Gastrointestinal Drugs Advisory Committee

Questions for NDA 21-597, Serostim for SBS

1. The primary endpoint of this study was change in Total IPN volume from week 2 to week 6. Pairwise comparisons of results of the primary endpoint yielded statistically significant differences between the recombinant human growth hormone (rh-GH)-containing arms and the control group. Are the findings in the table below clinically meaningful? In your response consider the definition of the primary endpoint and the duration of study treatment.

Changes in Total IPN Volume

Mean Change in Total IPN Vol.			Difference in Total IPN Volume [L/wk] (p-value)	
Group A rhGH (n=16)	Group B rhGH + GLN (n=16)	Group C GLN (n=9)	Group B vs C	Group A vs C
-5.9	-7.7	-3.8	-3.9 (<0.001)	-2.1 (0.043)

Baseline IPN Requirements:
Group A: 10.3 L/wk
Group B: 10.5 L/wk
Group C: 13.5 L/wk

2. Secondary endpoints were change in Total IPN calories and change in IPN or lipid frequency. Pairwise comparisons of the results of these secondary endpoints yielded statistically significant differences between the rh-GH-containing arms and the control group. Are the findings in the table below clinically meaningful?

Secondary Efficacy Analysis

Treatment Groups				
Group A rhGH (n=16)	Group B rhGH + GLN (n=16)	Group C GLN (n=9)	Group B vs C	Group A vs C
Change in Total IPN Calories [kcal/wk] / (p-value)				
-4338.3	-5751.2	-2633.3	-3117.9 (<0.001)	-1705.0 (0.005)
Change in IPN or Lipid frequency [d/wk] (p-value)				
-3.0	-4.2	-2.0	-2.2 (<0.001)	-1.0 (0.025)

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Continued

3. The primary endpoint was change in Total IPN volume. Only 1 of the 3 components (IPN volume) was recorded between week 6 and 18. Is the measurement of IPN volume adequate to demonstrate durability of effect? If not, what do you recommend as a minimum follow up period?

4. The data were primarily derived from a single, nutritional support tertiary care center. Are these data generalizable to the population of short bowel syndrome patients?

5. Are there specific safety concerns considering the potential for long term use of rh-GH in the treatment of short bowel syndrome patients?

6. Do the data support the safety and effectiveness of rh-GH alone or in co-therapy with glutamine in patients with short bowel syndrome? Are there any additional studies that you would recommend, e.g., dose finding?