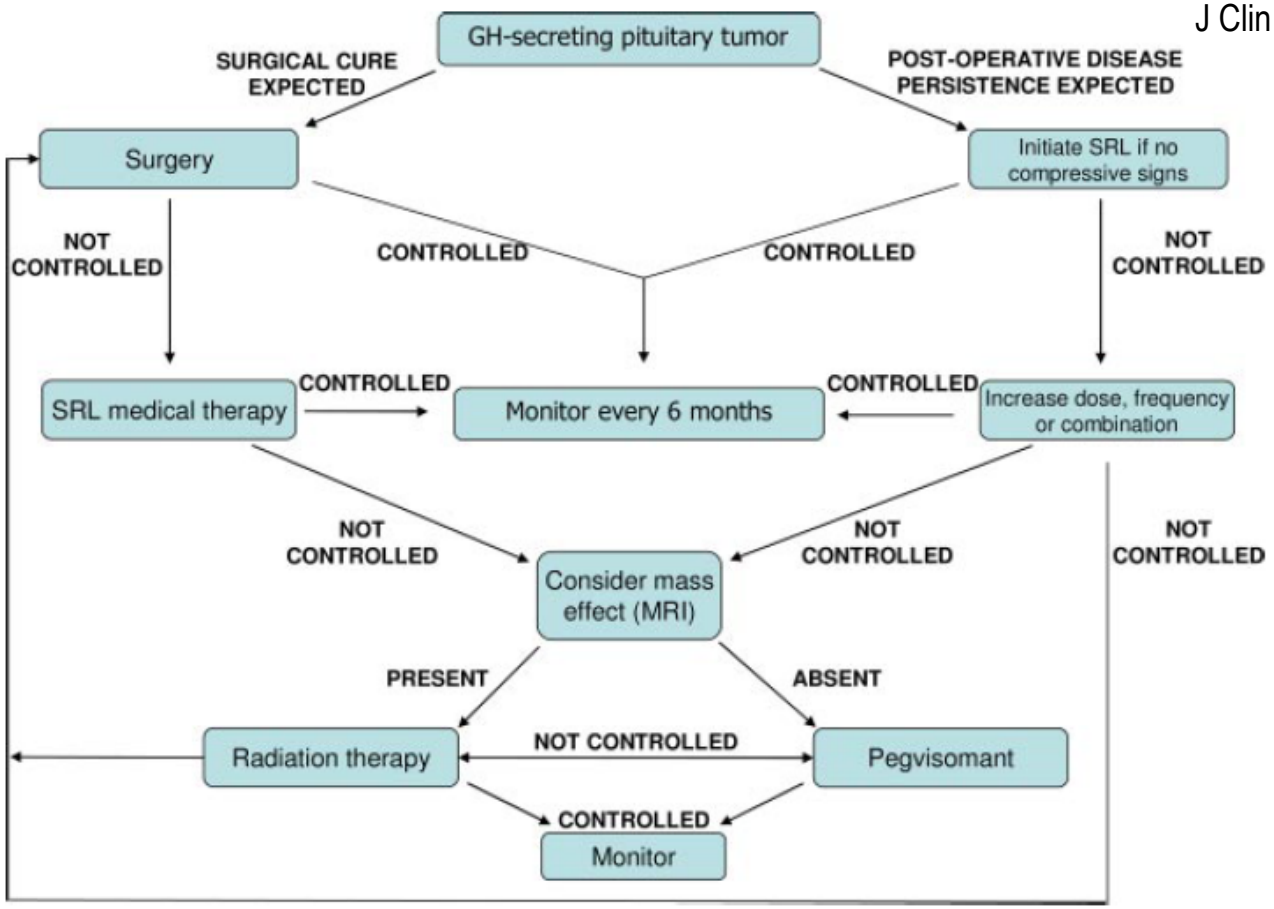


FIG. 1. Summary of management strategy for patients with acromegaly. First level, Surgery SR; SRL DR. Second level, SRL SR; monitor SR; increase dose DR. Third level, MRI DR. Fourth level, Radiation DR; Pegvisomant DR. Fifth level, Monitor SR; back to surgery SR. Control is defined by GH and IGF-I measurements as outlined in the text.

MANIFESTO

First-line therapy of acromegaly: A statement of the A.L.I.C.E. (Acromegaly primary medical treatment Learning and Improvement with Continuous Medical Education) study group

A. Colao[1], E. Martino[2], P. Cappabianca[3], R. Cozzi[4], M. Scanarini[5], E. Ghigo[6], and the participants of the A.L.I.C.E. (Acromegaly primary medical treatment Learning and

J. Endocrinol. Invest. 29: 1017-1020, 2006

Chirurgia

→ adenomi intrasellari (micro o macro)

→ Pazienti con deterioramento significativo del campo visivo oppure in situazioni di emergenza come ipertensione endocranica e apoplessia del tumore

Radioterapia

→ Mai

Eccezionalmente:

- *indisponibilità di altri trattamenti*
- *Preferenza del paziente*

Terapia medica

→ in tutti i casi in cui **non** è indicata la chirurgia come 1° linea

Attenzione!! I pazienti con severe complicanze cardiocircolatorie e/o respiratorie sono candidati alla terapia medica di 1° linea prima dell'intervento, anche quando questo è indicato

MANIFESTO

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A. Colao[1], E. Martino[2], P. Cappabianca[3], R. Cozzi[4], M. Scanarini[5], E. Ghigo[6], and the participants of the A.L.I.C.E. (Acromegaly primary medical treatment Learning and Improvement with Continuous Medical Education) study group

J. Endocrinol. Invest. 29: 1017-1020, 2006

Raccomandazioni

I. Gli interventi chirurgici devono essere effettuati in centri dove sono disponibili chirurghi esperti, dedicati alla patologia ipofisaria (≥50 interventi/anno). In queste condizioni la morbidità è <2% e la mortalità <0.1%. Preferibile una chirurgia con tecnica microchirurgica/endoscopica.

II. La radioterapia dovrebbe essere somministrata mediante tecnologia stereotassica

III. La terapia medica di 1° linea deve essere quella con formulazioni depot di analoghi della somatostatina

TERAPIA DELL'ACROMEGALIA

Oggi → **Chirurgia**
Farmacoterapia
Radioterapia

- Bromocriptina
- Cabergolina
- Octreotide-LAR
- Lanreotide ATG
- Pegvisomant

- Chirurgia: Controllo di GH/IGF-I in 50% (80% micro, 50% macro, 10% adenomi giganti)
- DA: Controllo GH/IGF-I in <10% (bassi livelli ormonali più iperprolattinemia)
- SRL: Controllo GH/IGF-I e crescita del tumore in 50-75%
- Pegvisomant: Controllo di IGF-I in 80-97%
- Radioterapia: Controllo GH/IGF-I in funzione del tempo 25-30% dopo 5 anni, 50-60% dopo10 anni, 75-80% dopo15 anni

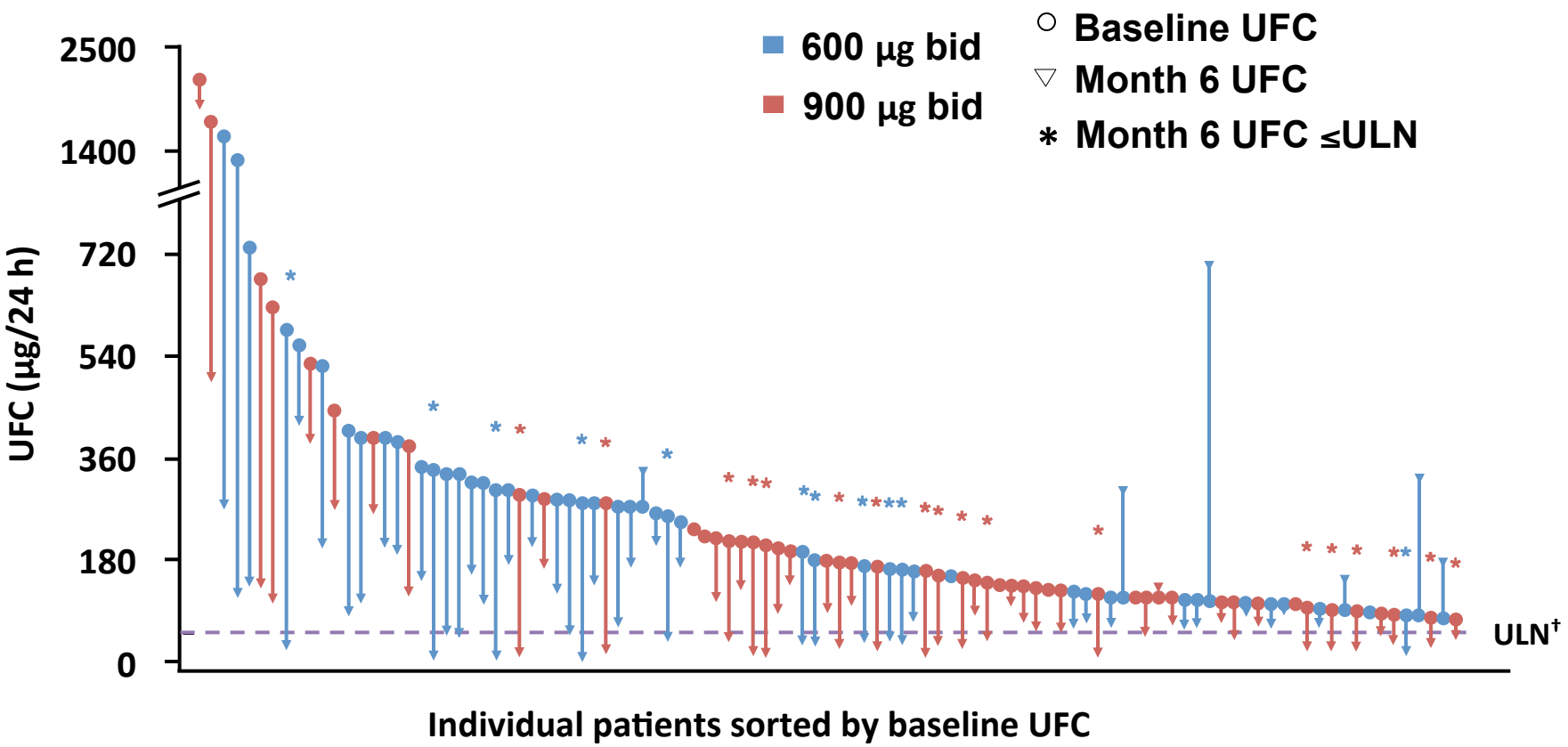
Domani

- Alte dosi di SRL
- Differenti schemi di terapia
- Trattamenti combinati
- Nuovi farmaci

