# A Multi-sensor Algorithm Predicts Heart Failure Events in Patients with Implanted Devices

## Results from the MultiSENSE Study

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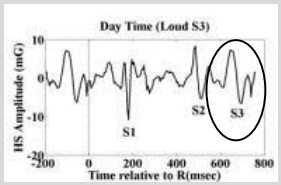
on behalf of the MultiSENSE investigators

# Heart Failure Monitoring Solution

**Goal:** Develop an alert algorithm for the early notification of worsening heart failure by combining information from a diverse set of implanted sensors chosen to target the different aspects of heart failure pathophysiology associated with common signs and symptoms of worsening heart failure.

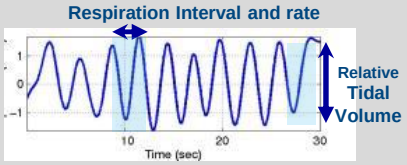
## Heart Sounds

Signs of elevated filling pressure (S3)



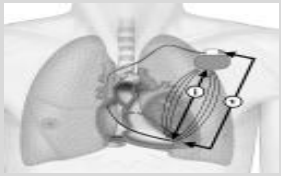

## Respiration

Rapid breathing and reduced tidal volume – shortness of breath



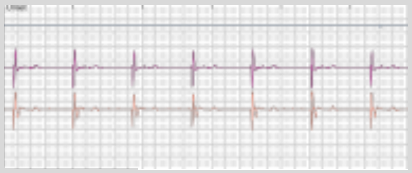

## Thoracic Impedance

Fluid accumulation and pulmonary edema



## Heart Rate

Indicator of cardiac status



## Activity

Global patient status and fatigue

# MultiSENSE Trial Design

- International, multi-center, non-randomized, clinical study designed to
  1) develop and
  2) prospectively evaluate

  a multi-sensor index and alert for the early detection of worsening heart failure

**Key inclusion criteria**

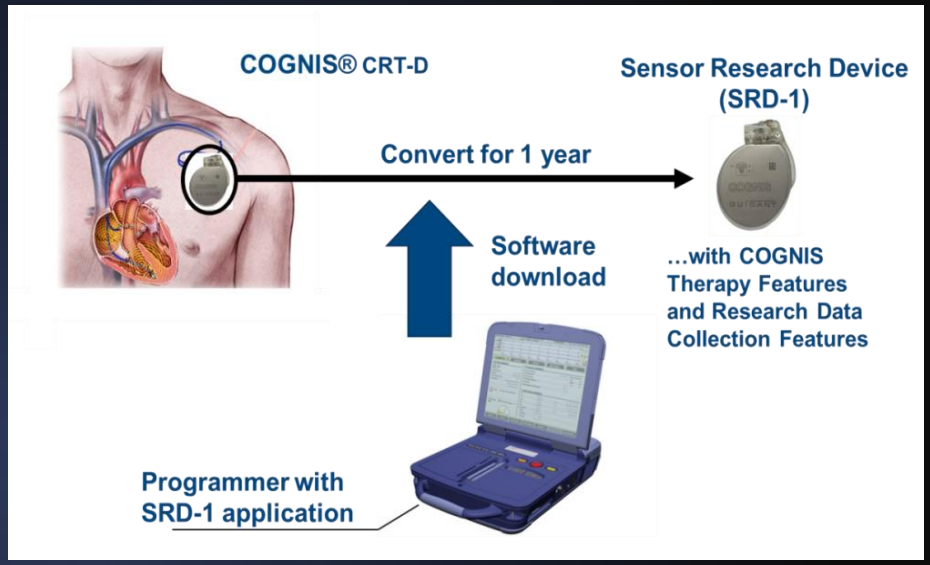
- Age 18 or above
- Currently implanted with a COGNIS CRT-D system
- NYHA Class II, III or IV within the last 6 months

**Key exclusion criteria**

- Documented as pacemaker dependent
- A history of appropriate tachycardia therapy within 1 week prior to enrollment
- Likely to undergo lead or PG revision
- Subjects that have received a heart or lung transplant
- Receiving mechanical circulatory transplant
- A life expectancy of less than 12 months

# MultiSENSE Study Design

- *Investigational software* was downloaded into cardiac resynchronization defibrillator devices (CRT-D) to enable high resolution data collection.




- Treating clinicians, investigators and clinical event committee members were *blinded* to the investigational sensor data.

