

AWARD NUMBER: W81XWH-19-1-0848

TITLE: Novel Topical Antibiotic Therapy to Reduce Infection After Operative Treatment of Fractures at High Risk of Infection: TOBRA-A Multicenter RCT

PRINCIPAL INVESTIGATOR: Robert V. O'Toole, MD

CONTRACTING ORGANIZATION: Department of Orthopaedic Surgery
University of Maryland School of Medicine
Baltimore 22 S. Greene St. Shock Trauma,
Baltimore, MD 21201

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14. ABSTRACT <p>Background: Infection after treatment of high-energy military fractures is very common and continues to cause significant morbidity. Recently, a study showing the use of local vancomycin powder around metal hardware used to treat these at-risk fractures results in a reduced risk of infection. The powder is thought to create a kill zone around the metal, prevent bacterial colonization, and therefore reduce the rate of postoperative infection. Specific Aims: Our primary specific aim is to demonstrate that the infection rate (defined by CDC criteria) is lower in patients with at-risk fractures treated with standard of care as well as local vancomycin and tobramycin than patients treated with standard of care and vancomycin alone. Additional specific aims include investigation of the potential development of antibiotic resistance and examining bacterial sensitivities in patients who become infected in the treatment group and comparing the proportion of additional complications such as wound dehiscence and nonunion. Study Design: The proposed study is a multi-center prospective open label randomized controlled trial. The study will accumulate patients from 50 core civilian and 1 military center to ensure generalizability. The study group will be a set of tibial plateau and pilon fractures previously shown to be at high risk of infection treated with plate and screw fixation. 1900 participants (950 per treatment arm) will be enrolled from METRC trauma centers over 24 months. Participants will be recruited during hospitalization for the initial injury. Military Benefit and Clinical Impact: Infection is a very common and serious complication associated with the treatment of high-energy military extremity trauma. Fixation of fractures in these injuries involves the use of metal implants. Plates and screws become colonized with bacteria and lead to high rates of infection that are not treated well with intravenous antibiotics. If the proposed study demonstrated the utility of this technology, it would have a dramatic effect on reducing the morbidity associated with extremity trauma. Further, a positive result could revolutionize the approach to prophylaxis against surgical site infection after orthopaedic fracture care in both the military and civilian arenas by moving the field toward technologies that focus on local antibiotics associated with the implanted devices. As of 9/30/22, 314 participants have been enrolled. There are 26 sites actively screening/enrolling and other participating sites' status can be found in the attachment. The study team is actively engaged with the rest of the participating sites on the administrative approval process.</p>									
15. SUBJECT TERMS Surgical site infection (SSI); vancomycin; tobramycin; topical antibiotics; tibial plateau; pilon; fracture fixation; orthopaedic surgery; trauma; METRC									
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1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose, and scope of the research.*

This study will build upon the success of the VANCO study (Contract Number: W81XWH-10-2-0134, FDA IND #119891) which enrolled 980 patients into a randomized controlled trial investigating topical Vancomycin powder versus no powder in patients having plate and screw fixation for fractures at risk of surgical site infection. The PI, Co-PI and most of the research team that led the VANCO study will serve similar roles in the current study. The proposed study design is a pragmatic, prospective, randomized controlled trial comparing deep surgical site infection rates in patients treated with either local Vancomycin powder or local Vancomycin and Tobramycin powders at the time of fracture fixation (in addition to standard of care). This study design will provide the highest quality evidence to investigate our hypothesis that the use of local Vancomycin and Tobramycin powders will be effective at decreasing deep surgical site infection in these at-risk patients. Participants (950 per treatment arm) will be enrolled from METRC trauma centers over a 24-month period and followed for 12 months following definitive fracture fixation surgery. Participants will be recruited during hospitalization for the initial injury.

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

Surgical site infection (SSI); vancomycin; tobramycin; topical antibiotics; tibial plateau; pilon; fracture fixation; orthopaedic surgery; trauma; METRC

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?

