Practical Management of Pediatric Growth Hormone Deficiency With Lonapegsomatropin-tcgd

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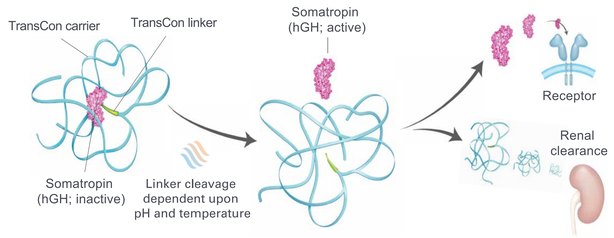
BACKGROUND

- Lonapegsomatropin-tcgd (SKYTROFA®; TransCon® human growth hormone [hGH]), a prodrug of somatropin, is the first FDA-approved once-weekly treatment indicated for children ≥ 1 year of age who weigh ≥ 11.5 kg with growth hormone deficiency (GHD; **Figure 1**)[1]
- Efficacy and safety evaluated in three phase 3 clinical trials: heiGHt trial in treatment-naïve participants, fliGHt trial in participants previously treated with daily somatropin, and enliGHten open-label extension trial[2-4]
  - Pivotal phase 3 heiGHt trial: lonapegsomatropin-tcgd was noninferior to daily somatropin
    - Annualized height velocity (least squares mean): 11.2 (lonapegsomatropin-tcgd) vs 10.3 (daily somatropin) cm/year; $P = 0.009$
    - Demonstrated a comparable safety profile[4]
  - Lonapegsomatropin-tcgd adverse event (AE) profile, similar to daily somatropin:[2-4]
    - Consistent across phase 3 studies and the majority were categorized as mild or moderate and unrelated to study drug
    - No serious treatment-emergent AEs (TEAEs) related to study drug
    - Low rates of injection site reactions and immunogenicity
  - Most common TEAEs (enliGHten through week 104): upper respiratory tract infection (21.1%), nasopharyngitis (11.1%), cough (8.7%), and pyrexia (8.4%)[2]

Figure 1. Lonapegsomatropin-tcgd (TransCon® hGH) Design[4,5]



- Lonapegsomatropin is a prodrug of somatropin with once-weekly administration and designed to provide sustained release of active, unmodified somatropin
- The unmodified, unbound somatropin released from lonapegsomatropin has the identical 191 amino-acid sequence and size (22 kDa) as endogenous growth hormone

Table 1. Top Reason for Preference of Once-Weekly Lonapegsomatropin-tcgd vs Daily Somatropin in the fliGHt Trial[3]

Top 3 Reasons for Preference (most important in bold):

Child (n = 99)	Parent / Caregiver (n = 142)
• **How often I need to get injections**	• **How often my child needs to get injections**
• Less annoyed by the injections	• Less interference with my child's activities
• Less interference with my activities	• Less interference with my activities

Participants ≥ 9 years old at the time of enrollment and their parents completed the Preference Questionnaire–Child and the Preference Questionnaire–Parent, respectively, at Weeks 6 and 13.Treatment preference (PQ-C and PQ-P) at week 13 are shown here.

- Once-weekly lonapegsomatropin-tcgd was preferred vs daily somatropin injection (84% of children and 90% of caregivers in the fliGHt trial; **Table 1**)[3]
- 94% of participants rated the lonapegsomatropin-tcgd Auto-Injector device as easy to use in the enliGHten trial[2]

UNMET NEEDS IN PEDIATRIC GHD TREATMENT

- Daily somatropin has been the standard of care for decades, but poor adherence is associated with suboptimal growth outcomes[7]
- Burdens of daily injections in pediatric GHD include:[8,9]
  - Difficulty using injection devices
  - Pain and/or bruising with injection
  - Child's aversion to injection
  - Interference with daily life

PURPOSE

- Discuss practical techniques and clinical pearls for pediatric endocrinology nurses working with lonapegsomatropin-tcgd for the treatment of pediatric GHD

