AWARD NUMBER: W81XWH-15-1-0115

TITLE: Phase I Trial of Intratumoral Administration of NIS-Expressing Strain of Measles Virus in Unresectable or Recurrent Malignant Peripheral Nerve Sheath Tumor

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CONTRACTING ORGANIZATION: Mayo Clinic and Foundation
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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
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4. TITLE AND SUBTITLE
Phase I Trial of Intratumoral Administration of NIS-Expressing Strain of Measles Virus in Unresectable or Recurrent Malignant Peripheral Nerve Sheath Tumor

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-15-1-0115

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Mayo Clinic and Foundation
200 First Street SW Rochester, MN
55905-0002

8. PERFORMING ORGANIZATION REPORT

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
Study approved by Mayo IRB on April 18, 2016, and by USAMRMC/ORP/HRPO on May 6, 2016. All study staff completed IRB training. Dose volume charts have been developed to facilitate pharmacy orders. Study opened for enrollment on May 17, 2016. Study coordinators identified and assigned to the study by Mayo Clinic Cancer Center.
Three patients have been enrolled in the study. They completed treatment per protocol and continue the follow up. None of the treated patients experienced side effects. With the first 3 patients we have completed the first dose level. We are continuing recruitment for the second dose level.

15. SUBJECT TERMS
Neurofibromatosis 1, Malignant Peripheral Nerve Sheath Tumor(MPNST), MV-NIS, Oncolytic Virus, Measles Virus

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	10	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION:

Malignant peripheral nerve sheath tumors (MPNST) is the major complication contributing to early mortality and overall decrease in life expectancy in Neurofibromatosis 1 patients. Oncolytic viruses can selectively infect and destroy tumor cells. Our preliminary data confirm that MPNST cells are highly susceptible to MV-NIS. We are conducting Phase I clinical trial to determine safety of intratumoral administration of MV-NIS. Protocol includes MV-NIS injections under ultrasound or CT guidance, *in vivo* monitoring of distribution and kinetics of virus using SPEC/CT or planar gamma camera imaging after TC-99m administration and assessing changes in tumor size by using WHO criteria. Our correlate studies will explore the time course of viral gene expression, virus elimination and humoral and cellular immune response to the injected virus.

2. KEYWORDS:

Neurofibromatosis 1, malignant peripheral nerve sheath tumor (MPNST), MV-NIS, oncolytic virus, measles virus

3. ACCOMPLISHMENTS:

The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?

Major Task 1: Prepare Protocol for Phase I Clinical Trial --completed
Major Task 2: Coordinate Study Staff for Clinical Trial I--completed
Major Task 2: Conduct Phase I Clinical Trial---study open and recruitment in progress
Major Task 3: Perform Correlate Studies
Subtask 1: Evaluate virus incorporation and persistence in MPNST after injection
Subtask 2: Assess viremia and viral shedding

What was accomplished under these goals?

1. Received Mayo IRB approval on 04/18/2016
2. The US Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) reviewed the protocol and found that it complies with applicable DOD, US Army, and USAMRMC human subjects protection requirements. Approval Received on May 6, 2016.
3. All stuff completed IRB training
4. Developed drug dose volume chart to facilitate pharmacy orders once patients start enrolling
5. Study opened for patient enrollment on May 17, 2016 to Mayo Clinic in Rochester
6. Study coordinators identified and assigned to the study by Mayo Cancer center
7. Three patients treated per protocol, completed first dose level

8. Study modification approved by Mayo IRB on April 20, 2017 included administrative changes to the consent and protocol

Protocol Summary

- Clarification of Week 6 imaging assessment only be done if uptake on prior imaging
- Updated time from injection of tracer to imaging to one hour
- Added Heparin tubes for assessment of immune response
- For viral shedding assessments, made Day 15 mandatory and Day 28 and Week 6 contingent upon Day 8 and/or Day 15 results
- Minor text and formatting edits throughout
- Updated the tissue collection at Week 6 to specify that the collection is not dependent on positive SPECT

Consent Summary

- Added to Sections 5 and 6 that patients are to wear masks during clinic visits for 12 days after the injection.
- Removed unneeded exclusion language from Section 6
- Classification added to Section 5

What opportunities for training and professional development has the project provided?

Nothing to report

How were the results disseminated to communities of interest?

Nothing to report

What do you plan to do during the next reporting period to accomplish the goal?

Continue patient accrual and procedures per protocol

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report

What was the impact on other disciplines?

Nothing to report

What was the impact on technology transfer?

Nothing to report

What was the impact on society beyond science and technology?

Nothing to report

5. **CHANGES/PROBLEMS:** The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

Nothing to report

Actual or anticipated problems or delays and actions or plans to resolve them

The study is now open and actively recruiting eligible patients, however, the IRB approval was longer than anticipated due to administrative delays.

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Received Mayo IRB approval on 04/18/2016.
The US Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) reviewed the protocol and found that it complies with applicable DOD, US Army, and USAMRMC human subjects protection requirements. Approval Received on May 6, 2016.
Annual IRB progress report approved by Mayo IRB 1/11/2017

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications.

  Nothing to report

Books or other non-periodical, one-time publications.

Nothing to repost

Other publications, conference papers and presentations.

Nothing to report

- **Website(s) or other Internet site(s)**

Nothing to report

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report

- **Other Products**

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Dusica Babovic-Vuksanovic
Project role: PI
Person months worked: 22
Contribution to projects: submitted quarterly reviews, coordinated activities needed for study opening for accrual
Funding support: this award

Name: Scott Okuno
Project role: co-PI
Person months worked: 14
Contribution to projects: patient accrual
Funding support: this award

Name: Jennifer Picket
Project role: study coordinator
Person months worked: 2
Contribution to projects: coordination of study procedures
Funding support: this award

Name: Jaclynn Wessling
Project role: study coordinator
Person months worked: 1.5
Contribution to projects: coordination of study procedures
Funding support: this award

Name: Jodi Klocke
Project role: study coordinator
Person months worked: 8
Contribution to projects: coordination of study procedures
Funding support: this award

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: N/A

QUAD CHARTS: N/A

9. APPENDICES: N/A