SOM-230
SSR-DA ligandi

Change in UFC from baseline to month 6

in the 103 patients with baseline and month-6 UFC measurements



Median percent UFC change from baseline was -47.9% in both groups

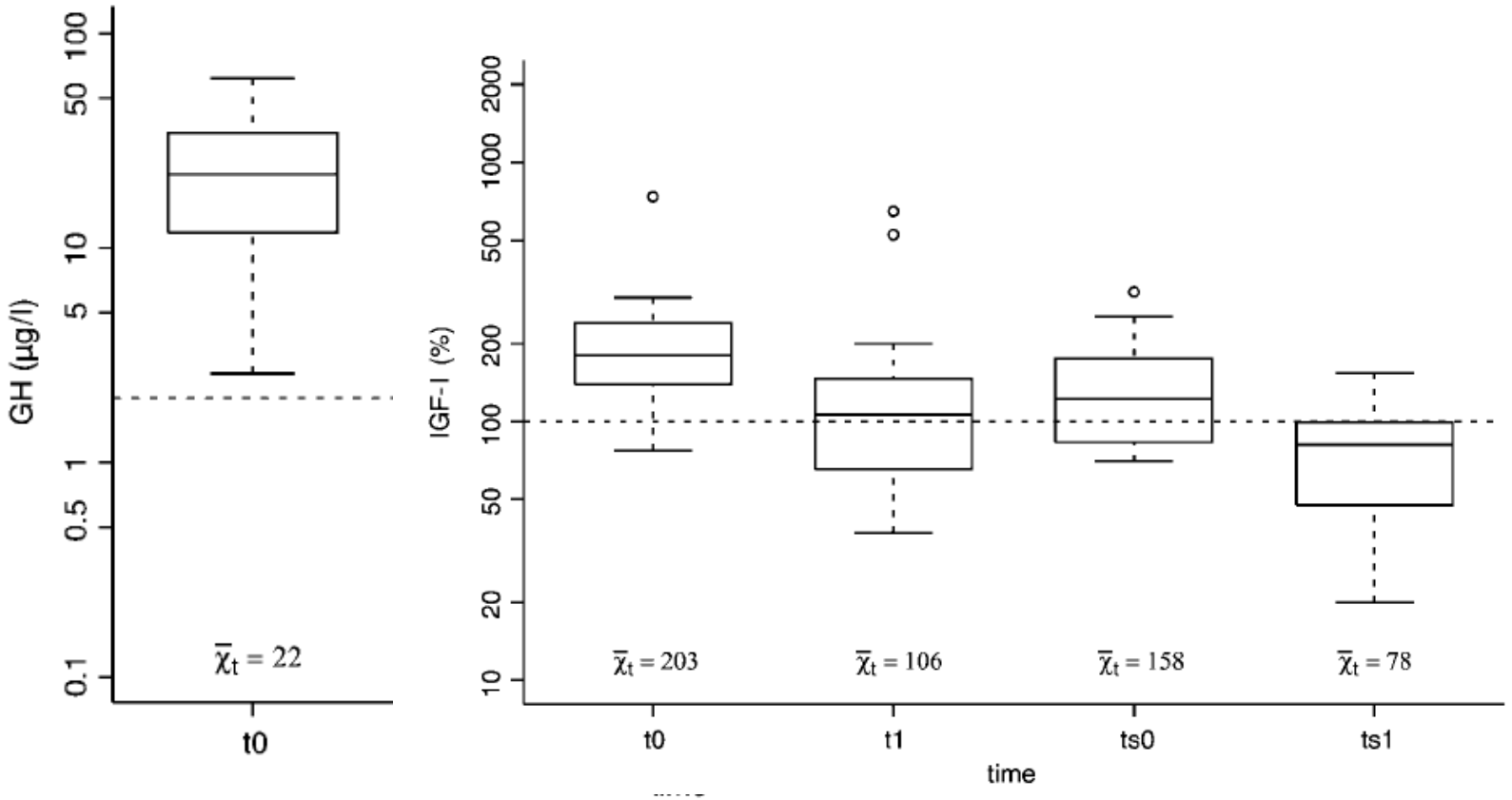
†Reference line is the upper limit normal UFC, which is 52.5 µg/24 h (145 nmol/24 h)

European Journal of Endocrinology (2005) **152** 61–66 ISSN 0804-4643

CLINICAL STUDY

Gross total resection or debulking of pituitary adenomas improves hormonal control of acromegaly by somatostatin analogs

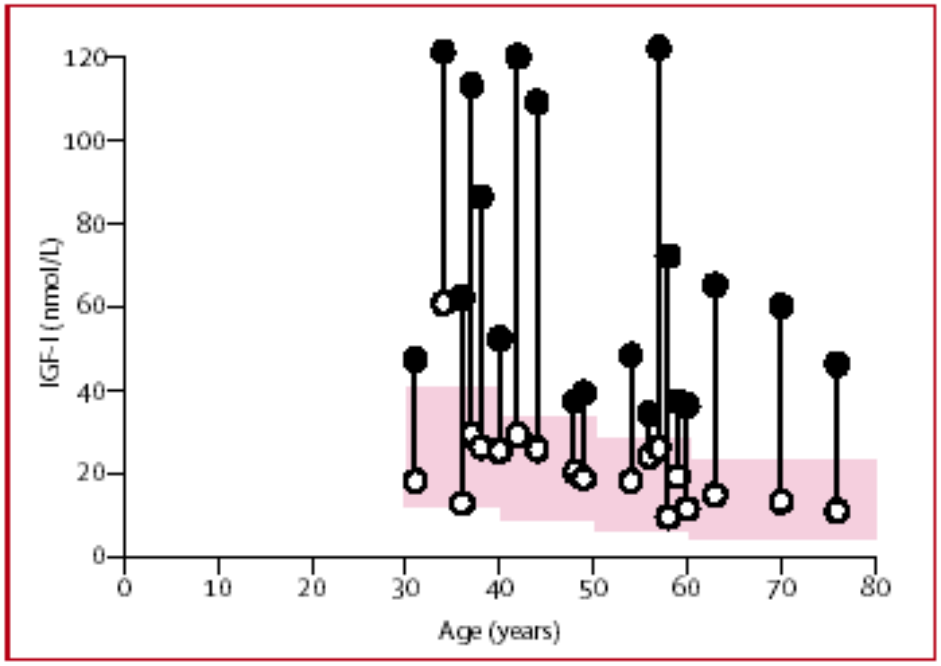
Patrick Petrossians, Liliane Borges-Martins, Consuelo Espinoza[2], Adrian Daly, Daniela Betea, Hernan Valdes-Socin, Achille Stevenaert[1], Philippe Chanson[2] and Albert Beckers



Combined therapy with somatostatin analogues and weekly pegvisomant in active acromegaly

J Feenstra, W W de Herder, S M T H ten Have, A W van den Beld, R A Feelders, J A M J L Janssen, A J van der Lely

www.thelancer.com Published online April 21, 2005



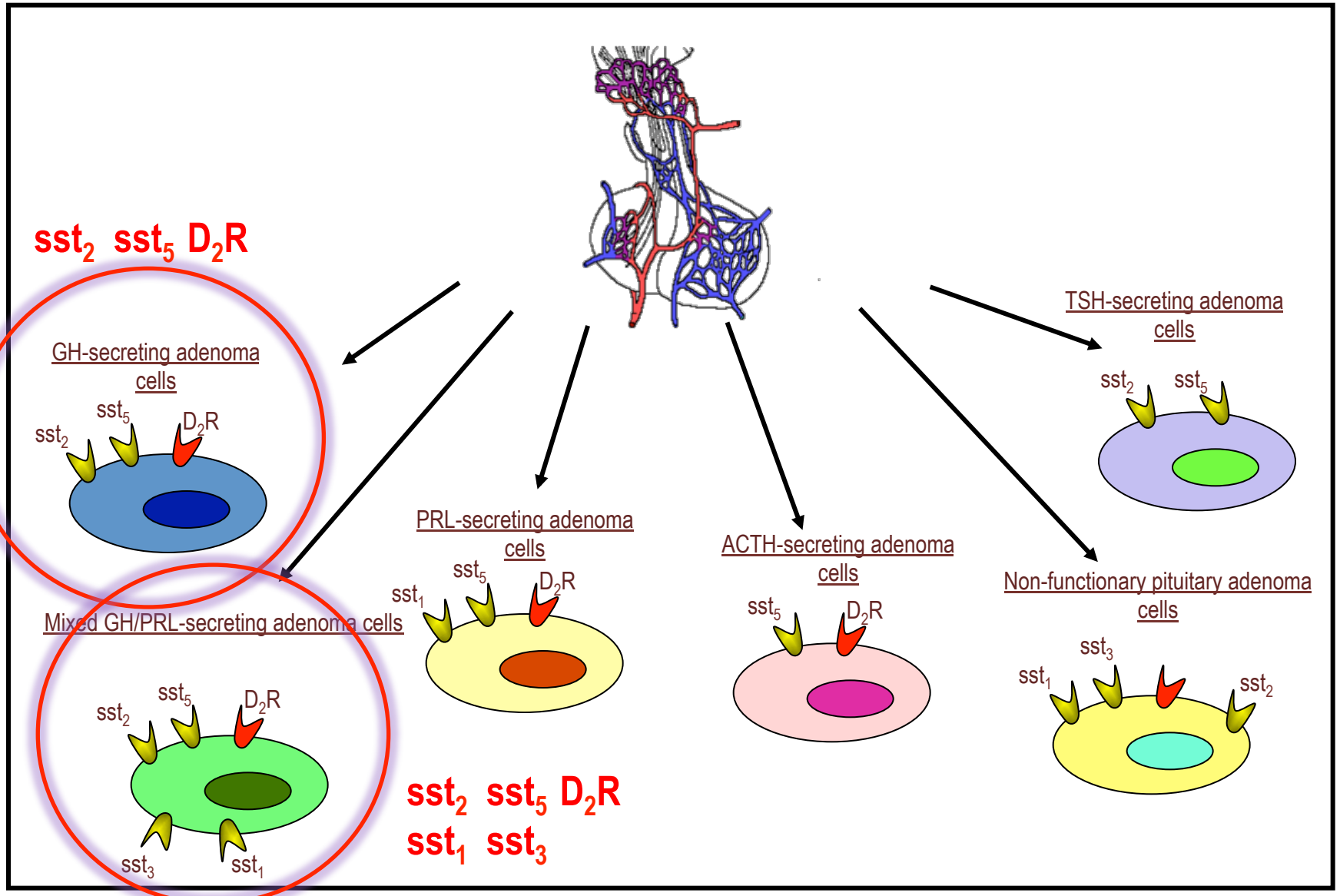
After 6 mo IGF-I normal in 18/19 patients (95%)
20 mg of GHRA daily = 65 mg/ weekly
Pts achieving normal IGF-I levels with 40 mg of GHRA daily as monotherapy save € 58,000 per year with the combination therapy

