IGF-1 Monitoring During Growth Hormone Treatment in Children with GHD

Rationale behind IGF-1 monitoring:
During rhGH treatment, reliable IGF-1 monitoring is valuable for assessing efficacy and safety, evaluating adherence and ensuring correct dosage[1]

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IGF-1 levels can be used in conjunction with other clinical parameters, like height velocity, **to measure efficacy and safety of rhGH therapy**[2–4]

IGF-1 SDS is the preferred measure of serum IGF-1 levels, values should remain in the normal range, between:[5–7]
-2 and +2 SDS

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Despite the difference in IGF-1 profiles across daily rhGH and LAGH products, efficacy and safety outcomes are similar[8]

When monitoring mean IGF-1 levels, samples should be collected at **4 days post-somatrogon injection**[2]

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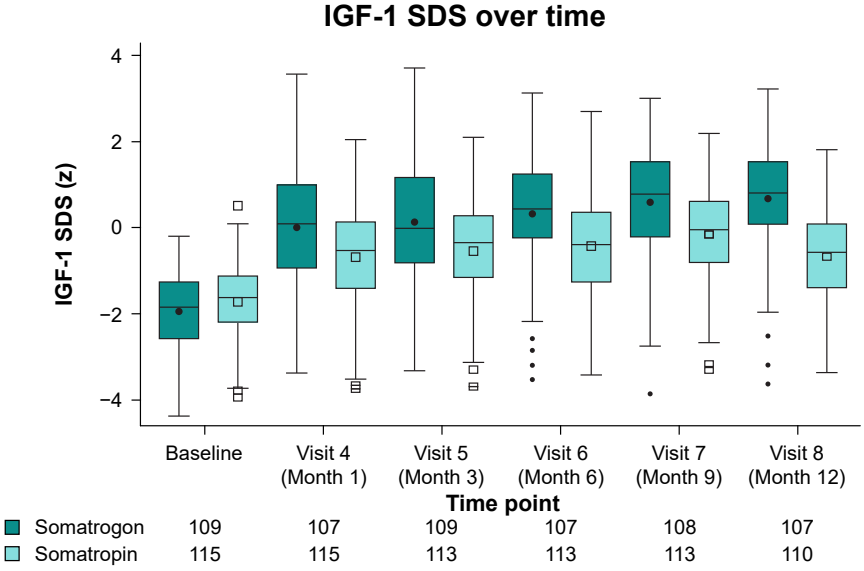
Despite the difference in IGF-1 profiles following injection with either daily rhGH or somatrogon, efficacy and safety outcomes are similar for both[8,9]

12-month Phase 3 study[9]



The mean IGF-1 SDS in the **somatrogon** group was:
- At baseline was **−1.95**
- After month 1, approached 0
- After 12 months was **0.65** (range **−3.64 to 3.22**)

The mean IGF-1 SDS in the **somatropin** group was:
- At baseline was **−1.72**
- Across the 12 months, remained near 0 (range **−0.69 to −0.16**)

−2 **+2**

IGF-1 SDS

For up to 5 years, patients treated with **somatrogon** had a mean IGF-1 SDS that remained between **−2 and +2**

Phase 2 OLE study[10]

	Total year 1 (N=48)	Year 2 (N=44)	Year 3 (N=43)	Year 4 (N=38)	PEN (N=40)
IGF-1 SDS (Z) at end of year					
n	43	41	38	1	35
Mean, SD	0.64 (0.96)	0.65 (1.08)	1.05 (0.82)	0.29 (-)	1.29 (0.81)
Median	0.58	0.68	1.09	0.29	1.25
Minimum, maximum	-1.66, 2.64	-2.23, 2.69	-0.96, 2.92	0.29, 0.29	-0.34, 2.71

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Figures were adapted from Deal CL et al. 2022[9] and Ngenla, Prescribing information, Israel.[2]
BMI, body mass index; CI, confidence interval; GHD, growth hormone deficiency; IGF-1 insulin-like growth factor 1; LAGH, long acting growth hormone; LSM, least square mean; OLE, open label extension; PEN, somatrogon delivery via a prefilled pen device; rhGH, recombinant human growth hormone; SD, standard deviation; SDS, standard deviation score.

