Ex-Vivo Cell Therapy Platform for Immune Reprogramming in Autoimmunity

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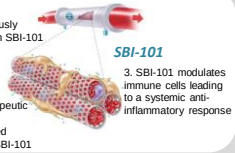
The Sentien Approach: Bringing Blood to the MSCs

Bioactive molecules secreted by MSCs are the primary source of activity of these therapeutically promising cells. We have engineered a system to maximize delivery of therapy from MSCs to circumvent the half-life issues that have hindered MSC transplantation. This system overcomes the dosing constraints of IV infusion and potentiates a broad range of biological responses unparalleled in single molecule therapeutics.

Product Concept: Sentien is developing a combination product (SBI-101) that integrates allogeneic MSCs within an extracorporeal, blood contacting device to fundamentally change the administration route. **Instead of bringing MSCs to the blood, our product brings blood to the MSCs.**

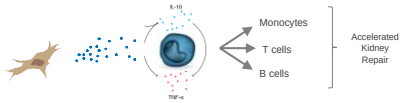


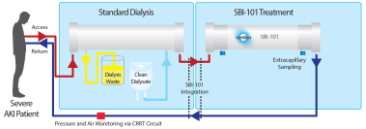
Background: SBI-101-01 trial

Sentien currently has an ongoing Phase I/II clinical trial investigating SBI-101 in Acute Kidney Injury (AKI): Double blind, randomized, controlled, study at 2 doses to establish safety and pharmacologic POC (NCT03015623). Miller et al., Kidney Int Rep. 2018

MSC Secreted Factors → Systemic Immunomodulation → Immune Cell Reprogramming

Therapeutic Hypothesis of MSC-Mediated Blood Reprogramming





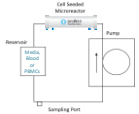
All patients were on Continuous Renal Replacement Therapy (CRRT)

8-10 US based clinical sites
CRRT only (control)
CRRT + 250M cells (low dose)
CRRT + 750M cells (high dose)

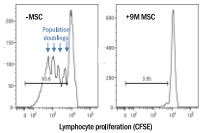
Endpoints:
1: Safety
2: Renal specific efficacy
Exploratory: PK/PD biomarkers

An interim analysis was performed on the low dose cohort (N=4 in each group).

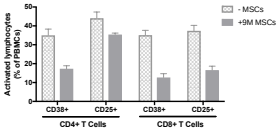
Mini-SBI-101 R&D Setup with Healthy PBMCs



Sentien has developed a miniaturized bioreactor system (mini-SBI-101) that enables detailed study of MSC effects on blood cells in the R&D setting. MSCs are seeded onto microreactors which are then perfused using a pump. This miniaturized reactor system enables detailed study of MSC effects on blood cells.

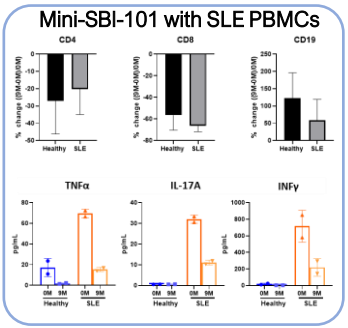


MSCs in bioreactor inhibit lymphocyte proliferation. CFSE labelled PBMCs were activated with PHA and IL-2 and perfused through the MSC reactor for 5 days. **Lymphocyte doublings were significantly reduced in the presence of MSCs**



T cell activation surface markers CD38 and CD25 are reduced in the presence of MSCs in bioreactor.

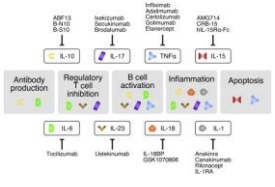
R&D of Mini-SBI-101 with PBMCs from Autoimmune Donors



PBMCs from donors with either SLE or MS are responsive to MSCs within the Bioreactor. PBMCs were activated with PHA and IL-2 and perfused through the MSC reactor for 5 days. PBMCs were then collected to assess immunophenotypic changes. Deceases in T-cell markers CD4 and CD8 were noted, as well as increases in B-cell marker CD-19. Further, changes in the cytokine milieu were assessed by ELISA comparing between cellular and acellular treatment groups. Decreases in pro-inflammatory cytokines were noted following exposure to MSCs.

Preliminary data supports broadening clinical application into autoimmunity conditions including SLE and MS

Summary



A treatment option which could balance multiple dysregulated cytokine levels would provide a significant advancement in the treatment of autoimmune diseases. Here we have shown the R&D scaled mini-SBI-101 simultaneously modulated multiple targets associated with autoimmune disease.

For more information regarding how SBI-101 may provide a therapeutic option for the regulation of cytokine storm associated with **COVID-19**, please see:

Poster #836 Clinical Evidence for Immune Reprogramming with Extracorporeal Mesenchymal Stromal Cell Therapy

Ex-vivo MSC therapy using SBI-101 technology has promise for many clinical applications requiring systemic immunotherapy for tissue repair and regeneration.

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