REVIEW

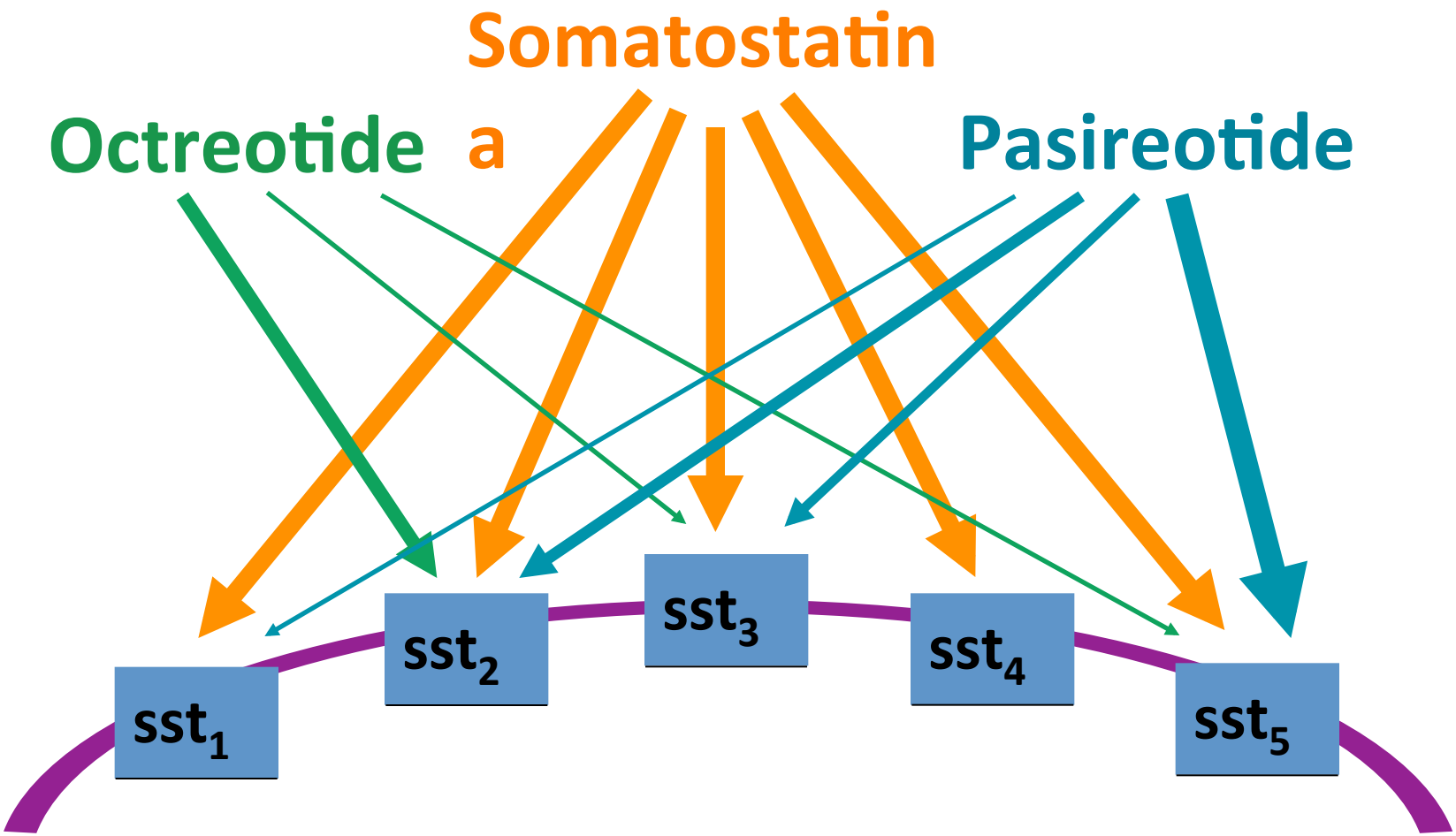
Journal of Molecular Endocrinology (2009) **42**, 1–10

The clinical–molecular interface of somatostatin, dopamine and their receptors in pituitary pathophysiology

Diego Ferone, Federico Gatto, Marica Arvigo, Eugenia Resmini, Mara Boschetti, Claudia Teti, Daniela Esposito and Francesco Minuto



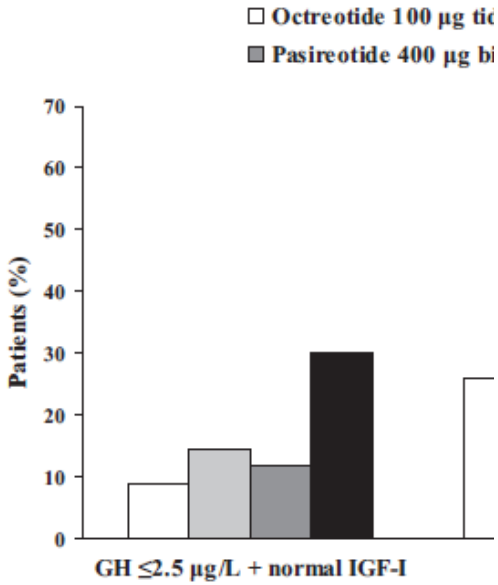
Più ampio profilo di interazione del pasireotide con i sottotitpi di recettore della somatostatina

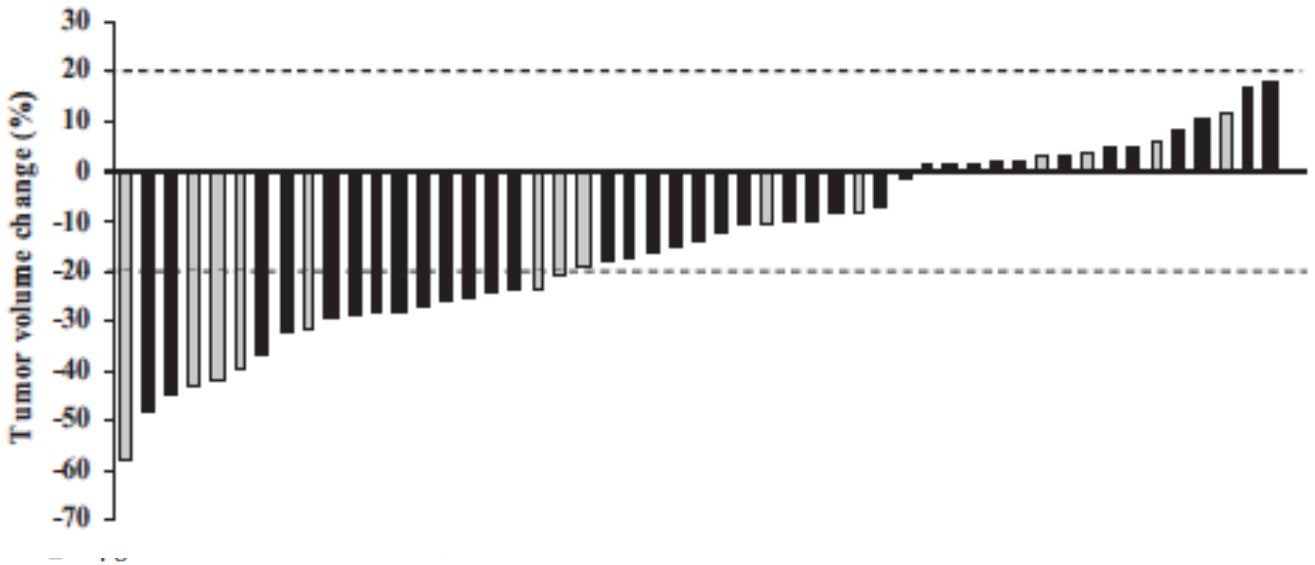


Pasireotide (SOM230) Demonstrates Efficacy and Safety in Patients with Acromegaly: A Randomized, Multicenter, Phase II Trial

S. Petersenn, J. Schopohl, A. Barkan, P. Mohideen, A. Colao, R. Abs, A. Buchelt, Y.-Y. Ho, K. Hu, A. J. Farrall, S. Melmed, B. M. K. Biller, and the Pasireotide Acromegaly Study Group

"..After 4 wk of octreotide, 9% of patients achieved a biochemical response. After 4 wk of pasireotide 200–600 g sc bid, 19% of patients achieved a biochemical response, which increased to 27% after 3 months of pasireotide; 39% of patients had a more than 20% reduction in pituitary tumor volume.."