- The study data were chronologically allocated into a:

**Development Set** — Used to develop the composite index and alert algorithm

**Test Set** — *Sequestered* and used for independent validation of algorithm performance.

# Event and Alert Classification

Independent clinical events committee (CEC) Adjudication:

**Heart Failure Events (HFE)**

***Primary*** cause of event was worsening heart failure and

- is ***admitted*** for HF and receives an augmented HF regimen with oral or intravenous medications, or
- receives unscheduled ***intravenous*** decongestive therapy that does not involve formal in-patient hospital admission, regardless of the setting

**True Positive Alerts**

- Onset before a usable HFEs
- Recovery no earlier than ***30 days*** before usable HFEs

**HF Related Alerts**

- Same onset and recovery window but *broader set of HF events*:
  - hospitalizations with a ***secondary*** cause of HF,
  - outpatient visits with a primary cause of HF and augmented ***oral*** medication changes,
  - HFEs that did not meet sensor ***data availability*** criteria or occurred within 45 days of device conversion

**Unexplained Alerts**

- All other alerts

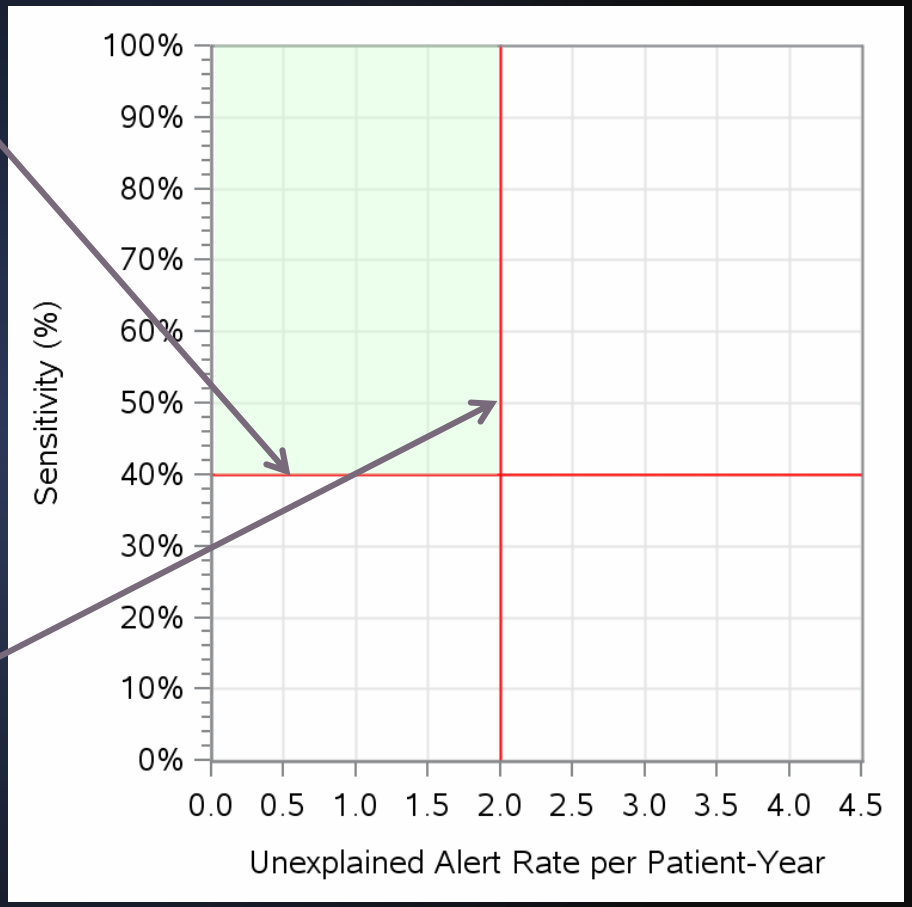
# Predefined Endpoints

**Endpoint 1: Sensitivity for detecting usable heart failure events >40%.**

- An exact two-sided 95% confidence interval (CI) for the sensitivity calculated based on the binomial distribution and the lower bound tested against a performance goal of 40%.

**Endpoint 2: Unexplained alert rate (UAR) per patient year <2.0**

- A two-sided 95% CI for the unexplained alert rate calculated based on the negative binomial distribution and the upper bound tested against the performance goal of 2.0.



