mice, whereas MAP gel alone, whole islets alone, or dissociated islets alone did not restore normoglycemia. In recent syngeneic epididymal fat pad transplants using 400 dissociated mouse islets, MAP gel significantly enhanced dissociated islet cell transplantation outcomes (n=6), as evidenced by rapid glycemic control and prolonged functional β-cell survival for up to 70 days post-transplantation. This platform enhances β-cell replacement therapy and long-term diabetes management. Furthermore, MAP gel demonstrated immunomodulatory properties. Cytokine profiling at 7 days post-implantation of 1 million Beta TC-6 cells mixed with MAP scaffolds or NP gels showed that MAP gel reduced pro-inflammatory cytokine expression, including IFNγ, IL-6, IL-1α, IL-1β, IL-10, IL-17, and TNFα. A significant decrease in IL-10 levels was observed in the MAP scaffold group, indicating a shift toward a less inflammatory microenvironment, which could promote beta cell survival.

Conclusions: MAP gel is a promising biomaterial for islet transplantation, supporting graft survival and function at multiple sites, including the kidney capsule and epididymal fat pad. Its ability to enhance islet engraftment, regulate local immune responses, and improve glycemic control makes it a compelling platform for advancing diabetes treatment strategies, including β-cell replacement therapy.

CITATION INFORMATION: Ma M., Chhabra P., Roosa C., Bates J., Cook J., Griffin D., Brayman K. Microporous Annealed Particle (MAP) Gel as a Novel Scaffold for Beta-Cell Replacement Therapy: Enhancing Engraftment and Immunomodulation in a Murine Model AJT, Volume 25, Issue 8 Supplement 1

DISCLOSURES: K. Brayman: None.

Abstract# RF14.4

SR-02, a Pancreatic Islet Replacement Therapy Transplanted to the Omentum

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Purpose: Islet replacement therapy is an alternative to whole pancreas transplant to restore glucose control to patients of type 1 diabetes (Rickels 2019). Allogeneic cadaveric islets (Lantidra), and an experimental, embryonic stem cell-derived product (Zimislecel), are infused to the portal hepatic circulation with concurrent immune suppression. Pancreatic cell clusters infused to the portal vein can cause microvascular obstruction injury that stimulates a local inflammatory reaction harmful to the infused cells. This uncertainty complicates the delivery of a calculated therapeutic dose and likely reduces the potency of the cell product. Furthermore, the surviving cell clusters are dispersed throughout the liver parenchyma, making their tracking, or removal (for safety reasons) impossible.

Methods: SR-02 is a novel stem-cell derived Islet replacement therapy that is administered into an omental pouch in lieu of the portal vein. The clusters are immobilized within the pouch with a surgical fibrin sealant. This allows a precise application of a calculated dose, which can be visualized radiographically and retrieved without causing long-term complication to the patient. SR-02 is manufactured to meet 21 CFR part 210 and 211 requirements and is currently being evaluated in a phase 1/2 clinical study (NCT06651515).

Results: A required feature of omental administration is the ability to remodel the implant site to form a niche, including microvascularization, capable of supporting a functional extra-pancreatic endocrine pancreas. Nonclinical studies have shown that the implant coordinates with host omental tissue to create a graft with structural features of a native pancreas. In particular, the bolus of implanted endocrine cell clusters become the organized endocrine cell clusters and ribbons separated by host stroma reminiscent of the distribution of islets in the pancreas. This implies coordination between host and implant to remodel the combined graft. Fibrosis and encapsulation of the allogeneic implant were not observed, suggesting stable integration into the remodeled tissue. SR-02 cells were reprogrammed from mature islet tissue of a pancreas from a highly compatible, healthy organ donor. Administration of this cell product is therefore not be limited to patients of certain ABO blood types.

Conclusions: The retrievability of the graft without immune suppression withdrawal enables the implant of clusters to patients on immune suppression therapy due to an existing organ transplant and enables the implant of clusters that have been modified to reduce or eliminate immune-targeted rejection. SR-03, a version of the Seraxis stem cell line has also been modified and is in nonclinical development. Omental administration and elimination of de novo systemic immune suppression therapy will make islet replacement therapy widely accessible to millions of patients in need.

CITATION INFORMATION: Rust W., Welsch C., Mazanet R. SR-02, a Pancreatic Islet Replacement Therapy Transplanted to the Omentum AJT, Volume 25, Issue 8 Supplement 1

DISCLOSURES: W. Rust: Employee; Seraxis, Inc.

