Growth Hormone- Indications Landscape
Presentation Outline

• Growth Hormone
  • Growth Hormone: Indications
  • Growth Hormone Deficiency in Children
  • Turner Syndrome
  • Small for Gestational Age
  • Chronic Renal Disease
  • Noonan Syndrome
  • Achondroplasia
  • Growth Hormone Deficiency in Adults
  • Conclusions
Growth Hormone

- A 191-amino acid polypeptide hormone secreted by anterior pituitary gland
- Also known as somatropin
- Important endogenous factor responsible for body growth
- Transported from the brain, attaches itself to the surface of the cells in the body
- New local hormone is produced in the cells, causing cells to divide or to produce proteins
- GH and Insulin are dichotomous cousins
  - GH- fasts hormone
  - Insulin- feasts hormone

Evolution of Growth Hormone

- First human pituitary GH isolated in 1945
- Exogenous GH used to treat in variety of disorders
- GH formulations are exclusively obtained by genetic engineering
- The various formulations of GH available in market include:
  - Genotropin¹
  - Serostim²
  - Zorbtive³
  - Humatrope⁴
  - Nutropin⁵
  - Nutropin-AQ or Protropin⁶
  - Norditropin⁷
  - Omnitrope⁸

Physiology and Metabolic Action

GHRH + Somatostatin

GH → IGF-I

Carbohydrate metabolism
Fat (lipid) metabolism
Bone metabolism
Protein metabolism
Water and sodium homeostasis

• Growth Hormone
• **Growth Hormone: Indications**
  • Growth Hormone Deficiency in Children
  • Turner Syndrome
  • Small for Gestational Age
  • Chronic Renal Disease
  • Noonan Syndrome
  • Achondroplasia
  • Growth Hormone Deficiency in Adults
• Conclusions
FDA- Approved Indications for GH

- Growth hormone deficiency
- Turner syndrome
- Chronic renal failure
- Prader-Willi syndrome
- Small for gestational age
- Idiopathic short stature
- AIDS wasting
- Noonan syndrome
Other Indications

- Short Bowel Syndrome (SBS)
- Short stature homeobox gene (SHOX)
# Norditropin®: Approved Indications

## Paediatrics
- Growth hormone deficiency
- Turner syndrome
- Chronic renal failure
- Small for gestational age
- Noonan syndrome
- Achondroplasia

## Adults
- Pronounced growth hormone deficiency in known hypothalamic-pituitary disease
- Childhood onset growth hormone insufficiency
Final Adult Height in Short Stature Patients vs. Normal

- GHD
- SGA, CRD
- TS, NS
- Hypochondroplasia
- Achondroplasia

180
160
140
120
100

Normal
GHD
• Growth Hormone
• Growth Hormone: Indications
• Growth Hormone Deficiency in Children
• Turner Syndrome
• Small for Gestational Age
• Chronic Renal Disease
• Noonan Syndrome
• Achondroplasia
• Growth Hormone Deficiency in Adults
• Conclusions
GHD in Children

- Absence or insufficient production of GH
  - Short stature and growth retardation
  - Prevalence range: 1 in 3500 to 1 in 7000\(^1\)
  - Untreated adult:\(^2\)
    - reduced height,
    - an average of 4.7 SDs below the mean

- GH therapy\(^2\)
  - Normalises growth during childhood
  - final height can be within 1 SD of the norm
  - Approx. 85% of the children obtain an adult height within the normal range\(^3\)

---

Increase in Growth with GH Therapy: Clinical Evidence

IGF-I-based GH dosing\(^1\)
- Maintains serum IGF-I concentrations within target range
- Improves growth responses with higher GH dose

GH therapy\(^2\)
- Significant increase in Growth velocity and growth velocity SD scores
- Increase in IGF-I and IGFBP-3 levels and in their SD scores

**Norditropin®: Recommended Dosing: GHD in Children**

**Indication**
Treatment of children with growth failure due to growth hormone insufficiency

**Recommended dosing**
25 to 35 microgram/kg/day or 0.7 to 1.0 mg/m²/day

- Dosage and administration schedule should be individualized
- Serum IGF-I levels may be useful for dose titration
- Failure to increase growth rate, during the first year of therapy, indicates the need for close assessment of compliance and evaluation for other causes of growth failure
Presentation Outline

