Bari,
7-10 novembre 2013

GH E FARMACOECONOMIA

Venerdi 8 novembre 2013

COME MONITORARE LA TERAPIA

ROBERTO CASTELLO
MEDICINA GENERALE/ENDOCRINOLOGIA
AZ. OSPEDALIERA UNIVERSITARIA
VERONA

Maggio 4° scudetto Capello

1996

5 Luglio Dolly e Ian Wilmut

20 Novembre Wojtyla e Castro

Aprile scontro Prodi-Berlusconi

Linee Guida

Bari,
7-10 novembre 2013

CONSENSUS STATEMENT

Consensus guidelines for the diagnosis and treatment of adults with GH deficiency II: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia

Eur J Endocrinol 2007

Ken K Y Ho on behalf of the 2007 GH Deficiency Consensus Workshop Participants

AACE Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR GROWTH HORMONE USE IN GROWTH HORMONE-DEFICIENT ADULTS AND TRANSITION PATIENTS – 2009 UPDATE: EXECUTIVE SUMMARY OF RECOMMENDATIONS

Complete guidelines are available at www.aace.com

David M. Cook, MD, FACE;
Kevin C.J. Yuen, MD;
Stephen F. Kemp, MD, PhD, FACE;
Mary Lee Vance, MD

Endocrine Pract 2009

European Journal of Endocrinology (2013) 169 R1–R14 ISSN 0804-4643

REVIEW
THERAPY OF ENDOCRINE DISEASE

EUR J ENDO 2013

Long-term effects of recombinant human GH replacement in adults with GH deficiency: a systematic review

Natasha M Appelman-Dijkstra*, Kim M J A Claessen*, Ferdinand Roelfsema, Alberto M Pereira and Nienke R Biermasz

Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline

JCEM 2011

Mark E. Molitch, David R. Clemmons, Saul Malozowski, George R. Merriam, and Mary Lee Vance

Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline

Bari,
vembre 2013

1.1 We recommend that patients with childhood-onset GHD who are candidates for GH therapy after adult height achievement be retested for GHD unless they have known mutations, embryopathic lesions causing multiple hormone deficits, or irreversible structural lesions/damage (1/⊕⊕⊕⊕).

PER QUALI PAZIENTI

1.2 We recommend that adult patients with st… hypothalamic/pituitary disease, surgery o… these areas, head trauma, or evid… hormone deficiencies be co… for ac-quired GHD (1/⊕⊕…

INTENTION TO TREAT

…opathic GHD in adults is very rare, and stringent …teria are necessary to make this diagnosis. Because in the absence of suggestive clinical circumstances there is a signif-icant false-positive error rate in the response to a single GH stimulation test, we suggest the use of two tests before mak-ing this diagnosis. The presence of a low IGF-I also increases the likelihood that this diagnosis is correct (2/⊕◯◯◯).

Molitch et al, JCE&M 2011, 96: 1587-1609

TARGET :SICUREZZA

CONTROINDICAZIONI

- Neoplasie in atto
- Retinopatia diabetica proliferante
- Ipertensione intracranica benigna

ATTENZIONE

- Età fertile/ Gravidanza
- Diabete con complicanze
- Residui di tumori ipofisari

Caso clinico

Bari,
7-10 novembre 2013

Clinical presentation of **Sheehan syndrome**: "…hypopituitarism can be mild, moderate, or severe, and part or total. Decreased endocrine function can be restricted to one hormone or can affect all hormones secreted by adenohypophysis cells. Clinical presentation varies and is dependent on the age of the patient, rapidity of onset, nature and causes of the pathological process, and the proportion of affected adenohypophysis cells. Mild hypopituitarism can remain undetected for years…"

"Sheehan syndrome", Kalman Kovacs, Lancet 2003; 361:520-22

SINDROME DI SHEEHAN

Bari,
7-10 novembre 2013

- Inizia GH 0.5 mg / die.
- IGF-1 = 198 ng/ml ((58°c) dopo 3 mesi
- Comparsa di alcuni sintomi: artralgie, edema alle mani, ritenzione

Cosa fare a questo punto?

Bari,
7-10 novembre 2013

- Ridurre GH a 0.3 mg/ die
- Ridurre GH a 0.2 mg/die
- Sospendere la terapia con GH

CASO CLINICO

- Sospensione del GH.
- IGF-1 = 56 ng/ml (<3°c).
- Scomparsa dei sintomi

Cosa fare a questo punto ?

Bari,
7-10 novembre 2013

- Riprendere GH con 0.2 mg/day
- Riprendere con GH 0.3 mg/day
- No GH

CASO CLINICO

Bari,
7-10 novembre 2013

- GH era ripreso a 0.3 mg/day.
- Dopo 2 mesi: IGF-1 = 182 ng/ml (52°c).
- Lamenta solo modico edema

MESSAGGI

Bari,
7-10 novembre 2013

- DOSE DI PARTENZA
- IMPORTANZA VALORI DI IGF-1
- TIMING PER IL FOLLOW-UP
- SINTOMI
- DICOTOMIA TRA VALORI IGF-1 E SINTOMI
- RISULTATI CLINICI ATTESI

American Association of Clinical Endocrinologists (AACE)

Starting dose:

- Age **<30 years, 0.4–0.5 mg/day** (may be higher for patients transitioning from paediatric treatment)
- Age **30–60 years, 0.2–0.3 mg/day**
- Age **>60 years, 0.1–0.2 mg/day**
- Use lower GH doses (0.1–0.2 mg/day) in all patients with diabetes or who are susceptible to glucose intolerance

At 1–2-month intervals:

- Increase dose in **increments of 0.1–0.2 mg/day based on clinical response, serum IGF1 levels, side effects and individual considerations such as glucose intolerance**. Longer time intervals and smaller dose increments may be necessary in older patients
- Aim for **serum IGF1 levels in the middle of the normal range appropriate for age and sex**, unless side effects are significant.
- Consider a trial of higher GH doses to determine whether this provides further benefit as long as the serum IGF1 levels remain within the normal range and the patient does not experience side effects