The specific aims of the study are as follows:

- Specific Aim 1: Compare the proportion of deep surgical site infections (SSI) of the study injury within 365 days of definitive fracture fixation surgery in patients allocated to receive a combination of local Vancomycin and Tobramycin powders compared to patients allocated to local Vancomycin powder.
- Specific Aim 2: A series of sensitivity analyses will be conducted to look at alternative measures of deep SSI under Specific Aim 1. These sensitivity analyses will consider the following alternative endpoints of deep SSI: infection by gram-negative bacteria, infection by gram-positive bacteria, polymicrobial pathogenic infections, culture-negative infections, and cellulitis/skin infections.
- Specific Aim 3: To compare the safety of treatment with a combination of local Vancomycin and Tobramycin versus Vancomycin powder alone as measured by the proportion of antibiotic resistance in each arm.

The tasks and milestones set forth to meet the aims of the project, as stated in the approved scope of work, are shown in the table below. Items not yet completed and marked with an asterisk (*) in the

status column below have additional information specifically addressed in other sections of this report.

<u>Tasks and Milestones</u>	<u>Timeline</u>	<u>Status</u>
Major Task 1: Study Initiation		
<ul style="list-style-type: none"> • Submission of an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) 	Oct 2019-Nov 2019	Completed
<ul style="list-style-type: none"> • Refine eligibility criteria, exclusion criteria, and screening protocol 	Oct 2019-Nov 2019	Completed
<ul style="list-style-type: none"> • Finalize consent form & human subject protocol 	Oct 2019-Nov 2019	Completed
<ul style="list-style-type: none"> • Develop case report forms (CRFs) for data capture, program, and pilot test REDCap 	Oct 2019-Dec 2019	Completed
<ul style="list-style-type: none"> • Coordinate with Sites for IRB protocol submission 	Oct 2019-Dec 2022	Started (90%)*
<ul style="list-style-type: none"> • Coordinate with Sites for IRB review 	Oct 2019-Dec 2022	Started (90%)*
<ul style="list-style-type: none"> • Coordinate with Sites for Military 2nd level IRB review (ORP/HRPO) 	Oct 2019-Dec 2022	Started (60%)*
<ul style="list-style-type: none"> • <i>Milestone:</i> Local IRB approval at MCC and UMD 	Mar 2021	Completed
<ul style="list-style-type: none"> • <i>Milestone:</i> HRPO approval for all protocols and local IRB approval through required participating sites 	June 2021-Dec 2021	Started (60%)*
<ul style="list-style-type: none"> • <i>Milestone:</i> FDA IND Approval 	Mar 2020	Completed
Major Task 2: Training Research Staff		
<ul style="list-style-type: none"> • Develop and conduct training for Research Coordinators on procedures for screening and consenting patients, study procedures, and data collection/reporting. 	Feb 2020-May 2020	Completed
<ul style="list-style-type: none"> • Certify sites to begin screening and enrolling patients 	May 2021-Dec 2022	Started (50%)*
<ul style="list-style-type: none"> • Conduct study initiation calls with each site to ensure procedures are in place 	Feb 2020-Dec 2022	Started (80%)*
<ul style="list-style-type: none"> • <i>Milestone:</i> Research Staff Trained 	June 2021	Started (70%)*
Major Task 3: Conduct Study		
<ul style="list-style-type: none"> • Clinical site Research Coordinators will screen and enroll eligible study patients 	May 2021-April 2023	Started*
<ul style="list-style-type: none"> • Generate and distribute monthly enrollment and follow-up reports; provide ongoing training and support to address problems with enrollment as they are identified 	July 2021-Mar 2023	Started
<ul style="list-style-type: none"> • Generate and distribute data quality reports to monitor data completeness; check for errors and inconsistencies 	March 2022-July 2023	Started