- Growth Hormone
- Growth Hormone: Indications
- Growth Hormone Deficiency in Children
- **Turner Syndrome**
- Small for Gestational Age
- Chronic Renal Disease
- Noonan Syndrome
- Achondroplasia
- Growth Hormone Deficiency in Adults
- Conclusions
Turner Syndrome

- Congenital disorder in females
  - Complete or partial absence of the second sex chromosome (45,X)\(^1\)
  - Affects approx. 3% of all female foetuses\(^2\)
  - Prevalence: 1 in 2000 live female births\(^3\)
  - Short stature and infertility\(^3\)
  - Untreated adults have an\(^4\)
    - Avg. height of 143–147 cm,
    - Much more than 2 SDs below the normal

Turner Syndrome: Clinical Features

**Short stature**¹
- Average adult stature 20 cm shorter than target height

**Cardiovascular system**¹
- Aortic coarctation
- Bicuspid aortic valve
- Conduction abnormalities

**Genitourinary system**¹,²
- Ovarian failure
- Renal malformation

**Characteristic facial features**¹,²
- Ptosis
- Hypertelorism
- Retrognathic face
- Micrognathia
- Ear malformations

**Other manifestations**¹,²
- Melanocytic nevi
- Hyperlipidemia
- Hypertension
- Wide-spaced nipples/poor breast development
- Tooth anomalies
- Strabismus
- Hyperopia
- Hearing loss
- Webbed neck
- Thyroiditis

Effect of Dose on Attainment of Normal Height

- 70% patients achieved final height within normal range
- A greater % of patients treated with GH dose of 0.067 mg/kg/day or up to 0.089 mg/kg/day reached normal final height
- Mean changes from baseline to final height SDS correspond to mean height gains of
  - 4.5 cms (dose A: 0.045 mg/kg/day)
  - 9.1 cms (dose A: 0.067 mg/kg/day)
  - 9.4 cms (dose A: 0.089 mg/kg/day)

Benefits of GH Therapy in Turner Syndrome: Clinical Data

• In addition to height gain, GH therapy in women with turner syndrome has beneficial effects on blood pressure and body proportion\(^1,2\)

• Height gain from GH improved patient’s health related quality of life that positively influenced psychosocial functioning\(^3,4\)

• Reduced cardiovascular risk factors with GH treatment
  – Decreases total cholesterol and LDL and increase HDL\(^5\)
  – Positive effect of the biophysical properties of the aortic wall\(^6\)

Turner Syndrome: On-going Monitoring and Specialist Care

**Pediatric Endocrinologist** – Growth/pubertal development

**Pediatrician** – Growth and development, overall health

**Geneticist** – Genetic screening

**Gynecologist** – Evaluation of gonadal function/estrogen replacement

**Cardiologist** – Assess and address cardiac anomalies

**Neonatologist** – Assess newborn abnormalities

*Other specialist may be consulted to address other deficits associated with Turner syndrome.

**Norditropin®: Recommended Dosing - Turner Syndrome**

**Indication**
Growth failure in girls due to gonadal dysgenesis (Turner syndrome)

**Recommended dosing**
45 to 67 microgram/kg/day or 1.3 to 2.0 mg/m²/day

**Before starting treatment it is recommended to measure**
- Fasting blood glucose
- IGF-I level
- Thyroid function (tested regularly)

**Monitoring of growth of hands and feet**
Otological evaluation in girls
Presentation Outline

• Growth Hormone
• Growth Hormone: Indications
• Growth Hormone Deficiency in Children
• Turner Syndrome
• **Small for Gestational Age**
• Chronic Renal Disease
• Noonan Syndrome
• Achondroplasia
• Growth Hormone Deficiency in Adults
• Conclusions
Small for Gestational Age

• Guidelines definition¹
  – Birth length and/or weight of 2 or more standard deviations (SD) scores below the mean or less than 3rd percentile for gestational age

• Approx. 10% of SGA children fail to exhibit catch up growth by 2 years²

• Decreased growth due to insensitivity to GH and low IGF-1 levels²

Causes of SGA

Maternal
- Infections
- Medical conditions
- Substance abuse
- Pregnancy pathology
- Age, height, birth weight
- Ethnic background

