

**Regenerative Medicine Minnesota
Progress Report
Due: 2/28/2018**

Grant Title: Phase I/II Study of Human Chorionic Gonadotropin and Epidermal Growth Factor Supplementation (Pregnyl®) to Support Tolerance and Repair as Adjunct Therapy in High-Risk or Refractory Acute Graft-Versus-Host Disease

Grant Number: RMM 102516 004

Principal Investigator: Shernan Holtan, MD

Project Timeline: 3/1/2017 - 2/28/2019

Progress to Date:

For each specific aim in your proposal, please describe progress and obstacles and/or achievements. Please address any deviations from estimated timelines and limit *total* response to 2000 words. Figures and tables are allowed.

Primary Objective, Phase I. Establish the maximum tolerated dose of Pregnyl in: (a) high-risk; and (b) steroid-refractory aGVHD, preceding testing for clinical efficacy.

We have enrolled 26 patients on the Pregnyl protocol to date, and we are near complete for clinical and laboratory analysis for the first 25.

We have achieved the maximum dose level written into the protocol with no dose-limiting toxicities to date. Because of differing outcomes between steroid-dependent and steroid-refractory acute GVHD patients (see figure on next page), we have modified the protocol to allow for further dose escalation within the steroid-refractory population.

Going forward, we have formally split the study into 3 arms, high-risk (Arm 1), steroid-dependent (Arm 2a), and steroid-refractory (Arm 2b) to allow continued dose-escalation within arm 2b. This protocol modification was approved by the IRB in March 2018 and is pending approval from the FDA.

In summary, we have achieved the primary objective of phase I for Arms 1 and 2a, and we will continue to dose-escalate in Arm 2b.

Phase Objective, Phase II. Define (a) the proportion of patients demonstrating a complete or partial response to Pregnyl and (b) the optimal therapeutic EGF level associated with clinical response.

While our current results are clearly better than historical controls, we wish to continue to dose-escalate steroid refractory patients, given lack of dose-limiting toxicities, to see if we determine a higher but still tolerable dose for this group of patients with a very poor prognosis.

Secondary Endpoint. Determine the tissue repair/regeneration vs. damage/inflammation plasma profile associated with aGVHD response to Pregnyl.

These analyses are ongoing, and we plan to submit the results from the first 25 patients for presentation at the American Society of Hematology this fall.

Please list any of the following that have resulted from the Minnesota Regenerative Medicine grant funding:

Publications and/or manuscripts submitted for publication: *None, analyses pending*

Disclosures/patents: *None, analyses pending*

Grant applications and/or awards: *None, analyses pending. I am submitting an R01 in an effort to secure funding for this study to expand in April 2018 (earliest start date December 2018, if awarded).*

Reporting to all Minnesotans:

Briefly and using lay language, please describe your overall progress and how it is significant to the patients in need of regenerative medicine therapies in Minnesota. This will be used on the RMM website to demonstrate how funds are being used to advance the health of all Minnesotans.

Acute graft-versus-host disease is a potentially fatal complication of blood and marrow transplantation. Through our clinical trial funded by Regenerative Medicine Minnesota, we are developing a simple, low-cost, and effective treatment to help support patients in their recovery from the disease. We are finding the best dose of a hormone supplement called Pregnyl® and testing if it can help speed the repair of damaged organs and tissues. We are encouraged by our initial results, and we hope that our study will lead to improved survival and quality of life for patients with acute graft-versus-host disease in Minnesota and around the world.

Thank you sincerely for your support of our clinical trial. Watching patients recover faster and better than expected has been a tremendous joy that words cannot express.