1. Kildemoes RJ et al. *J Clin Endocrinol Metab* 2021;106:567–576; 2. Ngenla, Prescribing information, Israel.; 3. Chong YM et al. *Anticancer Res* 2007;27:1617–1624; 4. Laron Z. Mol Pathol 2001;54:311–316; 5. Blum WF et al. *Endocr Connect* 2018;7:R212–R222; 6. Kos S et al. *Eur J Endocrinol* 2019;181:L1–L4; 7. Chanson P et al. *J Clin Endocrinol Metab* 2016;101:3450–3458; 8. Bidlingmaier M et al. *J Clin Endocrinol Metab* 2021;106:e2367–e23694; 9. Deal CL et al. *J Clin Endocrinol Metab.* 2022;107:e2717–e2728; 10. Zadik Z et al. *J Pediatr Endocrinol Metab* 2023;36:261–269.

March 2024 EM-ISR-SMA-0020

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12-month Phase 3 study[2]

Efficacy of **once-weekly somatrogon** was **non-inferior** to **once-daily somatropin** based on height velocity at 12 months

Efficacy of somatrogon compared to somatropin in paediatric patients with GHD at month 12

Treatment parameter	Treatment group		LSM difference (95% CI)
	Somatrogon (N=109)	Somatropin (N=115)	
	LSM estimate	LSM estimate	
Height velocity (cm/year)	10.10	9.78	0.33 (-0.24, 0.89)
Height standard deviation score	−1.94	−1.99	0.05 (-0.06, 0.16)
Change in height standard deviation score from baseline	0.92	0.87	0.05 (-0.06, 0.16)

Somatrogon and IGF-1 Monitoring in Clinical Practice[2]

Somatrogon dose may be adjusted as necessary, based on:[2]

- Growth velocity
- Body weight
- Adverse reactions
- Serum IGF-1 levels

Refer to the summary of product characteristics for more information on dose adjustment protocols[2]

IGF-1 levels in the clinic[2]

To determine mean IGF-1 SDS levels, IGF-1 samples should be drawn on **day 4 after dose administration**

Some patients may require **>1 dose reduction**

Target dose adjustments to achieve average IGF-1 SDS levels between **−2 and +2**

When IGF-1 concentrations exceed the mean reference value by > 2 SDS, **reduce dose by 15%**

← PREVIOUS

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Rationale Behind IGF-1 Monitoring

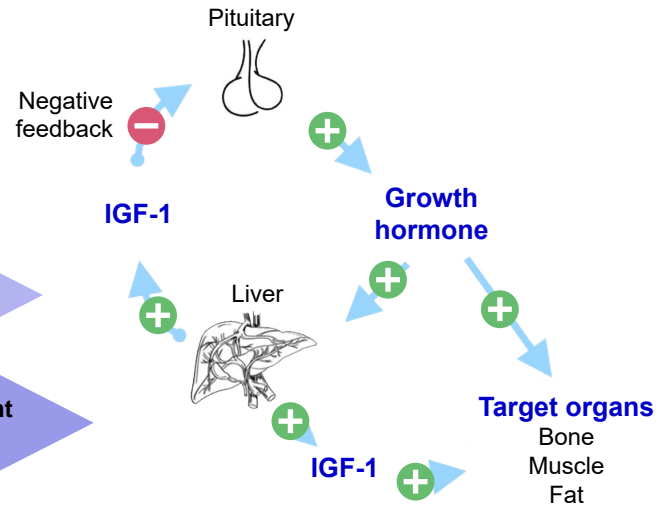
Growth hormone acts via the GH/IGF-1 axis to increase production of IGF-1[1–3]

Together, GH and IGF-1 stimulate metabolic changes and trigger growth[1–3]

rhGH will increase serum levels of IGF-1 via the same GH/IGF-1 axis[1,3]

IGF-1 levels increase in a dose-dependent manner during rhGH treatment[1]

The GH/IGF-1 axis[2,3]



IGF-1 levels are an indicator for bioavailable GH, therefore, can be used in conjunction with other clinical parameters, like height velocity, to measure efficacy and safety of rhGH therapy[1–3]

IGF-1 testing is essential to:

- **Adjust rhGH treatment dosing, to optimise efficacy and manage adverse events**[4]
- **Follow adherence and long-term safety of rhGH treatment**[4,5]
- **Assess GH status to help predict response to rhGH therapy in individual patients**[5]

Figure adapted from Chong YM et al. 2007.[2]
GH, growth hormone; IGF-1, insulin-like growth factor 1; rhGH, recombinant human growth hormone.

1. Ngenla, Prescribing information, Israel; 2. Chong YM et al. *Anticancer Res* 2007;27:1617–1624; 3. Laron Z. *Mol Pathol* 2001;54:311–316; 4. Kildemoes RJ et al. *J Clin Endocrinol Metab* 2021;106:567–576; 5. Blum WF et al. *Endocr Connect* 2018;7:R212–R222.