Fetal
- Chromosomal or other genetic defects
- Congenital anomalies
- Intra-uterine infection
- Multiple gestation
- Fanconi-, Bloom- or Down- syndrome

Placental
- Insufficiency
- Abruption
- Infarction
- Structural anomalies

Treating SGA Children with GH

• Aims
  - To normalise height in early childhood
  - To maintain normal height gain during childhood
  - To achieve adult height within normal target range

• Short-term studies in Europe
  - GH treatment showed a significant improvement in growth with a near doubling of height velocity and weight gain¹

• Long-term studies: Dutch-Norditropin study
  - Randomized, double-blind, dose-response study
  - Accessed the long-term efficacy and safety of GH treatment in short SGA children²

Long-term Studies: Dutch-Norditropin® Study

- SGA Children- randomly assigned to one of two GH dose groups, 0.033 or 0.067 mg/kg/day
- Significant improvement in height SDS from baseline (p<0.0001) in both groups
- Untreated group achieved a mean adult height SDS of -2.3 (0.7) after approx. 7.5 years’ follow-up
- Graph: Compared to untreated short children born SGA, those treated with GH had significant gain in adult height SDS

Efficacy and Safety of Long-term GH in SGA

**Efficacy**
- Treatment is effective
- Normalisation of height during childhood could be achieved
- 98% children obtain a height within the target range

**Safety**
- Treatment is safe and well-tolerated
- No associated increase in glucose intolerance
- At the recommended GH doses, IGF-I levels are maintained in the normal range (or < 2.5 SD)

Benefits of GH Therapy in SGA: Clinical Evidence

- GH treatment in very young SGA children (2-5 years), without spontaneous catch-up growth was associated with
  - Accelerated growth without any side effects\textsuperscript{1}
  - Significant Improvement in health related quality of life\textsuperscript{2}

- Adequate growth recovery with no excessive bone age acceleration or adverse effects on carbohydrate metabolism was observed in pre-term SGA patients (2–4 years) on GH treatment\textsuperscript{3}

- GH treatment in short children born SGA without signs of persistent catch-up growth leads to a normalization of AH, even with low GH dose\textsuperscript{4}

---

Norditropin®: Recommended Dosing - SGA

**Indication**
Treatment of short children born small for gestational age

**Recommended dosing**
33 to 67 microgram/kg/day or 1.0 to 2.0 mg/m²/day

**Most frequently reported adverse events – SGA**
- Influenza-like illness
- Upper respiratory tract infection
- Bronchitis
- Gastroenteritis

**Additional Adverse Events**
- Abdominal pain
- Otitis media
- Pharyngitis
- Arthralgia
- Headache
- Gynecomastia
- Increased sweating

**Norditropin® [package insert]. 2012**
• Growth Hormone
• Growth Hormone: Indications
• Growth Hormone Deficiency in Children
• Turner Syndrome
• Small for Gestational Age
• **Chronic Renal Disease**
• Noonan Syndrome
• Achondroplasia
• Growth Hormone Deficiency in Adults
• Conclusions
Chronic Renal Disease

• Growth retardation is often a clinical manifestation in children\(^1\)
• Causes:\(^2\)
  – Disturbances in GH/IGF-1 axis
  – insensitivity to the action of GH
  – Decreased bioavailability due to low levels of free IGF-1
• Incidence in children
  – Non-terminal renal failure -4.5 per million total population
  – End-stage renal disease - 1-1.5 per million total population

Rationale for GH treatment in CRD

• Renal failure causes an increase in abnormal forms of IGFBP-3 in the circulation
  – Believed to reduce the bioavailability of IGF-I and inhibit the growth stimulating effect of IGF-I in the circulation

• GH treatment can overcome the inhibitory effects of IGFBP-3 and thus restore normal growth rate

• The clinical benefit on muscle mass and reduced adiposity, as well as improved growth, support the hypothesis that this effect is through hepatic IGF-I synthesis in addition to any local (e.g. growth plate) increase in IGF synthesis

Long-term Effects on Growth and Puberty

- Sustained improvement in height SDS
- No adverse effects on renal function or bone maturation
- Height SDS is positively associated with gain in height
- Initiation of GH at younger age results in better final SDS height

