**Effects of Energy Dosing on Efficacy and Safety in an Open-Label Study of Endoscopic Pulsed Electric Field Induced Electroporation in Type 2 Diabetes (REGENT-1 Trial)**

**Aim:** The ReCET™ System (endoscopic Re-Cellularization via Electroporation Therapy) uses pulsed electric field (PEF), to induce apoptotic-like cell death followed by regeneration. We evaluated energy dose-responsive effects of the intervention on metabolic outcomes.

**Methods:** REGENT-1 is a multi-center, open-label study of endoscopic PEF therapy at three doses in T2D adults on 1-4 non-insulin agents. Group 1) Gen 1 catheter 600V, single treatment (n=12); Group 2) Gen 1 catheter, 600V, double treatment (n=18); and Group 3) Gen 2 catheter (increased treated surface area [TSA]), double treatment 750V (n=21). The primary endpoint was serious adverse events (SAEs). Secondary endpoints included metabolic changes at 24 and 48 weeks.

**Results:** Among 51 participants (age 52.9±7.9 years, BMI 31.4±3.5 kg/m², baseline HbA1c 8.7±0.9%[72±9mmol/mol]), one intervention-related SAE occurred. Other device or procedure-related adverse events (76 events in 47/51 participants) were mild and transient, such as sore throat. Increased PEF dosing (two applications, and higher voltage plus larger catheter diameter) correlated with glycemic, insulin-resistance, weight, and lipid reductions at 24 and 48 weeks. (**Table 1**)

**Conclusions:** PEF-induced duodenal regeneration with the ReCET System resulted in improved metabolic outcomes that were dose-dependent. These promising findings suggest that further research is warranted.

**Table 1: Changes in Glycemic/Metabolic Outcomes**

|  |  |  |
| --- | --- | --- |
|  | Change from Baseline at Week 24 (95% Confidence Interval) | Change from Baseline at Week 48 (95% Confidence Interval) |
|  | Group 1 | Group 2 | Group 3 | Group 1 | Group 2 | Group 3 |
| ∆HbA1c (%) | 0.09(-0.65,0.84) | -0.81(-1.42,-0.21) | -1.35(-1.91,-0.79) | 0.03(-0.65,0.72) | -1.00(-1.57,-0.43) | -1.70(-2.22,-1.18) |
| ∆Body weight (%) | -1.78(-4.5,0.94) | -4.93(-7.12,-2.74) | -5.99(-8.02,-3.98) | -1.23(-4.17,1.70) | -1.79(-4.20,1.19) | -6.16(-8.37,-3.95) |
| ∆Fasting glucose (mmol/L) | -0.21(-1.58,1.17) | -2.60(-3.72,-1.48) | -3.30(-4.37,-3.30) | 0.68(-0.78,2.14) | -2.30(-3.50,-1.10) | -3.66(-4.79,-2.53 |
| ∆HOMA-IR | 0.20(-0.63,1.03) | -1.23(-1.87,-0.59) | -0.97(-1.59,-0.35) | 1.42(-0.02,2.86) | -0.90(-2.04,0.24) | -1.17(-2.31,-0.03) |
| TIR (%) | 68.4(56.2, 80.5) | 76.3(66.5, 86.2) | 84.7(75.6, 93.7) | 68.2(55.6, 80.8) | 71.5(61.0, 82.1) | 86.1(77.4, 96.2) |
| ∆Total Cholesterol(mmol/L) | -0.64(-1.30,0.03) | -0.13(-0.68,0.42) | -0.41(-0.91,0.10) | -0.55(-1.12,-0.00) | -0.37(-0.84,0.10) | -0.82(-1.24,-0.40) |
| ∆LDL (mmol/L) | -0.60(-1.23,0.03) | -0.09(-0.41,0.60) | -0.28(-0.74,0.18) | -0.244(-0.75,0.26) | -0.11(-0.53,0.31) | -0.56(-0.93,-0.18) |
| ∆HDL (mmol/L) | 0.03(-0.06,0.12) | 0.05(-0.02,0.12) | 0.03(-0.35,0.91) | 0.01(-0.09,0.11) | 0.54(-0.03,0.14) | -0.02(-0.09,0.06) |
| ∆Triglycerides (mmol/L) | -0.32(-0.99,0.36) | -0.67(-1.23,-0.11) | -0.42(-0.92,0.09) | -0.50(-1.14,0.14) | -0.75(-1.29,-0.22) | -0.74(-1.22,-0.26) |