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14. ABSTRACT

The current state of the science leaves neuro-oncology providers aware of their patients' distress, yet without guidance for evidence-based treatment. Previous trials of evidence-based treatment for patients in this context did not include individuals with brain cancer. The purpose of this study is to assess the feasibility and acceptability of CALM, an evidenced-based treatment which aims to relieve distress following a brain cancer diagnosis, to meet military and civilian needs. Although research suggests CALM reduces distress in patients with advanced cancer, it has not been tested in brain cancer populations. Additionally, there may be a potential need for adaptations for this population, which will be studied in this trial. The first study is a single-arm, mixed-methods, Phase IIa, proof-of-concept trial (N=15) to inform CALM adaptations for Service Members, Veterans, their beneficiaries, and civilians with brain metastases. Upon completion of the Phase IIa/b trial, we will conduct a 2-year multi-arm randomized Phase IIc Pilot Trial (N = 60). CALM is being delivered individually to participants by trained CALM interventionists via telehealth. Recruitment goal for phase IIa/b was met on 5/4/23 with 15/15 participants recruited. Five patients withdrew before study completion. Ten patients have completed their course of CALM therapy.

15. SUBJECT TERMS
None listed.

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1. Introduction

The current state of the science leaves neuro-oncology providers aware of their patients' distress, yet without guidance for evidence-based treatment. Previous trials of evidence-based treatment for patients in this context did not include individuals with brain cancer. The purpose of this study is to assess the feasibility and acceptability of Managing Cancer and Living Meaningfully (CALM), an evidenced-based psychotherapeutic treatment which aims to relieve distress following a brain cancer diagnosis, to meet military and civilian needs. Although research suggests CALM reduces distress in patients with advanced cancer, it has not been tested in brain cancer populations. Additionally, there may be a potential need for adaptations for this population, which will be studied in this trial. The first study is a single-arm, mixed-methods, Phase IIa/b, proof-of-concept trial (N=15) to inform CALM adaptations for SMs, Veterans, their beneficiaries, and civilians with brain metastases (bMET). Upon completion of the Phase IIa/b trial, we will conduct a 2-year multi-arm randomized Phase IIc Pilot Trial (N = 60). Following stratification for type of brain cancer (Primary Brain Tumor or bMET), participants will be randomized in a 2:1 design using a random number generator to either the CALM intervention or the treatment as usual control group.

Participants are being recruited from the VCUHealth and VCU Massey Cancer Center. CALM will be delivered individually to participants by trained CALM interventionists via telehealth. For both studies, psychological and behavioral assessments will take place at 3 timepoints (pre-intervention, post-intervention, and 3-month follow-up). Brief feasibility and acceptability surveys will be completed following each session, and an exit interview will be conducted within 1-month post-intervention completion.

2. Keywords

Managing Cancer and Living Meaningfully, CALM, Brain Cancer, Brain Metastases, Quality of Life, Depression, Death Anxiety, Psychology

3. Accomplishments

What were the major goals of the project?

The table below is adapted from the original SOW first phase tasks. Projected completion dates and actual completion dates/months are detailed. Subtasks that are *italicized* were executed differently than the originally SOW, but were approved by the VCU IRB and the DOD before enrollment began. The numbers (representing grant month) and dates in parentheses indicate when an ongoing task began.