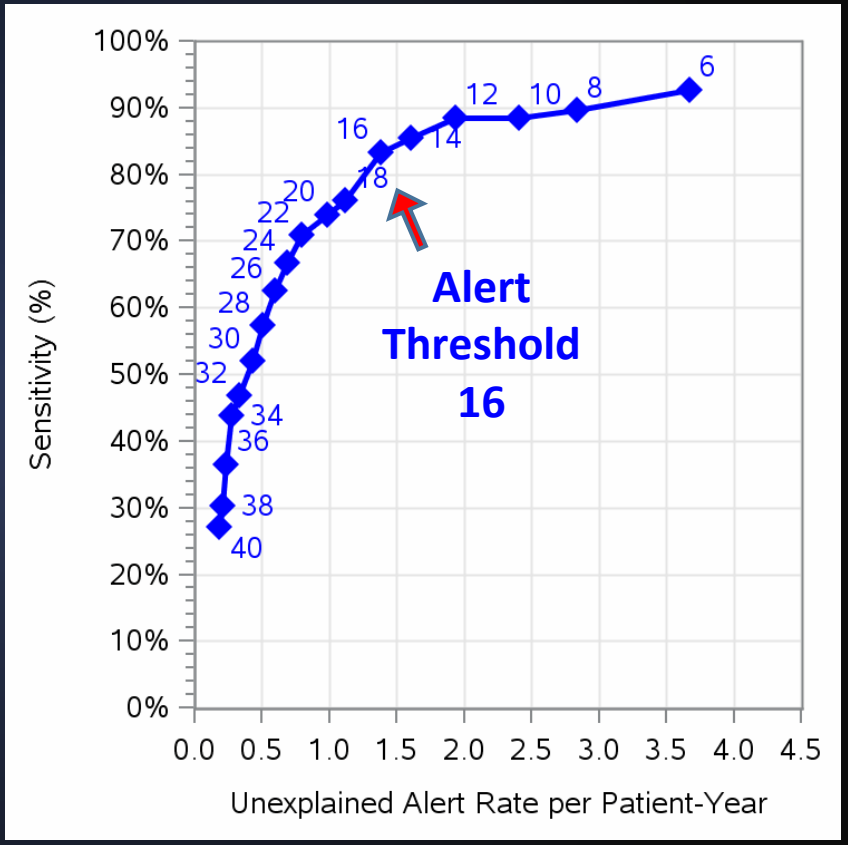
# Baseline Characteristics

| Characteristic | Measurement | Develop. (N=531) | Test (N=443) | P-value |
|---|---|---|---|---|
| Age at Implant (years) | Mean ± SD | 66.3 ± 10.9 | 66.8 ± 10.3 | 0.51 |
| Gender [N (%)] | Male | 387 (73) | 314 (71) | 0.50 |
| Race [N (%)] | White, Not Of Hispanic Origin | 367 (75) | 285 (79) | 0.31 |
| United States [N (%)] | Yes | 491 (92) | 362 (82%) | <0.0001 |
| Body Mass Index (kg/m2) | Mean ± SD | 30.2 ± 6.7 | 30.5 ± 6.9 | 0.48 |
| Renal Disease [N (%)] | Yes | 143 (27) | 101 (23) | 0.13 |
| Ischemic Etiology [N (%)] | Yes | 277 (52) | 217 (49) | 0.31 |
| NYHA Class [%] | I / II / III / IV | 5 / 64 / 27 / 0 | 4 / 64 / 25 / 1 | 0.30 |
| LVEF (%) | Mean ± SD | 29.3 ± 11.5 | 29.7 ± 11.4 | 0.63 |
| Systolic Blood Pressure (mmHg) | Mean ± SD | 121 ± 19 | 125 ± 19 | 0.009 |
| Diastolic Blood Pressure (mmHg) | Mean ± SD | 71 ± 11 | 73 ± 11 | 0.02 |
| NT-proBNP (pg/mL) | Mean ± SD | 2142 ± 5290 | 1576 ± 3023 | 0.07 |
| Sodium (mEq/L) | Mean ± SD | 139 ± 3 | 140 ± 3 | 0.03 |
| Hematocrit (%) | Mean ± SD | 39.3 ± 4.8 | 40.3 ± 5.0 | 0.004 |
| Serum Creatinine (mg/dL) | Mean ± SD | 1.4 ± 0.9 | 1.3 ± 0.7 | 0.08 |
| Concomitant Medications [N (%)] | Ace-Inhibitors/ARBs | 436 (83) | 354 (81) | 0.42 |
| | Beta Blockers | 490 (94) | 405 (93) | 0.70 |
| | Diuretics | 399 (76) | 340 (78) | 0.50 |
| | Anticoagulants | 462 (88) | 356 (82) | 0.005 |