RESULTS

AUTO-INJECTOR USE

- Lonapegsomatropin-tcgd auto-injector provides a fully automated reconstitution of the lyophilized drug[1]
- Practice the auto-injector with the patient and caregiver in the clinic[11]
- Once the green top is pressed against the skin, the auto-injector will inject automatically[11]
- We recommend waiting 10 minutes after injection before checking for local reactions

IGF-1 MONITORING AND ESTIMATION

- Because lonapegsomatropin-tcgd is administered once-weekly, the IGF-1 profile differs from that of daily somatropin[12]
- To estimate average weekly IGF-1 with lonapegsomatropin-tcgd on any day following a prior dose, a predication curve and calculation has been developed (**Figure 2, 3**)[12]
  - Based on a single blood draw at any time after steady state (> 5th dose)[10,12]
  - We recommend scheduling a blood draw with enough time to make dose changes before next medication shipment
  - Calculate the average IGF-1 SDS using the time since last dose administration (to the nearest ½ day)[12]

Average IGF-1 SDS = measured IGF-1 SDS – correction factor

Figure 2. Average Weekly IGF-1 SDS Prediction Curve[12]

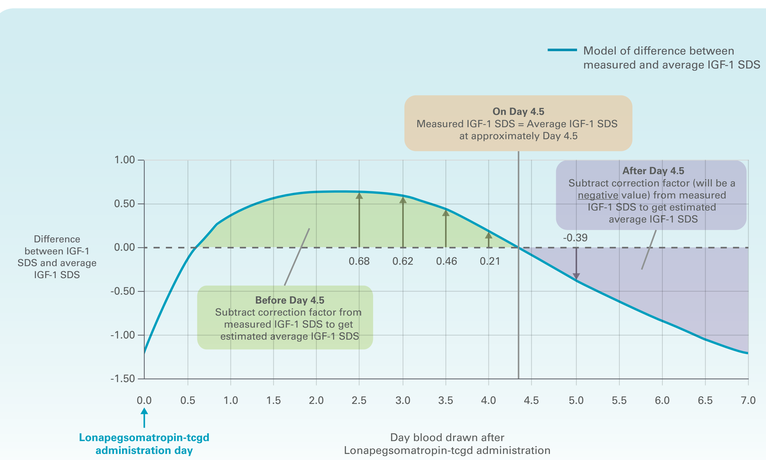


Figure 3. Average IGF-1 SDS Correction Factors[12] and Case Studies

Day	Correction Factor*	90% Prediction Interval†
0	–1.22	–1.80, -0.65
0.5	–0.12	–0.46, 0.22
1.0	0.39	–0.07, 0.86
1.5	0.60	0.16, 1.04
2.0	0.67	0.32, 1.02
2.5	0.68	0.43, 0.93
3.0	0.62	0.45, 0.78
3.5	0.46	0.33, 0.59
4.0	0.21	0.06, 0.36
4.5	**–0.09**	**–0.31, 0.13**
5.0	–0.39	–0.68, –0.09
5.5	–0.64	–1.01, –0.26
6.0	–0.85	–1.29, –0.42
6.5	–1.07	–1.57, –0.57
7.0	–1.22	–1.77, –0.68

Average IGF-1 SDS Calculation Case Study #1
- Patient injects on Sunday PM (Day 0)
- Blood is drawn on Wednesday AM (Day 2.5)
- Measured IGF-1 SDS is 2.0
- Correction factor at Day 2.5 is 0.68

1.32 average IGF-1 SDS = **2.0** measured IGF-1 SDS – **0.68** correction factor

Average IGF-1 SDS Calculation Case Study #2
- Patient injects on Wednesday PM (Day 0)
- Blood is drawn on Monday PM (Day 5.0)
- Measured IGF-1 SDS is 0.9
- Correction factor at Day 5.0 is -0.39

1.29 average IGF-1 SDS = **0.9** measured IGF-1 SDS – **-0.39** correction factor

*Correction factor represents the predicted difference between actual IGF-1 SDS and average IGF-1 SDS by time between dosing and blood draw. Predictions are most accurate between Days 2.5 and 5. Correction factors for average IGF-1 concentration are also available.[12]
†The 90% Prediction interval is the confidence interval for the correction factor.

