

Award Number: W81XWH-10-2-0177

TITLE: The Use of Novel Therapies to Reconstitute Blood Cell Production and Promote Organ Performance, using Bone Marrow Failure as a Model

PRINCIPAL INVESTIGATOR: Adrianna Vlachos, M.D.

CONTRACTING ORGANIZATION: The Feinstein Institute for Medical Research
Manhasset, NY 11030

REPORT DATE: October 2011

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;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE October 2011		2. REPORT TYPE Annual		3. DATES COVERED 28 September 2010 - 27 September 2011	
4. TITLE AND SUBTITLE The Use of Novel Therapies to Reconstitute Blood Cell Production and Promote Organ Performance, using Bone Marrow Failure as a Model				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-10-2-0177	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Adrianna Vlachos, M.D. E-Mail: avlachos@nshs.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) The Feinstein Institute for Medical Research Manhasset, NY 11030				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
13. SUPPLEMENTARY NOTES					
14. ABSTRACT Diamond Blackfan anemia (DBA) is a rare inherited red cell aplasia. Mutations have been described in ribosomal protein genes. Currently standard therapy includes corticosteroids, red cell transfusions or stem cell transplantation; however all are fraught with many side effects. Leucine is one of the branched chain amino acids and has been shown to upregulate protein translation. This is a pilot study to test the feasibility of administering leucine to 50 patients with DBA, monitoring for clinical hematologic response and side effects. The study has not yet opened due to some delays. It has also required multiple revisions in the site-specific and master protocols. In addition the manufacturing company has a shortage of Leucine due to a factory issue since May 2011. At present we have procured adequate product and it is being set into capsular form. Since the protocol has not yet opened there is no scientific progress for this study at this time.					
15. SUBJECT TERMS None provided.					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 4	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	4
Reportable Outcomes.....	4
Conclusion.....	4
References.....	4
Appendices.....	4

INTRODUCTION:

Diamond Blackfan anemia (DBA) is a rare inherited red cell aplasia. Mutations have been described in ribosomal protein genes. Currently standard therapy includes corticosteroids, red cell transfusions or stem cell transplantation; however all are fraught with many side effects. Leucine is one of the branched chain amino acids and has been shown to upregulate protein translation. This is a pilot study to test the feasibility of administering leucine to 50 patients with DBA, monitoring for clinical hematologic response and side effects.

BODY:

The study has not yet opened for a variety of reasons. Initially the protocol was delayed due to the unanticipated need for an investigational new drug (IND) distinction from the Food and Drug Administration (FDA). The protocol also went through multiple revisions as site-specific and master protocols were required. The protocol was reviewed by our local institutional review board (IRB) for preliminary approval, pending the approval of the Department of Defense (DOD) and the FDA, but has required multiple modifications. In addition, the manufacturing company has a shortage of Leucine due to a factory issue since May 2011. The local IRB did not approve administration of the product in powder form due to inaccurate measurements with the initially proposed "scoop" method. We inquired as to the cost of packaging the product into capsular form. At present we have procured adequate product and it is being set into 250mg capsules. At this size capsule we can administer to small children (as the protocol starts at age 2 years) as well as adults. Our local Office of Research Compliance is requesting a Site Monitoring Plan to comply with the FDA IND requirements. We are awaiting a cost quote for this service and will need to procure funds for this, if this is mandated. Since the protocol has not yet opened there is no scientific progress for this study. The revisions will be sent to all three agencies (DOD, IRB and FDA). We have not had any charges to this grant as the protocol is not open.

KEY RESEARCH ACCOMPLISHMENTS:

- There are no key research accomplishments to date as the study is not opened yet.

REPORTABLE OUTCOMES:

- There are no key research accomplishments to date as the study is not opened yet.

CONCLUSION:

There are no results to report at this time as the study has not yet opened.

REFERENCES:

There are no references to report at this time as the study has not yet opened.

APPENDICES:

There are no appendices.

SUPPORTING DATA:

There are no supporting data.