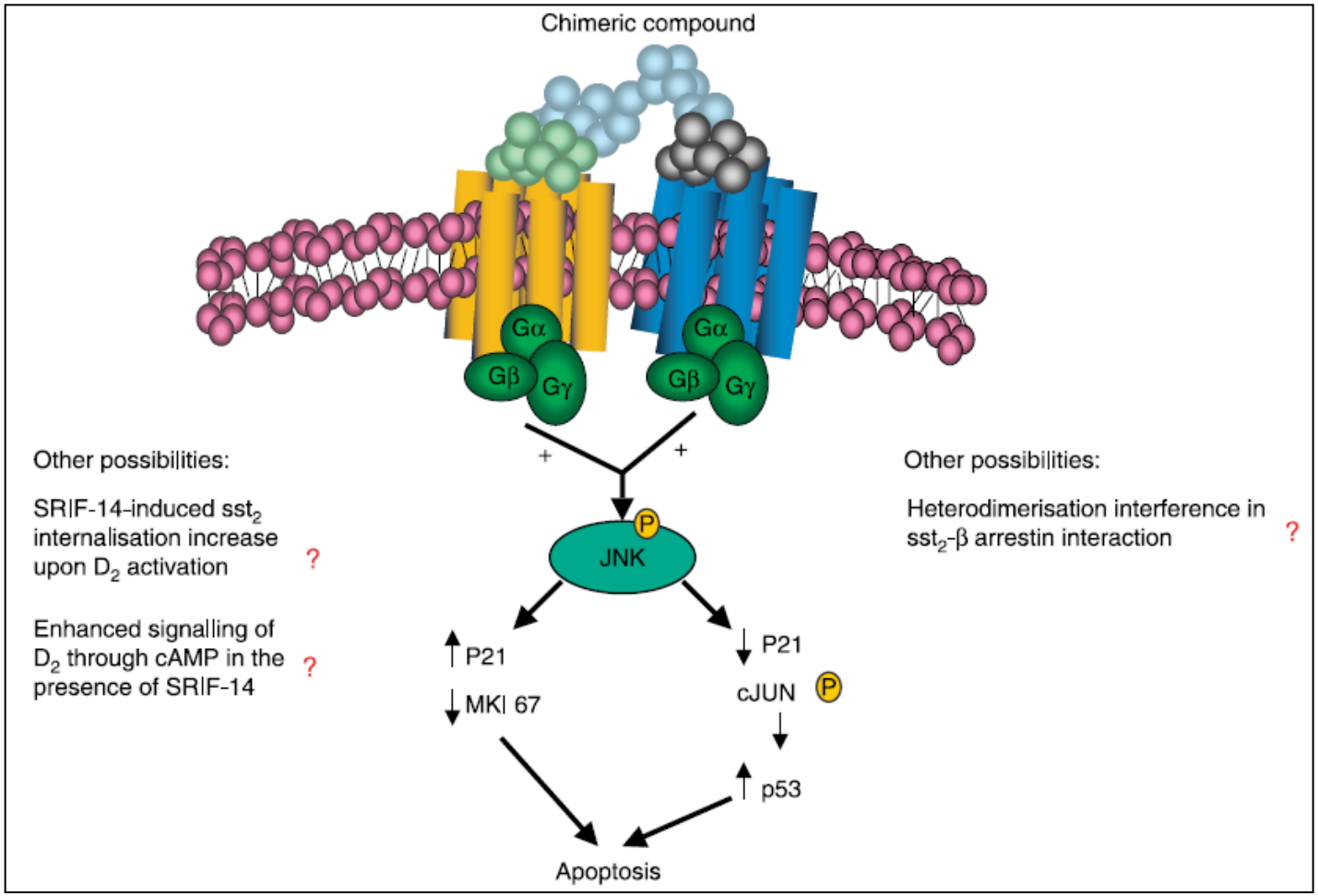


REVIEW

Journal of Molecular Endocrinology (2009) **42**, 361–370

The clinical–molecular interface of somatostatin, dopamine and their receptors in pituitary pathophysiology

Diego Ferone, Federico Gatto, Marica Arvigo, Eugenia Resmini, Mara Boschetti, Claudia Teti, Daniela Esposito and **Francesco Minuto**

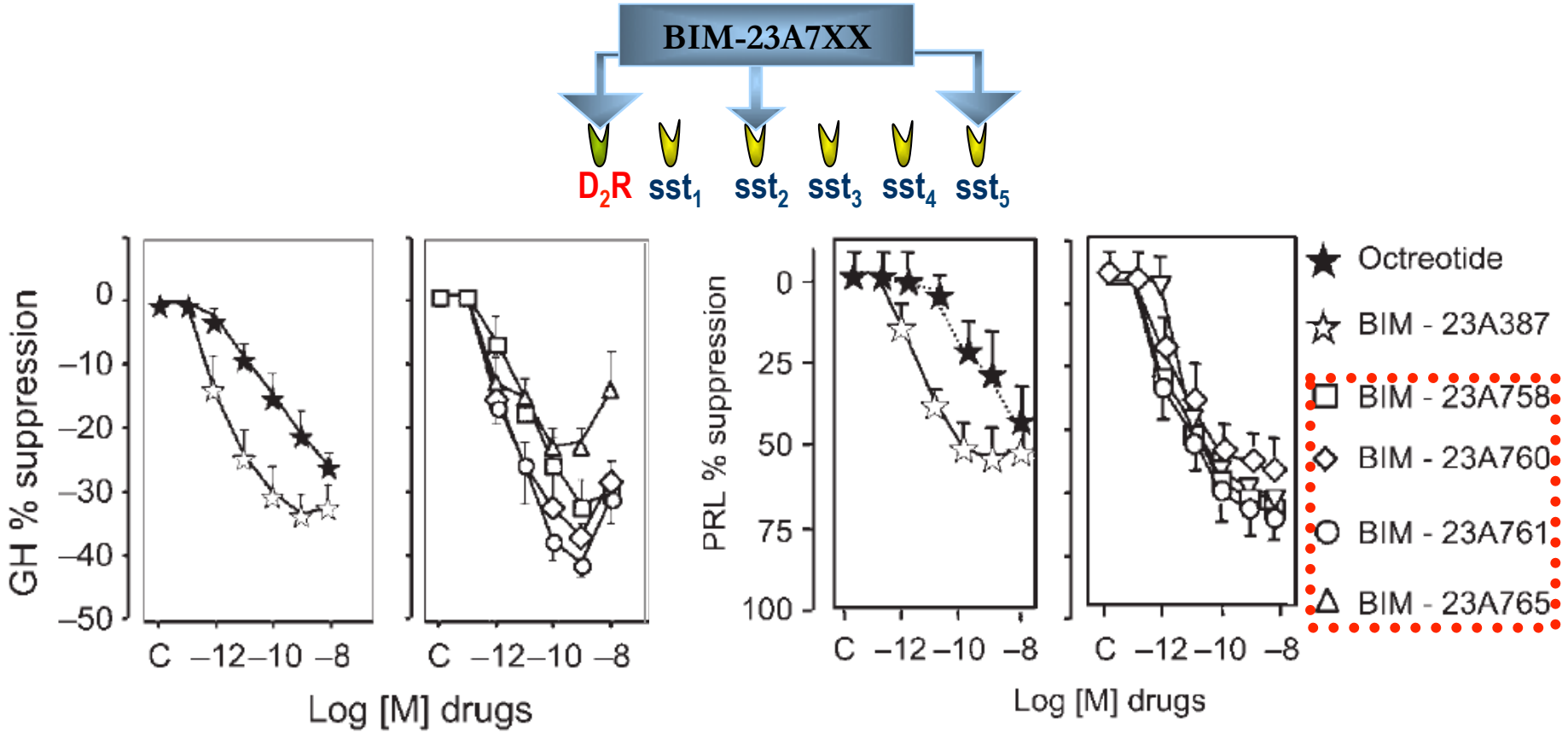


European Journal of Endocrinology (2005) **153** 135–141 ISSN 0804-4643

EXPERIMENTAL STUDY

Efficacy of chimeric molecules directed towards multiple somatostatin and dopamine receptors on inhibition of GH and prolactin secretion from GH-secreting pituitary adenomas classified as partially responsive to somatostatin analog therapy

P Jaquet, G Gunz, A Saveanu, H Dufour[1], J Taylor[2], J Dong[2], S Kim[2], J-P Moreau[2], A Enjalbert and M D Culler[2]



Conclusioni-1

La chirurgia è ancora l'approccio iniziale nell'acromegalia, anche se sempre meno frequente, grazie al rapporto costo/beneficio, ma deve essere praticata in centri con alta esperienza

I. Prima di ogni intervento dovrebbe esser praticata un'attenta valutazione integrata del paziente

II. Le complicanze non sono rarissime: l'ipopituitarismo è la più frequente, mentre l'iponatriemia la più severa. La disfunzione surrenalica sub-clinica deve essere sempre presa in considerazione per la sua pericolosità

III. Evitare un approccio troppo aggressivo: la terapia medica è molto efficace nella magior parte dei casi, inoltre il *tumor debu*lking può migliorare la risposta al trattamento farmacologico

IV. La chirurgia, come seconda linea di terapia, può essere curativa in molti casi di macroadenoma

Conclusioni-2

La terapia medica con analoghi della somatostatina è di importante ausilio

I. Come prima linea di trattamento nella maggior parte dei casi di macroadenoma, ed induce *shrinkage* (del 50% in 45% dei casi entro i 12 mesi) e controllo del GH ed IGF-I (30-50% dei casi entro i 12 mesi)