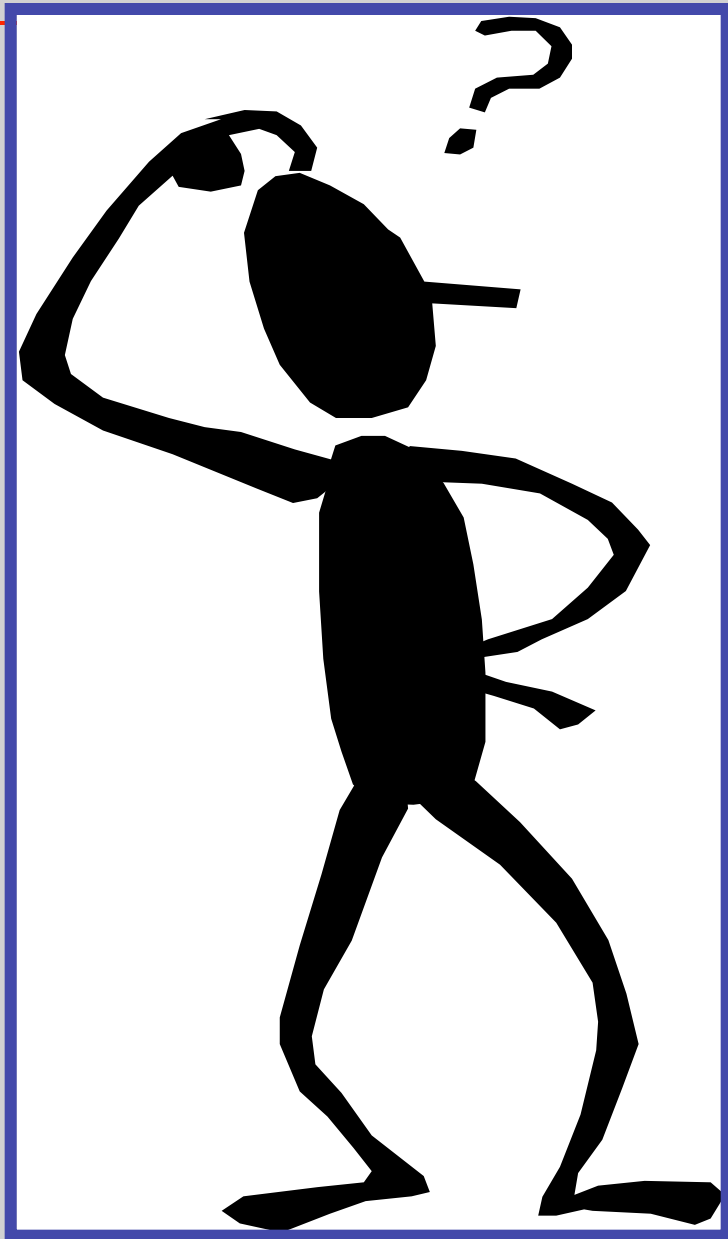
Monitor at 6-month intervals once maintenance doses are achieved.

- Monitoring should include clinical evaluation and assessment of side effects, serum IGF1 and fasting glucose levels. The **lipid profile should be assessed annually**, and **QoL measurements may be done every 6 or 12 months**. If the initial bone DXA scan is abnormal, repeat evaluations at 2–3-year intervals are recommended. If pituitary microadenomas or post-surgery residual pituitary tumour is still present, periodic MRIs should be undertaken. Patients on concurrent thyroid, glucocorticoid and gonadal hormone replacement may need dose adjustments after starting GH replacement therapy

Gasco V. GH therapy in adult GH deficiency: A review of treatment schedules and the evidence for low starting doses. EJE(2013) 168 R55–R66

Bari,
7-10 novembre 2013

Gli effetti del trattamento con rhGH: come monitorarli?



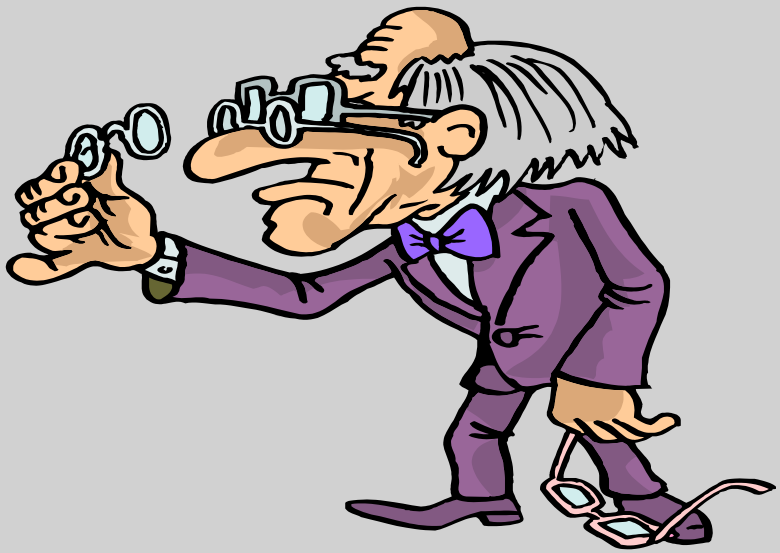
Monitoraggio della terapia con GH

Bari,
7-10 novembre 2013

TARGET

Dosaggio degli indici biochimici dell'azione del GH	Risposta clinica	Sicurezza	Interazione
Markers biochimici	Indicatori clinici Mortalità?	Comparsa di eventi avversi	Estrogeni, Tiroide Cortisolo

Il target terapeutico per il paziente adulto



Marker biochimico

Bari,
7-10 novembre 2013

IGF-1

- miglior marker biochimico dell'azione del GH
- utile per individuare il sovradosaggio

Marker biochimico

Bari,
7-10 novembre 2013

E' indispensabile escludere fattori che possano interferire sui livelli serici di IGF-1:

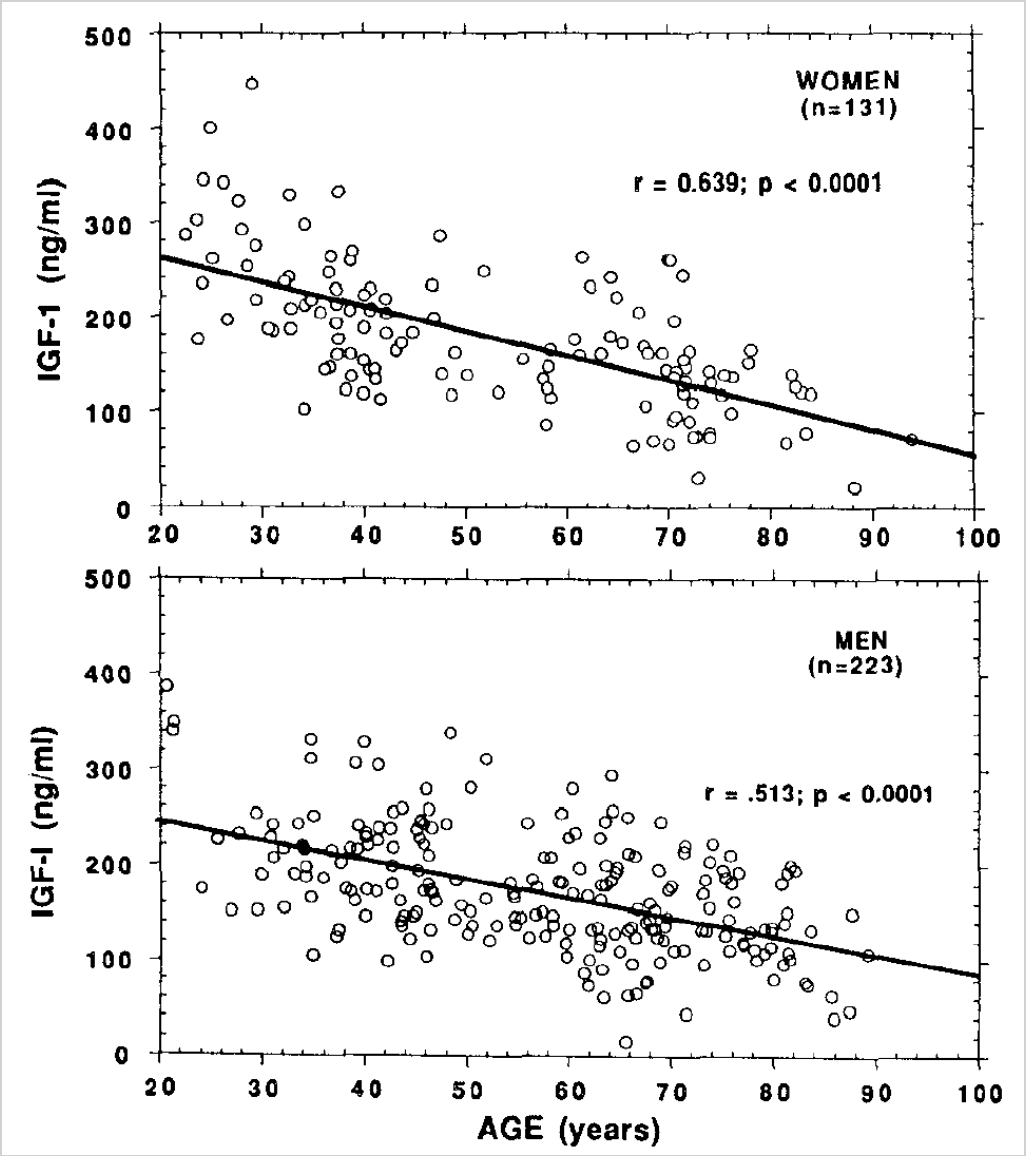
- ipotiroidismo
- stato nutrizionale
- malattie intercorrenti
- malattie epatiche o renali
- terapia sostitutiva con estrogeni per os

