THERAPEUTIC ADVANCES in
Endocrinology and Metabolism

Plain Language Summary of Publication

Comparing the efficacy and safety of weekly somatrogon with daily somatropin to treat children with growth hormone deficiency: a plain language summary of publication

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Summary

- The efficacy of weekly **somatrogon** injections was no different from that of daily **somatropin** injections to treat children who don't make enough growth **hormone** to grow adequately.
  - Efficacy refers to how well a drug works in a clinical trial.
  - Children treated with weekly **somatrogon** had an increased growth rate, similar to that of children treated with daily **somatropin**.
- The safety of weekly **somatrogon** injections was similar to that of daily **somatropin** injections.

How to say...

- **Somatrogon** <Soh-MA-troh-gon>
- **Somatropin** <Soh-MA-troh-pin>
- **Hormone** <HOR-mone>

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The original scientific article on which this summary is based was published in *The Journal of Clinical Endocrinology & Metabolism* and can be accessed for free at: https://academic.oup.com/jcem/article/107/7/e2717/6566444. **The details of the original article are as follows:** *Cheri L. Deal, Joel Steelman, Elpis Vlachopapadopoulou, Renata Stawerska, Lawrence A Silverman, Moshe Phillip, Ho-Seong Kim, CheolWoo Ko, Oleg Malievskiy, Jose F. Cara, Carl L. Roland, Carrie Turich Taylor, Srinivas Rao Valluri, Michael P. Wajnrajch, Aleksandra Pastrak, and Bradley S. Miller.* Efficacy and safety of weekly **somatrogon** vs daily **somatropin** in children with growth **hormone** deficiency: a phase 3 study. *J Clin Endocrinol Metab* 2022; 107(7): e2717–e2728.

The purpose of this plain language summary is to help you to understand the findings from recent research.

- **Somatrogon** is used to treat growth **hormone** deficiency (the condition under study that is discussed in this summary). Approval varies by country; please check with your local healthcare provider for more details.
- The results of this study may differ from those of other studies. Physicians/providers should make treatment decisions based on all available evidence and not on the results of a single study.

Keywords: growth **hormone**, growth **hormone** deficiency, **somatrogon**, **somatropin**

What did this study look at?

What is growth hormone deficiency?

- Children with growth **hormone** deficiency (GHD for short) don't make enough growth **hormone** to grow adequately.
  - Growth **hormone** is a chemical messenger that the body needs to grow.
  - An important way that growth **hormone** works is by getting the body to produce more of another **hormone** called insulin-like growth factor 1 (IGF-1 for short).
  - Growth **hormone** and IGF-1 work together to cause the body to grow taller.
  - Children with GHD grow more slowly than children with normal levels of growth hormone.
  - If not treated, children with GHD do not reach an optimal adult height.

What is somatropin?

- **Somatropin** (sold by Pfizer under the brand name Genotropin) is a type of human growth **hormone** that is made in a laboratory.
  - It has been used as a treatment for GHD for more than 30 years.
  - **Somatropin** treatment can increase the growth rate of children with GHD, allowing them to reach an optimal adult height.
  - It needs to be injected under the skin every day because the body gets rid of **somatropin** quickly.
    - These injections are usually done at home by the child or their parents/caregivers.
  - Despite being prescribed **somatropin** treatment, some children with GHD do not reach a normal height as adults.
    - This could be caused by children missing some of their **somatropin** injections.
    - For **somatropin** treatment to be effective, parents/caregivers must make sure children take all their growth **hormone** injections, which means injections must be given every day.
  - Some children with GHD and their parents or caregivers feel that having **somatropin** injections every day is a physical and emotional burden. This is because they think that injections:
    - can be painful and sometimes cause bruising/bleeding; and
    - interfere with everyday life and activities.

What is somatrogon?