Abstract# RF14.5

CD40L Co-Stimulation Blockade as a Non-Toxic Calcineurin Inhibitor-Free Immunosuppression for Beta Cell Replacement Therapy: Preliminary Results from a Pilot Clinical Study

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Purpose: Islet transplantation holds promise as a functional cure for type 1 diabetes, but the nephrotoxicity, neurotoxicity, and islet toxicity of calcineurin inhibitors (e.g., tacrolimus) limits its broader clinical application. Tegoprubart (Eledon Pharmaceuticals), a novel monoclonal antibody targeting CD40 ligand CD40L), offers a potential alternative. This study evaluates the safety and efficacy of tegoprubart in recipients of cadaveric islet transplants.

Methods: Three patients with type 1 diabetes and problematic hypoglycemia have been enrolled in this single-center, phase 1/2 clinical trial. Induction immunosuppression included anti-thymocyte globulin, followed by tegoprubart (20 mg/kg IV every three weeks after an initial loading dose) and mycophenolate for maintenance therapy.

Results: Patient 1 (42-year-old female, BMI 29) reduced insulin requirements from 80 to 30 units/day after a single-donor intraportal islet transplantation (363,000 IEQ, 4,092 IEQ/kg). A second transplant led to insulin independence within one week, sustained for 8 months.Patient 2 (32-year-old female, BMI 20) achieved insulin independence one month after a single-donor islet transplantation (326,000 IEQ, 6,700 IEQ/kg), with HbA1c improving from 8.5% to 5.8% at seven weeks. She has remained insulin-free for 7 months with stable graft function with A1c of 5.0. Patient 3 (37-year-old male, BMI 30) maintained stable islet graft function (IEQ 375,000, 4,086IEQ/kg) and reduced HbA1c from 9.9% to 7.0% three months post-transplant. All patients had an uncomplicated post-transplant course, with no adverse events, donor-specific antibodies, or immunologic rejection. No opportunistic infections occurred. Compared to historical controls receiving tacrolimus-based immunosuppression, patients treated with tegoprubart experienced a greater reduction in insulin requirements after a single islet transplant (≥60 units/day vs. 40 units/day) and 2.5-fold higher islet engraftment efficiency (AUC C-peptide/blood glucose during MMTT, standardized per transplanted islet mass).

Conclusions: Preliminary data from the first three patients indicate that tegoprubart with mycophenolate is well-tolerated and effective in preventing islet graft loss, with no unexpected adverse events. Further studies are warranted to validate these findings.

CITATION INFORMATION: Wojcik N., Juengel B., Appelbaum N., Juszczyk A., Basto L., Escobedo M., Wang L., Tibudan M., Klein T., Barth R., Fung J., Witkowski P. CD40L Co-Stimulation Blockade as a Non-Toxic Calcineurin Inhibitor-Free Immunosuppression for Beta Cell Replacement Therapy: Preliminary Results from a Pilot Clinical Study AJT, Volume 25, Issue 8 Supplement 1

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Abstract# RF14.6

The Role of microRNAs as Biomarkers of Pancreas Transplant Rejection; EMPAR Study

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Purpose: Pancreas transplant rejection diagnosis remains difficult. Certain microRNAs (miRNAs) are associated with vascular inflammation, T and B cell proliferation, and beta cell dysfunction and therefore might be dysregulated during rejection and may serve as potential biomarkers for rejection.

Methods: EMPAR is the first prospective study examining the role of a combination of novel biomarkers for pancreas rejection including islet beta cell specific cell free DNA, trypsinogen, and selected miRNAs. 9 patients with new SPK transplant and 10 admitted with pancreas dysfunction or any infection have been recruited so far. Circulating miRNAs were extracted from plasma using a miRNAeasy kit (Qiagen) in the presence of UniSp2/4/5 spike-in RNAs. RNA was subjected to reverse transcription (RT) in the presence of UniSp6 and Cel-miR-39-3p spike-in RNAs and subsequently used for quantitative PCR (qPCR) with the miRCURY LNA system and probes hsa-miR-375-3p, hsa-miR-148a-3p, hsa-miR-150-5p, hsa-miR-409-3p, hsa-miR-125b-5p, UniSp2/4/6 and Cel-miR-39-3p. MiRNA baseline CT values, normalised to UniSp2, of patients who were admitted for transplantation or admitted without rejection were compared to samples post-perfusion (PP), samples 1-month post-transplant and to samples of patients who were admitted for rejection (R).

Results: MiR-148a-3p PP CT values were 0.85 higher than baseline values (mean difference CI 0.73-0.97, p=0.04) suggesting a significant downregulation whereas they did not change in a consistent way for the rest. miR-148a-3p values returned to base line 1-month post-transplant. Interestingly miR-150-5p CT values were 1.86 higher 1-month post transplantation compared to baseline (mean CT difference CI