The PROMISE Study: An Evaluation of the Safety and Accuracy of the Next Generation 180-Day Long-term Implantable Eversense CGM System

Abstract OR-149
Session 3-CT-OR06, 0800-1000
Sunday, June 27, 2021

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(NCT03808376) Garg et.al.: Submitted to Diabetes Technology and Therapeutics: 2021

Disclosure Information

- Advisory Boards Consulting fees*: Medtronic, Novo-Nordisk, Zealand, Lifescan Diabetes Institute and Eli Lilly
- Research grants*: Eli Lilly, Novo-Nordisk, Merck, Lexicon, Medtronic, Dario, NCI, T1D Exchange, NIDDK, JDRF, Animas, Dexcom, Sanofi and Senseonics
- No stocks in any device or pharmaceutical company

*All Research grants and Honoraria through University of Colorado Denver

Background

- The Eversense CGM system is the only long-term implantable CGM system approved for use
- Key attributes include:
  - Fluorescent-based optical methodology
  - Transmitter placed on the skin over the sensor allows for
    - On-body vibratory alerts
    - Mild silicone-based adhesive with low rates of skin irritation
  - No interference with Paracetamol or Vitamin C
  - Inserted and removed by certified health care providers in a short in-office procedure
- Pivotal studies have shown a MARD of:
  - 8.5% for the 90-day US product
  - 9.4% for the 180-day European system

Purpose

- To evaluate the safety and accuracy of the next-generation Eversense CGM System for up to 180 days, the PROMISE Study was conducted at 8 clinical research sites in the USA.
  - Two sensor systems were studied
- Materials and Methods
  - 181 subjects with 10 clinic visits, between day 1-180, lasting up to 10 hours, comparing CGM and reference glucose from YSI 2300 glucose analyzer (YSI)
  - Hyperglycemia and hypoglycemia challenges to assess glucose between 40-400mg/dL
  - 96 of the 181 subjects had 2 sensors, one in each arm
    - 53 had a second sensor identical to the primary sensor
    - 43 subjects had a second sensor with specific chemistry modifications (Sacrificial Boronic Acid {SBA} sensor) to reduce oxidation of the glucose-binding indicator chemistry
- The CGM prompts 2 calibrations/day to day 21, after it can prompt 1 calibration/day

Baseline Patient Characteristics

Demographic	Value
Gender n (%)	
Male	85 (47.0)
Female	96 (53.0)
Age (years)*	48.6 (14.9)
Ethnicity n (%)	
Hispanic	23 (12.7)
Non-Hispanic	158 (87.3)
Race n(%)	
Caucasian	**163 (90.1)**
Black or African American	**10 (5.5)**
Asian	**4 (2.2)**
American Indian or Alaska Native	**2 (1.1)**
Native Hawaiian or Other Pacific Islander	**0 (0.0)**
More than One Race Self-Identified	**2 (1.1)**

Mean duration of diabetes, 22.0 years; 69.6% with Type 1; Mean HbA1c, 7.6%

Accuracy by Glucose Range: Primary Sensor

YSI Glucose Range (mg/dL)	Number of Paired CGM and YSI Reference Points	Mean Percent 20/20% of Reference	Mean Absolute Relative Difference, MARD (%)	Median Absolute Relative Difference (%)
Overall	**49613**	**92.9**	**9.1**	**6.7**
40 – 60	2281	89.4	9.4	7.0
61 – 80	5270	92.2	8.8	7.0
81 – 180	19001	90.9	9.0	6.7
181 – 300	14578	94.7	7.7	5.9
301 – 350	6862	96.5	7.1	5.9
351 – 400	1510	93.9	8.0	6.3

Precision Analyses: 53 paired primary sensors

Paired ARD was 10.1%, percent coefficient of variation was 7.1%

Comparison between Primary and SBA Sensors

	Primary Sensors # of Paired Points – 49.613	SBA Sensors # of Paired Points – 12,034
% with 20/20%	92.9%	93.9%
Overall MARD	**9.1%**	**8.5%**
Day 1 MARD	11.0%	11.2%
Day 180 MARD	10.4%	7.4%
MAD between 40-60 mg/dL	**9.4%**	**7.5%**
MAD between 61-80 mg/dL	**8.8%**	**7.7%**
Survival to 180 days	**65%** **98% day 90, 90% day 120,** **74% day 150**	**90%** **96% day 90 and day 120** **94% day 150**

Alert Rate Performance Comparing Primary and SBA Sensors

Glucose Level mg/dL	Event Detection Rate %		True Alert Rate %	
	Primary Sensor	SBA Sensor	Primary Sensor	SBA Sensor
60	87	90	68	73
70	93	94	87	84
180	99	99	94	93
240	98	98	92	91

Safety

- HbA1c
  - 7.6% at baseline, 7.2% at day 90, 7.3% at day 180
- Adverse Events
  - No SAEs related to device or insertion/removal procedures
  - No unanticipated AEs or UADEs
- Procedure
  - 279 sensors (85 single sensors + 96 dual sensors + 2 replacements)
    - 558 insertion/removal procedures
  - **No failure to remove sensor on first attempt**
  - **2 mild skin infections**
    - Incision infection rate in 1.1% of subjects or 0.36% of the total insertion and removal procedures

Summary

- The effectiveness measurements for the primary sensors:
  - **9.1% Overall MARD**
  - **92.9% of the CGM readings within 20/20% of YSI values**
  - **8.8 - 9.4% MAD for hypoglycemia range**
  - **87-99% event detection rates**

- The effectiveness measurements for the subset of **SBA sensors**:
  - **8.5% Overall MARD**
  - **93.9% of CGM readings were within 20/20% of YSI values**
  - **<8% MAD for hypoglycemic range**
  - **90-99% event detection rates**
  - **7.4% MARD at end of sensor life**

  - The addition of SBA to sensor chemistry appears to result in sensors with slower indicator degradation kinetics increasing sensor longevity and improving sensor accuracy

Conclusion

- As shown by the PROMISE study, the next-generation Eversense CGM system:
  - **Safe and accurate for up to 180 days, particularly in hypoglycemia ranges**
  - **Allows for a single calibration/day** on most days of system wear
  - With many unique features, this system should be considered a welcomed addition to options available for real-time CGM

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