Marker biochimico

Bari,
7-10 novembre 2013

IGF-I levels in normal women and men in the Baltimore Longitudinal Study on Aging; the decrease with age in mean (± 1 SD) IGF-I is shown by decade

(Corpas, Endocrine Rev. 1993)



Target terapeutico per il paziente adulto?

Bari,
7-10 novembre 2013

A che livello dobbiamo mettere l'asticella?

Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline

5.2 Remarks

A commonly used target for IGF-I is the upper half of that range, although no published studies offer specific guidance in this regard. Clinical benefits may not become apparent for

IGF-I (ng/ml): valori mediani
5th, 25th, 75th and 95th percentile per età

Bari,
7-10 novembre 2013

Age-range	Median	Percentiles			
		2.5th	25th	75th	97.5th
25-39	206	95.6	154.0	254.0	366.7
40-59	147	60.8	118.0	188.3	297.7
≥ 60	103	34.5	68.3	149.0	219.8

IGF-I (ng/ml): valori mediani
5th e 95th percentile per età e sesso

Bari,
7-10 novembre 2013

	29 – 40 anni (mg/L)	41 – 50 anni (mg/L)	51 – 60 anni (mg/L)	61 -75 anni (mg/L)
Maschi				
5 percentile	125	89	94	98
95 percentile	302	241	231	225
Femmine				
5 percentile	124	97	99	91
95 percentile	306	273	254	220

Marker biochimico

Bari,
7-10 novembre 2013

- I pazienti con GHD insorto in età adulta hanno in circa il 50% dei casi, normali livelli basali di IGF-1

Thoren et al, J Clin Endocrinol Metab, 82: 223, 1997

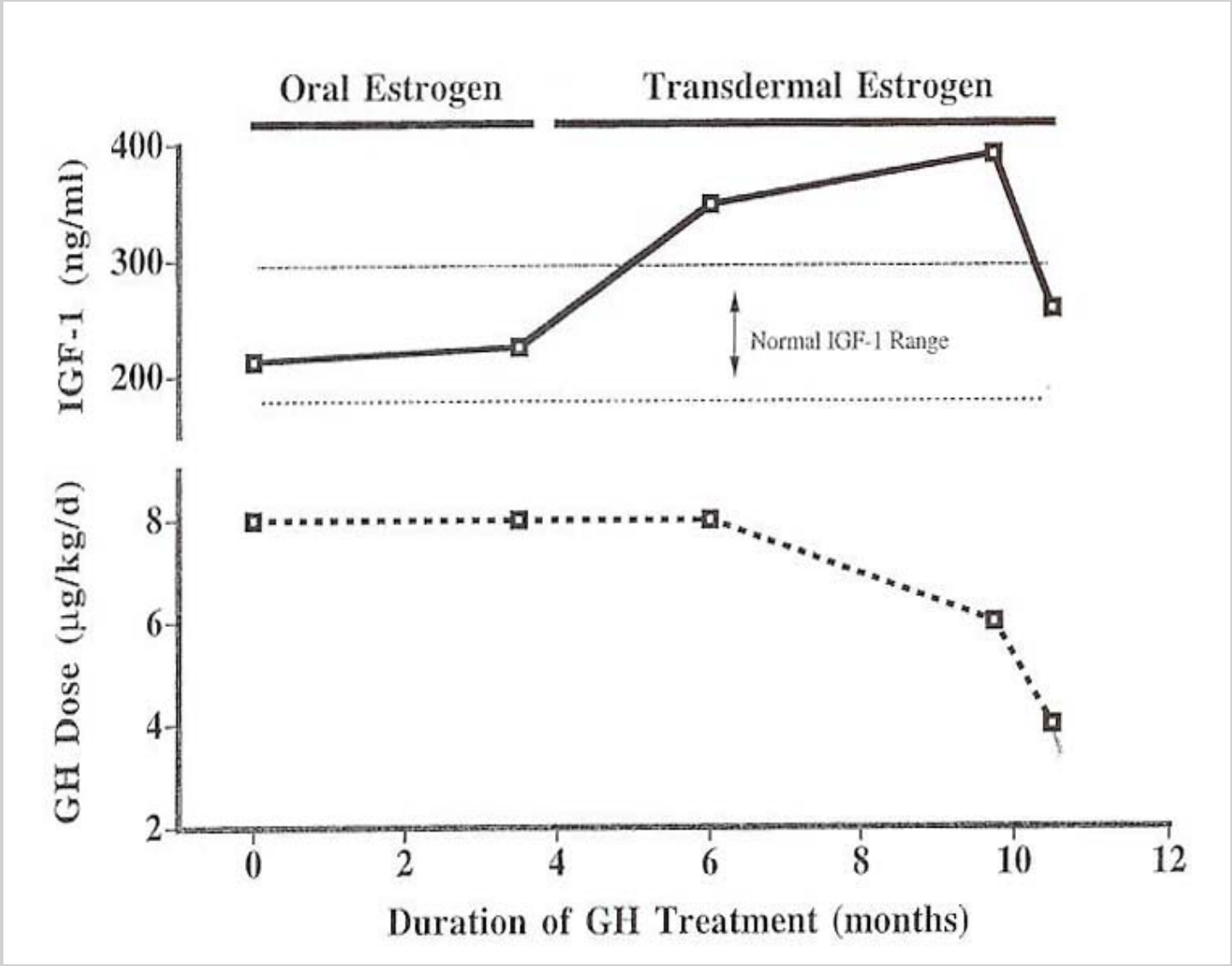
- 36% dei pazienti con livelli di IGF-1 tra 0 e + 2 DS ha sintomi persistenti da eccesso di GH

de Boer et al, Horm Res, 48: 21, 1997

Lo stretto monitoraggio clinico è necessario, particolarmente nei pazienti con normali livelli circolanti di IGF-1

Modificazioni dei livelli di IGF-1 e della dose di GH in donne GHD in terapia sostitutiva

Bari,
7-10 novembre 2013



Cook et al, JCEM 1999

IGF-1 controlli: quando?

