

# Growth Hormone Therapy: What's New?



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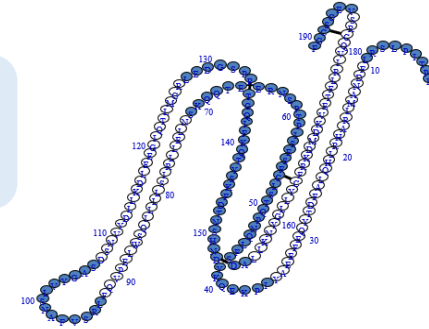


# Agenda

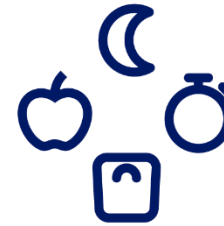
- Background
- GH physiology & Metabolic Effects
- Causes of GH deficiency & GH therapy
- Daily GH therapy
- Weekly GH therapy “somapacitan & Somatrogen”
- First Clinical Experience in Managing Children with GHD Treated with Somapacitan: KSA
  - 72-week efficacy & safety outcomes
- Conclusions

# Growth hormone: Physiology

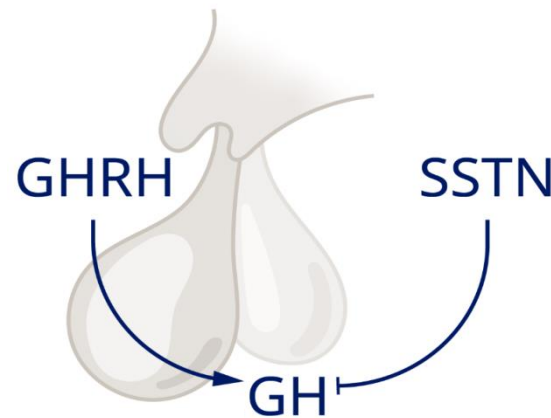
**GH is a 191 amino acid polypeptide hormone**



GH is **secreted** by somatotroph cells in the **anterior pituitary gland** in a **pulsatile** fashion.<sup>1-2</sup>



Nutrition, exercise, body composition and deep sleep onset play key roles in the stimulation of GH secretion.<sup>2</sup>



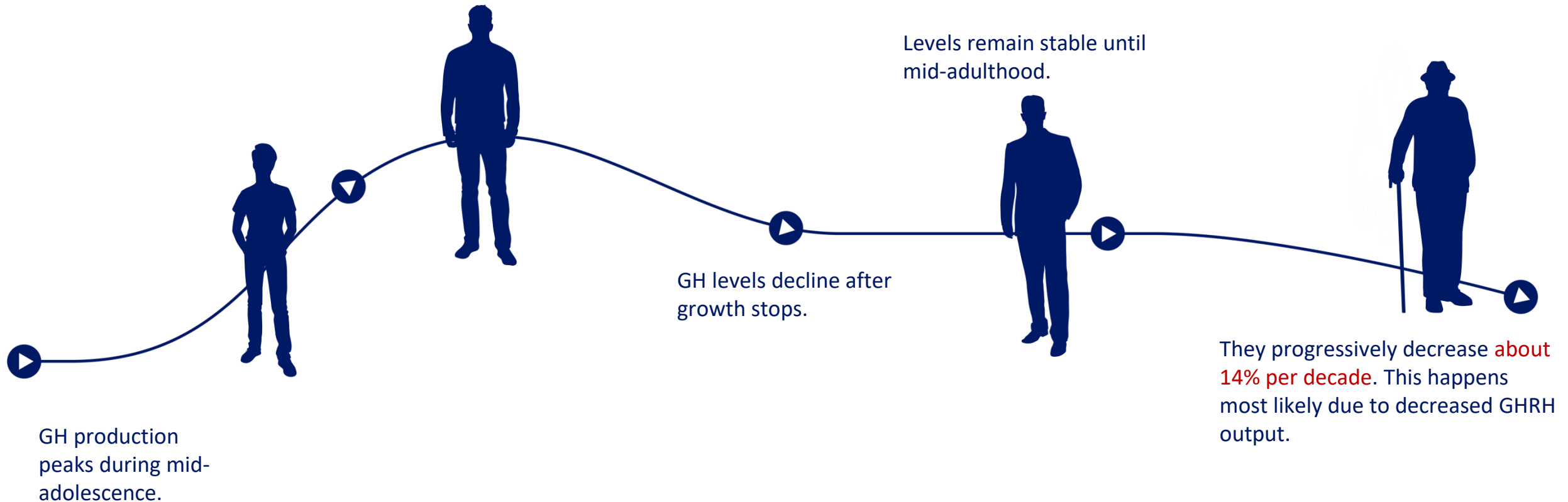
# Growth hormone: Physiology

Growth hormone is secreted in pulses (after infancy)



# Growth hormone: Physiology

**GH secretion is increased in puberty then decreases subsequently.**



GH, growth hormone, Melmed S., N Engl J Med, 2019;380:2551–62.

# Metabolic effects of GH

- In general, growth hormone stimulates protein anabolism in many tissues:
  - Increases amino acid uptake, increases protein synthesis & decreases oxidation of proteins.
  - Promotes linear growth.
  - Increase bone formation & bone mass.
  - Increase active muscle mass.
  - Anabolic effects.
- Increase lipolysis & redistribution of fat:
  - Growth hormone enhances the utilization of fat by stimulating triglyceride breakdown and oxidation in adipocytes
- Growth hormone has anti-insulin activity, because it suppresses the abilities of insulin to stimulate uptake of glucose in peripheral tissues and enhance glucose synthesis in the liver.
- Positive self - esteem.

# Growth hormone Deficiency

## Causes GH deficiency

### Syndromes with concomitant GHD<sup>2</sup>

- Septo-optic dysplasia (SOD), optic nerve atrophy
- Midline face defects ( Cleft lip /palate)
- Holoprosencephaly
- Pituitary aplasia or hypoplasia
- Most of the CNS abnormalities are associated with multiple pituitary hormonal deficiencies.

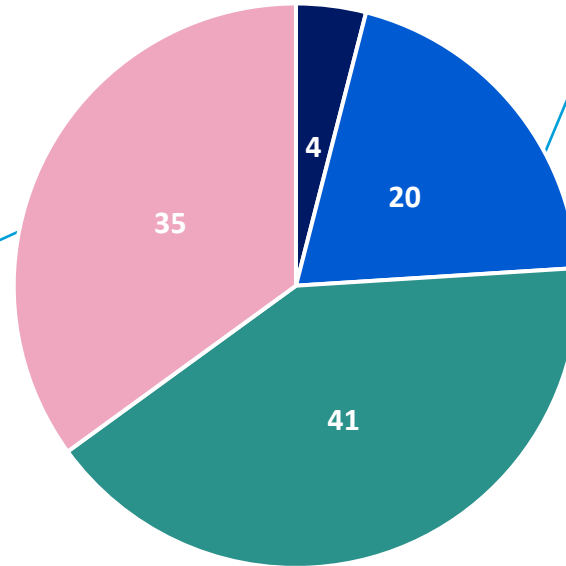
### Acquired GHD<sup>1</sup>

#### CNS insults:

- Trauma.
- Infection.
- Surgery.
- Radiation therapy.