<ul style="list-style-type: none"> • <i>Milestone:</i> The first patient enrolled at the principal investigator’s site. 	June 2021	Completed
<ul style="list-style-type: none"> • <i>Milestone:</i> All patients enrolled 	Mar 2023	
<ul style="list-style-type: none"> • <i>Milestone:</i> All patient follow up complete 	Mar 2024	
Major Task 4: Outcome Adjudication		
<ul style="list-style-type: none"> • Develop data presentation profiles of cases ready for the adjudication 	Jan 2022-Jan 2023	Started
<ul style="list-style-type: none"> • Convene adjudication committee to determine study outcomes for records that have been fully completed. 	Jan 2022-May 2024	Started
<ul style="list-style-type: none"> • <i>Milestone:</i> Outcome Adjudication Completed 	May 2024	
Major Task 5: Data Analysis and Report Writing		
<ul style="list-style-type: none"> • Develop final analysis files 	Jan 2024-Jul 2024	
<ul style="list-style-type: none"> • Conduct analysis and write final reports and peer-reviewed publications 	Mar 2024-Sep 2024	
<ul style="list-style-type: none"> • Disseminate results published in peer-reviewed journals and presentation at professional and scientific meetings 	Mar 2024-Sep 2024	
<ul style="list-style-type: none"> • <i>Milestone:</i> Report findings from the final analysis 	Sep 2024	

What was accomplished under these goals?

For this reporting period describe 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting

As of September 26, 2022, 932 patients were screened, and 314 participants have been enrolled. Please refer to the end of the report (pg 16-22) for the screening/enrollment and follow-up progress of the study. Enrollment is close to enrollment goal per unit time but the overall enrollment is delayed over a year because of COVID issues, delay in contract, and the problems related to the central IRB requirement.

There are twenty sites actively screening and enrolling patients out of the twenty-six sites certified. There are three additional sites with HRPO approval waiting for certification to begin screening activity, 1 site waiting for HRPO approval, and 2 sites preparing for HRPO submission. We are continuing to work through the process of reliance agreements, local cede reviews, and central IRB submissions with other participating sites. There are 2 sites waiting for Pearl sIRB approval, 14 sites waiting for local IRB approval, and additional 5 sites in the preparation stage. Please refer to the attached appendix for the detailed list of the participating site status.

As the screening and enrollment activity has started across multiple sites, the coordinating center started sending out regular summary reports and data queries. Also, monthly site research coordinator meetings have been held since February 2022. The adjudication committee is reviewing the early discontinuation cases in real-time. Additional communications with sites are in place via emails or phone calls to address any questions or issues. Most recent DSMB meeting was held on August 30, 2022 and the board members found that the study is safe and ethical to continue.

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

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report

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

If this is the final report, state “Nothing to Report.”

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

The next reporting period will be focused on enrollment, data collection, and gaining the necessary approvals to begin enrollment at the rest of the participating sites. Key activities will include:

1. Enrollment: We will continue enrolling and anticipate the pace to increase as more sites are certified.
2. FDA: We plan to submit an information amendment to the FDA addressing items that were not part of the clinical hold.
3. IRB: We will continue to add sites to Pearl IRB and develop reliance agreements.
4. Adjudication: The adjudication committee will continue reviewing new cases with enrolled patients. We will begin holding regular committee meetings.
5. Site management: Administrative tasks associated with securing site participation will continue.
6. Screening and enrollment: Sites will begin screening and enrollment after completing the study training and certification process.
7. Data quality checks: Summary reports will be provided to the sites regularly. Data queries, will be sent out to sites to ensure data quality of the study.
8. Monthly check-in meetings: Monthly check-in calls will continue to address any questions as the sites are implementing the study.

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?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- transfer of results to entities in government or industry;
- instances where the research has led to the initiation of a start-up company; or
- adoption of new practices.

Nothing to report

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- improving public knowledge, attitudes, skills, and abilities;
- changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or
- improving social, economic, civic, or environmental conditions.

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

Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to report

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

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

The delay caused by the new requirement for a single IRB is continuing to impact the certification timeline of the sites. Because the use of an sIRB is fairly new to most of our participating sites, it is slowing down both local and central IRB submission processes. We are providing extra time and effort for additional meetings and communications as our plan is to certify as many sites as possible before the next technical report.