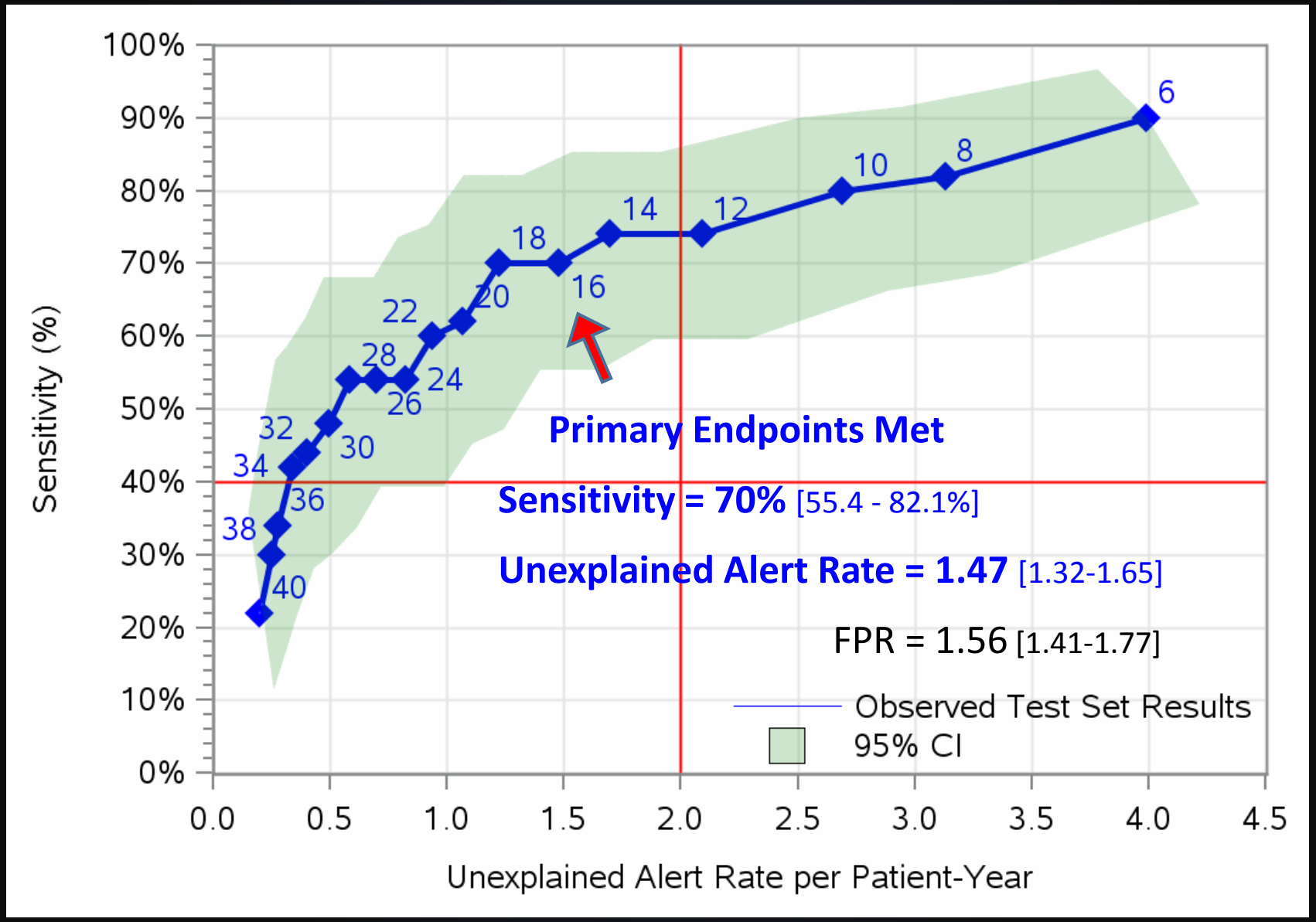
# Alert Development

- Development data set:
  - 500 patients with SRD-1 Conversion
  - Median Follow-up time 324 days
  - 64 patients (12.8%) with heart failure events (HFE)
  - 127 total HFEs
- Sensor feature trends assessed for meaningful associations with HFE

**Composite index (HeartLogic™)**
**Accelerometer-based first and third heart sounds,**
**thoracic impedance,**
**respiration rate,**
**a ratio of respiration rate to tidal volume,**
**heart rate,**
**patient activity**

