Weekly Somatrogon Practicalities in Interpreting IGF-1

This interactive document is intended to provide guidance in interpreting IGF-1 values when using the Long Acting Growth Hormone Somatrogon. For more information, contact your Pfizer medical contact.

Somatrogon is a fusion protein of rhGH and and 3 copies of the carboxy-terminal peptide (CTP) of human chorionic gonadotropin[1,2]

Click here to learn more

Reliable IGF-1 monitoring, in conjunction with other clinical parameters, is valuable to measure **efficacy and safety** of rhGH therapy[3-6]

Click here to learn more

IGF-1 SDS is the preferred measure of serum IGF-1 levels; values should remain in the normal range, between.[2,7-9]
-2 and +2 SDS

Despite the difference in **IGF-1 profiles** across daily rhGH and LAGH products, efficacy and safety outcomes are similar[10,11]

The best estimate of mean IGF-1 level is represented by the level on day **4** post- somatrogon injection[4,10,11]
An **IGF-1 estimation table** is available to estimate the mean IGF-1 from samples **drawn on other days**[12]

Click here to learn more

- LAGH has a significantly different PD profile from Daily GH: IGF-1 profile fluctuations are greater with LAGH. Despite this difference, efficacy and safety outcomes are similar for both.[10,11]
- Random IGF-1 levels may not be representative of the average IGF-1 exposure.[3,4,10,11]

Conceptual representation of the Somatrogon PD model [3,4]

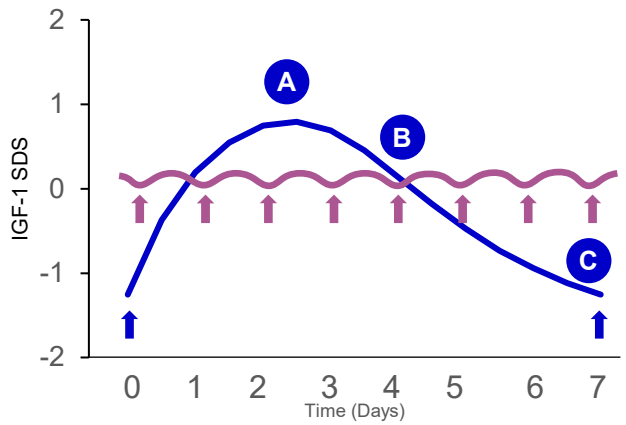
Peak IGF-1 level occurs at Day 2 post dose;
Mean IGF-1 level over the dosing interval occurs at Day 4 post dose.

A **Day 2**: Samples collected here will overestimate average IGF-1

B **Day 4** Samples collected best estimate average IGF-1

C **Day 5-7**: Samples collected will underestimate average IGF-1

For up to 5 years, patients treated with Somatrogon generally had a mean IGF-1 SDS that remained between −2 and +2[10].



PD= Pharmacodynamic; LAGH = Long Acting Growth Hormone; CI, confidence interval; GHD, growth hormone deficiency; IGF-1 insulin-like growth factor 1.
1. Deal CL et al. *J Clin Endocrinol Metab.* 2022;107:e2717–e2728. 2. Somatrogon injection [summary of product characteristics]. LPDGEN012023 3. Kildemoes RJ et al. *J Clin Endocrinol Metab* 2021;106:567–576; 4. Fisher et al. *Horm Res Paediatr* 2017;87:324–332 5. Chong YM et al. *Anticancer Res* 2007;27:1617–1624; 6.Laron Z. Mol Pathol 2001;54:311–316; 7. Blum WF et al. *Endocr Connect* 2018;7:R212–R222; 8. Kos S et al. *Eur J Endocrinol* 2019;181:L1–L4; 9. Chanson P et al. *J Clin Endocrinol Metab* 2016;101:3450–3458;10. Bidlingmaier M et al. *J Clin Endocrinol Metab* 2021;106:e2367–e23694 11. Zadik Z et al. *J Pediatr Endocrinol Metab* 2023;36:261–269. March 2024.
12. Pfizer Data on File REFSMT1303, PFIZER Inc. March 2024.

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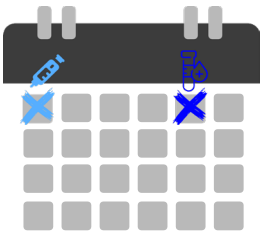
Somatrogon and IGF-1 Monitoring in Clinical Practice[2]

- Day 4 post dose is recommended[3]



If IGF-1 sampling occurs on an alternate day, use the **IGF-1 Estimation Table[4]**

- The IGF-1 Estimation table has been developed to predict mean IGF-1 and IGF-1 SDS values based on IGF-1 measurement at different timepoints during the dosing interval following Somatrogon treatment[4]

- **How to use the table[4]**
  - A Table of Adjustments required to calculate Mean IGF-1 SDS and IGF-1 has been developed.
  - The calculation formula to use depends on the time since last dose and is specified in the column, for mean IGF-1 SDS and IGF-1, respectively

Practical example of calculation

1. Fisher DM, et al. *Horm Res Paediatr*. 2017;87:324-332. **2.** Deal C, et al. *J Clin Endocrinol Metab*. 2022;107:e2717-e2728.
3. somatrogon injection [summary of product characteristics]. LPDGEN012023. 4. Pfizer Data on File REFSMT1303, PFIZER Inc. 2024

