**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**

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| --- | --- | --- | --- |
|  | Baseline Value | Week 12 | Week 48 |
|  | All Subjects | All SubjectsN=51 | Gen1600VSingle (Grp 1)N=12 | Gen1Double (Grp 2)N=18 | Gen2750VDouble (Grp 3)N=21 | All SubjectsN=48 | Gen1600VSingle (Grp 1)N=12 | Gen1Double (Grp 2)N=16 | Gen2750VDouble (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 functionΦtot [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 |