

# Sudden Unexplained Death in Epilepsy in Patients Treated with Brain-Responsive Neurostimulation

DEVINSKY O, ET AL. *EPILEPSIA*. 2018, JAN 16; 00:1-7

## SUMMARY

- SUDEP is the most common cause of epilepsy-related death.
- The risk of SUDEP is higher with medically intractable partial onset and secondarily generalized seizures, as well as in patients with frequent seizures, a long duration of epilepsy and those taking a large number of AEDs.
- The SUDEP rate for patients treated with the RNS System is favorable compared to patients with treatment-resistant epilepsy and epilepsy surgery candidates.
- Review of data from patients treated with the RNS System demonstrates that not all SUDEPs follow seizures.

## METHODS

**Study Design:** All patient deaths were assessed by an independent SUDEP adjudication committee and cases of possible, probable and definite SUDEP were determined.

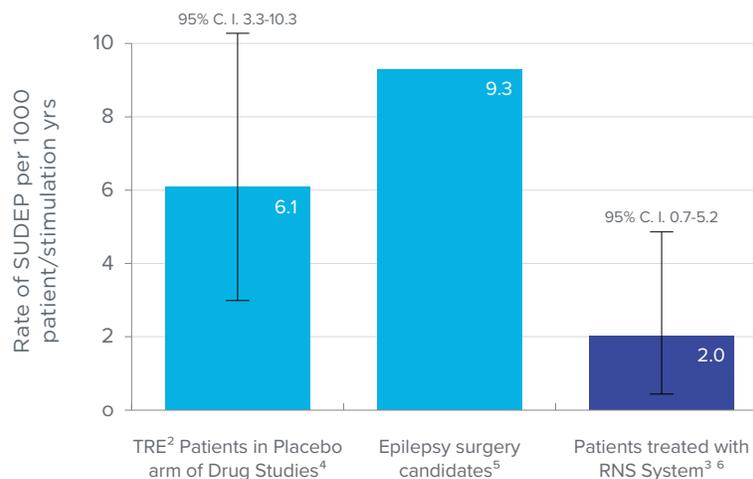
**Population:** 707 patients treated either as part of clinical trials or as part of clinical care following FDA approval.

**Primary Outcome:** SUDEP rates and 95% confidence intervals (CIs) in patients being treated with the RNS System in the clinical trial and post-market setting.

**Secondary Outcome:** RNS System electrographic findings at the time of SUDEP events.

## KEY RESULTS

SUDEP rate for patients treated with the RNS System is favorable compared to patients with treatment-resistant epilepsy and epilepsy surgery candidates.





## KEY RESULTS (CONT)

**For all patients treated with the RNS System (N=707), the SUDEP rate was:**

- 2.0/1000 over 2,036 patient stimulation years<sup>1</sup>
- 2.3/1000 over 2,208 patient implant years

**This compares favorably to the SUDEP rate observed in:**

- Treatment resistant epilepsy patients randomized to the placebo arm of AED trials (6.1/1000 patient years)
- Epilepsy surgery candidates (9.3/1000 patient years)

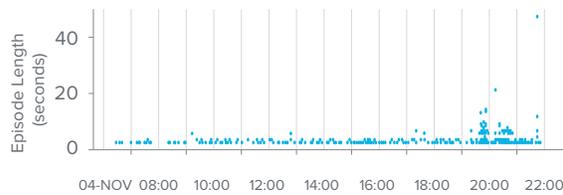
The upper limit of the 95% CI for the rate of SUDEP in patients being treated with brain responsive neurostimulator is below that of the SUDEP rate for the treatment resistant epilepsy patients randomized to the placebo arm of AED trials and patients who are candidates for epilepsy surgery.

## ADDITIONAL OBSERVATIONS

The RNS System recorded electrographic activity at time of death for 5 probable/definite SUDEP events.

- Three had increased epileptiform activity in the hours prior to death
- One had no abnormal activity recorded leading up to the event
- One patient had no data available

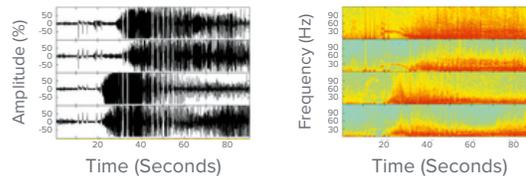
**Figure 1: Patient 4 (Definite SUDEP)**



**Exhibit:** Patient 4 had increased detections and 3 episodes during which the electrocorticographic activity caused a saturation of the amplifiers (electrographic seizures) in the 3 hours before detections ceased.

- **Figure 1** shows that at approximately 19:00, the number and duration of detected episodes increased.
- In **Figure 2**, the ECoG at 21:45 shows an electrographic seizure (typical of the patient's clinical seizures) that was triggered by detection of a prolonged episode.

**Figure 2: Patient 4 (Definite SUDEP)**



### Footnotes

1. 1/5 of the patients did not have stimulation enabled at the time of SUDEP.
2. TRE = Treatment Resistant Epilepsy
3. RNS System data represents SUDEP rate per 1000 stimulation years.
4. Ryvlin P, Cucherat M, Rheims S; Lancet Neurol. 2011; 10:961-8.
5. Dasheiff, R.M., 1991. J Clin Neurophysiol 8, 216-222.
6. Devinsky O, Friedman D, et al. Epilepsia. 2018; 1-7.

**R<sub>x</sub> Only**

The RNS System is an adjunctive therapy for adults with refractory, partial onset seizures with no more than 2 epileptogenic foci. See important prescribing and safety information in the RNS® System labeling. Refer to the labeling for a description of the RNS® System and its components, indications for use, contraindications, warnings, cautions, adverse events and instructions for use. The manuals are available at [www.NeuroPace.com](http://www.NeuroPace.com).

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