LONAPEGSOMATROPIN-TCGD DOSING

- Recommended initial dose: 0.24 mg hGH/kg body weight, once-weekly[1]
- Weight-based dosing brackets determine cartridge (**Table 2**)[1]
  - Initial dose calculation is the same for treatment-naïve patients and those switching from daily somatropin[1]
    - Wait at least 8 hours between the final dose of daily somatropin and the first dose of once-weekly lonapegsomatropin-tcgd[1]
  - Lonapegsomatropin-tcgd demonstrated a predictable linear dose-response with average IGF-1 SDS[2,10]
    - Moving up or down one dose bracket corresponds to an average IGF-1 change of 0.3 SDS[2]
- To avoid missed doses, lonapegsomatropin-tcgd can be taken 2 days before or 2 days after the scheduled dosing day. Resume once-weekly dosing for the next dose at the previously scheduled dosing day[1]

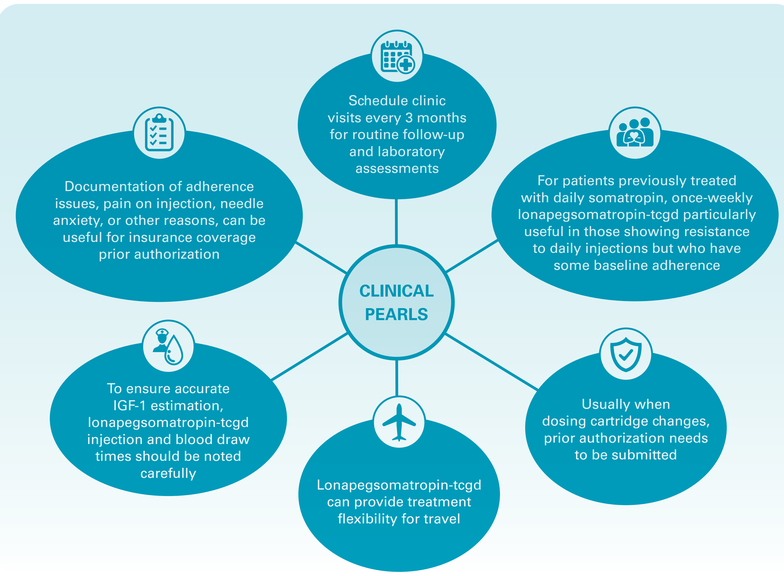
Table 2. Weight-based Dosing Brackets[1]

Weight (kg)	Cartridge(s) (mg hGH)	Weight (kg)	Cartridge(s) (mg hGH)
11.5 – 13.9	3.0	35.0 – 41.9	9.1
14.0 – 16.4	3.6	42.0 – 50.9	11.0
16.5 – 19.9	4.3	51.0 – 60.4	13.3
20.0 – 23.9	5.2	60.5 – 69.9†	7.6 x 2
24.0 – 28.9	6.3	70.0 – 84.9†	9.1 x 2
29.0 – 34.9	7.6	85.0 – 100†	11.0 x 2

Every cartridge dose corresponds to a unique color.
†Patients requiring a dose greater than the 13.3-mg cartridge will need to inject 2 cartridges per weekly dose. The **same dose strength must be used** for both doses in those patients requiring a double dose.[1]

CLINICAL IMPLICATIONS

Figure 4. Pediatric Endocrinology Nurses and Advanced Practitioners Play a Critical Role in the Multidisciplinary Management With Once-Weekly Lonapegsomatropin-tcgd Treatment



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