Bari,
7-10 novembre 2013

1. **Ogni 4 settimane fino a quando è stato raggiunto il range, poi ogni 6-12 mesi***
2. **Annualmente**
3. **Dopo 3 mesi dall' inizio della terapia e poi ogni 6 mesi**

*Drake W.M. et al. *Endocrine Reviews* 2001 22(4):425-450

Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline

5.0 Treatment regimens

5.1 We recommend that GH dosing regimens be individualized rather than weight-based and start with low doses and be titrated according to clinical response, side effects, and IGF-I levels (1/⊕⊕⊕⊕).

5.2 We recommend that GH dosing take gender, estrogen status, and age into consideration (1/⊕⊕⊕⊕).

5.3 We suggest that during GH treatment, patients be monitored at 1- to 2-month intervals during dose titration and semiannually thereafter with a clinical assessment and an evaluation for adverse effects, IGF-I levels, and other parameters of GH response (2/⊕⊕◯◯).

Molitch et al, JCE&M 2011, 96: 1587-1609

ALTRI PARAMETRI

Bari,
7-10 novembre 2013

1. Evaluation of QoL (NHP etc.), IGF-1, glucose and lipids yearly, DXA every 2 ys.

2. **Clinical examination (BMI), lipids, glucose every 6 mo., DXA every 18-24 mo, Neuropsychological tests when required**

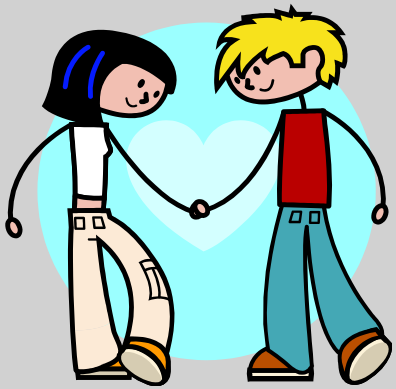
3. Clinical examination (BMI), lipids and glucose yearly

*Drake W.M. et al. *Endocrine Reviews* 2001 22(4):425-450

Bari,
7-10 novembre 2013

Sicurezza clinica a lungo termine del GH Stanno tutti bene ?

Le evidenze nell'adulto



- **rischi neoplastici "de novo"? persistente residuo della lesione iniziale la terapia con GH potrebbe indurre una ri-espansione della lesione tumorale?**

- **iperglicemia e diabete mellito ? Se il paziente è già affetto da diabete mellito: è corretto iniziare la terapia con rhGH? Quali rischi e attenzioni ?**

- **sindrome metabolica: la terapia con GH potrebbe apportare un miglioramento o un peggioramento nel quadro clinico sopra descritto?**

Terapia con rhGH e residuo adenomatoso

Bari,
7-10 novembre 2013

Hypothalamic/pituitary tumor recurrence

There is no evidence that hypothalamic or pituitary tumor recurrence is influenced by GH replacement therapy. Before GH replacement therapy is initiated, pituitary imaging should be performed. Good clinical practice predicates that patients with residual tumors should be monitored regularly; GH replacement therapy does not impose a need for intensifying follow-up.

Eur J Endocrinol 2007, 157(6): 695-700

R35. No data are available to suggest that GH therapy is associated with causing or accelerating recurrences of pituitary-region tumors; therefore, we recommend continued long-term surveillance of patients with pituitary-region tumors regardless of whether or not these patients are treated with GH therapy (**Grade D; BEL 4**).

Endocrine Pract 2009, 15 Suppl 2: 1-29

TABLE 3. Incidence of recurrent and secondary tumors and mortality rates

	GHRT	Control	*P* value
Tumor recurrence	6 (5.5%)	8 (7.3%)	0.7835
Childhood onset	0	4	ns
Adult onset	6	4	ns
Secondary tumor	5 (4.5%)	3 (2.7%)	0.7215
Childhood onset	5	2	ns
Adult onset	0	1	ns
Total (primary outcome)	11 (10%)	11 (10%)	1.00
Mortality	7 (6.4%)	15 (13.6%)	0.03

ns, Not significant.

Discussion

The present study further supports the safety of GHRT in a large group of patients primarily treated with brain irradiation for benign and malignant disease. Mortality was lower in the GH-treated group and neither the risk of secondary tumors nor the frequency of recurrent disease was increased.

TABLE 4. Characteristics of patients with secondary tumors

	Primary diagnosis	Secondary tumor	Sex	Age at primary diagnosis (yr)	Total radiation dose (Gy)	Follow-up (yr)	GH duration (yr)
GHRT	Medulloblastoma	Meningioma	F	8	4500	23	8
	Medulloblastoma	Meningioma	F	5	5000	22	2
	Medulloblastoma	Meningioma	F	5	5000	25	6
	Astrocytoma	Meningioma	M	13	4500	28	9
	Optic glioma	Malignant nerve sheath tumor, Neurofibromatosis 1	M	5	4750	18	5
Control	Acute lymphocytic leukemia	Meningioma	F	4	2500	33	n/a
	Pinealoma	Meningioma	F	13	4500	14	n/a
	Astrocytoma	Oligodendroglioma	F	27	4250	17	n/a

F, Female; M, male; n/a, not available.

Assessment of primary cancers in GH-treated adult hypopituitary patients: an analysis from the Hypopituitary Control and Complications Study

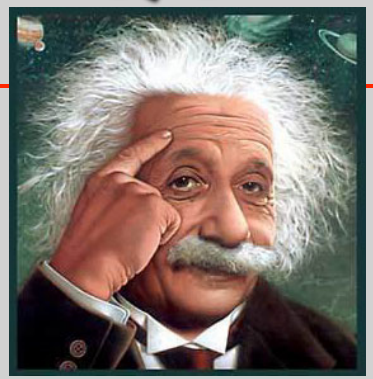
Table 3 Primary invasive cancer incidence by country for GH-treated adult hypopituitary patients in HypoCCS. SIRs were calculated for reference population cancer rates from SEER program (24) for the USA, and from GLOBOCAN (23) for all other countries.