Benefits of GH Therapy in CRD: Clinical Evidence

• Significant improvement in body length without adverse effects in infants with growth retardation secondary to chronic renal failure\(^1\)

• Beneficial effect on CVD risk markers in adult HD patients\(^2\)
  – Increase lean body mass (LBM), IGF-I and serum high-density-lipoprotein

• Improves LBM, other markers of mortality and morbidity, and health-related quality of life in adult patients who are on maintenance HD\(^3\)

• Improves height and concomitantly bone modeling / remodeling, beneficial for bone matrix mineralization\(^4\)

• Growth Hormone
• Growth Hormone: Indications
• Growth Hormone Deficiency in Children
• Turner Syndrome
• Small for Gestational Age
• Chronic Renal Disease
• **Noonan Syndrome**
• Achondroplasia
• Growth Hormone Deficiency in Adults
• Conclusions
Noonan Syndrome

- Autosomal dominant disorder\textsuperscript{1}
- Occurs in 1:1000 to 1:2500 live births\textsuperscript{2}
- No gender predominance\textsuperscript{1}
- Shares clinical features with\textsuperscript{3}
  - Turner syndrome
  - Neurofibromatosis type 1
  - LEOPARD syndrome
  - Cardiofaciocutaneous syndrome
  - Watson syndrome
  - Costello syndrome

Noonan Syndrome: Clinical Features

**Characteristic facial features**
- Broad, high forehead
- Hypertelorism
- Low-set, posteriorly rotated ears with a thick helix
- High-arched palate
- Micrognathia
- High-arched eyebrows
- **Short neck with excess nuchal skin**
- Epicanthic folds
- Downward-slanting palpebral fissures

**Congenital heart defects**
- Pulmonary valve stenosis
- Hypertrophic obstructive cardiomyopathy
- Atrial and ventricular septal defects
- Persistent ductus arteriosus

**Short stature**
- Up to 83% of patients have short stature

**Other clinical manifestations**
- Sunken chest
- Skeletal disorders
- Low posterior hairline
- Undescended testicles at birth
- Lymphatic abnormalities
- Increased bruising/bleeding
- Mental retardation/learning disabilities
- **Poor eyesight**
- Disproportional sitting height vs. height

---

Noonan Syndrome: Other Clinical features

- Excess nuchal skin
- Sunken chest
- Eye - strabismus, refractive error, ptosis

Growth and Development in Noonan Syndrome

• Children with Noonan Syndrome (NS) are not GH deficient but
  – show abnormalities in the GH-IGF-I axis

• Early Development
  – Normal weight and length at birth
  – Failure to thrive and feeding difficulties in 63% of patients

• Puberty
  – Growth spurt reduced or absent
  – Bone development delayed

• Mean adult height
  – Men: 162.5 cm
  – Women: 152.7 cm
  – Both values below third percentile

Increase in height with GH Therapy in Noonan Syndrome

- GH therapy in children increased height velocity (cm/year) during the first 2 years of treatment\(^1\)

- In pre-pubertal patients with short stature, GH treatment induced a mean height gain from baseline of 1.7 SDS—corresponding to 10.4 cm\(^2\)

**Indication**
Treatment of children with short stature associated with Noonan syndrome

**Recommended dosing**
Up to 0.066 mg/kg/day

**Most frequently reported adverse events – Noonan syndrome:**
- Upper respiratory infection
- Gastroenteritis
- Ear infection
- Influenza
- Scoliosis
Noonan Syndrome: On going Monitoring and Specialist Care

**Van der Burgt I. Orphan J Rare Dis. 2007;2(4):1-6.**

**Patient’s Age (Years)**

- **Birth–1 month**
  - Address:
    - Diagnosis
    - Cardiac Anomalies
    - Lab Studies
    - Chromosomal/DNA Analysis
    - Genetics Counseling
  - 1 month–1 year Address:
    - Growth and Development
    - Cardiac Anomalies
    - Coagulopathies
    - Cutaneous Manifestations

- **1-5 Years**
  - Address:
    - Growth and Development
    - Cardiac Anomalies
    - Coagulopathies
    - Cutaneous Manifestations