#### CNS neoplasm:

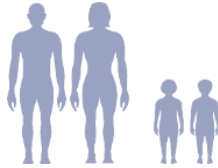
- Craniopharyngioma.
- Hypothalamic tumors.
- Brain tumors close to pituitary stalk.



### Congenital GHD<sup>1</sup>

Present from birth, as a result of genetic mutations or structural defects in the brain

5-30% of short stature patients is associated with GHD which affected first-degree relative with the same genetic cause of GHD



### Idiopathic GHD<sup>1</sup>

No known or diagnosable cause

Can be present at any point during childhood



# GH therapy

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Lessons learned since recombinant human GH was introduced to the market in 1985

- 1 High level of GH safety has lasted more than 39 years because of:
  - Jacob Creutzfeldt disease relationship to pituitary-derived GH.
  - Potential association between GH & leukemia.
- 2
  - Initially, growth hormone was injected **intramuscularly**.
  - In 1985, it was shown as effective when administered as a subcutaneous injection.
- 3
  - Early in its use, growth hormone was administered twice weekly; this was increased to 3 times weekly when the higher frequency resulted in an increased growth response.
  - Daily administration is now the recommended use.
  - **Once weekly administration** is currently available for children & adult with Growth Hormone deficiency.



# GH therapy

## Benefits of GH Therapy



Improve linear growth <sup>1,2</sup>



Body composition changes producing a reduction in total and visceral fat and increase in lean body mass <sup>3</sup>



Improvement in CV function and lipids



Increases bone mineral density<sup>1</sup>



Improves memory, alertness & concentration and improved QOL<sup>1</sup>

GH, growth hormone; GHD, growth hormone deficiency; QOL: quality of life

1. Growth Hormone Research Society. *J Clin Endocrinol Metab* 2000;85:3990–3; 2. Grimberg *et al.* *Horm Res Paediatr* 2016;86:361–97

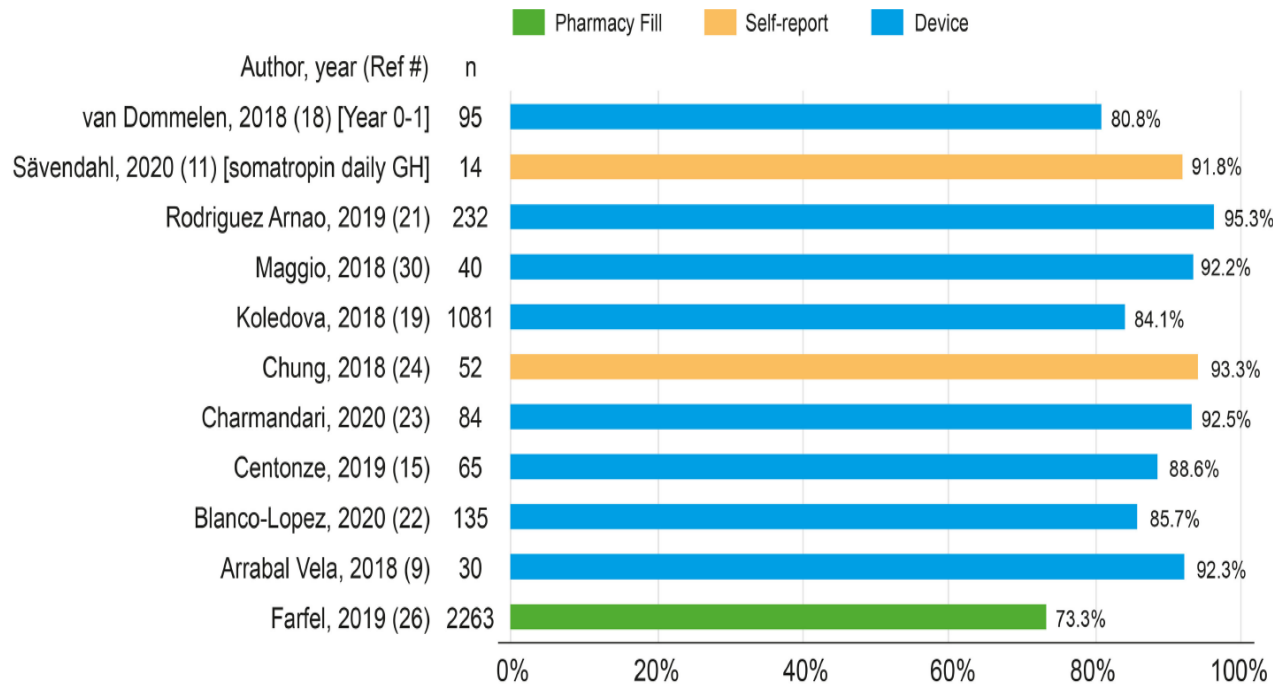
<b>Year of initial FDA approval</b>	<b>Indications for GH treatment</b>
1985	Pediatric growth hormone deficiency
1993	Growth failure secondary to chronic renal failure up to the time of renal transplantation
1996	Adult growth hormone deficiency
1996	HIV wasting in adults
1996	Turner syndrome
2000	Prader-Willi syndrome
2001	Small for gestational age
2003	Idiopathic short stature
2003	Short bowel syndrome
2006	<i>SHOX</i> gene deficiency
2007	Noonan syndrome

# Factors influencing the response to GH?

- Indication of GH therapy ( GH Deficiency, Turner Syndrome, SGA...).
- Age of starting GH therapy.
- Pubertal status.
- GH dose.
- GH dose titration 3-6 monthly.
- **Treatment adherence**
- Birth Weight (SGA).
- Concomitant medication.
- Associated co-morbidity.
- Rarely, development of GH antibodies.
- Cultural believes (spreading not true side effects).
- Family education and uncertain worries on side effects.
- Limited parents' information on GH therapy.