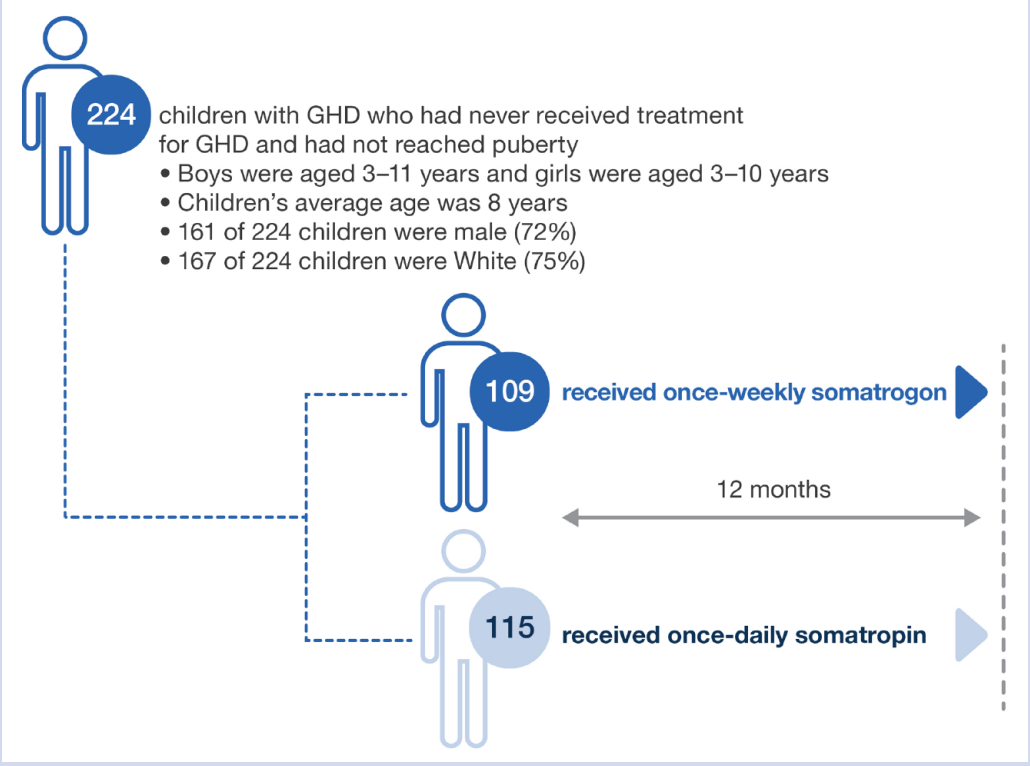
- **Somatrogon** is a recently developed treatment for children with GHD and has been approved in several countries.
  - **Somatrogon** is a long-acting growth **hormone**, so it works in the body for longer than **somatropin**.
  - **Somatrogon** only needs to be injected once a week, which means that people with GHD may be less likely to miss injections.

What was the purpose of this study?

- In this study, researchers compared the efficacy and safety of once-weekly **somatrogon** with once-daily **somatropin** in children with GHD.
  - Efficacy is how well a drug works in a clinical trial.
- To understand the efficacy of both treatments, researchers looked at:
  - how fast the children grew after 6 and 12 months of treatment (also known as height velocity); and
  - the height of the children receiving treatment compared to the average height of children without GHD (these children were the same age and sex as those being treated).
- Researchers also looked at:
  - whether the children's bones were developing at the right speed for their age (also known as bone maturation); and
  - whether treatment increased IGF-1 in the body to normal levels or above normal levels.

Who took part in this study?

- This study was carried out from December 2016 to August 2019 at 83 centers in 21 countries (Argentina, Australia, Belarus, Bulgaria, Canada, Colombia, Georgia, Greece, India, Israel, the Republic of Korea, Mexico, New Zealand, Poland, the Russian Federation, Spain, Taiwan, Turkey, Ukraine, the UK, and the USA).
  - Children were randomly placed in either the once-weekly **somatrogon** group or the once-daily **somatropin** group, where they received that treatment for 12 months.



