Product-Based Research

016–TransCon GH as a Long-Acting Growth Hormone for the Treatment of Pediatric Growth Hormone Deficiency

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Background: With growth hormone (GH) receptors present on virtually all cells, GH replacement therapy should aim for the same exposure and tissue distribution as endogenous GH and current daily GH therapies. The challenge to developing a long-acting GH (LAGH) is to establish the same safety, efficacy, and tolerability of daily GH, which includes maintaining GH and IGF-1 levels within the physiological range. To create a LAGH, two approaches have been used: 1) combine unmodified GH with a prolongation technology, or 2) modify GH providing a longer half-life. TransCon GH is a LAGH prodrug in development for pediatric growth hormone deficiency (GHD) with GH transiently bound to an inert carrier. It was designed to release unmodified GH over 7 days to achieve the same exposure, safety, efficacy, and tolerability as daily GH with more convenient once weekly dosing. This profile was successfully demonstrated in the Phase 2 trial in pediatric GHD. TransCon GH is also being developed with an autoinjector for ease of administration and improved adherence.

Aims: We aim to present the topline 52-week pivotal Phase 3 results of TransCon GH in treatment of pediatric GHD.

Methods: The phase 3 heiGHt trial was designed to compare safety, tolerability, and efficacy of weekly TransCon GH versus daily GH over 52 weeks in treatment-naive prepubertal children with GHD. Study endpoints include annualized height velocity (AHV), IGF-1 response, immunogenicity, and safety.

Results: Top-line 52-week results of the heiGHt trial (N = 161) including AHV, Δ height SDS, IGF-1 levels, Δ bone age, and adverse events, will be available for presentation at PENS 2019.

Conclusions: Only LAGHs based on unmodified GH have succeeded in providing both accelerated height velocity as well as reducing truncal adiposity in line with currently available daily GH therapies. Top-line data from the pivotal heiGHt trial of TransCon GH, a LAGH prodrug releasing unmodified GH, will be available in March 2019.

Clinical Implications: A GH prodrug that provides sustained release of unmodified GH for the treatment of pediatric GHD would likely maintain the same tissue distribution as endogenous GH, with comparable efficacy, safety, tolerability, with the benefit of improved compliance due to weekly dosing via an autoinjector.

http://dx.doi.org/10.1016/j.pedn.2019.02.023

017–Real-world and Clinical Trial Glycemic Outcomes Comparison of Young Patients with T1D Using the MiniMed™ 670G System

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Background: The MiniMed™ 670G system with SmartGuard™ Auto Mode automatically adjusts basal insulin delivery every 5 minutes based on sensor glucose (SG) values. The system's at-home safety and effectiveness have been demonstrated in two separate multi-center pivotal trials consisting of participants with type 1 diabetes (T1D) aged 7-13 years and 14-75 years.

Aims: To compare real-world glycemic data of patients aged 7-13 years using the MiniMed™ 670G system with data reported during the system pivotal trial in participants aged 7-13 years.

Methods: System data from the real-world cohort (n=105, 7-13 years, mean±SD 10.4±1.2 years) were voluntarily uploaded to CareLink™ Personal software from Mar 2017-Dec 2017, de-identified, and retrospectively analyzed. These data included time spent below, within, and above target glucose range (70-180 mg/dL, 3.9-10 mmol/L) during a ~2-week period in Manual Mode followed by a 12-week period with Auto Mode enabled. The real-world data were compared with that from pivotal trial participants (n=105, 10.8±0.8 years) who underwent a 2-week run-in phase in Manual Mode followed by a 12-week study phase with Auto Mode enabled. Analyses were conducted with a Wilcoxon signed-rank test.

Results: For the real-world cohort (~10,000 days of system use), median Auto Mode usage was 79.9% and the mean percentage of time in target glucose range (TIR) increased from 56.4±16.3% to 67.1±9.1% ($p<0.001$) during Manual Mode and Auto Mode, respectively. The average SG was 178±26 mg/dL (9.9±1.4 mmol/L) and 161±16mg/dL (8.9±0.9 mmol/L) for the Manual Mode and Auto Mode periods, respectively. For the pivotal trial cohort (~13,000 days of system use), median Auto Mode usage was 80.6% and the mean TIR increased from 56.2±11.4% and 65.0±7.7% ($p<0.001$), respectively; while the average SG was 169±22 mg/dL (9.4±1.2 mmol/L) and 162±12 mg/dL (9.0±0.7 mmol/L), respectively.

Conclusions: The real-world CareLink™ Personal and pivotal trial outcomes data of children with T1D using the MiniMed™ 670G automated insulin delivery system displayed similar trends in improved glycemic metrics.

Clinical Implications: Clinical trial and real-world outcomes data can help to set appropriate expectations for managing glycemic control in young patients utilizing the MiniMed™ 670G system.

http://dx.doi.org/10.1016/j.pedn.2019.02.024