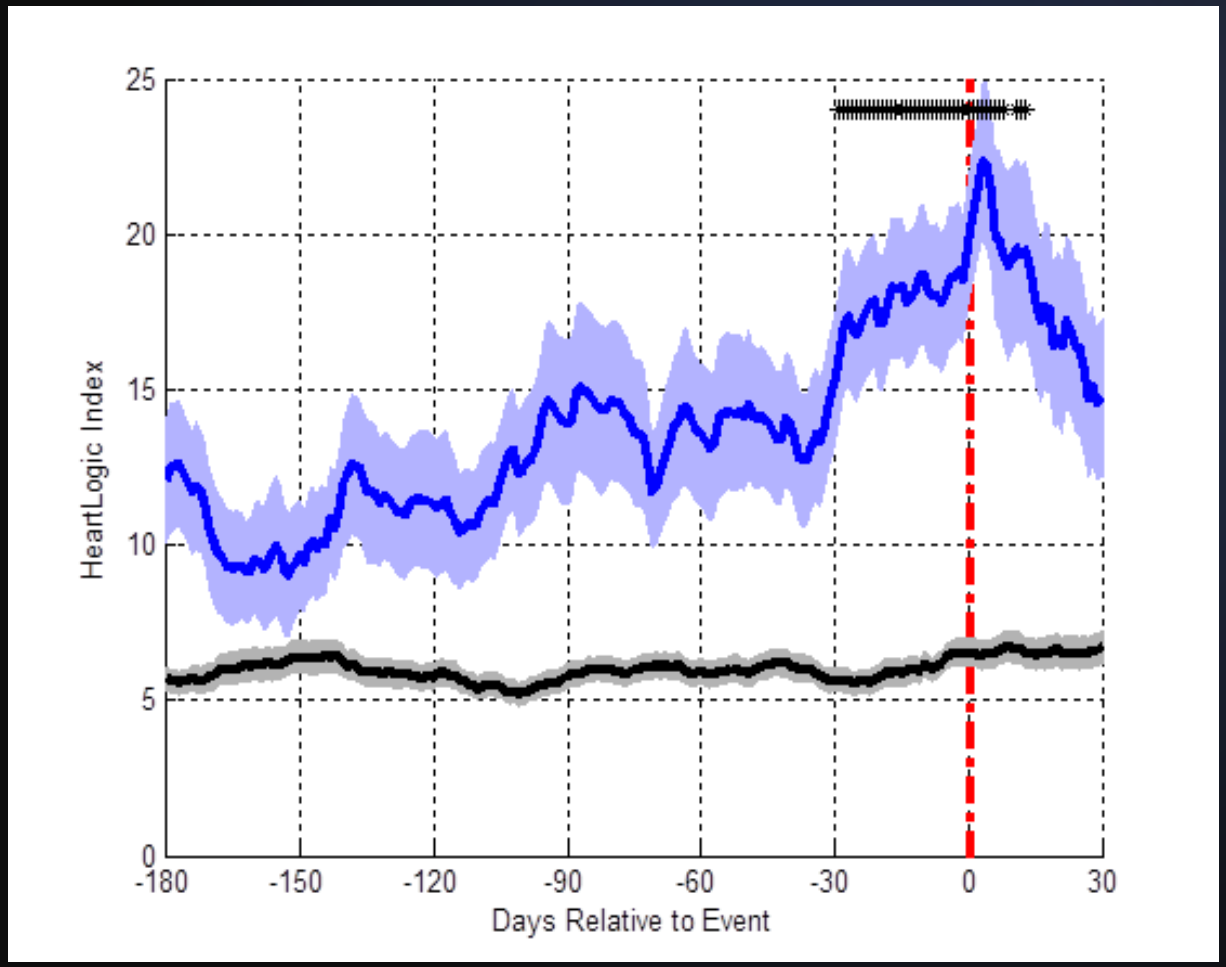


# Primary Endpoints



# HeartLogic Index Trends

Median Time from Alert Onset to HFEs was 34 days




Index Leading to Heart Failure Event, Mean ± SEM

Non-Event Patient Index, Mean ± SEM

Event day or last available index date

* p<0.05; rank sum test; days -180 to -90

# Limitations

- Further studies will be needed to establish whether this type of heart failure alert can improve patient outcomes.
- The HeartLogic alert was studied only in patients who have a CRT-D indication and implant
- Patients were enrolled in the Development and Test Set cohorts sequentially rather than in a randomized format
- This study was limited by a 1 year duration of follow-up
- Some events were excluded because of inadequate data (due to non-compliance with study related data collection).

# Conclusion

- A multi-sensor index and alert algorithm was established
- Alert performance was validated in an independent patient data set.
- Pre-specified performance goals were exceeded:
  - Sensitivity = 70%
  - UAR = 1.47 alerts / patient-year
- The multi-sensor algorithm provides a timely alert predicting impending HF decompensation.
  - Median time to alert = 34 days
  - Additional alert thresholds provide options for increased sensitivity or decreased unexplained alert rates.

# Thank you on behalf of MultiSENSE investigators

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