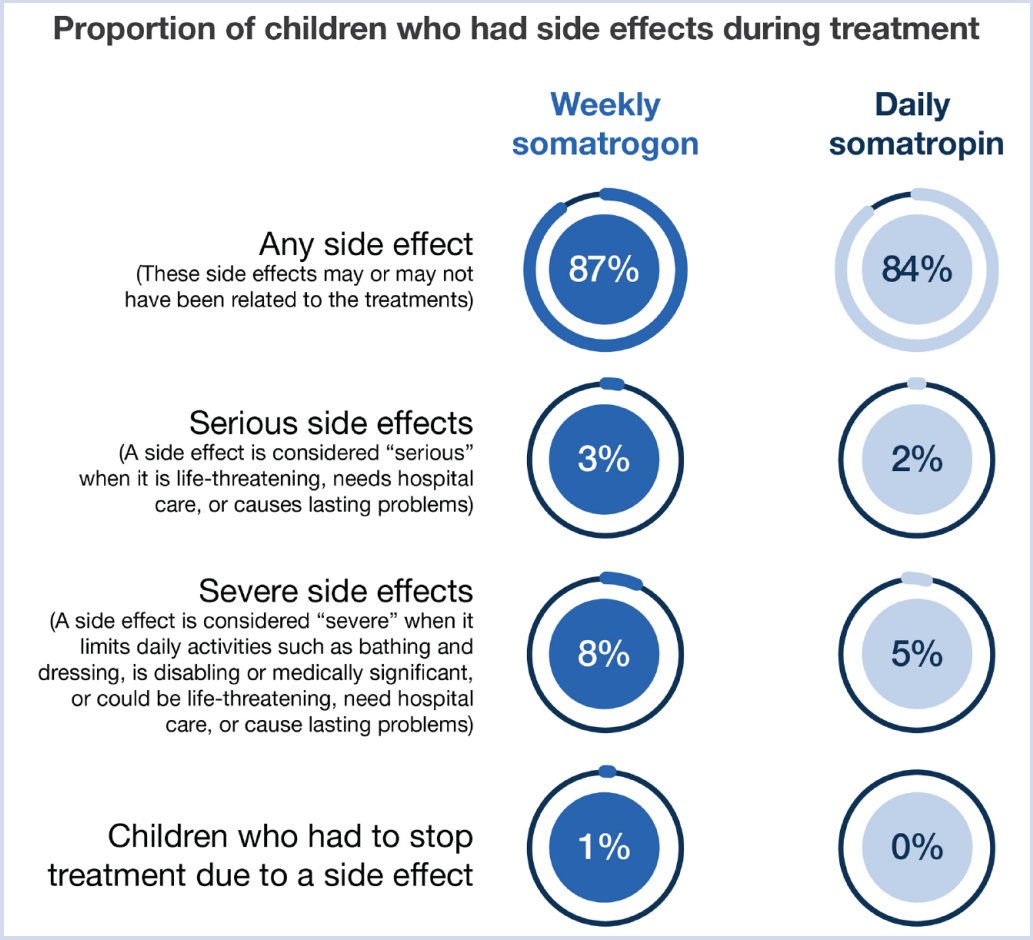
What were the results of the study?