Country	*n*	Observed cases	Expected cases	SIR (95% CI)
Denmark	151	7	5.48	1.28 (0.51–2.63)
Germany	435	5	9.85	0.51 (0.16–1.18)
Italy	833	5	11.52	0.43 (0.14–1.01)
Sweden	348	15	18.87	0.79 (0.44–1.31)
The Netherlands	439	16	16.12	0.99 (0.57–1.61)
UK	462	10	11.27	0.89 (0.43–1.63)
USA	3165	71	75.79	0.94 (0.73–1.18)
Other countries[a]	1007	13	12.72	1.02 (0.54–1.75)
Total	6840	142	161.63	0.88 (0.74–1.04)

CI, confidence interval; SIR, standardized incidence ratio.
[a]Sum of countries where expected case count was <5: Austria, Belgium, Canada, Czech Republic, France, Hungary, Iceland, Norway, and Spain.

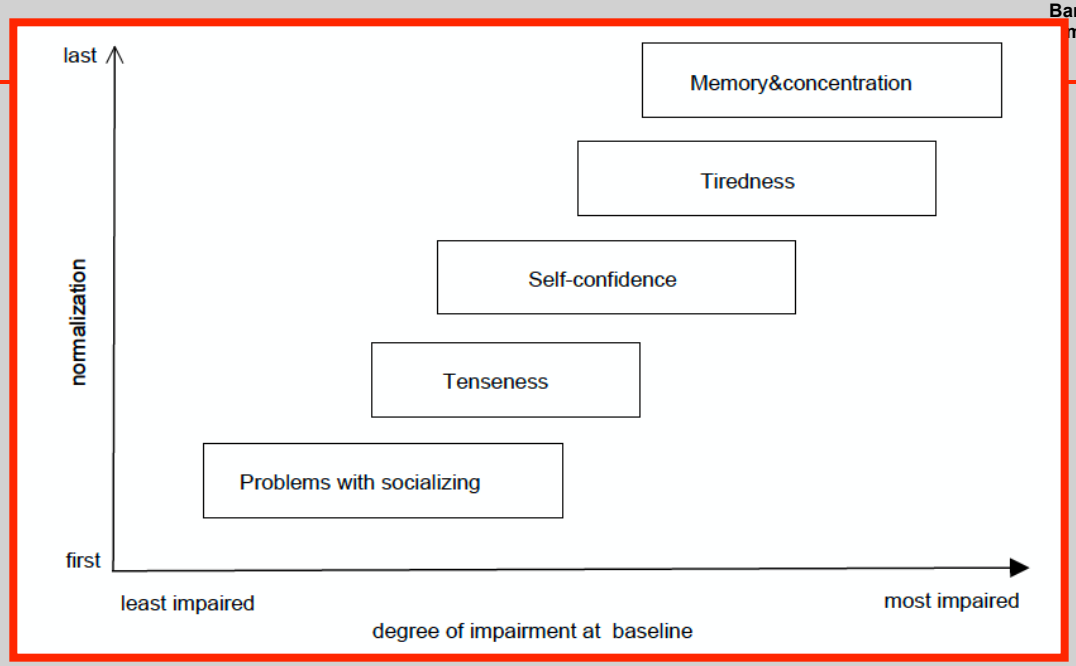
Child et al, EJE 2011

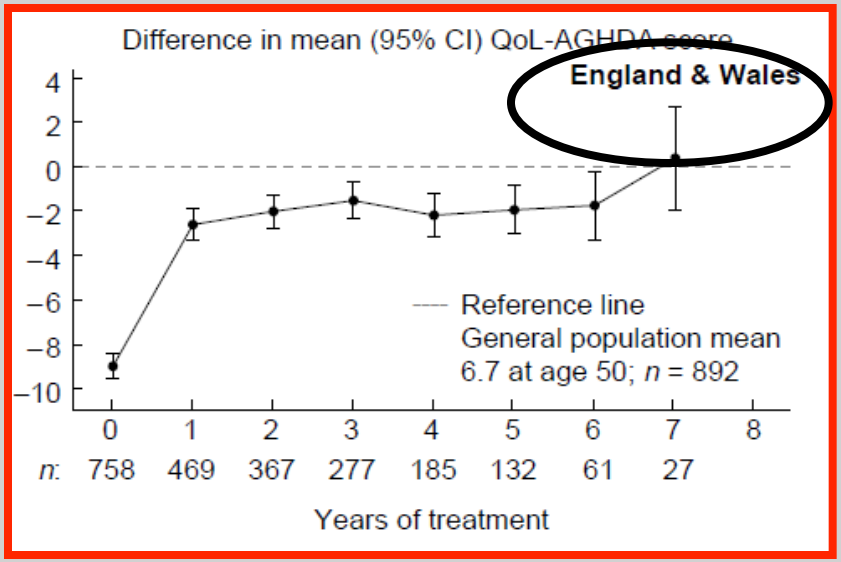
QUALITA' DI VITA

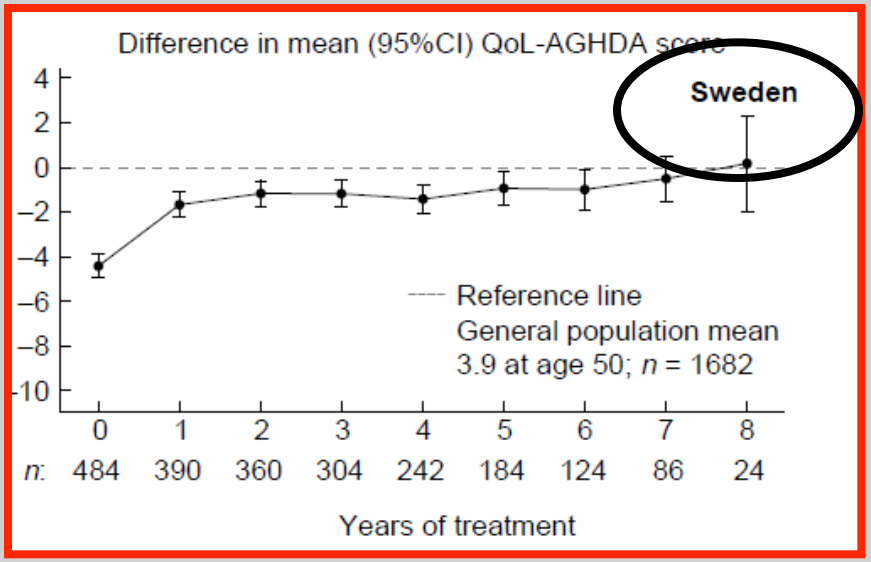


SCALE

- aspetti fisici
- aspetti psicologici
- aspetti sociali

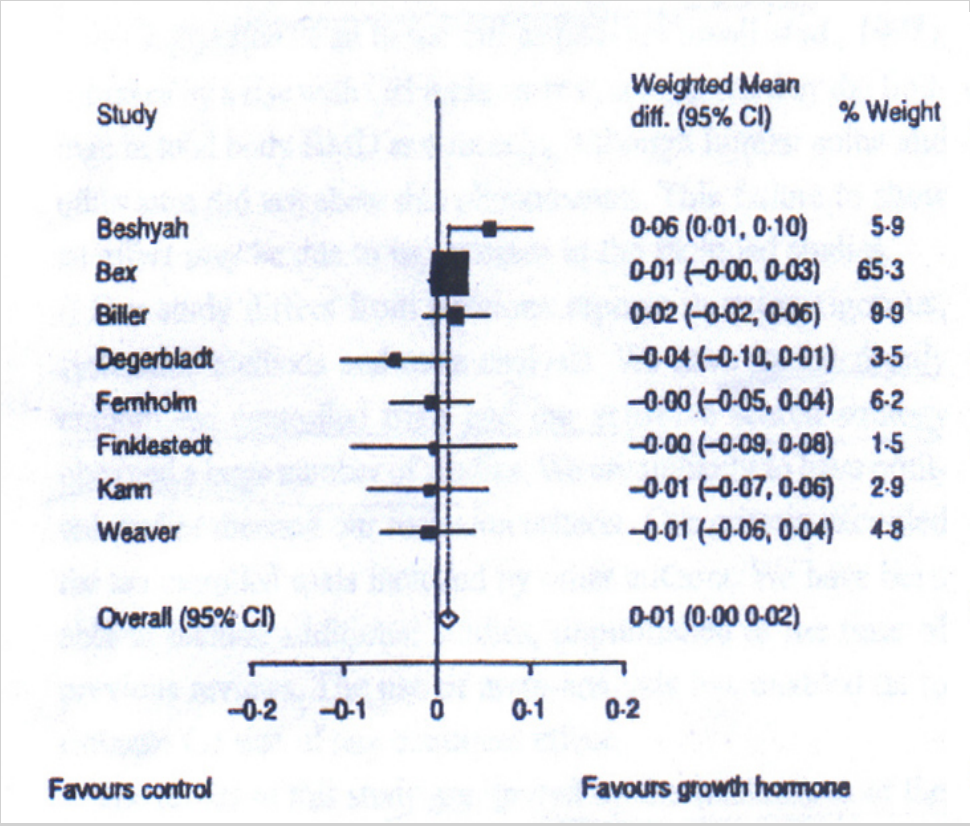


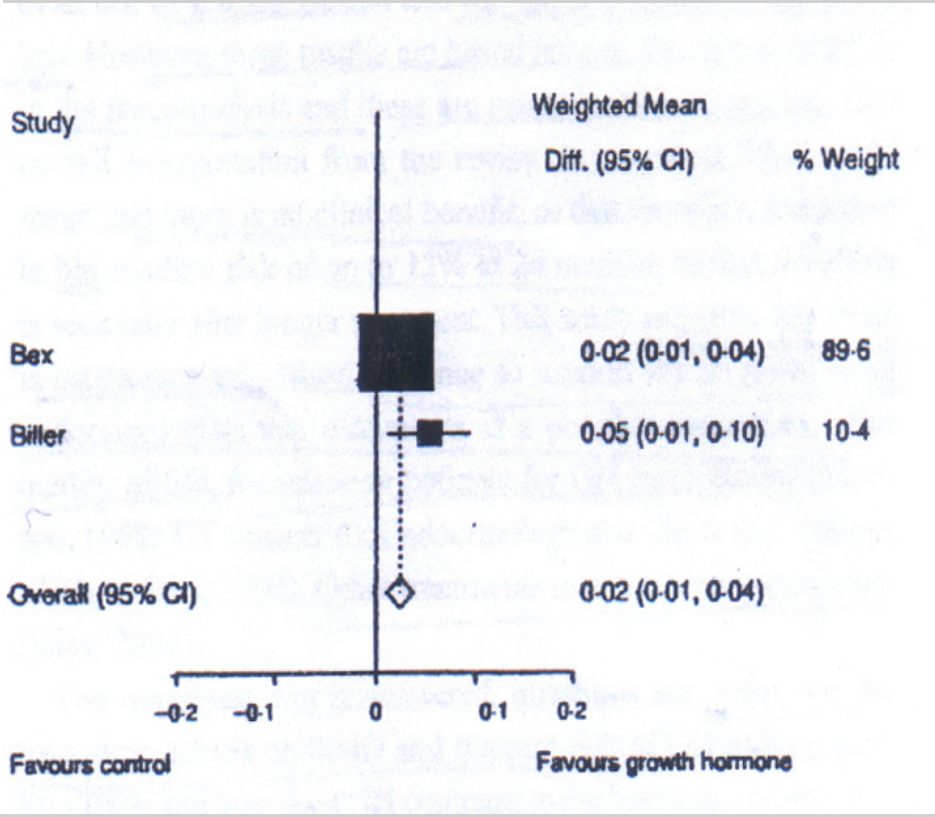




KOLTOWSKA EJE 2006

Effetto sulla massa ossea in GHD: metanalisi





Davidson et al, Clin Endocr 2004

European Journal of Endocrinology (2013) **168** 745–753 ISSN 0804-4643

CLINICAL STUDY

Fifteen years of GH replacement improves body composition and cardiovascular risk factors

Mariam Elbornsson[1,2], Galina Götherström[1,2], Ingvar Bosæus[3], Bengt-Åke Bengtsson[1,2], Gudmundur Johannsson[1,2] and Johan Svensson[1,2]

Table 4 Effects of 15 years of GH replacement in 156 adults with adult-onset GHD on body composition corrected for body weight, serum lipid profile, fasting plasma glucose, and blood HbA1c. All values are shown as the mean (S.E.M.).