As mentioned in the previous report, limited staff available to process the contracts and extensions at the University of Maryland (prime site) is causing a delay for the sites that require fully executed contracts or extensions prior to Pearl sIRB/HRPO submission or to begin screening/enrollment activity. After a status review with the prime site, it may seem that a few sites that require revisions on the contracts may not be able to begin screening/enrollment activity until year 2023. The average time to process revisions can take at least 3 months at the prime site.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

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. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report

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

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.

Example:

Name: Mary Smith
 Project Role: Graduate Student
 Researcher Identifier (e.g. ORCID ID): 1234567
 Nearest person month worked: 5

Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.

Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)

Name:	Robert O'Toole
Project Role:	Principal Investigator
ORCID ID:	0000-0002-5628-6584
Effort:	10%
Contribution:	Dr. O'Toole led the overall project effort and has overseen the development of the study protocol and submission of the IND application to the FDA.
Name:	Manjari Joshi
Project Role:	Co-Investigator
ORCID ID:	Not available
Effort:	5%
Contribution:	Dr. Joshi has provided oversight and expertise on all project matters related to infectious disease.
Name:	Nathan O'Hara
Project Role:	Co-Investigator
ORCID ID:	0000-0003-0537-3474
Effort:	15%
Contribution:	Mr. O'Hara has managed all administrative aspects of the project at the lead institution and contributed to the development of the protocol.
Name:	Renan Castillo
Project Role:	MCC Principal Investigator
ORCID ID:	0000-0003-0473-5891
Effort:	15%
Contribution:	Dr. Castillo contributed to the development of protocol and statistical planning as well as led all project efforts at the METRC Coordinating Center.
Name:	Anthony Carlini
Project Role:	MCC Co-Investigator

ORCID ID: Effort: Contribution:	0000-0003-1419-4515 15% Mr. Carlini has organized all project efforts across institutions and has developed/drafted study documents and reports.
Name: Project Role: ORCID ID: Effort: Contribution:	Suna Chung MCC Project Director Not Available 30% Ms. Chung has organized all project efforts across institutions and has developed/drafted study documents and reports.
Name: Project Role: ORCID ID: Effort: Contribution:	Richard Thompson Biostatistician 0000-0001-8378-4426 15% Dr. Thompson has oversight and expertise on all project matters related to statistical planning.
Name: Project Role: ORCID ID: Effort: Contribution:	Susan Collins Study Manager Not Available 60% Ms. Collins corresponded with participating centers, organized site survey responses, and drafted the consent documents and case report forms.
Name: Project Role: ORCID ID: Effort: Contribution:	Elias Weston-Farber Programmer Not Available 30% Mr. Weston-Farber supports the analysis of the data under the supervision of the study investigators.
Name: Project Role: ORCID ID: Effort: Contribution:	Paige Sullivan Programmer Not Available 30% Ms. Sullivan supports programming of the REDCap database under the supervision of the study investigators.
Name: Project Role: ORCID ID: Effort: Contribution:	Christopher Pierce Data Analyst Not Available 45% Mr. Pierce supports the analysis of the data under the supervision of the study investigators.
Name: Project Role: ORCID ID: Effort: Contribution:	Chris Witczak Financial Analyst Not Available 6% Mr. Witczak set up the study account and prepared subaward paperwork for participating centers.

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

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site); and*

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.*

An updated Quad Chart is included as Attachment 1.

- 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.*

Please see page 16 for the summary report.

