

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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REPORT DATE: JUL 2018

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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Introduction

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 of principle for this type of approach.

Keywords

Avance® nerve graft, autologous bone marrow stem cells (BMSC), nerve autograft, peripheral nerve repair

Accomplishments

During the course of year 3 of this study, both sites (WRNMMC and BAMC) were up and running with regulatory approvals completed at the local and secondary review levels.

To date, the study is on-going for patient recruitment and follow-up. A no cost extension was requested with the Q3 report to extend the study for an additional year to allow for completion of the major tasks and milestones set out for this project. Study teams at both sites are fully trained on the protocol and procedures for this project.

The study team at WRNMMC has consent 2 patients to the date of this report. The surgeries have been performed, and follow-up is ongoing.

The study team at BAMC have consented 6 patients, but are only continuing to follow 4 of the 6 because one of the 6 had a gap over 7cm, which disqualifies that patient from participation, and in the other, the surgeon did not use the graft during the surgical procedure.

There have been no adverse events at either site. The study has enrolled, and is following, 6 of 12 (50%) of the total enrollees in the proposal.

Bringing Curtis Hand Center on board to bring in additional subjects is in process, and will be complete within Q1 of year 4. Curtis Hand Center personnel will be trained in this protocol as soon as the subaward is complete.

Impact

Military combat injuries to the extremities from blast, fragmentary, and ballistic injury can result in a spectrum of musculoskeletal trauma to include injuries to the soft tissues, vessels, nerves, and bone. It has been reported that while body armor has decreased the mortality associated with combat trauma, there is actually an increase in severe traumatic injury to the upper extremity in the surviving warrior. The incidence and prevalence of extremity injury has been on the rise significantly in the 21st century, with 54% of all casualties seen to involve extremity injury in 2006 up from 22% just 3 years prior. Costlier still is the fact that 65% of inpatient care is devoted to such wounds which are known to have the highest long-term costs associated with them – both a drain on military medical resources. The proposed phase I safety study complements the ongoing DoD and VA areas of interest by decreasing the burden of wounded warriors in the short term by lessening length of rehabilitation, and in the long term by reducing recidivistic chronic ailments. Moreover, these wounded service members have often sustained injuries to multiple limbs, often deeming the autograft sites unviable. The recent availability of the only commercially viable peripheral nerve allograft (Avance®, AxoGen Inc.) presents an attractive alternative to harvesting autograft by offering numerous benefits to the patient, including decreased operative time and no donor site morbidity. Furthermore, while the efficacy of these options has already been documented, there are limitations on the expected level of recovery and on the length of discontinuity that can be treated. The addition of a Warriors own BMSC's is expected to further improve outcomes and has shown a long safety record and is a standard point-of-care procedure. This proposed phase I safety trial, has the potential for establishing a safety record for the synergistic effect of the allograft and autologous stem cells leading to the acceleration and translation of advances in knowledge into new treatment algorithms for combat related injuries through evidence-based practices for the peripheral nerve repair.

Changes/Problems

There have been major personnel changes on this award over the course of this year, although none have come from key personnel. The program manager for this award did leave HJF, and his workload has been picked up by the clinical research nurse. A replacement program manager will be starting with the program on 30 July 2018.

Delays were also encountered during the process of reviewing and approving the subaward for MedStar/Curtis National Han Center. These have been addressed, and the document is circulating for signatures.

Products

No products have been generated to date.

Participants and Other Collaborating Organizations

WRNMMC, SAMMC, Cleveland Clinic and Curtis National Hand Center are all collaborating on this project. Work at both WRNMMC and SAMMC is managed through HJF directly. The subaward to the Cleveland Clinic is complete, and work is ongoing.

The subaward to MedStar/Curtis National Hand Center has been reviewed by legal teams at both institutions, and is being circulated for final execution.

Special Reporting Requirements

None

Appendices

None