# "Challenges and Considerations Against Daily Growth Hormone Therapy"

Mean 12-month adherence among 11 rhGH studies



**83 % Mean Adherence ranges for once daily GH injection  
(4,091 Patient from 2018 till 2020)**

**14.3 % - 44.8 %**

**Suboptimal treatment ranges for  
once daily GH injection**

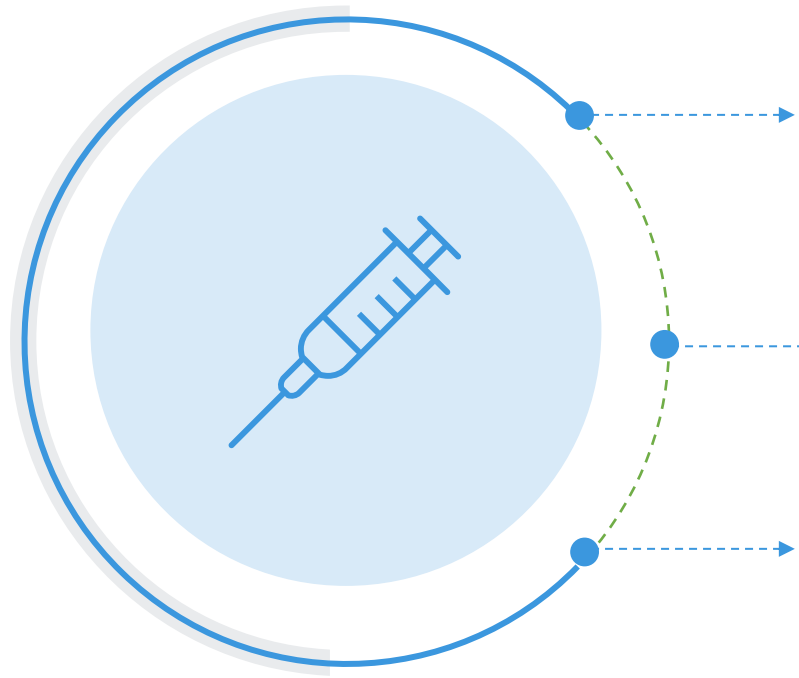
**3,091 Patient from 2018 till 2020**

**78 % - 88 %**

**Adherence ranges to  
once daily GH injection**



# Daily injections may present challenges for pediatric and adult patients initiating & maintaining therapy<sup>1</sup>



**Patients may struggle with the need for long-term daily injections<sup>1</sup>**: The perceived pain of injections may affect compliance<sup>3,4</sup>

**Life circumstances can interfere with daily injections<sup>1</sup>**: **50%** of parents reported that GH treatment interferes with family travel<sup>5,a</sup>

**Some patients and their caregivers may prefer alternative GH treatment options<sup>2</sup>**

<sup>a</sup> Based on data gathered via focus groups or telephone interviews of 31 parents of children with GHD aged 4 to 12 years. A total of 51 concepts related to the burden of GH treatment were discussed in parent/guardian interviews, and emotional well-being and interference were identified as the 2 domains of treatment burden for parents. GH, growth hormone.

1. Christiansen JS, et al. Eur J Endocrinol. 2016;174(6):C1-C8; 2. McNamara M, et al. Patient Prefer Adherence. 2020;14:781-793; 3. Kappelgaard AM, et al. Horm Res. 2004;62(3):98-103; 4. Laursen T, et al. Basic Clin Pharmacol Toxicol. 2006;98(2):218-221; 5. Brod M, et al. Patient. 2017;10(5):653-666.

## "Weekly Growth Hormone Therapy: Two Available Preparations in Saudi Arabia"

Somapacitan & Somatrogen

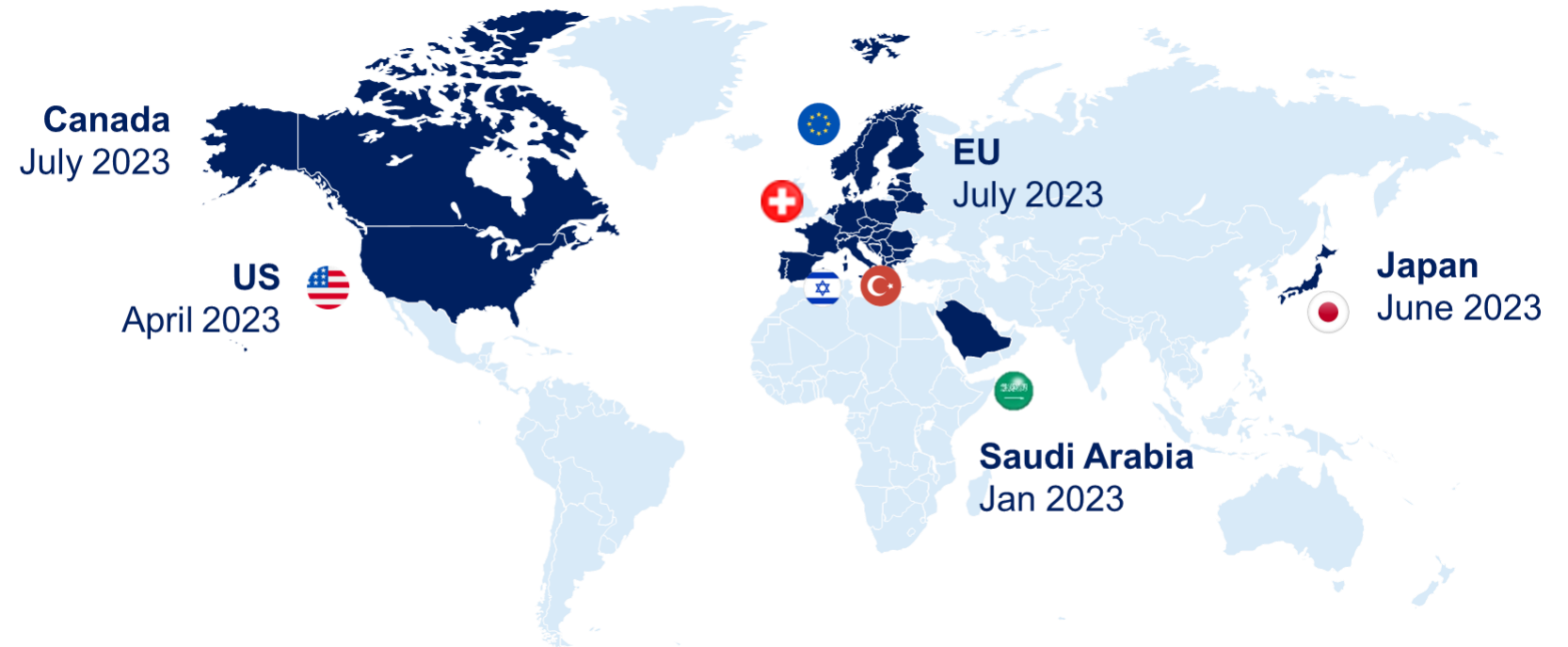
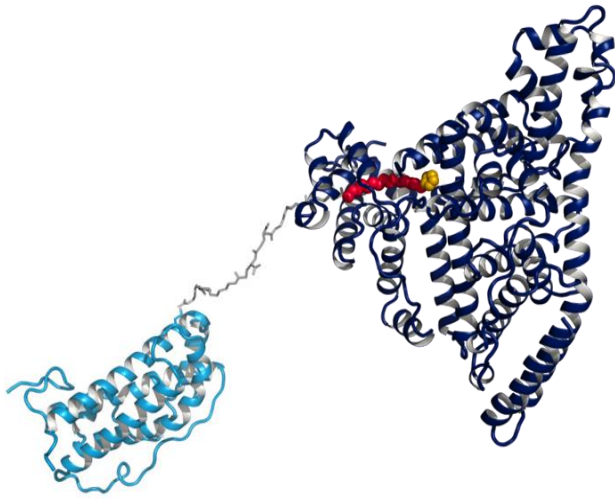
# Somapacitan

Once-weekly growth hormone for the treatment of Children & Adults with GHD



Karolinska  
Institutet

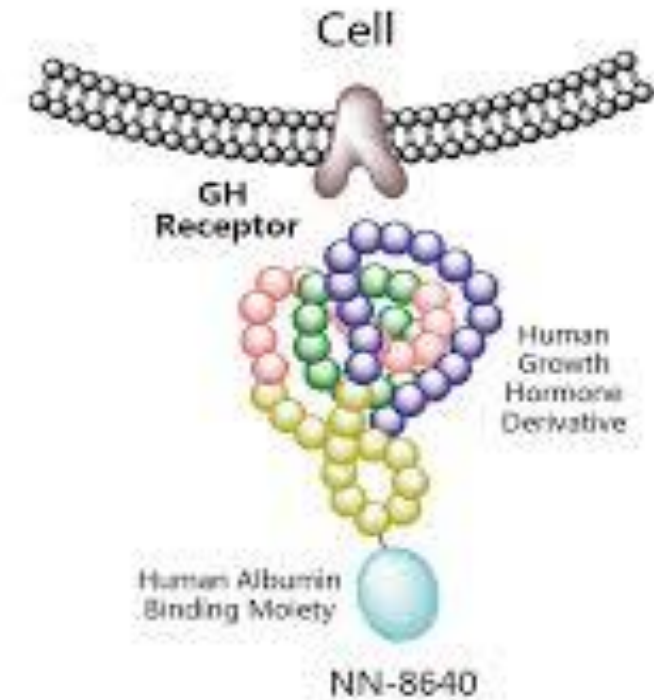
KAROLINSKA  
UNIVERSITY HOSPITAL



Growth hormone and linker are scaled, **GHR**, growth hormone receptor; **MW**, molecular weight; 1. Battelino et al. Clin Endocrinol (Oxf) 2017;87:350–8; 2. Rasmussen et al. J Clin Endocrinol Metab 2014;99:E1819–29; 3. Rasmussen et al. J Clin Endocrinol Metab 2016;101:988–98; 4. Thygesen et al. Growth Horm IGF Res 2017;35:8–16

# "Somapacitan: A Once-Weekly Growth Hormone Preparation"

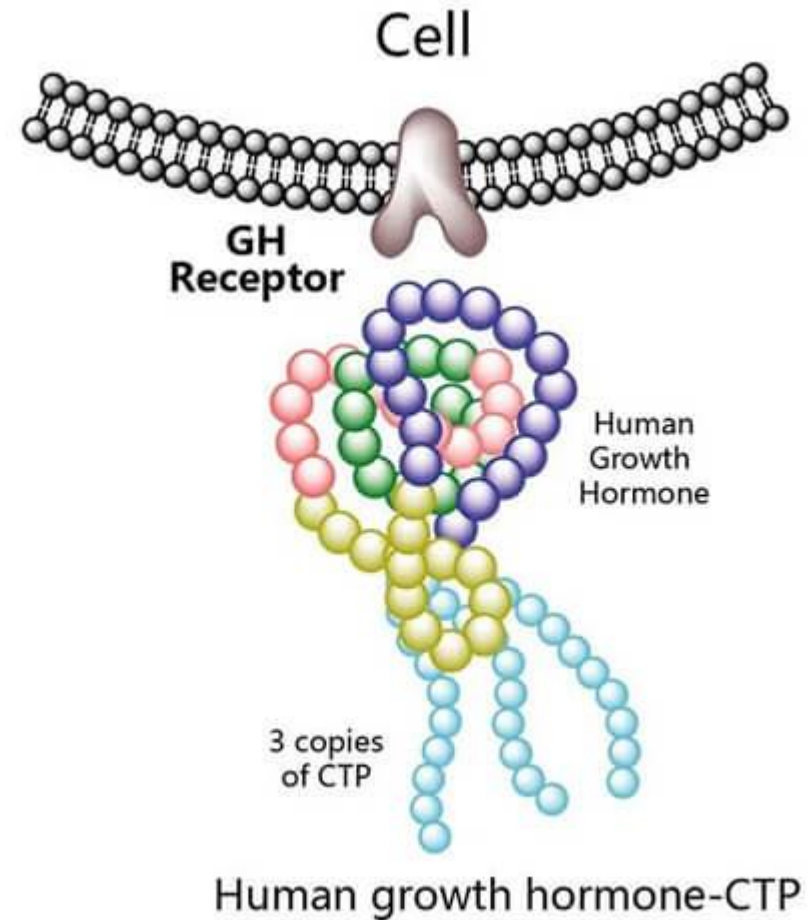
- Somapacitan is a reversible albumin-binding GH analog. The binding to albumin in the bloodstream prolongs the half-life of the hormone, allowing it to be administered weekly while maintaining steady therapeutic levels.
- The slow release of the active hormone ensures continuous GH activity over the course of the week, providing comparable growth-promoting effects to daily GH therapy.



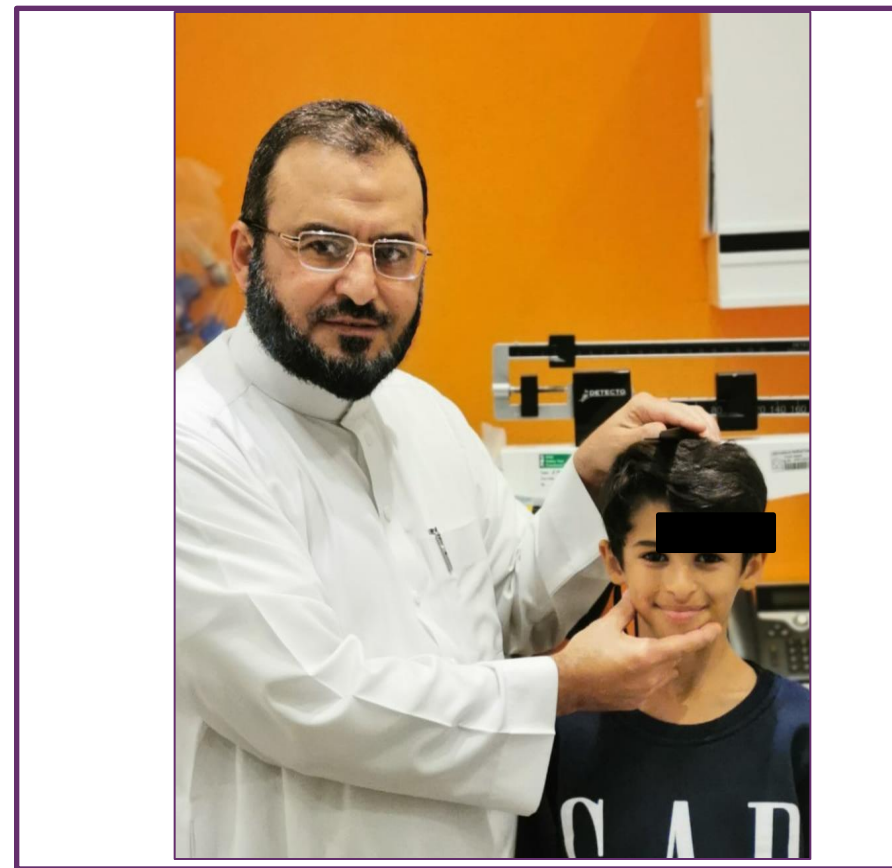


# " Somatogon : A Once-Weekly GH Preparation"

- Somatogon consists of human GH with three copies of the carboxy-terminal peptide (CTP) from the beta-subunit of human chorionic gonadotropin (hCG).
- The addition of these CTPs extends the drug's half-life in the bloodstream, leading to sustained levels of GH over the course of a week.



# "Efficacy and Safety of Weekly Somapacitan in Growth Hormone Deficiency: A 72-Week Study at a Single Centre in Jeddah, Saudi Arabia."



## Study Design & Population:

- This single-center observational cohort study was conducted at King Abdulaziz University to evaluate the efficacy and safety of weekly Growth Hormone (GH) therapy in children diagnosed with GHD.
- The study spanned 72 weeks, from March 1, 2023, to July 31, 2024.

## Criteria used in study to diagnose Growth Hormone Deficiency:

- Childhood growth hormone deficiency (GHD) was diagnosed based on a combination of clinical and biochemical criteria.
- Clinically, GHD was suggested by a slower growth rate relative to peers, and the diagnosis was confirmed if one or more of the following conditions were met:
- Two distinct GH stimulation tests (glucagon and clonidine) showing GH levels  $\leq 10$  ng/ml.- Insulin-like growth factor-I (IGF-I) levels below the standardized reference range for age and sex.
- Height falling below -2 standard deviations (SD) for age, sex, and race.
- Poor height velocity, defined as below the 25th percentile for  $\geq 1$  year or crossing major percentile lines on growth charts.
- Additionally, other medical conditions that could impact growth were systematically excluded.

"Inclusion criteria encompassed 184 children undergoing treatment with somapacitan"

Non-  
adherent to  
daily GH

Needle  
phobia

Transition  
phase  
patients

Injection  
site pain

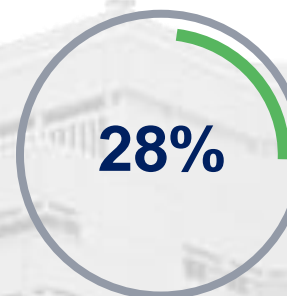
Family  
preference

Social  
reasons

# "Overview of the Characteristics of 184 Children with Growth Hormone Deficiency"

## Percentage of Patients Naïve & Switching

Switching (52)



Naïve (132)

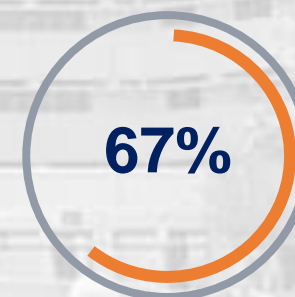


## Percentage of patients according to gender

Female (60)



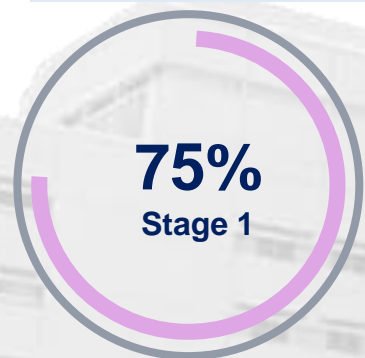
Male (124)