- **5-12 Years**
  - Address:
    - Growth/skeletal age
    - Cardiac Anomalies
    - Vision/Hearing
    - Delay in Puberty

- **12-21 Years**
  - Address:
    - Growth/skeletal age
    - Cardiac Anomalies
    - Family Planning/Fertility
    - Genetics counseling
    - Resolution of coagulopathies

**Specialists by Age Group**

- **1 Month**
  - Pediatric Endocrinologist, Hematologist

- **1 Year**
  - Clinical Geneticist, Cardiologist, Pediatrician

- **5 Years**
  - Gynecologist/Urologist

- **11-12 Years**
  - Gynecologist/Urologist

- **21 Years**
  - Gynecologist/Urologist
Presentation Outline

• Growth Hormone
• Growth Hormone: Indications
• Growth Hormone Deficiency in Children
• Turner Syndrome
• Small for Gestational Age
• Chronic Renal Disease
• Noonan Syndrome
• **Achondroplasia**
• Growth Hormone Deficiency in Adults
• Conclusions
Achondroplasia: Incidence, Cause and Signs

• Most common of the identified skeletal dysplasias
  – Incidence: 1 in 25000 live births
  – Cause: Mutation of the fibroblast growth factor receptor-3 (FGFR3) gene on human chromosome 4

• Signs and symptoms
  – Short stature with arms and legs disproportionate to trunk length
  – Prominent forehead, a flat area at the base of the nose, a protruding jaw and poor dental structure
  – Adults exhibit forward curve to the lower spine, bowed legs and often elbows that cannot be straightened fully

Achondroplasia

• Diagnosis
  – X-Ray or gene test
• Dose/Treatment duration
  – 0.05 mg/kg/day & average 5 years treatment
• Average height
  – Men: 131.6 cm
  – Women: 123.5 cm
• Clinical evidence
  – GH treatment of children with achondroplasia was shown to improve height without adverse effect on trunk-leg disproportion¹

¹ Hertel et al. Acta Paediatr. 2005;94:1402-10
Presentation Outline

• Growth Hormone
• Growth Hormone: Indications
• Growth Hormone Deficiency in Children
• Turner Syndrome
• Small for Gestational Age
• Chronic Renal Disease
• Noonan Syndrome
• Achondroplasia
• Growth Hormone Deficiency in Adults
• Conclusions
GHD in Adults- Definition

- Criteria for severe GH deficiency in adult life and during transition period, as defined by the Growth Hormone Research Society\(^1\)
  - A peak GH response of < 3 µg/l during an ITT or glucagon tests in patients- Adult life GHD
    - with signs and symptoms of hypothalamic-pituitary disease
    - receiving cranial irradiation or tumor treatment
    - with TBI and subarachnoid hemorrhage (SAH)
    - receiving GH therapy during childhood
  - A peak GH response of <6 µg/L during an ITT in patients- Transition period GHD

Causes of GHD in Adults

- Craniopharyngioma
- Non-functioning pituitary adenoma
- Pituitary hormone secreting tumours
- Surgery
- Irradiation
- Idiopathic
- Trauma
- Other

- Prolactin-secreting pituitary adenoma
- Gonadotrophin-secreting pituitary adenoma
- Pituitary tumour secretory status unknown
- ACTH-secreting pituitary adenoma
- GH-secreting pituitary adenoma

GHD in Adults: Patient Characteristics

<table>
<thead>
<tr>
<th>Feature</th>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body composition</td>
<td>Abnormal body composition</td>
</tr>
<tr>
<td></td>
<td>↑ Waist: hip ratio</td>
</tr>
<tr>
<td>Bone mineral density</td>
<td>↓ Bone mass</td>
</tr>
<tr>
<td></td>
<td>↑ Fracture risk</td>
</tr>
<tr>
<td>Cardiovascular profile</td>
<td>↓ Lipid profile &amp; insulin sensitivity</td>
</tr>
<tr>
<td></td>
<td>↑ Risk of cardiovascular disease</td>
</tr>
<tr>
<td>Quality of life</td>
<td>↓ Quality of life</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>↓ Cognitive function</td>
</tr>
</tbody>
</table>