Summary of Adjustments required to Calculate Mean IGF-1 SDS and IGF-1

Interval (time after dose)	Adjustment to measured IGF-1 SDS to approximate mean IGF-1 SDS	Adjustment to measured IGF-1 to approximate mean IGF-1
>0 - 12 hours	IGF-1 SDS **+ 1.8**	IGF-1 (ng/mL) **x 2**
>12- 24 hours	IGF-1 SDS **+ 0.7**	IGF-1 (ng/mL) **x 1.3**
>24- 36 hours	IGF-1 SDS **- 0.1**	IGF-1 (ng/mL) **x 1**
>36 - 48 hours	IGF-1 SDS **- 0.5**	IGF-1 (ng/mL) **x 0.8**
>48- 60 hours	IGF-1 SDS **- 0.7**	IGF-1 (ng/mL) **x 0.8**
>60- 72 hours	IGF-1 SDS **- 0.7**	IGF-1 (ng/mL) **x 0.8**
>72- 84 hours	IGF-1 SDS **- 0.6**	IGF-1 (ng/mL) **x 0.8**
>84- 96 hours	IGF-1 SDS **- 0.3**	IGF-1 (ng/mL) **x 0.9**
>96 - 108 hours	No Adjustment	No Adjustment
>108 - 120 hours	IGF-1 SDS **+ 0.4**	IGF-1 (ng/mL) **x 1.1**
>120 - 132 hours	IGF-1 SDS **+ 0.7**	IGF-1 (ng/mL) **x 1.3**
>132 - 144 hours	IGF-1 SDS **+ 1.1**	IGF-1 (ng/mL) **x 1.5**
>144 - 156 hours	IGF-1 SDS **+ 1.4**	IGF-1 (ng/mL) **x 1.7**
>156 - <168 hours	IGF-1 SDS **+ 1.6**	IGF-1 (ng/mL) **x 1.9**

ADA=anti-drug antibody; IGF-1=insulin-like growth factor 1; PD=pharmacodynamic; PI, prediction interval; PK=pharmacokinetic; SDS=standard deviation score.

Pfizer Data on File REFSMT1303, PFIZER Inc. March 2024

Example: Correcting for a Day 2 sample

- Injection was given on a **Sunday at 4 pm** (Day 0)
- Blood sample was taken on **Tuesday, at 9 am**(day 2, >36 - 48 hours)
- IGF-1 SDS **observed** value was 1.27

  - The summary table gives adjustment formula of : **IGF-1 SDS - 0.5**

  - **The mean IGF-1 SDS calculated** from the sample drawn on day 2 was: 1.27 – 0.5 = **0.77**

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IGF-1=insulin-like growth factor 1; SDS=standard deviation score. Pfizer Data on File REFSMT1303, PFIZER Inc. March

Somatrogon is a fusion protein of hGH and 3 copies of the carboxy-terminal peptide (CTP) of human chorionic gonadotropin[1,2]

Clinical trials showed non inferiority of Somatrogon at a dose of 0.66 mg/kg/week versus daily somatropin at a dose of 0.034 mg/kg/day in Height Velocity at 12 month[1]

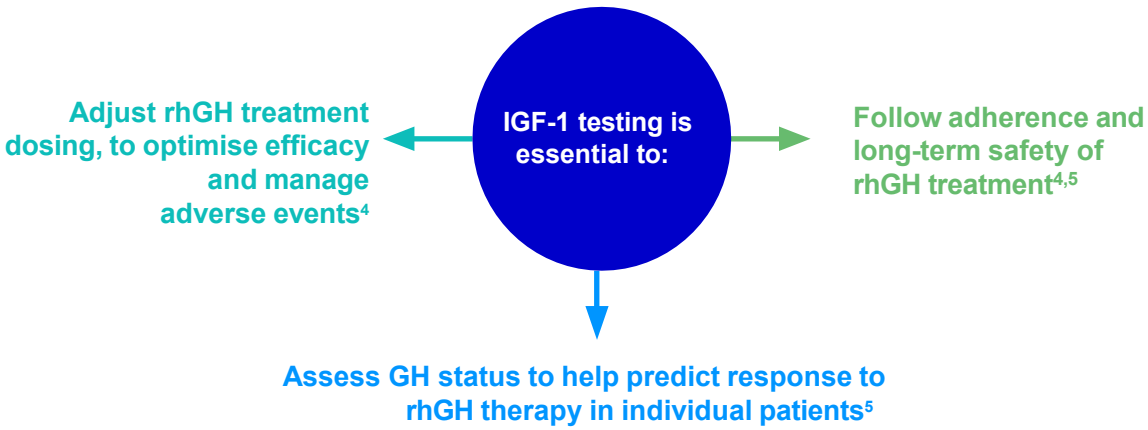
12 month phase 3 study

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 is a human growth hormone analog indicated for treatment of pediatric patients aged 3 years and older who have growth failure due to inadequate secretion of endogenous growth hormone[1,2]

1, . Deal CL et al. *J Clin Endocrinol Metab.* 2022;107:e2717–e2728. 2 Somatrogon injection [summary of product characteristics]. LPDGEN012023

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



−2 to +2
(50th percentile=0)

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

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GH, growth hormone; IGF-1, insulin-like growth factor 1; rhGH, recombinant human growth hormone.

1.Somatrogon injection [summary of product characteristics]. LPDGEN012023; 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.