**Pulsed electric field induced duodenal re-cellularization impact on insulin sensitivity and beta cell function: Results from REGENT-1, an open-label, prospective study in Type 2 diabetes**

**Introduction/Objective:** Type 2 diabetes (T2D) is marked by impaired beta-cell function and insulin resistance. Duodenopathy disrupts glucose regulation, presenting a novel therapeutic target. The Re-Cellularization via Electroporation Therapy (ReCET™) System uses non-thermal pulsed electric field (PEF) to regenerate duodenal mucosa and submucosa. The REGENT-1 study modelled MMTT data to assess the metabolic effects of ReCET™ on insulin sensitivity (SI), beta-cell function and disposition index (DI).

**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 tx (n=12); Group 2) Gen 1 catheter, 600V, double tx (n=18); and Group 3) Gen 2 catheter (increased treated surface area), double tx 750V (n=21). Mixed Meal Tolerance Tests (MMTT) assessed β-cell function (Φtot), SI, and disposition index (DI).

**Results:** Fifty-one participants (mean age 52.9 years, BMI 31.4 kg/m², HbA1c 8.7%) underwent PEF therapy. Significant improvements in Φtot, SI, and DI were observed at 12 weeks, with further gains by 48 weeks (both p<0.05). High-energy treatment showed the greatest DI improvement, with outcomes comparable to Roux-en-Y gastric bypass.

**Conclusions:** ReCET™ significantly improved SI and DI, with sustained benefits up to 48 weeks. High-energy treatment yielded optimal results. These findings highlight duodenal regeneration as a promising therapeutic target for T2D management.

**Table 1. REGENT-1 Changes in Efficacy Outcomes at 12 and 48 weeks after ReCET**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline Value | Week 12 | | | | Week 48 | | | |
|  | All Subjects | All Subjects  N=51 | Gen1  600V  Single (Grp 1)  N=12 | Gen1  Double (Grp 2)  N=18 | Gen2  750V  Double (Grp 3)  N=21 | All Subjects  N=48 | Gen1  600V  Single (Grp 1)  N=12 | Gen1  Double (Grp 2)  N=16 | Gen2  750V  Double (Grp 3)  N=19 |
| ∆HbA1c (%) | 8.7  ±0.93 | -1.04  ±0.91 | -0.44  ±0.59 | -1.04  ±0.80 | -1.40  ±1.19 | -1.02  ±0.61 | 0.03  ±0.69 | -1.00  ±0.67 | -1.70  ±0.52 |
| ∆Body weight (Kg) | 88.09  ±18.47 | -3.56  ±1.14 | -1.14  ±1.40 | -3.82  ±1.12 | -4.74  ±1.03 | -4.07  ±2.45 | -1.16  ±2.93 | -4.09  ±2.4 | -5.90  ±2.2 |
| Fasting glucose (mmol/L) | 9.79  ±2.38 | 8.36  ±2.41 | 9.2  ±2.89 | 8.36  ±2.67 | 7.92  ±1.84 | 7.61  ±1.87 | 8.51  ±1.69 | 7.71  ±2.14 | 7.02  ±1.57 |
| Fasting Insulin (mU/L) | 11.16  ±6.56 | 9.28  ±5.70 | 8.27  ±5.26 | 11.39  ±6.80 | 7.99  ±4.51 | 9.44  ±5.44 | 10.91  ±5.11 | 11.69  ±5.35 | 6.38  ±4.46 |
| Fasting C-Peptide (pmol/L) | 754.2  ±416.8 | 705.3  ±370.0 | 504.1  ±189.0 | 873.8  ±388.3 | 666.2  ±373.7 | 654.4  ±447.9 | 637.6  ±128.0 | 877.7  ±539.4 | 466.2  ±410.1 |
| HOMA-IR  (mg/dL mIU/L) | 5.07  ±3.12 | 3.46  ±2.43 | 3.16  ±2.11 | 4.28  ±3.07 | 2.89  ±1.78 | 3.32  ±2.01 | 4.47  ±2.34 | 3.81  ±1.59 | 2.10  ±1.50 |
| Beta Cell function  Φtot [10-9 min-1] | 19.08  ±13.08 | 32.41  ±35.06 | 40.3  ±9.43 | 27.5  ±9.68 | 32.23  ±16.6 | 27.19  ±20.41 | 18.0  ±10.9 | 28.0  ±21.6 | 33.03  ±15.9 |
| Sensitivity Index (SI)  [pmol/L/min]x10-4 | 3.0  ±3.2 | 12.5  ±27.0 | 9.12  ±12.0 | 3.71  ±2.62 | 22.4  ±7.6 | 48.5  ±13.9 | 6.73  ±1.1 | 10.6  ±3.9 | 12.7  ±7.8 |
| Disposition Index [pmol/L/min 10-9 min-1]x10-3 | 5.32  ±3.26 | 33.6  ±1.8 | 31.5  ±1.1 | 11.8  ±0.7 | 57.0  ±2.3 | 41.0  ±1.4 | 9.8  ±12.5 | 27.0  ±9.0 | 60.0  ±18.7 |