	Baseline (n=156)	1 year (n=154)	3 years (n=146)	5 years (n=136)	7 years (n=135)	10 years (n=125)	12 years (n=117)	15 years (n=109)	*P* value (10–15 years)
Body composition									
LST/weight (%)	62.2 (0.7)	65.2 (0.8)***	64.6 (0.8)***	64.8 (0.8)***	64.5 (0.8)***	64.3 (0.8)***	64.2 (0.8)***	63.7 (0.8)***	<0.01
ALST/weight (%)	28.3 (0.4)	29.8 (0.4)***	29.5 (0.4)***	29.5 (0.4)***	29.2 (0.4)***	28.8 (0.4)***	28.6 (0.4)	28.5 (0.4)	<0.01
BF/weight (%)	33.7 (0.8)	30.9 (0.8)***	31.5 (0.8)***	31.0 (0.8)***	31.7 (0.8)***	32.0 (0.8)***	32.3 (0.8)***	32.7 (0.8)**	<0.001
TF/weight (%)	20.7 (0.4)	18.9 (0.4)***	19.3 (0.5)***	19.5 (0.6)***	20.2 (0.5)*	20.5 (0.6)	20.5 (0.6)	21.2 (0.7)**	<0.001
Serum lipids									
TC (mmol/l)	6.0 (0.1)	5.8 (0.1)*	5.7 (0.1)***	5.5 (0.1)***	5.5 (0.1)***	5.4 (0.1)***	5.4 (0.1)***	5.5 (0.1)***	NS
LDL-C (mmol/l)	4.0 (0.1)	3.7 (0.1)***	3.6 (0.1)***	3.4 (0.1)***	3.4 (0.1)***	3.3 (0.1)***	3.2 (0.1)***	3.3 (0.1)***	NS
HDL-C (mmol/l)	1.2 (0.03)	1.3 (0.03)	1.3 (0.03)*	1.3 (0.03)*	1.3 (0.03)*	1.4 (0.07)***	1.4 (0.04)***	1.4 (0.04)***	NS
TG (mmol/l)	1.7 (0.1)	1.8 (0.1)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	1.8 (0.1)	1.8 (0.1)	1.8 (0.1)	NS
Glucose metabolism									
Glucose (mmol/l)	4.4 (0.05)	4.7 (0.05)***	4.6 (0.05)**	4.6 (0.05)**	4.7 (0.06)***	4.8 (0.06)***	4.8 (0.05)***	4.8 (0.06)***	NS
HbA1c (%)	5.0 (0.04)	5.0 (0.05)	4.9 (0.05)	4.8 (0.05)	4.7 (0.06)***	4.6 (0.07)***	4.6 (0.06)***	4.6 (0.06)***	NS

