

AWARD NUMBER: W81XWH-15-2-0026

TITLE: Clinical Evaluation of Decellularized Nerve Allograft with Autologous Bone Marrow Stem Cells to Improve Peripheral Nerve Repair and Functional Outcomes

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14. ABSTRACT The current award is a phase I safety study (n=12) evaluation of the synergistic effect of the co-treatments of a commercially available decellularized processed peripheral nerve allograft scaffold (Avance® Nerve Graft, AxoGen, Alachua FL) with autologous bone marrow stem cells (BMSC) for the reconstruction of mixed peripheral nerve gaps between 3 and 7 cm in length. Each treatment separately has been shown to have an established safety record. Avance has been used in more than 10,000 surgeries without a reported adverse event. The current standard of care for nerve injury, the autograft, has significant limitations: the source and quantities of autologous tissue needed for repairs are limited, and when faced with severe trauma these donor sites are not viable due to concurrent injury. Use of a decellularized nerve graft mitigates concerns of donor site morbidity, decreases surgical time and has substantially equivalent outcomes. Augmenting the scaffold with the patient's own BMSCs may allow for point of care treatment with the potential to enhance the regenerative ability of the wound-healing environment. The proposed use of an existing commercially available scaffold with an autologous stem cell transplant, both with proven safety records, would establish a safety profile and provide a proof					
15. SUBJECT TERMS Avance nerve graft, autologous bone marrow stem cells (BMSC), nerve autograft, peripheral nerve repair					
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1. INTRODUCTION:

The purpose of this study is to evaluate the safety of the nerve allograft and BMSC sequentially to repair peripheral nerve gaps of the ulnar and median nerves of the upper extremities between 2 and 7 centimeters (cm) in length. Subjects will be followed for 18 months post-surgery. Secondary outcomes will be examined to evaluate the efficacy of the co-treatment for nerve repair compared to Avance Nerve Graft and BMSC treatments alone. The study is designed to treat up to 24 patients using the sequential treatment of nerve allograft and BMSC. This is a prospective, observational trial to evaluate the safety of Avance nerve graft and BMSC and to measure the efficacy of the synergistic treatment for peripheral nerve repair.

2. KEYWORDS:

Avance nerve graft
Autologous Bone Marrow Stem Cells (BMSC)
Nerve autograft
Peripheral nerve repair

3. OVERALL PROJECT SUMMARY:

During Quarter 1 of Year 2 (July-September 2016), the team discussed and reviewed the protocol and Case Report Form (CRF) with the principal investigator (PI). The clinical research coordinator (CRC) made edits to protocol and CRF.

During Quarter 2 of Year 2 (October-December 2016), the team discussed and reviewed the protocol and Case Report Form (CRF) with the PI. The CRC made edits to protocol and CRF. The CRC created a flow chart to map out the study design. The team received initial feedback from Cleveland Clinic on the data to be collected during specimen analysis. The team created and revised the master budget. The master revised budget was approved.

During Quarter 3 of Year 2 (January-March 2017), the CRC updated the protocol, consent form, and CRF. The lead site master protocol was submitted to the Scientific Review Committee (SRC) at WRNMMC. Due to the new WRNMMC IRB 200-day review policy, the team shifted strategies to make SAMMC the lead site (instead of WRNMMC) and therefore, submit the lead site protocol to the BAMC IRB, the local IRB at SAMMC. The SRC lead site protocol submission at WRNMMC was withdrawn. The master protocol, consent form, and application form were updated according to BAMC IRB protocol templates. The master protocol was submitted to the SRC at SAMMC and received SRC approval. The lead site protocol was submitted to the BAMC IRB. An IAIR agreement was approved between the WRNMMC and BAMC IRBs. The CRC submitted HJF paperwork to create a sub-award for Cleveland Clinic. Clinical research manager (CRM) was hired at SAMMC.

During Quarter 4 of Year 2 (April-June 2017), SAMMC, the lead site, received IRB approval in May. HRPO approval was received in June. The WRNMMC performance site IRB submission was sent to the local IRB in June. The CNHC performance site IRB

submission was sent to the local IRB in June. Curtis National Hand Center is still waiting for the budget office to finalize their site specific budget. Budget and SOW for Curtis will have to be submitted to HJF to create the sub-award for CNHC. Cleveland Clinic sub-award has been finalized and processed by HJF on behalf of Cleveland Clinic. Still awaiting final approval and signature from Cleveland Clinic.

Subject enrollment is anticipated to begin in August at SAMMC, in August/September at WRNMMC, and in October at Curtis National Hand Center. It is still anticipated that all subjects will be enrolled before the end of year 3 (June 30, 2018). Follow-up of the research subjects may require a No Cost Extension (NCE) up to 1 year later.

The team is preparing for a two-day training/protocol review with all participating sites and vendors to be held at WRNMMC on July 13th and July 14th.

4. KEY RESEARCH ACCOMPLISHMENTS

No Key Research accomplishments beyond what was outlined in the overall project summary above have been accomplished.

5. CONCLUSION:

During the period of this report, the lead site has obtained IRB and HRPO approval and IRB review/approval is pending at the other two performance sites (WRNMMC and Curtis National Hand Center). Subject enrollment is anticipated to begin in August at SAMMC, in August/September at WRNMMC, and in October at Curtis National Hand Center. It is still anticipated that all subjects will be enrolled before the end of year 3 (June 30, 2018). Follow-up of the research subjects may require a No Cost Extension (NCE) up to 1 year later.

6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

Publications: Nothing to report

Abstracts: Nothing to report

Presentations: Nothing to report

7. INVENTIONS, PATENTS AND LICENSES:

Nothing to report

8. REPORTABLE OUTCOMES

Nothing to report

9. OTHER ACHIEVEMENTS:

Nothing to report

10. REFERENCES:

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11. APPENDICES:

None

12. TRAINING OR FELLOWSHIP AWARDS:

None

13. COLLABORATIVE AWARDS:

No collaborative awards were executed in year 2

14. QUAD CHART: