EDUCATION BRIEF
PEDIATRIC (AGES 2-6) HYBRID CLOSED LOOP PIVOTAL TRIAL RESULTS

Medtronic

HYBRID CLOSED LOOP (HCL) PIVOTAL TRIAL PURPOSE AND STUDY DESIGN[1]

The following pivotal trial data was submitted for FDA approval of Medtronic HCL therapy in patients ages 2-6 years old. The purpose of the pivotal trial was to test safety of HCL therapy in the study cohort of patients ages 2-6 years old. The trial was a single-arm, non-randomized study that took place in 7 sites in the United States and 1 site in Israel. Baseline A1C was obtained to compare as an endpoint before and after the pivotal trial.

The enrollment criteria & study design included:

- Ages 2-6 years old (n=46)
- Diagnosis of type 1 diabetes (T1D) >3months (average duration: 2.9 years)
- A1C <10% (average: 8.0%)
- Previously been on insulin pump therapy at least 90 days, with or without continuous glucose monitor (CGM)
- 2-week run-in period with pump and CGM (without HCL)
- Participants and families were then trained on HCL.
- Seven days after training, HCL was activated for the 3-month study period.
- Time in range (TIR) was collected to compare between the run-in and study period.

STUDY RESULTS[1]

The following results were seen in over 4,000 days of patient exposure to HCL therapy which included zero episodes or events of severe hypoglycemia and/or diabetic ketoacidosis (DKA).

Time in Range[1]

Day and Night (p<0.001)
HCL use: 84.9%

Sensor Glucose	Run-in % Time in Range	Study % Time in Range
> 300 mg/dL	5.2	3.7
> 180 mg/dL	41.0	33.0
71 – 180 mg/dL	55.4	63.6
≤ 70 mg/dL	3.6	3.5
≤ 54 mg/dL	0.8	0.8

Figure 1

Nighttime Only (p<0.001)
Overnight = 10:00PM-7:00AM

Sensor Glucose	Run-in % Time in Range	Study % Time in Range
> 300 mg/dL	5.1	2.9
> 180 mg/dL	44.2	29.8
71 – 180 mg/dL	52.8	67.4
≤ 70 mg/dL	2.9	2.8
≤ 54 mg/dL	0.6	0.7

Figure 2

For the full 24-hour time period, participants increased their TIR from 55% to nearly 64% - equivalent to almost 2 hours more per day in target range (70-180 mg/dL). Overall, time spent below range was unchanged; the improvement in time in range was from a reduction in time spent above range.

As you look at just the overnight period (10:00PM-7:00AM) results are similar. TIR went from 53% to 67%, equivalent to 1.3 hours per night increase in TIR.

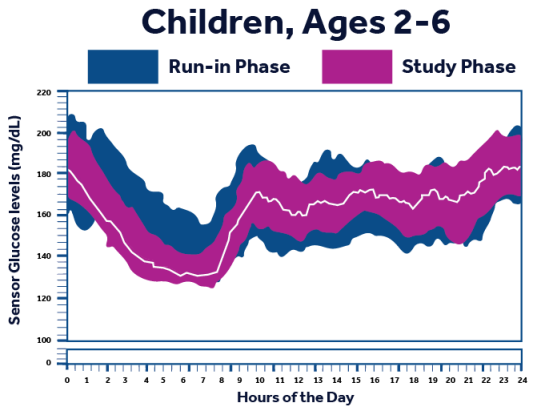

Figure 3

Variability[1]

This chart (Figure 3) shows the median variability from the run-in in blue, and the study phase in pink. You can see significantly improved variability and glycemia in the overnight period, with average glucose at target by wake-up. There is also an improvement in the daytime, suggesting better meal coverage.

A1C[1]

In this chart (Figure 4), you can see the changes in A1C in pediatric patients ages 2-6. The study participants attained an average A1C of 7.5% by the end of the study period. And overall, the A1C curve shifted to the left, indicating improved A1C.

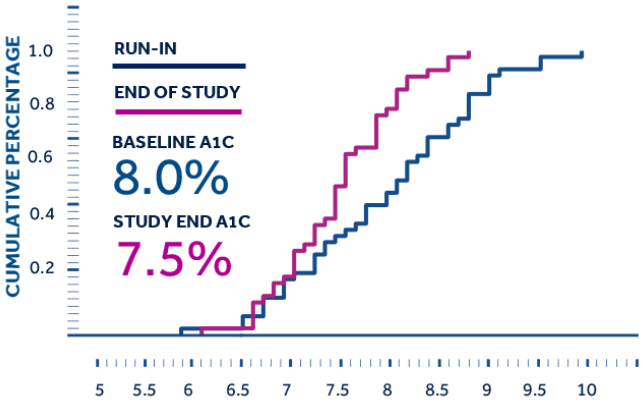

Figure 4

CONCLUSION

In review, the study achieved the primary endpoint and suggested safe usage for HCL in pediatric patients from 2-6 years old.

Since the pivotal study did not include a control group, no effectiveness claims can be made. The study had limitations, including a relatively small number of participants, no comparative control group, and a study period that lasted only three months. In addition, the amount of time the system was used in the Manual Mode was shorter than the time in HCL. Due to these study limitations, caution is advised when attempting to extrapolate these results to individual patient results. There could be significant differences.

References:
[1]Data on file from CEP302: Pivotal Trial (Ages 2-6). N=46. 2019; 10 US sites and 1 EMEA site.