The statistical analyses are based on a repeated-measures ANOVA followed by Student–Newman–Keuls *post hoc* test. *P* values (10–15 years) are based on

Rischio di DM durante terapia sostitutiva con rhGH

Bari,
7-10 novembre 2013

BMI (kg/ m²)	Casi osservati	SIR	IC 95%
< 20	0	0.0	0.0-2.3
20-24	5	0.3	0.1-0.7
25-29	18	0.6	0.4-0.9
30-34	30	2.2	1.5-3.1
> 35	23	3.8	2.4-5.7

Monson JP, dati KIMS

SINDROME METABOLICA

Bari,
7-10 novembre 2013

- La genesi della SM è multifattoriale e non [illegible]

L'incidenza di SM è maggiore in pazienti con GHD, anche dopo anni di terapia …
ma senza terapia come sarebbe aumentato il rischio cardiovascolare?

- Inoltre con il passare degli anni il rischio per patologie cardiovascolari aumenta per tutti…

Che effetto può avere la terapia sostitutiva con rhGH su tutti questi fattori?

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

The Journal of Clinical Endocrinology & Metabolism 89(5):2192–2199

doi: 10.1210/jc.2003-030840

Impact of Growth Hormone (GH) Treatment on Cardiovascular Risk Factors in GH-Deficient Adults: A Metaanalysis of Blinded, Randomized, Placebo-Controlled Trials

PATRICK MAISON, SIMON GRIFFIN, MARC [illegible]COUE-BEGLAH, NABILA HADDAD, BEVERLEY BALKAU, AND PHILIPPE CHANSON

Clinical Pharmacology (P.M.), Clinical Research Unit, Assistance Pubique-Hôpitaux de Paris, Henri Mondor University Hospital, F-94010 Créteil, France; Institut National de la Santé et de la Recherche Médicale U258 (P.M., M.N.-B., N.H., B.B.), F-94807 Villejuif, France; Institute of Public Health (S.G.), CB2 2SR Cambridge, United Kingdom; and Endocrinology and Reproductive Diseases (P.C.), Assistance Publique-Hôpitaux de Paris, Bicêtre University Hospital, and University Paris XI, F-94275 Le Kremlin-Bicêtre, France

European Journal of Endocrinology (2009) 161 S97–S106 ISSN 0804-4643

Adult GH deficiency throughout lifetime

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control data. Similarly, although data from KIMS indicate normal SMR in patients on long-term GH replacement, the impact of bias in patient selection for GH replacement and the favourable effects of enhanced clinical care render it difficult to define a precise beneficial effect of GH on mortality at the present time.

Bari,
7-10 novembre 2013

Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline

Mark E. Molitch, David R. Clemmons, Saul Malozowski, George R. Merriam, and Mary Lee Vance

J Clin Endocrinol Metab, June 2011, 96(6):1587–1609

3.5 We suggest that, although mortality is increased in patients with hypopituitarism and GHD has been implicated in this, GH has not yet been shown to improve mortality (2/⊕OOO).

3.6 We suggest that GH therapy of GH-deficient adults improves the quality of life of most patients (2/⊕⊕OO).

Bari,
7-10 novembre 2013

European Journal of Endocrinology (2013) **169** R1–R14 ISSN 0804-4643

REVIEW
THERAPY OF ENDOCRINE DISEASE

Long-term effects of recombi t human GH replacement in adults with GH deficiency ystematic review

Natasha M Appelman-Dijkstra*, Kim M J A , Ferdinand Roelfsema, Alberto M Pereira and Nienke R Biermasz

Effects of H on mortality

In summary, there is evidence for a moderate increased mortality rate despite long-term rhGH replacement, especially in females. Differences in pituitary disease, hormone replacement- and radiation therapies may account for differences between studies. However, as long-term studies on mortality are scarce, at this moment, no firm conclusions on the safety of long-term rhGH replacement can be drawn.

European Journal of Endocrinology (2013) **169** R1–R14 ISSN 0804-4643

Bari,
7-10 novembre 2013

REVIEW
THERAPY OF ENDOCRINE DISEASE

Long-term effects of recombinant human GH replacement in adults with GH deficiency: a systematic review

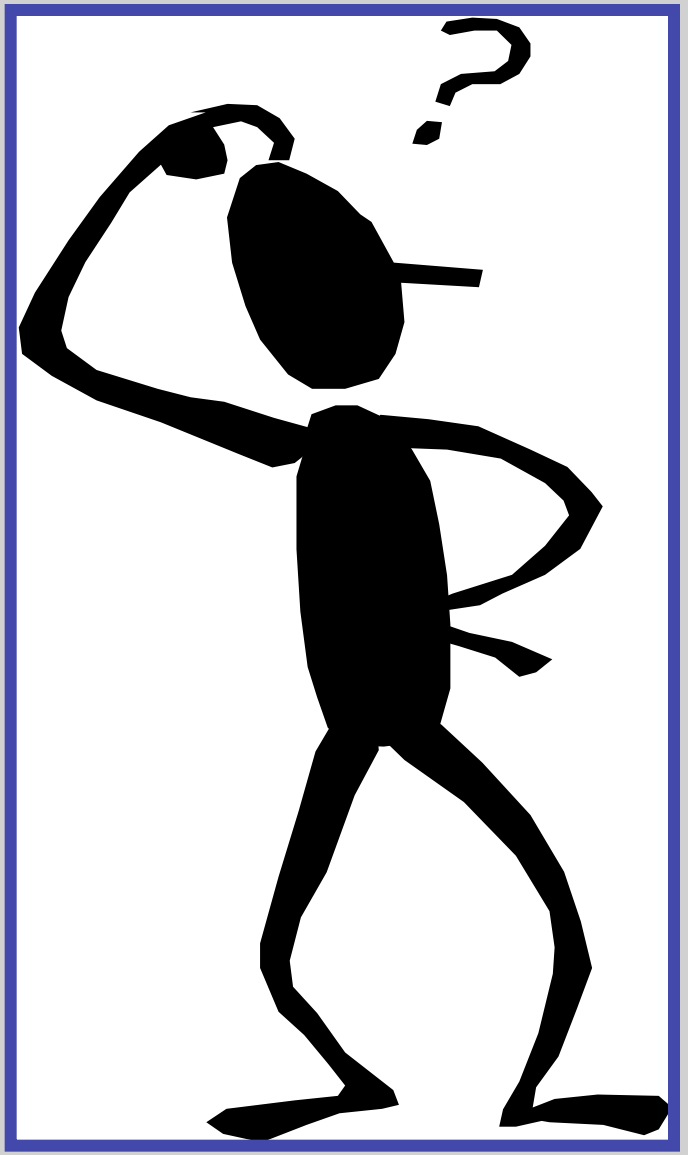
Natasha M Appelman-Dijkstra*, Kim M J A Claessen*, Ferdinand Roelfsema, Alberto M Pereira and Nienke R Biermasz