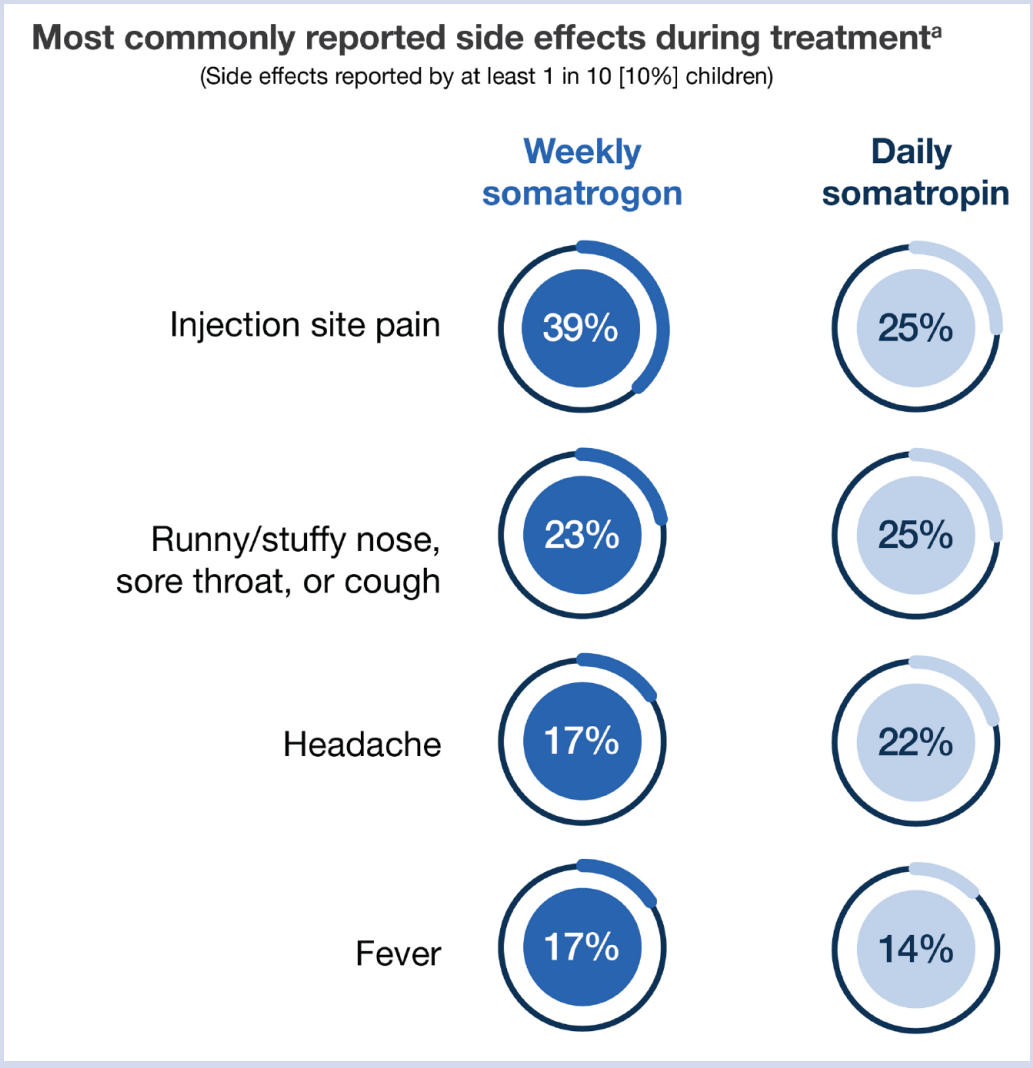
Efficacy

- After 12 months, children who had weekly **somatrogon** injections grew as quickly as children who had daily **somatropin** injections.
  - Both groups had an average height velocity of about 10 centimeters a year (or 4 inches a year).
  - The two treatments resulted in a similar growth rate (how quickly the children grew).
    - Based on this, the researchers concluded that the efficacy of weekly **somatrogon** injections was no different from that of daily **somatropin** injections for children with GHD.
- Children who had weekly **somatrogon** injections were similar to children who had daily **somatropin** injections in terms of:
  - how quickly they grew after 6 months of treatment;
  - how much closer they got to the average height (for their age and sex) after 6 and 12 months of treatment; and
  - how quickly their bones developed for their age.
- At the start of the study, children with GHD had IGF-1 levels that were much lower than the average level for children without GHD.
  - One month after having weekly **somatrogon** injections, children with GHD reached IGF-1 levels that were close to the average level.
  - After 12 months of treatment, the children's IGF-1 levels were slightly higher than average but were still within the normal range.
  - Children who had daily **somatropin** injections reached IGF-1 levels that were close to the average level between the first month and the end of the study.

Safety

- The percentage of children who experienced side effects was similar in both treatment groups.
  - A side effect is something (expected or unexpected) that happened after the treatment started.
  - These side effects may or may not have been related to the treatments received.
- Most of the side effects were mild or moderate in intensity.
- Of the 224 children in the study, none died during the study and one child stopped treatment due to side effects (redness and thickening of the skin where the injection was).
- Most cases of injection site pain reported by children were mild or moderate in intensity.
  - The number of children who reported injection site pain decreased over time.


Proportion of children who had side effects during treatment
Weekly somatrogon
Daily somatropin
Any side effect
(These side effects may or may not have been related to the treatments)
87%
84%
Serious side effects
(A side effect is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems)
3%
2%
Severe side effects
(A side effect is considered "severe" when it limits daily activities such as bathing and dressing, is disabling or medically significant, or could be life-threatening, need hospital care, or cause lasting problems)
8%
5%
Children who had to stop treatment due to a side effect
1%
0%


Most commonly reported side effects during treatment[a]
(Side effects reported by at least 1 in 10 [10%] children)
Weekly somatrogon
Daily somatropin
Injection site pain
39%
25%
Runny/stuffy nose, sore throat, or cough
23%
25%
Headache
17%
22%
Fever
17%
14%

What were the main conclusions reported by the researchers?