II. Come trattamento pre-operatorio migliora l'*outcome*, le complicanze e comorbidità sistemiche

III. Come trattamento adiuvante (post-chirurgico) è effecace in 60-70% dei casi (entro i 12 mesi)

IV. I trattamenti combinati SRL+pegvisomant o SRL+DA possono risultare di supporto in casi resistenti alla monoterapia

V. Nuovi schemi di trattamento (alte dosi) e nuovi farmaci sono in arrivo (pasireotide and dopastatine)

Systemic Complications of Acromegaly: Epidemiology, Pathogenesis, and Management

Endocrine Reviews 25(1):102–152

doi: 10.1210/er.2002-0022

ANNAMARIA COLAO, DIEGO FERONE, PAOLO MARZULLO, AND GAETANO LOMBARDI

TABLE 1. Clinical features of acromegaly

Direct effects of the tumor	
Headache visual impairment	Visual loss
	Temporal hemianopia of one or both eyes
	Quadrandopia
Hyperprolactinemia	Mixed tumoral secretion or pituitary stalk section
Hypopituitarism cavernous sinus syndrome	Hypothyroidism, hypogonadism, hypocorticism
Systemic effects of GH/IGF-I excess	
Soft tissue and skin changes	Acral enlargement
	Increased skin thickness and soft tissue hyperplasia
	Increased sweating
	Skin tags and acanthosis nigricans
Cardiovascular features	Biventricular hypertrophy
	Increased interventricular septum thickness (eccentric hypertrophy)
	Diastolic dysfunction at rest and/or systolic dysfunction on effort
	Diastolic heart failure
	Arrhythmias
	Hypertension
	Endothelial dysfunction and increased carotid IMT
Metabolic features	Impaired fasting glucose
	Impaired glucose tolerance
	Diabetes mellitus
	Insulin resistance
	Reduced total cholesterol and increased triglycerides
	Increased nitrogen retention
Respiratory features	Upper airway obstruction
	Macroglossia
	Sleep apnea
	Ventilatory dysfunction
Bone and joint features	Increased articular cartilage thickness
	Arthropathy/osteoarthritis
	Carpal tunnel syndrome
	Osteopenia
Other endocrine consequences	Multinodular thyroid goiter
	Thyrotoxicosis
	Hypercalciuria
	Hyperparathyroidism

Acromegalia: mortalità"

Determinanti per la sopravvivenza	P
Ultimo GH	< 0.0001
Ipertensione	< 0.02
Cardiopatie	< 0.03
Diabete	< 0.03
Durata sintomi	< 0.04

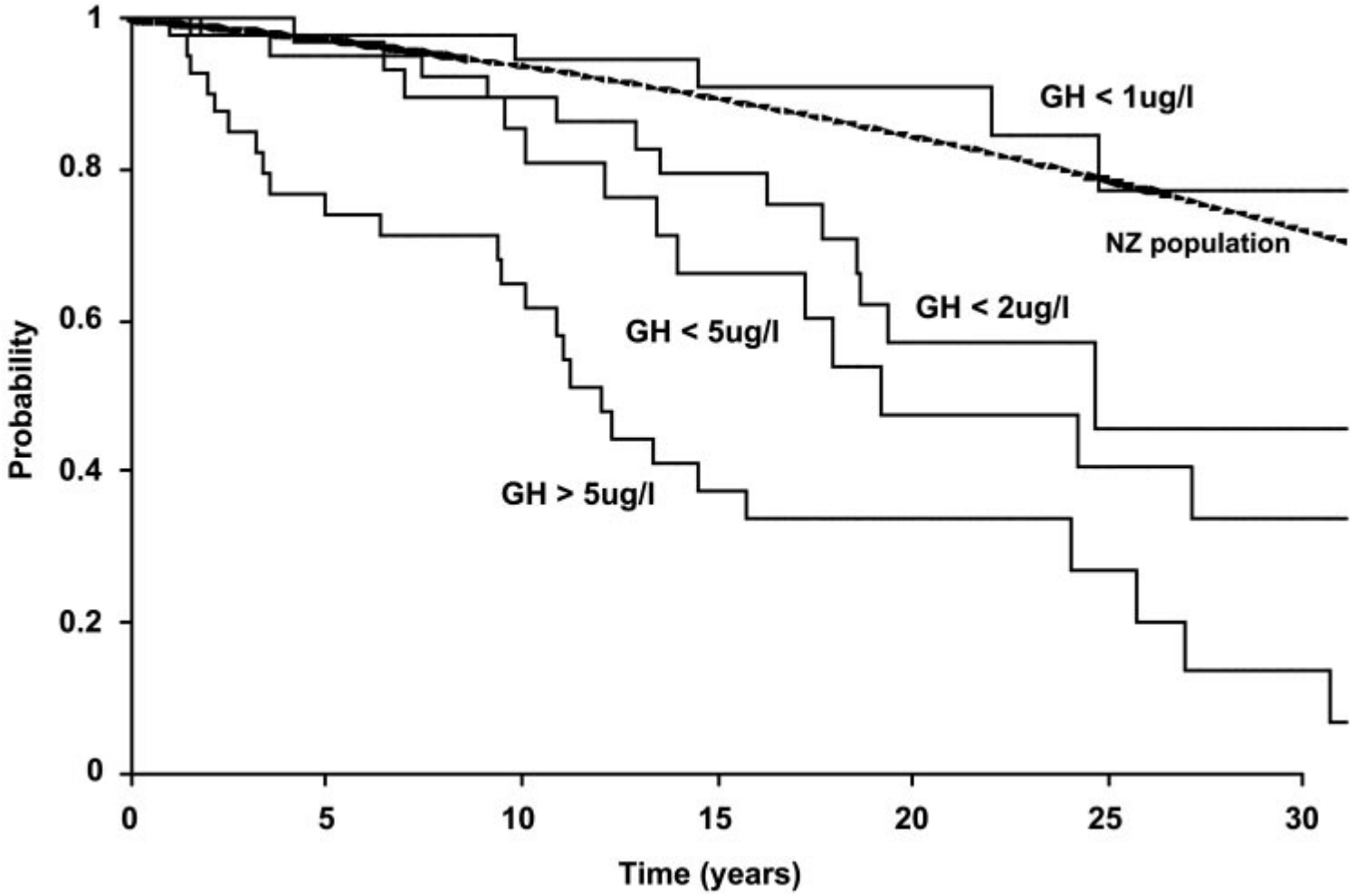
Cause di morte	
Cardiovascolari	60%
Respiratorie	25%
Tumori	15%

Da: Wright 1969; Alexander 1980; Nabarro 1987; Bengtsson 1988; Bates 1993; Etxabe 1993; Rajasoorya 1994; Swearingen 1998; Abosch 1998; Holdaway 2003. GES Barcelona 2003

Factors Influencing Mortality in Acromegaly

IAN M. HOLDAWAY, RAJA C. RAJASOORYA, AND GREG D. GAMBLE

Department of Endocrinology, Auckland Hospital (I.M.H.), and Department of Medicine, Auckland University School of Medicine (G.D.G.), Auckland 1, New Zealand; and Department of Medicine, Alexandra Hospital (R.C.R.), Singapore 159964

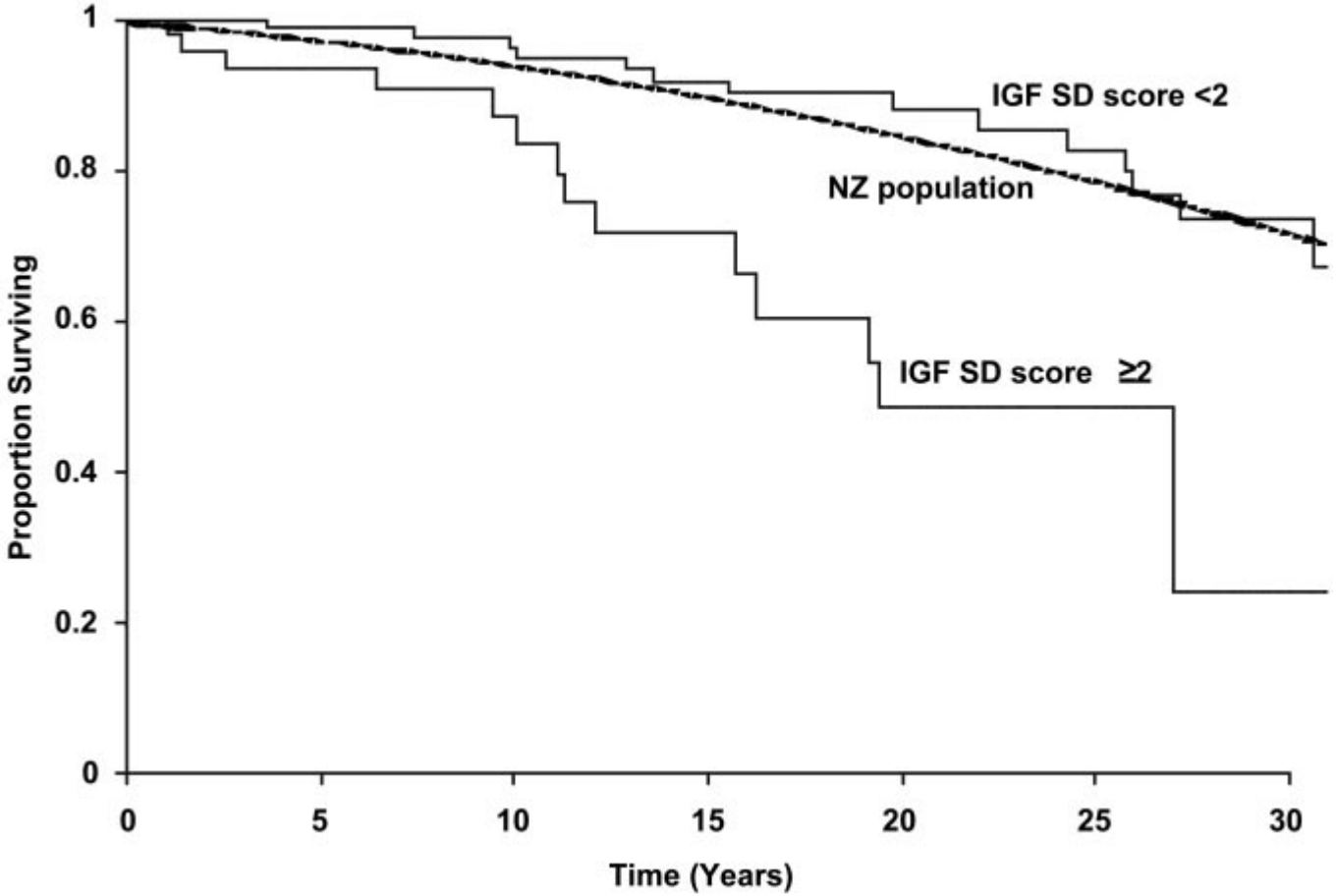


J Clin Endocrinol Metab 89: 667–674, 2004)

Factors Influencing Mortality in Acromegaly

IAN M. HOLDAWAY, RAJA C. RAJASOORYA, AND GREG D. GAMBLE

Department of Endocrinology, Auckland Hospital (I.M.H.), and Department of Medicine, Auckland University School of Medicine (G.D.G.), Auckland 1, New Zealand; and Department of Medicine, Alexandra Hospital (R.C.R.), Singapore 159964



J Clin Endocrinol Metab 89: 667–674, 2004)

Criteri di "Cura"

GH ≤ 2.5 μg/l e/o GH dopo OGTT≤ 1 μg/l

e

IGF-I normale per età

Giustina A et al, *JCE&M* 2000

"..The cutoff value for GH used within each individual center depends upon the reliability of the assay used and the ability of the laboratory to provide normative data with very high sensitivity assays.."