TOBRA Monthly Report Tables for 20220926

TABLE 1: Screening, Eligibility, and Enrollment by Site

Clinical Site	Screened, last 7 days	Enrolled, last 7 days	Screened, to date	Screened per day	Enrolled per day	Eligible, to date	Refused, to date	Non-enrolled for 'other' reasons	Early discontinuations (pre-enrollment)	Potential early discontinuations (pre-enrollment)	Consented & Randomized, to date
CAP e	1	0	67	0.20	0.06	25	2	3	0	0	20
CMC i	1	0	101	0.47	0.08	37	16	3	0	0	18
DAR l	0	0	11	0.10	0.09	11	1	0	0	0	10
HCM t	0	0	5	0.03	0.02	4	0	0	0	0	4
HOU k	0	0	80	0.33	0.11	68	13	29	0	0	26
HRV r	1	0	11	0.08	0.08	11	0	1	0	0	10
IFH c	1	1	33	0.11	0.03	21	2	9	0	0	10
MET j	2	0	61	0.25	0.04	21	6	5	0	0	10
MTH f	0	0	91	0.38	0.08	21	0	0	1	0	20
RIH s	0	0	25	0.17	0.02	5	1	1	0	0	3
SHS m	0	0	20	0.09	0.07	18	2	0	0	0	16
UCH n	0	0	4	0.02	0.02	4	0	0	0	0	4
UMD b	5	0	161	0.32	0.14	83	8	6	0	0	69
UMS g	5	1	53	0.29	0.15	40	5	8	0	0	27
UOK q	0	0	47	0.25	0.12	25	0	3	0	0	22
USC cc	0	0	3	0.23	0.08	3	0	2	0	0	1
UVA u	0	0	13	0.10	0.02	5	1	1	0	0	3
UWI d	1	0	68	0.22	0.05	21	2	3	0	0	16
VMC h	2	1	32	0.23	0.11	18	0	2	0	0	16
WFU p	1	0	45	0.27	0.05	10	1	0	0	0	9
TOTAL	20	3	932	.	.	451	60	76	1	0	314

TABLE 2: Reasons for Ineligibility by Site

Clinical Site	Screened, to date	Ineligible, to date	Failed inclusion criteria	Failed age criteria	Prior/ current deep SSI	Already received definitive fixation	Myonecrosis	Pregnant or lactating	Follow-up concerns	Vanco allergies	Tobra/ aminoglycoside allergies
CAP e	67	42	26	1	0	7	0	0	14	0	0
CMC i	101	64	61	2	0	2	0	1	0	0	0
DAR l	11	0	0	0	0	0	0	0	0	0	0
HCM t	5	1	0	0	0	0	0	0	1	0	0
HOU k	80	12	0	0	0	5	0	1	6	0	0
HRV r	11	0	0	0	0	0	0	0	0	0	0
IFH c	33	12	0	0	1	1	0	0	9	1	1
MET j	61	40	21	1	0	6	0	0	16	0	0
MTH f	91	70	39	0	0	20	0	0	16	0	0
RIH s	25	20	5	0	0	13	0	0	2	0	0
SHS m	20	2	0	0	0	0	0	0	2	0	0
UCH n	4	0	0	0	0	0	0	0	0	0	0
UMD b	161	78	66	0	1	1	0	0	10	0	0
UMS g	53	13	1	0	2	5	0	0	8	0	0
UOK q	47	22	0	0	4	18	2	0	1	0	0
USC cc	3	0	0	0	0	0	0	0	0	0	0
UVA u	13	8	3	0	0	2	0	0	1	0	0
UWI d	68	47	40	1	0	1	0	0	6	0	0
VMC h	32	14	6	1	0	1	0	0	6	0	0
WFU p	45	35	17	0	0	11	0	0	8	1	0
TOTAL	932	481	285	6	8	93	2	2	106	2	1