In summary, available literature on long-term rhGH replacement in adult GHD patients shows inconsistent results with respect to its expected beneficial effects, in the presence of several drawbacks to enable a definite interpretation. First, long-term studies were generally uncontrolled and lacked a control group (of non-treated GHD patients) enabling adjustment for subjective changes or changes due to ageing. Second, only a limited number of centres have reported their data, resulting in a low number of evaluable patients with a follow-up duration of ≥ 5 years of rhGH replacement with half of the long-term studies describing (part of) the same patient cohort. Especially the course of QoL during ongoing therapy is unestablished. With respect to the metabolic profile, rhGH therapy has shown prolonged, beneficial effects in the long-term for body composition, lipid profile, carotid IMT and BMD, but overall cardiovascular risk, as assessed by the prevalence of the MS, glucose levels and BMI appeared not to be influenced or was even negatively affected. Therefore, the benefit of long-term rhGH treatment should be a matter of ongoing research to enable adequate risk-benefit analyses and, in clinical daily practice, the benefits of rhGH should be considered carefully in each patient.

Gli effetti del trattamento con rhGH: come valutarli?

Bari,
7-10 novembre 2013

Tollerabilità
Sicurezza



EFFETTI AVVERSI DELLA TERAPIA CON GH

Pharmacological Reports 2007; 59: 500

Molto frequenti

- **NEL SITO DI INIEZIONE**
  (eritema, noduli,...)

Meno frequenti

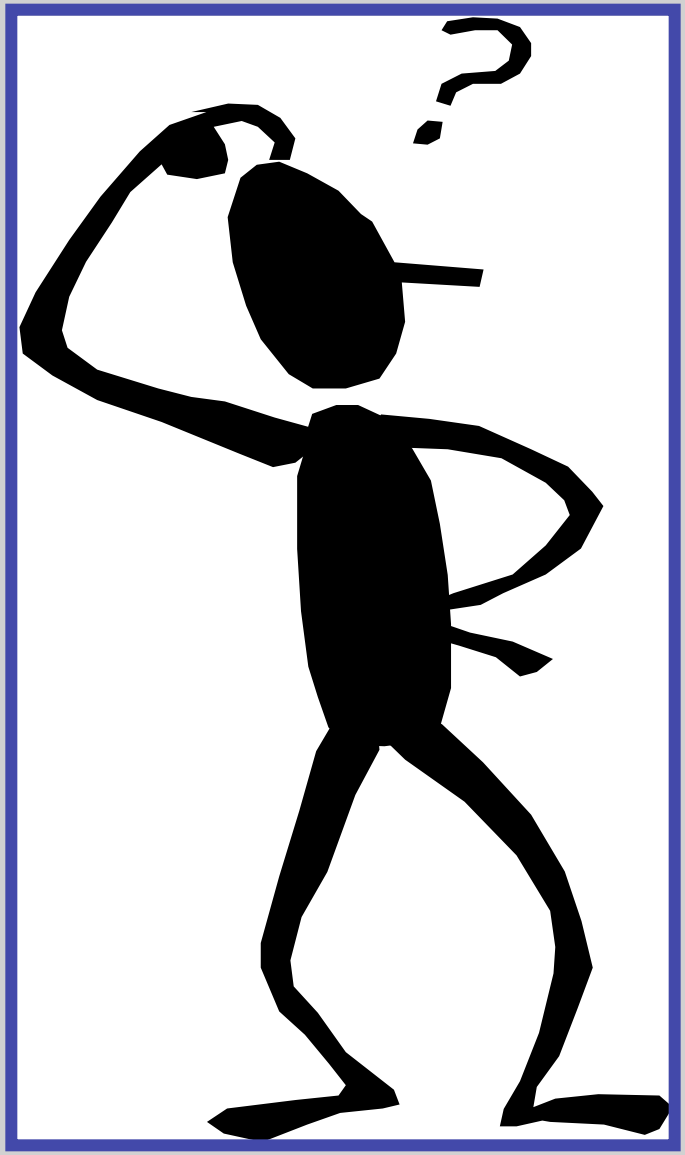
- **EFFETTI METABOLICI**
  Lieve edema
  Ritenzione

- **EFFETTI MUSC.-SCHELETRICI**
  Sindr. Tunnel carpale
  Artralgie, mialgie

TERAPIA CON GH

Bari,
7-10 novembre 2013

PER QUANTO TEMPO ?



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5.3 Values and preferences

It is unclear how long to administer GH therapy. If benefits are being achieved, there is no particular reason to stop treatment. On the other hand, if there are no apparent or objective benefits of treatment after at least 1 yr of treatment, discontinuing GH therapy may be appropriate.

R32. No data are available regarding the optimal length of GH replacement; therefore, we recommend that if patients on GH replacement report significant QOL benefits and objective improvements in biochemistry and body composition, then GH treatment should be continued indefinitely. However, if the patient reports neither subjective nor objective benefits, then it is reasonable to consider discontinuing GH treatment altogether (**Grade D; BEL 4**).

COMPLIANCE ALLA TERAPIA

Bari,
7-10 novembre 2013

- La mancata aderenza al trattamento è una delle principali ragioni per cui i pazienti non ottengono i benefici attesi dalla terapia
- Tale aspetto ha un impatto negativo anche sul sistema socio-sanitaro, in termini di costi dovuti ai farmaci non utilizzati e alle ospedalizzazioni correlate alle complicanze
- Gli interventi volti al miglioramento dell'aderenza al trattamento possono ottimizzare i benefici clinici ed evitare l'aumento dei costi
- Nel deficit dell'ormone della crescita (GHD), il dolore al sito di iniezione e la scomodità della somministrazione rappresentano le principali problematiche correlate alla riduzione dell'aderenza al trattamento

JOURNAL MEDICAL ECONOMICS 2011

Consensus Guidelines for the Diagnosis and Treatment of Adults with Growth Hormone Deficiency: Summary Statement of the Growth Hormone Research Society Workshop on Adult Growth Hormone Deficiency*

Bari,
7-10 novembre 2013

European Journal of Endocrinology (2007) **157** 695–700 ISSN 0804-4643

CONSENSUS STATEMENT

Consensus guidelines for the diagnosis and treatment of adults with GH d
associatio
Endocrinc
Endocrinc
of Austral

Ken K Y Ho on be
Pituitary Research Unit

J Clin Endocrinol Metab, June 2011, 96(6):1587–1609

SPECIAL FEATURE

Clinical Practice Guideline

lormone
ctice

Merriam,

GRAZIE PER L' ATTENZIONE