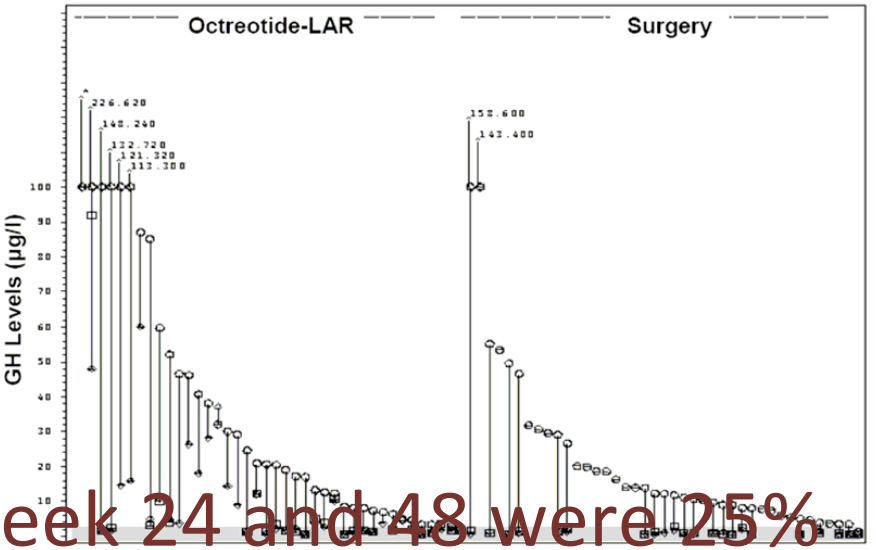
Melmed et al. Guidelines for Acromegaly Management: An Update JCE&M 2009

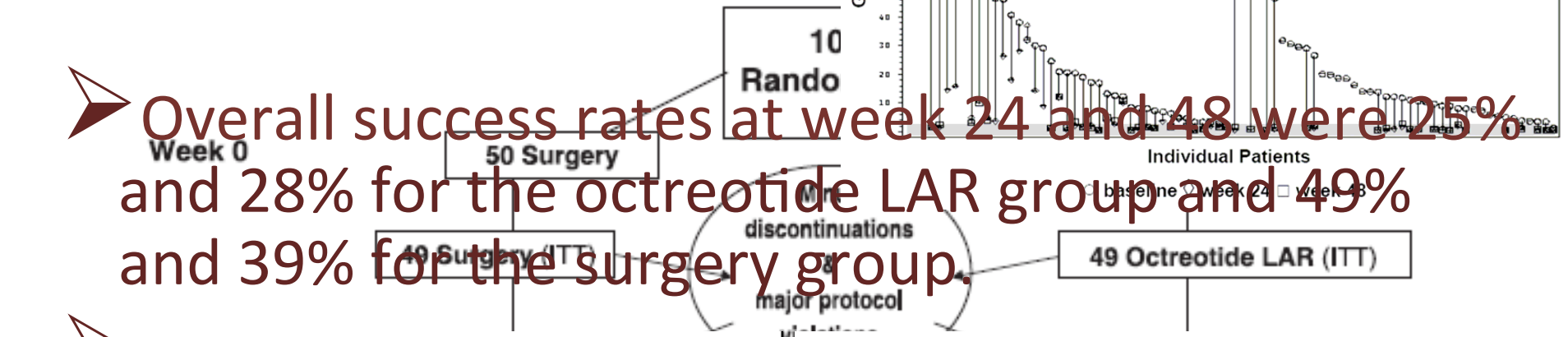
Clinical Endocrinology (2009) 70, 757–768 doi: 10.1111/j.1365-226

ORIGINAL ARTICLE

Octreotide LAR *vs.* surgery in newly diagnosed patients with acromegaly: a randomized, open-label, multicentre study

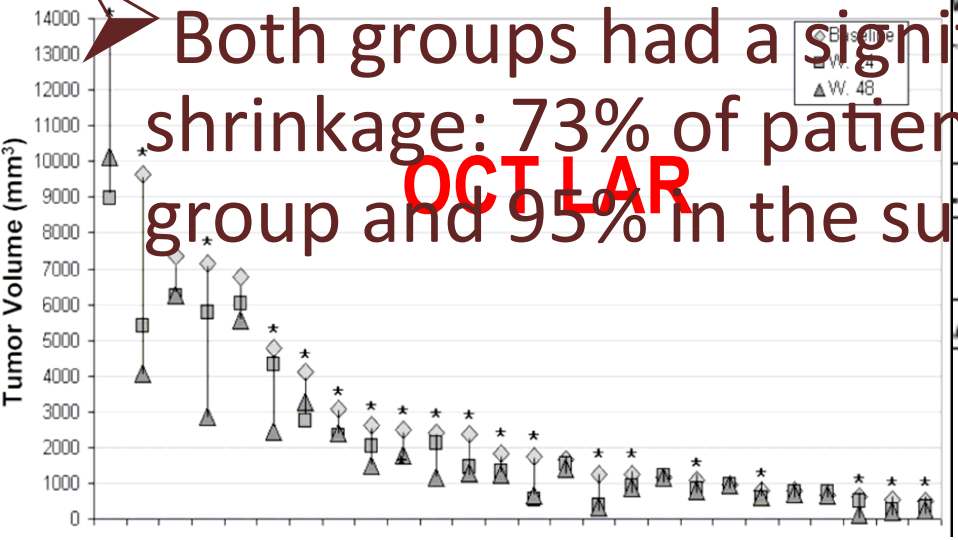
Annamaria Colao*, Paolo Cappabiancat, Philippe Caront, Ernesto De Menis§, Andrew J. Farrall¶, Monica R. Gadelha**, Abdel Hmissitt, Aled Rees‡‡, Martin Reincke§§, Mitra Safaritt, Guy T'Sjoen¶¶, Hakim Bouterfatt and Ross C. Cuneo***



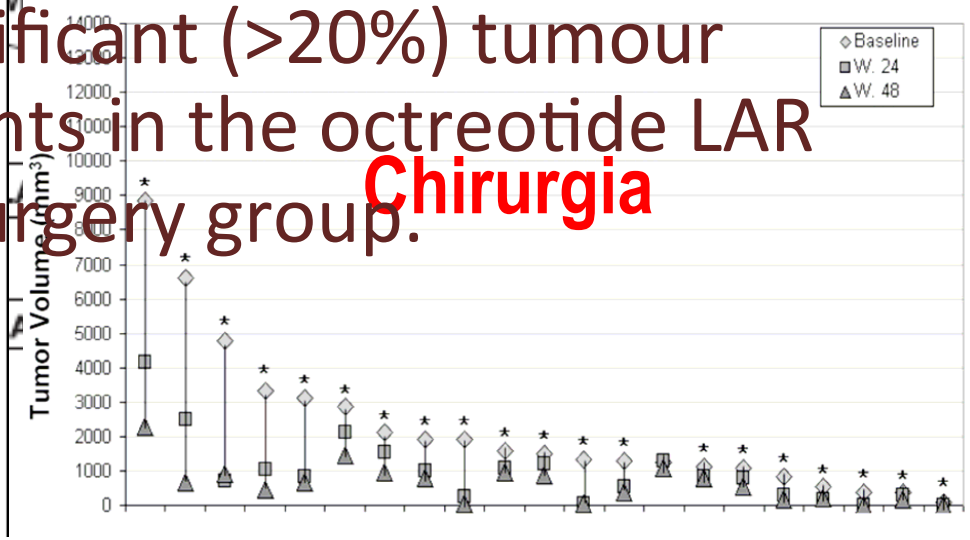


- Overall success rates at week 24 and 48 were 25% and 28% for the octreotide LAR group and 49% and 39% for the surgery group.
- Both groups had a significant (>20%) tumour shrinkage: 73% of patients in the octreotide LAR group and 95% in the surgery group.

OCT LAR



Chirurgia



Clinical Endocrinology (2009) 71, 237–245 doi: 10.1111/j.1365-22

ORIGINAL ARTICLE

Significant tumour shrinkage after 12 months of lanreotide Autogel-120 mg treatment given first-line in acromegaly

Annamaria Colao*, Renata S. Auriemma*, Alberto Reborat, Mariano Galdiero*, Eugenia Resminit, Francesco Minutot, Gaetano Lombardi*, Rosario Pivonello* and Diego Feronet