# Childhood Onset vs. Adult Onset GHD

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Childhood Onset GHD</th>
<th>Adult Onset GHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Younger</td>
<td>Older</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Most</td>
<td>Few</td>
</tr>
<tr>
<td>Organic</td>
<td>Few</td>
<td>Most</td>
</tr>
<tr>
<td><strong>Physical Findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final height</td>
<td>Short or normal</td>
<td>Normal</td>
</tr>
<tr>
<td>BMI</td>
<td>± Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>Lean body mass</td>
<td>Low</td>
<td>Normal or low</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>Normal to high</td>
<td>High</td>
</tr>
<tr>
<td>Bone density</td>
<td>Low in most cases</td>
<td>Normal (GHD after 30 yrs)</td>
</tr>
<tr>
<td><strong>Quality of Life</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional reaction</td>
<td>Severely abnormal</td>
<td>More affected</td>
</tr>
<tr>
<td>Energy level</td>
<td>Slightly to mildly abnormal</td>
<td>Severely abnormal</td>
</tr>
</tbody>
</table>

## Benefits of GH Therapy in Adults with GHD

<table>
<thead>
<tr>
<th>Feature</th>
<th>Benefit of GH therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body composition</td>
<td>Reduced body fat</td>
</tr>
<tr>
<td></td>
<td>Increased lean mass</td>
</tr>
<tr>
<td>Bone mineral density</td>
<td>Increased bone mass</td>
</tr>
<tr>
<td>Cardiovascular profile</td>
<td>Reduced intima wall thickness</td>
</tr>
<tr>
<td></td>
<td>Improved serum lipid profile</td>
</tr>
<tr>
<td></td>
<td>Increased fibrinolytic activity</td>
</tr>
<tr>
<td>Quality of life</td>
<td>Improved QoL</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>Improved cognitive function</td>
</tr>
</tbody>
</table>
Benefits of GH Therapy in Adults with GHD: Clinical Data

• Young adults with CO GHD, showed beneficial effect of continued GH treatment on BMD\textsuperscript{1}
  – 24 months of GH treatment was associated with 3.5% greater increase in BMD of the lumbar spine

• In patients with tibial fractures, GH treatment was found to significantly enhance fracture healing process particularly those with closed tibial fractures\textsuperscript{2}

• Long-term GH treatment in men with GHD resulted in a continuous increase in bone turnover\textsuperscript{3}
  – BMD was found to continuously increase in all regions, predominantly cortical bone

Norditropin®: Recommended Dosing- Adult GHD

**Indication**
- Pronounced growth hormone deficiency in known hypothalamic-pituitary disease
- Childhood onset GHD

**Recommended dosing**
It is recommended to start treatment with a low dose 0.1–0.3 mg/day and to increase the dosage gradually at monthly intervals in order to meet the need of the individual patient. Serum IGF-I can be used as guidance for the dose titration. Dose requirements decline with age. Maintenance dosages vary from person to person, but seldom exceed 1.0 mg/day (equal to 3 IU/day).
GH Therapy in GHDA: Summary

• GH replacement therapy in adults with GHD demonstrated beneficial effects which are maintained for up to 15 years
• GH replacement produces a clinically significant improvement in bone mineral density, improving the atherogenic risk profile
• GH therapy in patients with GHD was shown to improve body composition and quality of life – enabling them to resume normal daily life
Presentation Outline

- Growth Hormone
- Growth Hormone: Indications
- Growth Hormone Deficiency in Children
- Turner Syndrome
- Small for Gestational Age
- Chronic Renal Disease
- Noonan Syndrome
- Achondroplasia
- Growth Hormone Deficiency in Adults
- Conclusions
Conclusions

• GH therapy has many advantages including:
  – Improved linear growth
  – Body composition changes producing a reduction in total and visceral fat and increase in lean body mass
  – Improvement in cardiovascular function and lipids
  – Improved quality of life
  – Increase in bone mineral density
  – Improved memory, alertness, and concentration

• Increased frequency of GH administration was found to improve growth rate
Conclusions

• GH has been approved for many indications including:
  – Growth hormone deficiency
  – Chronic renal insufficiency
  – Turner Syndrome
  – Small for gestational age
  – Noonan Syndrome

• Early initiation of GH should be considered for to normalize heights in early childhood