TABLE 3: Discontinuations by Site

Clinical Site	Consented & Randomized, to date	Discontinuations, pre-t0						Eligible & Enrolled	Discontinuations, post-t0			
		Inappropriate Enrollment	Potential Inappropriate Enrollment	Late Ineligible	Potential late ineligible	Late Refusal	Potential late refusal		Participant withdrawal	Physician Withdrawal	Potential physician withdrawal	Death
CAP e	20	0	0	0	0	0	0	20	0	0	0	0
CMC i	18	0	0	1	0	0	0	17	0	0	0	0
DAR l	10	0	0	0	2	0	0	8	0	0	0	0
HCM t	4	0	0	0	0	0	0	4	0	0	0	0
HOU k	26	1	0	0	0	0	1	24	0	0	0	0
HRV r	10	0	0	0	0	0	0	10	0	0	0	0
IFH c	10	0	0	0	0	0	0	10	0	0	0	0
MET j	10	0	0	0	0	0	0	10	0	0	0	0
MTH f	20	0	0	4	0	0	0	16	0	0	0	0
RIH s	3	0	0	0	1	0	0	2	0	0	0	0
SHS m	16	0	0	0	0	0	0	16	0	0	0	0
UCH n	4	0	0	0	0	0	0	4	0	0	0	0
UMD b	69	0	0	3	0	0	0	66	0	0	0	0
UMS g	27	0	0	0	1	0	0	26	0	0	0	0
UOK q	22	0	0	1	0	0	0	21	0	0	0	0
USC cc	1	0	0	0	0	0	0	1	0	0	0	0
UVA u	3	0	0	0	0	0	0	3	0	0	0	0
UWI d	16	0	0	0	0	0	0	16	0	0	0	0
VMC h	16	0	0	0	0	0	0	16	0	0	1	0
WFU p	9	0	1	1	0	0	0	7	0	0	0	0
TOTAL	314	1	1	10	4	0	1	297	0	0	1	0

TABLE 4: Week 2 Follow-up

Clinical Site	Enrolled & Eligible	DF complete	DUE	Clinical Follow-up						Medical Record Review Status		
				Complete	Incomplete	Not started	missed	early	late	Complete	Incomplete	Not started
CAP e	20	18	18	17	0	1	0	2	0	17	0	1
CMC i	17	17	16	15	0	1	0	2	0	15	0	1
DAR l	8	8	8	6	0	2	0	0	0	6	0	2
HCM t	4	4	4	3	0	1	0	2	0	3	0	1
HOU k	24	24	24	22	0	1	1	1	0	22	0	2
HRV r	10	3	3	2	0	1	0	0	0	2	0	1
IFH c	10	9	8	7	0	1	0	0	0	7	0	1
MET j	10	10	10	10	0	0	0	0	0	10	0	0
MTH f	16	12	12	12	0	0	0	0	0	12	0	0
RIH s	2	2	2	2	0	0	0	0	0	2	0	0
SHS m	16	16	16	14	0	2	0	1	0	14	0	2
UCH n	4	0	0	0	0	0	0	0	0	0	0	0
UMD b	66	64	63	62	0	0	1	1	0	62	0	1
UMS g	26	25	24	20	0	4	0	1	0	20	0	4
UOK q	21	1	1	0	1	0	0	0	0	0	1	0
USC cc	1	1	0	0	0	0	0	0	0	0	0	0
UVA u	3	2	2	2	0	0	0	0	0	2	0	0
UWI d	16	16	16	16	0	0	0	1	0	16	0	0
VMC h	16	14	13	10	0	3	0	3	0	10	0	3
WFU p	7	7	7	7	0	0	0	0	0	7	0	0
TOTAL	297	253	247	227	1	17	2	14	0	227	1	19

TABLE 5: Month 3 Follow-up

Clinical Site	Enrolled & Eligible	DF complete	DUE	Clinical Follow-up						Medical Record Review Status		
				Complete	Incomplete	Not started	missed	early	late	Complete	Incomplete	Not started
CAP e	20	18	14	11	2	1	0	7	0	12	1	1
CMC i	17	17	12	7	3	2	0	2	0	10	0	2
DAR l	8	8	1	0	0	1	0	0	0	0	0	1
HCM t	4	4	2	2	0	0	0	1	0	2	0	0
HOU k	24	24	19	11	0	6	2	1	1	11	0	8
HRV r	10	3	0	0	0	0	0	0	0	0	0	0
IFH c	10	9	3	3	0	0	0	0	0	3	0	0
MET j	10	10	6	4	1	1	0	0	0	4	1	1
MTH f	16	12	6	3	0	3	0	0	0	3	0	3
RIH s	2	2	0	0	0	0	0	0	0	0	0	0
SHS m	16	16	10	6	1	3	0	1	0	7	0	3
UCH n	4	0	0	0	0	0	0	0	0	0	0	0
UMD b	66	64	54	49	0	4	1	1	0	49	0	5
UMS g	26	25	11	5	0	6	0	0	0	5	0	6
UOK q	21	1	1	0	0	1	0	0	0	0	0	1
USC cc	1	1	0	0	0	0	0	0	0	0	0	0
UVA u	3	2	2	1	1	0	0	2	0	2	0	0
UWI d	16	16	11	11	0	0	0	1	0	11	0	0
VMC h	16	14	4	2	0	2	0	0	0	2	0	2
WFU p	7	7	5	1	1	3	0	1	0	2	0	3
TOTAL	297	253	161	116	9	33	3	17	1	123	2	36