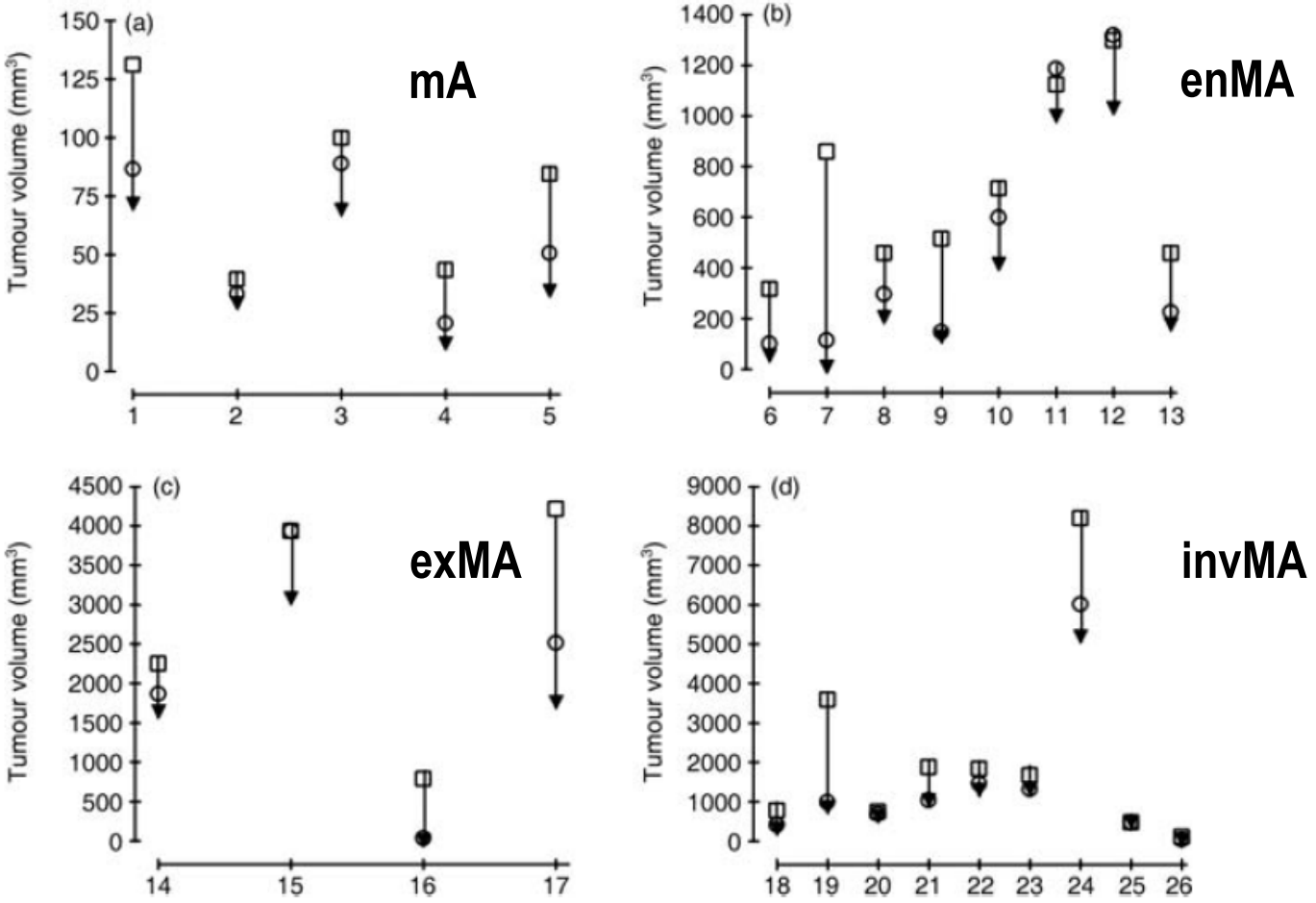


Fig. 3 Individual tumour volumes before and after 6 and 12 months of lanreotide-Autogel treatment in five patients with microadenoma (a), eight patients with enclosed macroadenomas (b), four patients with extrasellar macroadenomas (c), and nine with invasive adenomas (d). □, baseline; ○, 6 months; ▼, 12 months.

European Journal of Endocrinology (2009) **161** 331–338 ISSN 0804-4643

CLINICAL STUDY

High-dose intramuscular octreotide in patients with acromegaly inadequately controlled on conventional somatostatin analogue therapy: a randomised controlled trial

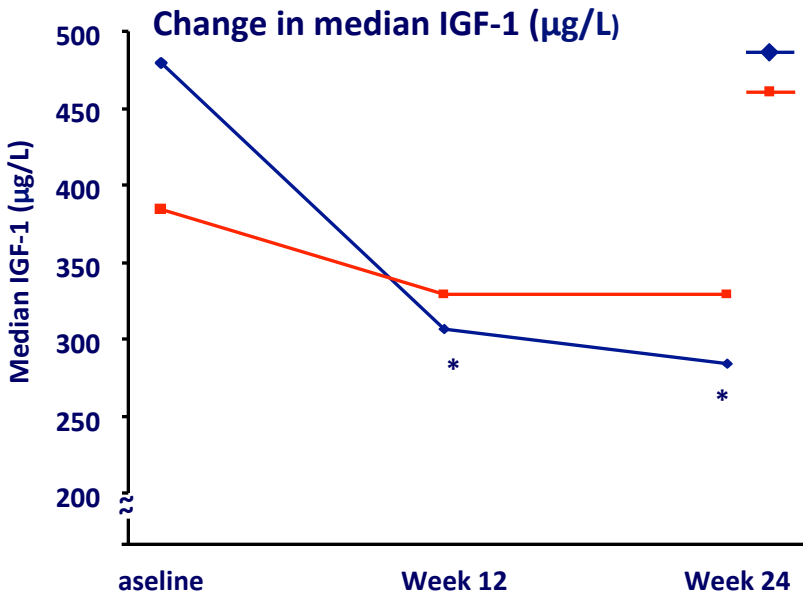
Andrea Giustina[1], Stefania Bonadonna[1], Giovanna Bugari[2], Annamaria Colao[3], Renato Cozzi[4], Salvatore Cannavo[5], Laura de Marinis[6], Ettore degli Uberti[7], Fausto Bogazzi[8], Gherardo Mazziotti[1], Francesco Minuto[9], Marcella Montini[10] and Ezio Ghigo[11]

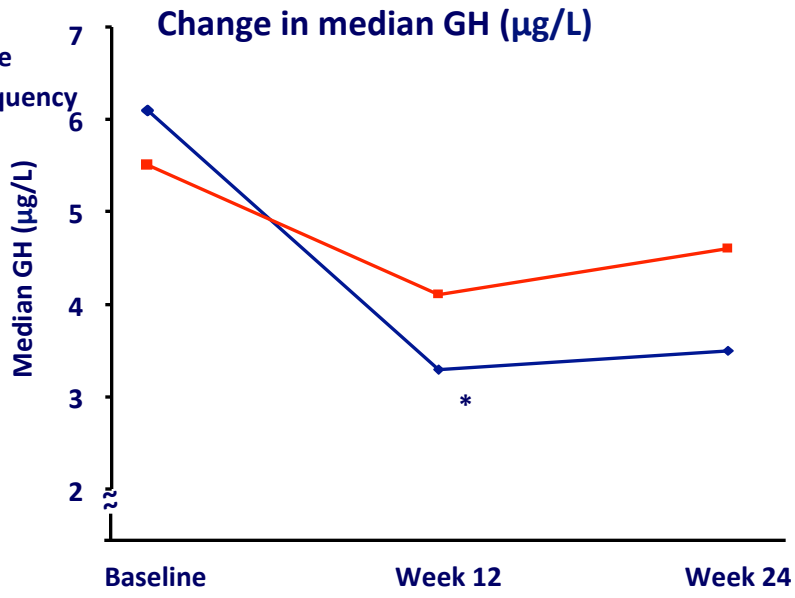
High dose group: octreotide LAR 60 mg q28d - High frequency group: octreotide LAR 30 mg q21d

Significantly more patients in the high-dose group achieved a reduction in IGF-1 at week 24 ($P<0.05$)

Median IGF-1 was significantly reduced in the high-dose group at week 24 ($P<0.05$)

Median GH was significantly reduced in the high-dose group at week 12 ($P<0.05$)