- The efficacy of weekly **somatrogon** injections was no different from that of daily **somatropin** injections in treating children with GHD.
- Children with GHD who were treated with weekly **somatrogon** had an increased growth rate, similar to that of children treated with daily **somatropin**.
  - Children in this study generally had IGF-1 levels in the normal range and their bones developed at a normal rate for their age.
- The safety of weekly **somatrogon** was similar to that of daily **somatropin**.
- Since **somatrogon** is injected less often than **somatropin** (once a week compared to once a day), children treated with **somatrogon** may be less likely to miss injections and may have a better quality of life.

Who sponsored this study?
This study was sponsored by OPKO Health.

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OPKO Health and Pfizer would like to thank all of the people who took part in this study.

Declarations

Ethics approval and consent to participate
As described in the original publication, the study was conducted in accordance with the International Conference on Harmonisation Guideline for Good Clinical Practice and the Declaration of Helsinki and was registered on ClinicalTrials.gov (NCT02968004). The study protocol was approved by the institutional review board and/or independent ethics committee of the participating study centers. Parents or guardians of each patient provided signed, informed, written consent before any study procedures were started.

Consent for publication
Not applicable.

Author contributions
Cheri L. Deal: Investigation; Writing – original draft; Writing – review & editing.

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Renata Stawerska: Investigation; Writing – original draft; Writing – review & editing.

Lawrence A. Silverman: Investigation; Supervision; Validation; Writing – original draft; Writing – review & editing.

Moshe Phillip: Investigation; Writing – original draft; Writing – review & editing.

Ho-Seong Kim: Investigation; Writing – original draft; Writing – review & editing.

CheolWoo Ko: Investigation; Writing – original draft; Writing – review & editing.

Oleg Malievskiy: Investigation; Writing – original draft; Writing – review & editing.

Jose F. Cara: Investigation; Writing – original draft; Writing – review & editing.

Carl L. Roland: Investigation; Writing – original draft; Writing – review & editing.

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Srinivas Rao Valluri: Formal analysis; Writing – original draft; Writing – review & editing.

Michael P. Wajnrajch: Investigation; Writing – original draft; Writing – review & editing.

Aleksandra Pastrak: Investigation; Supervision; Validation; Writing – original draft; Writing – review & editing.

Bradley S. Miller: Investigation; Writing – original draft; Writing – review & editing.

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Competing interests

C.L.D. is a consultant for Ascendis Pharma, EMD Serono, Novo Nordisk, Pfizer, Poxel, Lumos Pharma, Neurocrine Science, Levo, and Merck KGaA, and has participated in clinical trials sponsored by OPKO/Pfizer and Levo. E.V. is a principal investigator for clinical trials sponsored by Ascendis, OPKO, and Amgen and has participated in advisory boards for Ascendis, Novartis, and Pfizer. R.S. is a principal investigator for clinical trials sponsored by Ascendis and OPKO and has received research support from OPKO, Sandoz, and Pfizer. B.S.M. is a consultant for AbbVie, Ascendis Pharma, BioMarin, EMD Serono, Novo Nordisk, Orchard Therapeutics, Pfizer, Sandoz, Tolmar, and Vertice Pharma, and has received research support from Alexion, AbbVie, Amgen, Lumos Pharma, Novo Nordisk, OPKO, and Pfizer. L.A.S. has been an advisory board member for Pfizer and Ascendis, has received consulting fees from OPKO and Pfizer and has been an advisor and researcher for Novo Nordisk. M.P.'s institution has received research grants from OPKO. J.F.C., C.L.R., C.T.T., S.R.V., and M.P.W. are employees and stockholders of Pfizer. A.P. is an employee and stockholder of OPKO. J.S., H.S.K., C.W.K., and O.M. have no conflicts of interest to declare.

Availability of data and materials

Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.