## Percentage of patients according to Tanner stage

75%

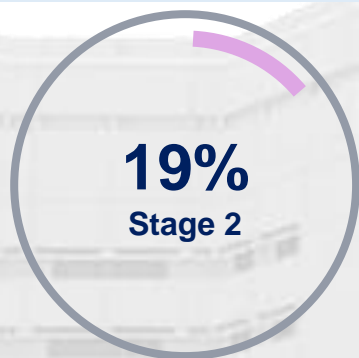
Stage 1



138 patients\*

19%

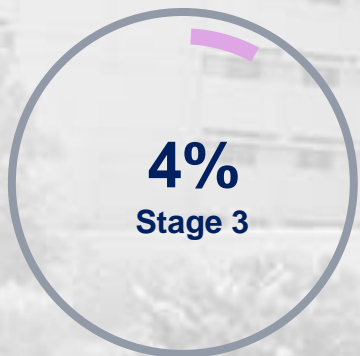
Stage 2



36 patients

4%

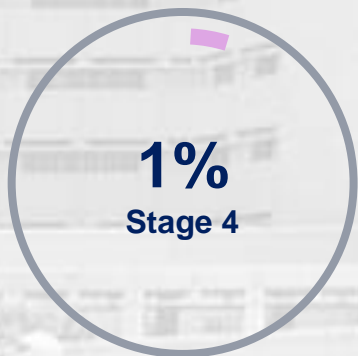
Stage 3



9 patients\*

1%

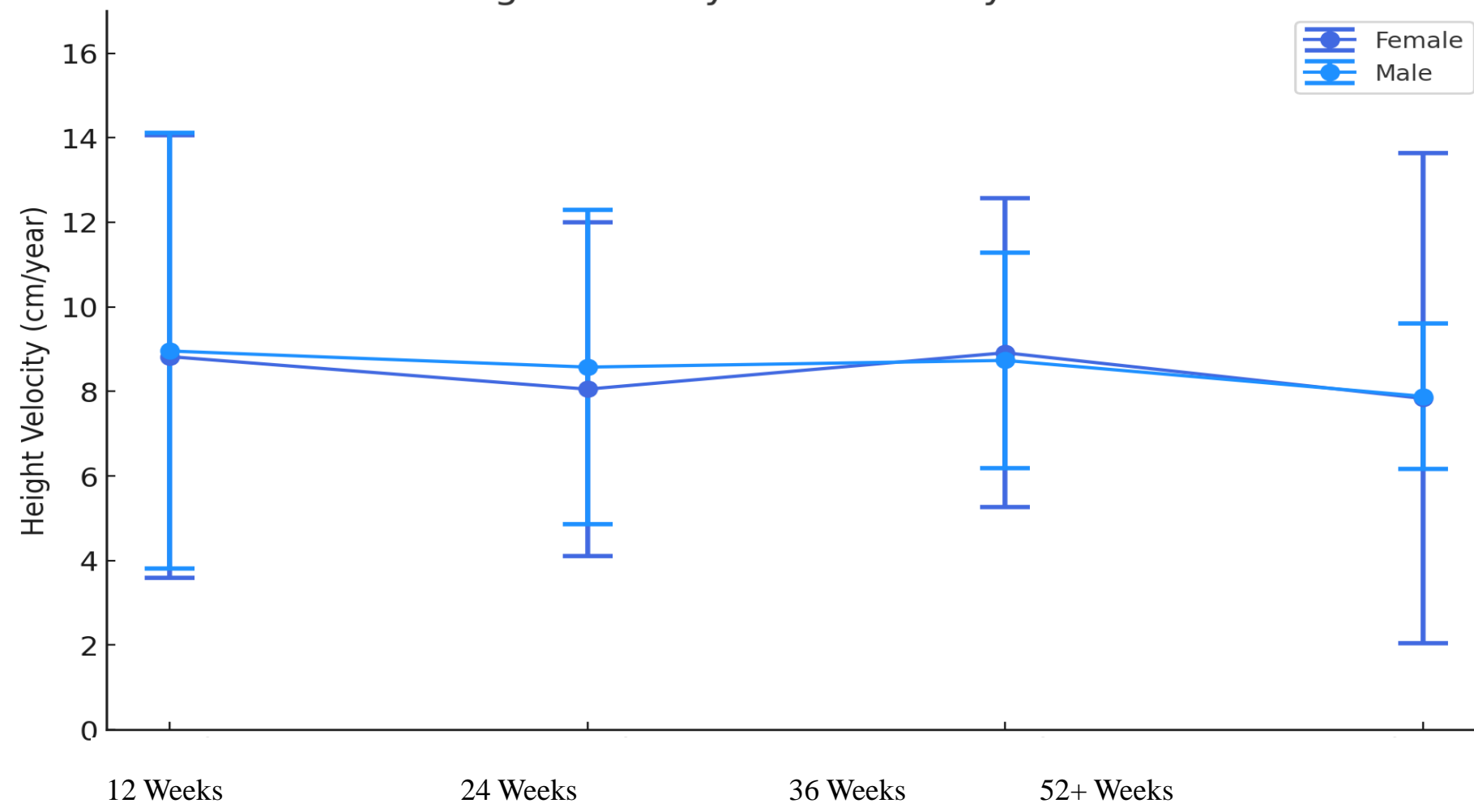
Stage 4



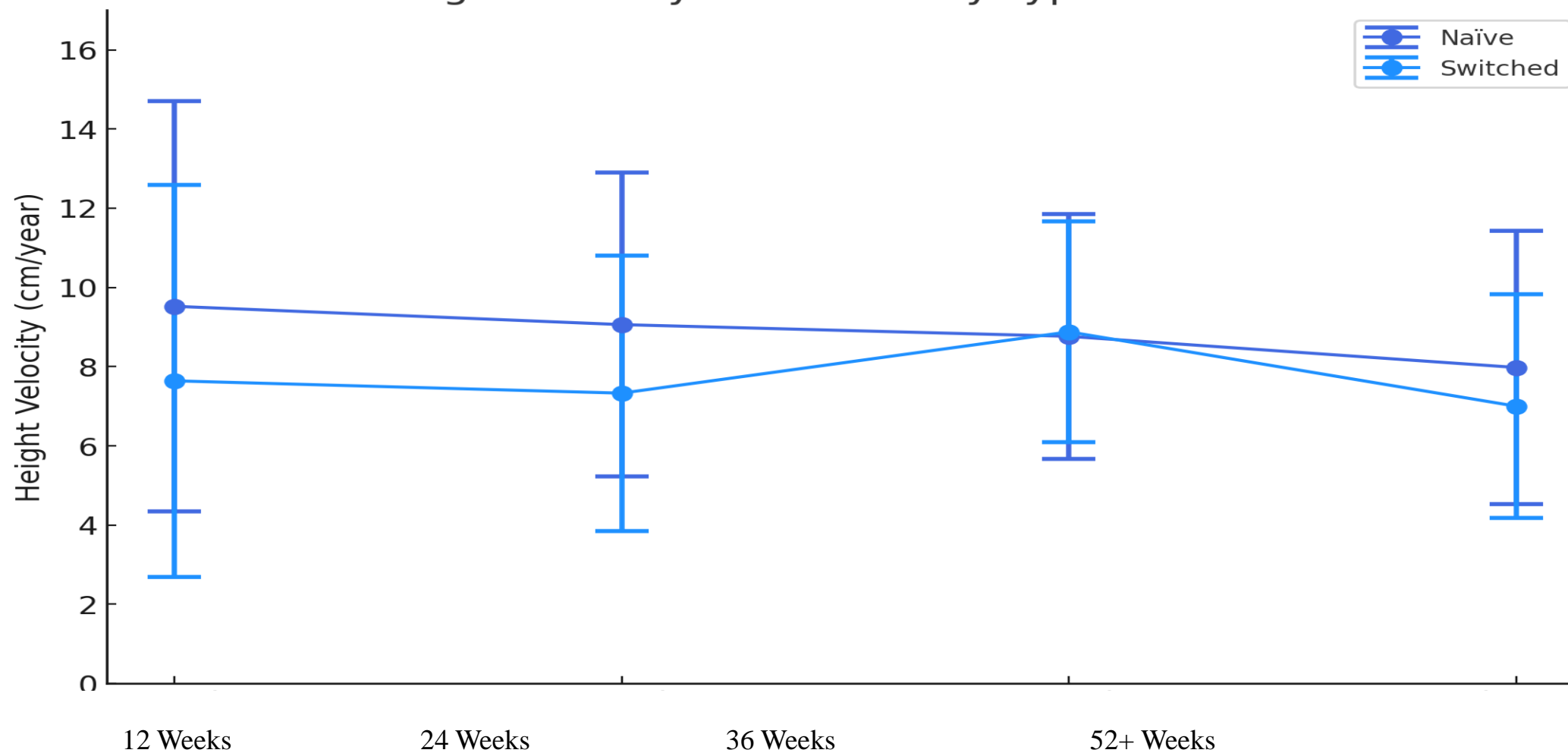
2 patients

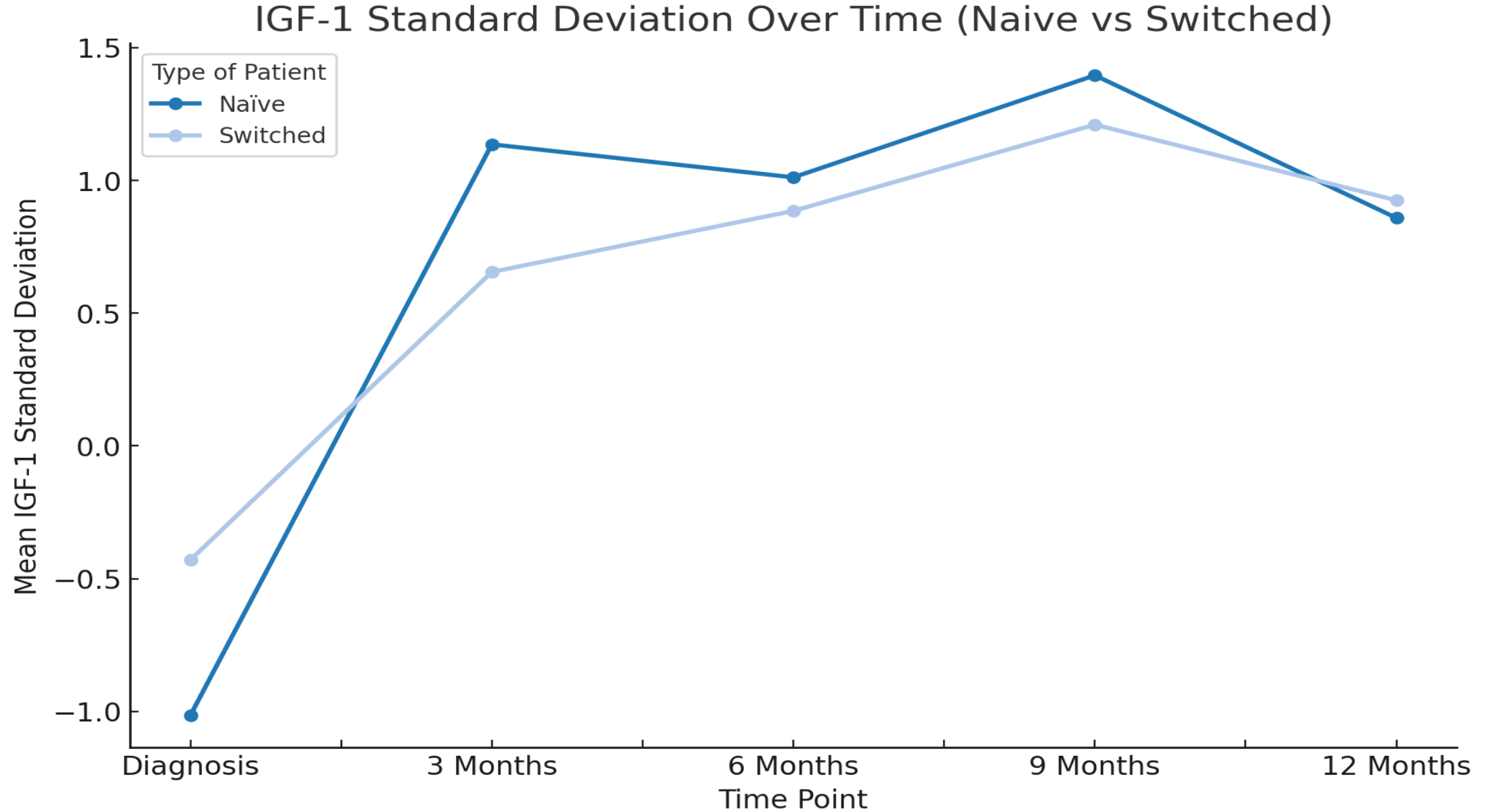


Height Velocity Over Time by Gender

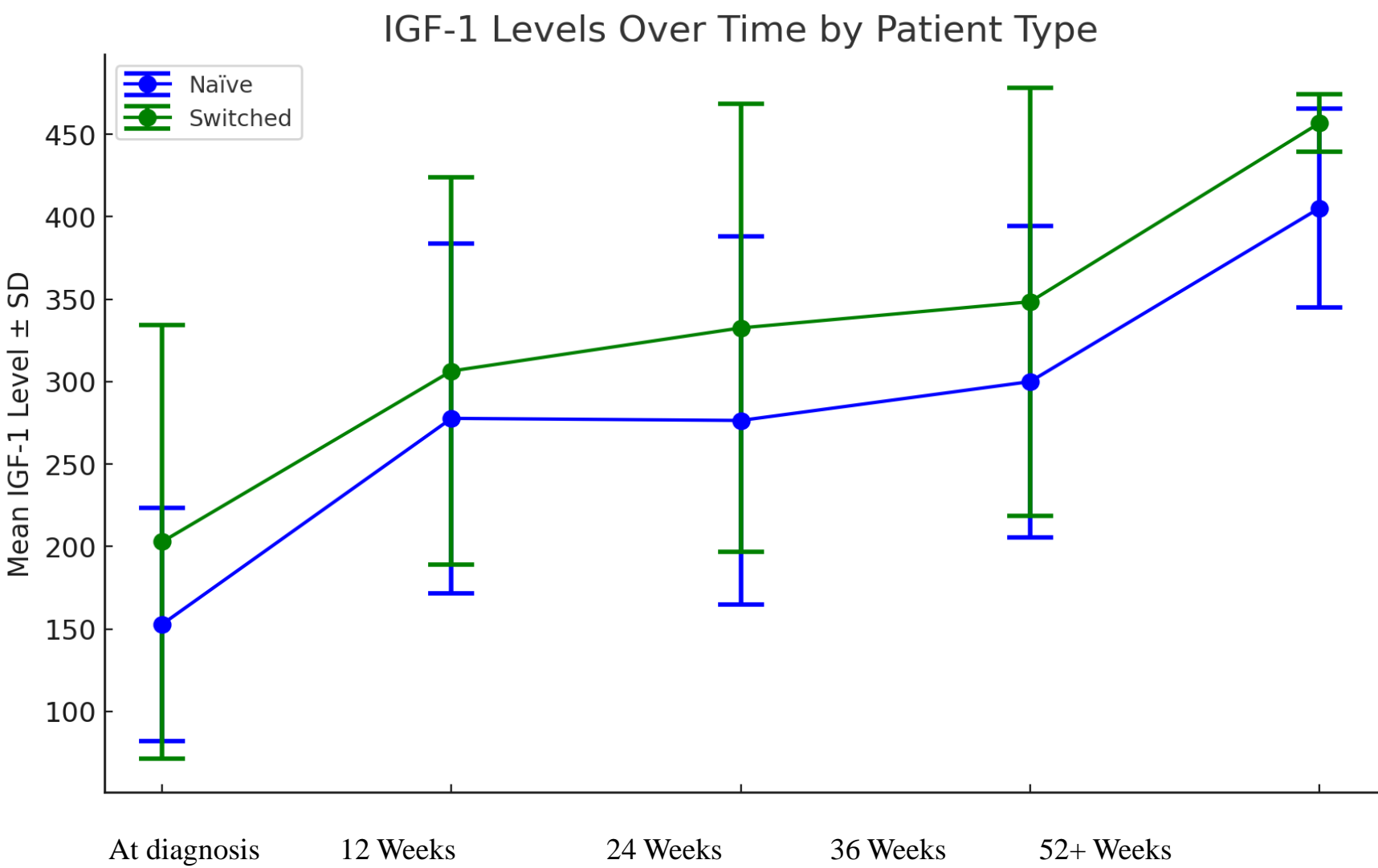


## Height Velocity Over Time by Type of Patient

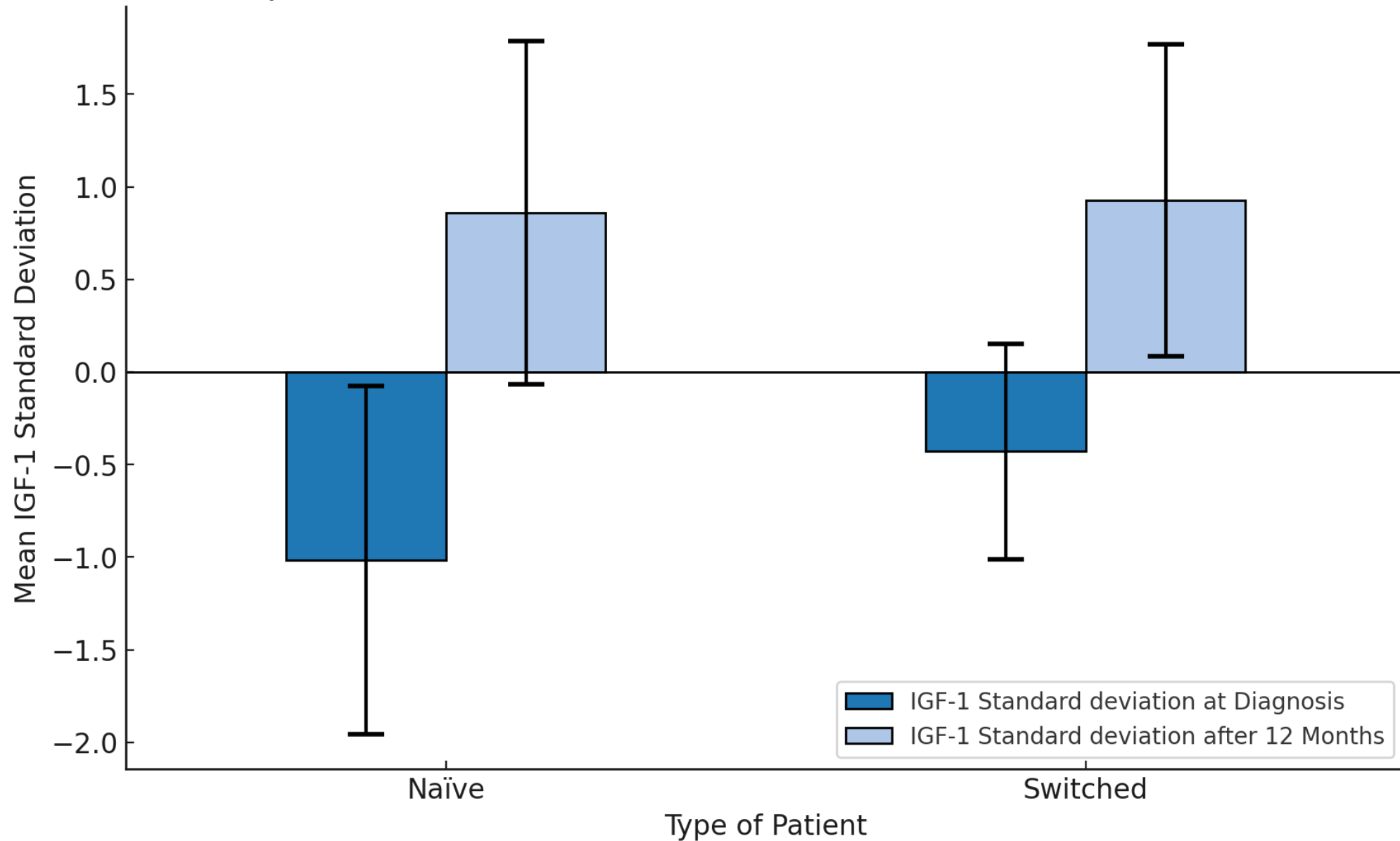








## Comparison of IGF-1 Standard Deviation (Baseline vs One Year)

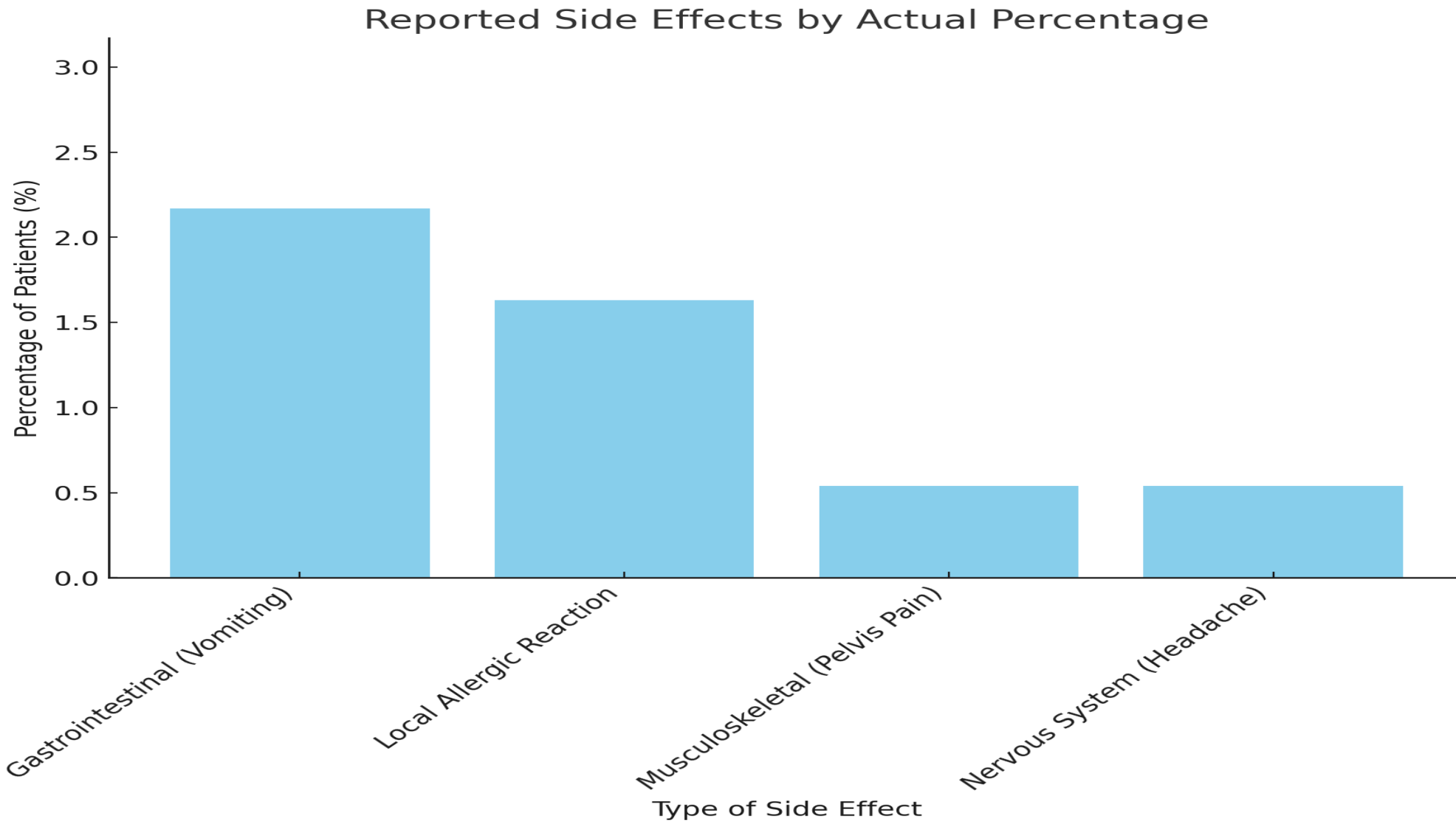


# Reported Adverse Medical Events

- The overall incidence of side effects was low, affecting just 4.89% of patients.
- The most common side effects were gastrointestinal issues (vomiting, 2.17%) and local allergic reactions (1.63%), with isolated cases of musculoskeletal pain & headaches (0.54% each).

# Reported Adverse Events

Side Effects	Pooled (Count)	Naive Patients (Count)	Switched Patients (Count)
No. of exposed patients	184	124	60
All events	9	7	2
Serious events	0	0	0
Severity			
Mild events	5	4	1
Moderate events	4	3	1
Severe events	0	0	0



# Conclusions

- **Clinical Efficacy:** Over the 72 weeks, patients demonstrated significant improvements in HV and IGF-1 levels, similar to results seen with daily GH treatments.
  - The study's outcomes align with broader evidence supporting somapacitan as an effective long-term therapy for GHD.
- **Safety Profile:** Adverse events were minimal and in line with expectations for GH therapy, with no new safety signals identified during the study period.
  - This safety profile confirms the global data supporting the use of somapacitan in pediatric populations.
- **Patient Compliance:** The reduced frequency of injections likely contributed to better adherence, an important factor in achieving optimal growth outcomes in children with GHD.