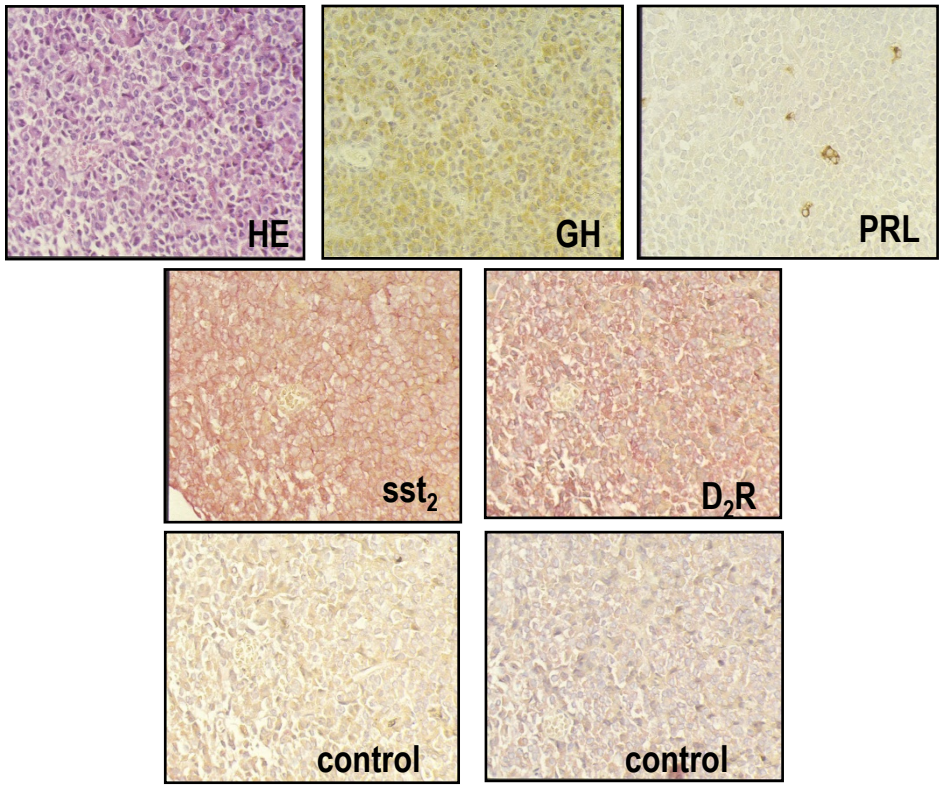


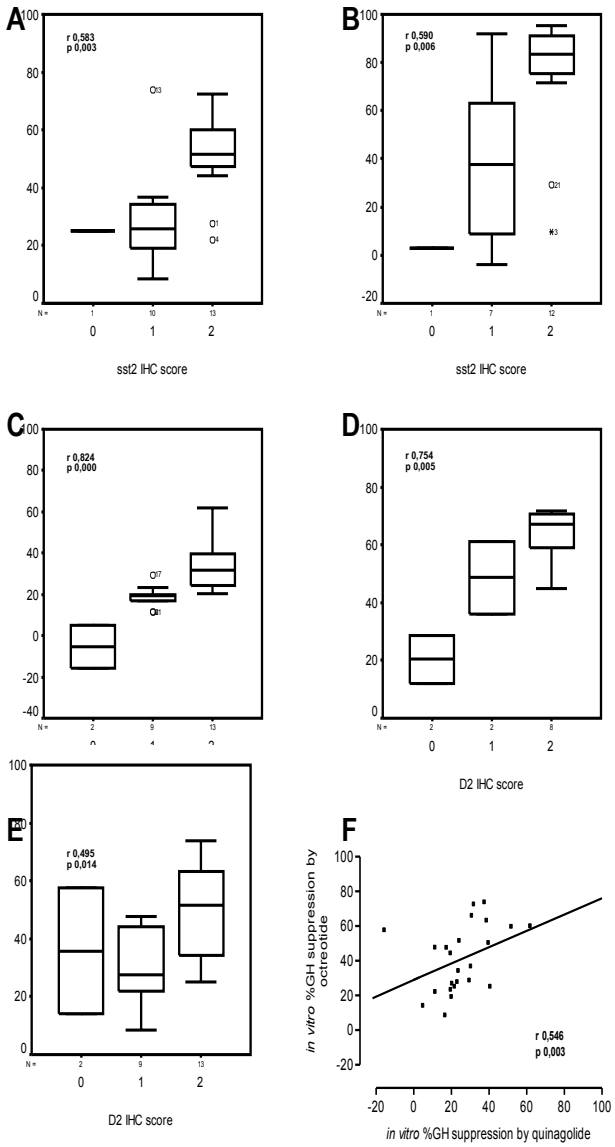
* $P<0.05$ versus baseline

Correlation of *in Vitro* and *in Vivo* Somatotropic Adenoma Responsiveness to Somatostatin Analogs and Dopamine Agonists with Immunohistochemical Evaluation of Somatostatin and Dopamine Receptor and Electron Microscopy

Diego Ferone, Wouter W. de Herder, Rosario Pivonello, Johan M. Kros, Peter M. van Koetsveld, Ton de Jong, Francesco Minuto, Annamaria Colao, Steven W. J. Lamberts, and Leo J. Hofland

J Clin Endocrinol Metab 93: 1412–1417, 2008





Clinical Endocrinology (2005) **63**, 477–481

LETTERS TO THE EDITOR

Re-evaluation of the efficacy of the association of cabergoline to somatostatin analogues in acromegalic patients

Cozzi R et al.

- 19 pazienti
- 12 mesi terapia OCT LAR o LAN
- No normalizzazione di IGF-I
- Aggiunta CAB dose da 1-3.5 mg /week

- GH < 2.5 µg/L in 4 (21%)
- Normalizzazione IGF-I 8 (42%)
- Risposta indipendente dai livelli di PRL

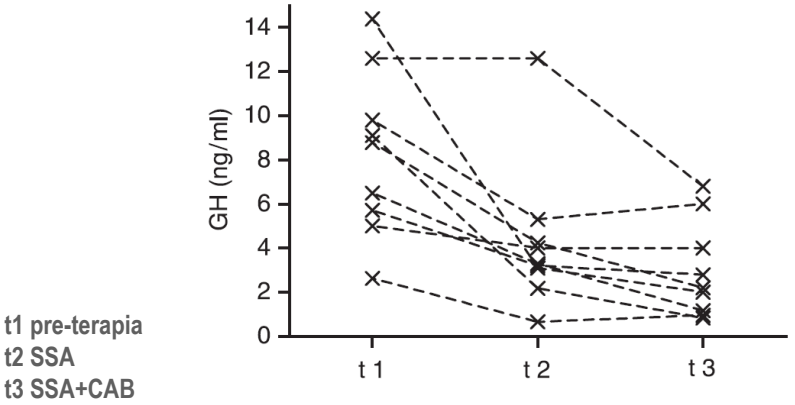


Fig. 1 Individual values of IGH (ng/ml) before medical treatment (t 1), with SA alone (t 2) and with the association of SA and DA (t 3).

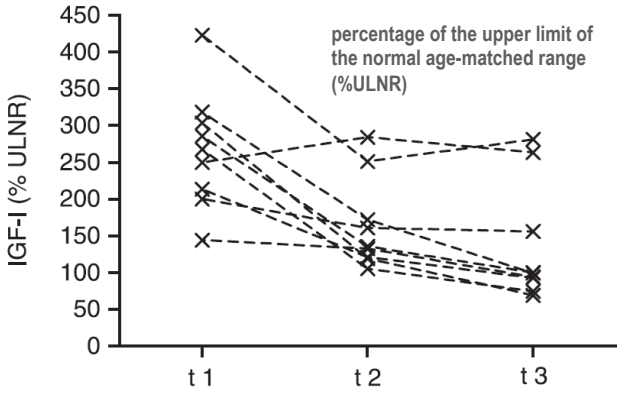


Fig. 2 Individual values of IGF-I (%ULNR) before medical treatment (t 1), with SA alone (t 2) and with the association of SA and DA (t 3).

European Journal of Endocrinology (2006) 154 467–477 ISSN 0804-4643

CLINICAL STUDY

Efficacy of 12-month treatment with the GH receptor antagonist pegvisomant in patients with acromegaly resistant to long-term, high-dose somatostatin analog treatment: effect on IGF-I levels, tumor mass, hypertension and glucose tolerance

Annamaria Colao, Rosario Pivonello, Renata S Auriemma, Maria Cristina De Martino, Martin Bidlingmaier[1], Francesco Briganti[2], Fabio Tortora[2], Pia Burman[3], Ione A Kourides[3], Christian J Strasburger[4] and Gaetano Lombardi

- 16 Pz. (9 ♀; età 28–61 anni)
- Pegvisomant alla dose di 10–40 mg s.c. al giorno per 12 mesi
- Titolazione ogni mese sulla base dell'IGF-I

	Before	After	P
Weight (kg)	83.5±15.0	85.7±13.6	0.055
Serum GH levels (μg/l)	22.9±24.0	34.5±40.4	0.29
Serum IGF-I levels (μg/l)	775.1±141.4	237.8±106.7	<0.0001
Tumor volume (mm^3)	1198±1234	1196±1351	0.37
Ring size (mm)	12.7±2.2	12.2±2.3	0.78
Systolic blood pressure (mmHg)	133.9±16.2	129.6±10.1	0.13
Diastolic blood pressure (mmHg)	87.1±13.6	86.2±7.1	0.70
Heart rate (bpm)	72.8±7.6	76.8±7.9	0.14
Total cholesterol levels (mmol/l)	5.3±1.0	5.5±0.8	0.43
HDL-cholesterol levels (mmol/l)	1.2±0.3	1.5±0.2	0.0017
Total/HDL-cholesterol ratio	4.5±1.0	3.7±0.6	0.0012
Triglyceride levels (mmol/l)	1.5±0.9	1.5±0.7	0.86
Glucose levels (mmol/l)	5.6±1.2	4.4±1.4	0.0012
HbA1c levels (%)	5.3±0.7	5.3±0.5	0.24
Insulin levels (mU/l)	12.4±6.7	8.1±3.0	0.0023
HOMA index	3.4±2.1	1.9±1.0	0.0017
Fibrinogen levels (mg/dl)	342.1±75.2	361.6±63.6	0.58
AST levels (U/l)	19.4±8.6	22.9±15.1	0.64
ALT levels (U/l)	18.6±14.0	40.1±61.2	0.017
Albumin levels (g/dl)	3.8±0.4	4.4±0.3	0.0002

OBIETTIVI DELLA TERAPIA

- Ridurre l’effetto massa
- Controllare l’eventuale ipersecrezione ormonale
- Compensare l’ipofunzione

L'IPERPROLATTINEMIA. Fisiopatologia, clinica e terapia
Camanni e Massara, 1987

Fig. 33 – *Normalizzazione della prolattinemia ottenuta in 2 pazienti con macroadenoma solo dopo alcuni mesi di trattamento con dosi elevate di bromocriptina. Nel caso P.P. è stata documentata anche la normalizzazione del reperto tomodensitometrico. L'area tratteggiata indica il "range" dei valori normali (risultati personali non pubblicati).*

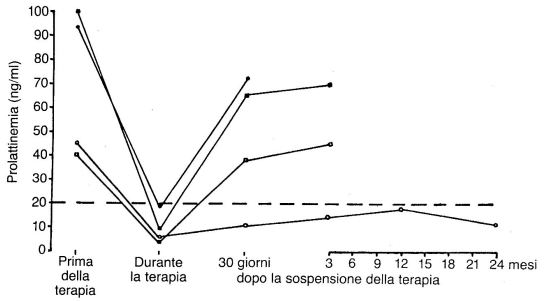


Fig. 32 – *Livelli plasmatici di PRL in 4 pazienti con microprolattinoma prima, durante terapia con bromocriptina e dopo la sospensione del farmaco (risultati personali non pubblicati).*

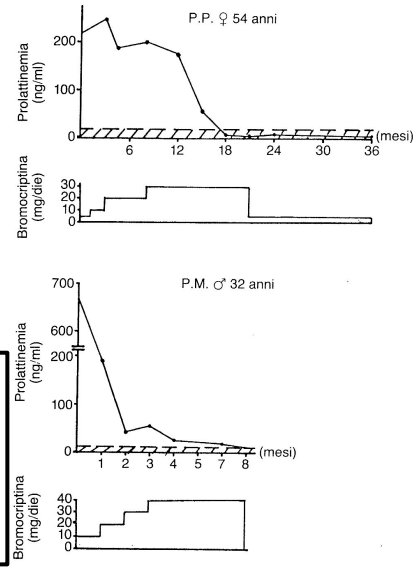


Fig. 33 – *Normalizzazione della prolattinemia ottenuta in 2 pazienti con macroadenoma solo dopo alcuni mesi di trattamento con dosi elevate di bromocriptina. Nel caso P.P. è stata documentata anche la normalizzazione del reperto tomodensitometrico. L'area tratteggiata indica il "range" dei valori normali (risultati personali non pubblicati).*