

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

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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. One patient was identified as a possible study participant, but before enrollment she required hospitalization for pulmonary embolus. Due to treatment with anticoagulants, the patient was not eligible for participation. We are continuing study enrollment.					
15. SUBJECT TERMS Neurofibromatosis 1, Malignant Peripheral Nerve Sheath Tumor (MPNST), MV-NIS, Oncolytic Virus, Measles Virus					
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

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:** Provide a brief list of keywords (limit to 20 words).

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

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 staff 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. One patient identified and evaluated for eligibility

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

Began charging the study after protocol activation, starting June 1, 2016. Anticipate increase in activity and associated higher levels of expense in next quarters.

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.

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 report

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: 10

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: 2

Contribution to projects: patient accrual

Funding support: this award

Name: Laurie Olsen-Holtorf

Project role: study coordinator

Person months worked: 2

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: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.

- 9. APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.