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Measuring IGF-1 in Practice

IGF-1 SDS is the preferred measure of IGF-1[1]

Multiple factors can affect serum IGF-1 measurements, including:[1–3]

Age

BMI

Other endocrine hormones

Nutritional status

Methodology

IGF-1 concentrations are often measured using commercially available immunoassay kits[1]

Measuring IGF-1 SDS accounts for factors that can affect IGF-1 concentrations like:[2,3]

- Age
- Gender
- Pubertal stage

–2 to +2
(50th percentile=0)

is the normal range in which IGF-1 SDS values should reside[1]

BMI, body mass index; IGF-1, insulin-like growth factor 1; SDS, standard deviation score.

1. Blum WF et al. *Endocr Connect* 2018;7:R212–R222; 2. Kos S et al. *Eur J Endocrinol* 2019;181:L1–L4; 3. Chanson P et al. *J Clin Endocrinol Metab* 2016;101:3450–3458.

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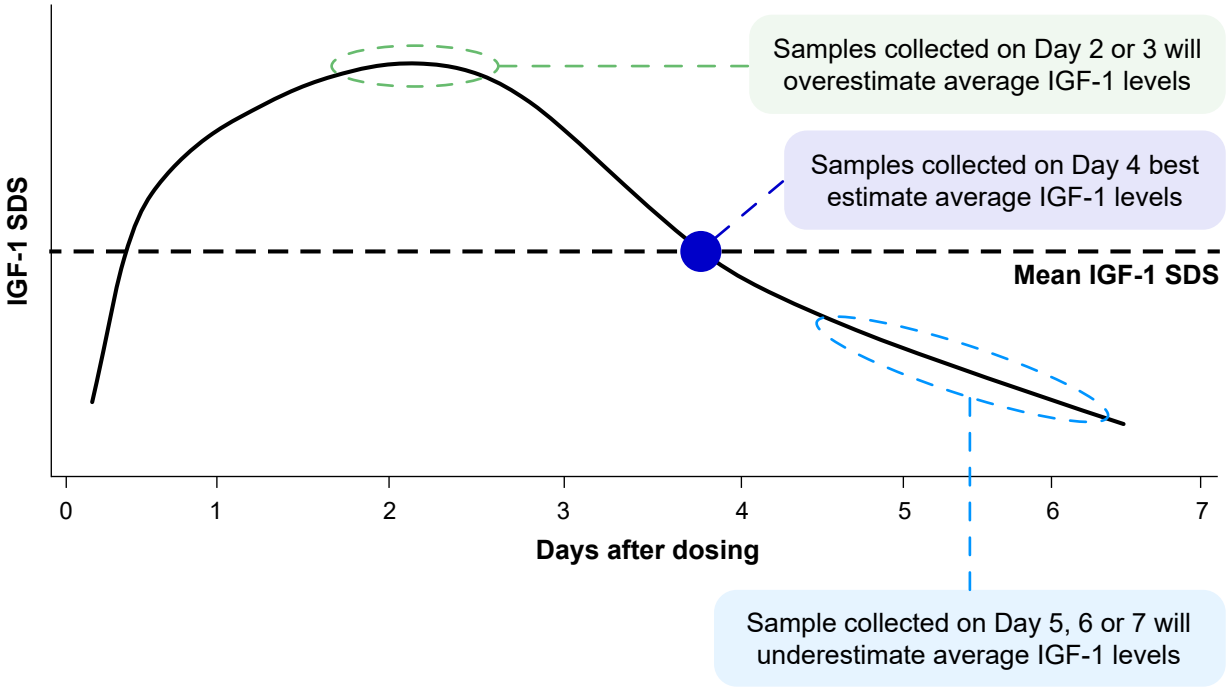
IGF-1 Samples Should be Drawn on Day 4 After Dose Administration[1–5]

Conceptual Representation of Somatorogon PD Profile[1,3]



Samples drawn outside of Day 4 should be interpreted with caution[3]

IGF-1, insulin-like growth factor 1; PD, pharmacodynamic; SDS, standard deviation score.

1. Fisher DM et al. *Horm Res Paediatr* 2017;87:324–332; 2. Fisher DM et al. *J Endocr Soc* 2020;4:A255–A256; 3. Bidlingmaier M et al. *J Clin Endocrinol Metab* 2021;106:e2367–e2369; 4. Deal CL et al. *J Clin Endocrinol Metab* 2022;107:e2717–e-2728; 5. Ngenla, Prescribing information, Israel.

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