TABLE 6: Month 6 Follow-up

Clinical Site	Enrolled & Eligible	DF complete	DUE	Clinical Follow-up						Medical Record Review Status		
				Complete	Incomplete	Not started	missed	early	late	Complete	Incomplete	Not started
CAP e	20	18	8	7	1	0	0	2	0	7	1	0
CMC i	17	17	2	2	0	0	0	2	0	2	0	0
DAR l	8	8	0	0	0	0	0	0	0	0	0	0
HCM t	4	4	1	0	0	1	0	0	0	0	0	1
HOU k	24	24	11	5	1	5	0	1	0	6	0	5
HRV r	10	3	0	0	0	0	0	0	0	0	0	0
IFH e	10	9	3	3	0	0	0	0	0	3	0	0
MET j	10	10	1	1	0	0	0	0	0	1	0	0
MTH f	16	12	0	0	0	0	0	0	0	0	0	0
RIH s	2	2	0	0	0	0	0	0	0	0	0	0
SHS m	16	16	1	0	0	1	0	0	0	0	0	1
UCH n	4	0	0	0	0	0	0	0	0	0	0	0
UMD b	66	64	36	31	1	3	1	2	0	31	1	4
UMS g	26	25	0	0	0	0	0	0	0	0	0	0
UOK q	21	1	0	0	0	0	0	0	0	0	0	0
USC cc	1	1	0	0	0	0	0	0	0	0	0	0
UVA u	3	2	0	0	0	0	0	0	0	0	0	0
UWI d	16	16	8	8	0	0	0	2	0	8	0	0
VMC h	16	14	0	0	0	0	0	0	0	0	0	0
WFU p	7	7	0	0	0	0	0	0	0	0	0	0
TOTAL	297	253	71	57	3	10	1	9	0	58	2	11

TABLE 7: Month 12 Follow-up

Clinical Site	Enrolled & Eligible	DF complete	DUE	Clinical Follow-up						Medical Record Review Status		
				Complete	Incomplete	Not started	missed	early	late	Complete	Incomplete	Not started
CAP e	20	18	0	0	0	0	0	0	0	0	0	0
CMC i	17	17	0	0	0	0	0	0	0	0	0	0
DAR l	8	8	0	0	0	0	0	0	0	0	0	0
HCM t	4	4	0	0	0	0	0	0	0	0	0	0
HOU k	24	24	0	0	0	0	0	0	0	0	0	0
HRV r	10	3	0	0	0	0	0	0	0	0	0	0
IFH c	10	9	0	0	0	0	0	0	0	0	0	0
MET j	10	10	0	0	0	0	0	0	0	0	0	0
MTH f	16	12	0	0	0	0	0	0	0	0	0	0
RIH s	2	2	0	0	0	0	0	0	0	0	0	0
SHS m	16	16	0	0	0	0	0	0	0	0	0	0
UCH n	4	0	0	0	0	0	0	0	0	0	0	0
UMD b	66	64	14	10	2	2	0	0	0	11	1	2
UMS g	26	25	0	0	0	0	0	0	0	0	0	0
UOK q	21	1	0	0	0	0	0	0	0	0	0	0
USC cc	1	1	0	0	0	0	0	0	0	0	0	0
UVA u	3	2	0	0	0	0	0	0	0	0	0	0
UWI d	16	16	0	0	0	0	0	0	0	0	0	0
VMC h	16	14	0	0	0	0	0	0	0	0	0	0
WFU p	7	7	0	0	0	0	0	0	0	0	0	0
TOTAL	297	253	14	10	2	2	0	0	0	11	1	2