Study AIM 1: To conduct a mixed-method Phase IIa Proof of-Concept Trial (N = 12) with post-session surveys and individual exit interviews to guide CALM adaptation in SMs,Veterans, their beneficiaries, and civilians with bMET.	Projected Task/ Milestone Completion (Month)	Approximate Projected End Date	Actual Completion (Month)	Actual Completion Date
Major Task 1: PRMC & IRB Submission & Approval				
Subtask 1: Finalize Protocol	1	9/15/2021	-2	7/1/2021
Subtask 2: Submit to Massey PRMC	1	9/15/2021	-2	7/22/2021
Subtask 3: Submit to VCU IRB / VA IRB	1	9/15/2021	1 to 2	9/20/2021
Subtask 4: Revise IRB	1 to 2	10/15/2021	2 to 5	1/3/2022
Subtask 5: Submit final approved protocol toclinicaltrials.gov	2	10/15/2021	2	10/7/2021
Milestone: Approval PRMC & IRB	3	11/15/2021	5	1/7/2022
Major Task 2: Recruit Participants				
Subtask 1: Identify Potential Eligible Participants	3 (every 3 months)	11/15/2021	7 to 19	3/23/2023
Subtask 2: Send Opt-Out Letters	3 (every 3 months)	11/15/2021	7 to 19	3/23/2021
Subtask 3: Screen for Eligibility/ Consent/ Enroll Participants	3 to 6	2/15/2023	8 to 21	5/3/2023
Milestone: All Patients Allocated to Interventionist (N = 15)	6	2/15/2023	21	5/3/2023
Major Task 3: Complete CALM Intervention				
Subtask 1: Prepare REDCap database	3 to 4	12/15/2021	1 to 4	12/15/2021
Subtask 2: Run CALM Intervention for (N = 15)	4 to 10	6/15/2022	23	7/25/2023
Subtask 3: Complete Post-Session Measures (Participant)	4 to 10	6/15/2022	23	7/25/2023

Subtask 4: Complete Post-Session Measures (Interventionist)	4 to 10	6/15/2022	23	7/25/2023
Subtask 5: Ongoing CALM Supervision	4 to 10	6/15/2022	23	7/25/2023
Subtask 6: Baseline / Post-Intervention Assessment Measures Completed & Entered into Database	4 to 10	6/15/2022	23	7/25/2023
Milestone: CALM Intervention Completed	10	6/15/2022	23	7/25/2023
Major Task 4: Exit Interviews				
Subtask 1: Complete Exit Interviews with Enrolled Participants	8 to 12	8/15/2022	24	8/11/2023
Milestone: Exit Interviews Transcribed and Coded	12	8/15/2022	Ongoing	Ongoing
Major Task 5: Data Analysis				
Subtask 1: Qualitative Thematic Analysis Performed	12 to 14	10/15/2022	Ongoing	Ongoing
Milestone: Quantitative Analysis Completed	15	11/15/2022	Ongoing	Ongoing
Major Task 6: Protocol Revisions				
Subtask 1: Review study findings with co-I's & patient advocates	15	11/15/2022	Ongoing	Ongoing
Subtask 2: Collaboratively decide on necessary adaptations	15	11/15/2022	Ongoing	Ongoing
Subtask 3: Develop any additional materials needed (e.g., session handouts; appointment cards)	15-16	12/15/2022	Ongoing	Ongoing
Milestone: Adapted CALM protocol for brain cancer	16	12/15/2022	TBD	TBD

What was accomplished under these goals?

1) **Major Activities**

We have received approval from our IRB and the DOD (Major Task 1) and completed recruiting participants and running the CALM intervention (Major Task 2 and 3). We are currently in follow-up data collection for Phase IIa/b.

2) **Specific Objectives**

We have recruited the anticipated 15 participants needed for the phase IIa/b trial. Ten of the participants completed the 6-session CALM intervention and their post-intervention / exit interview surveys. There were two participants who did not complete a first session (one withdrew due to interest and the other was lost to follow-up); as such they are not considered trial initiators. Three individuals withdrew following initiation of CALM (one after 1-session, one after 2-sessions, and one after 3- sessions). As such, thirteen participants will be considered as trial initiators.

3) **Significant Results/Key Outcomes**

We have preliminary findings: Of 21 patients demonstrating interest and screened, 15 enrolled in the study (73% female; 80% White; M_{age}=58yrs). All 15 participants completed baseline assessments, with 13 trial initiators. Ten participants have completed treatment, to date. Reasons for withdrawal include disinterest in intervention topics (*n*=1), lost to follow-up (*n*=2), lack of distress (*n*=1), and became too ill to participate (*n*=1). Retention is 66%. No adverse events were determined to be study-related.

4) **Other Achievements**

The regulatory process for the second iteration of this trial has been submitted to the VCU IRB for review on 8/8/2023.

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

Our CALM interventionists and members of the study team are provided ongoing supervision by CALM developer, Dr. Gary Rodin on a bi-weekly basis virtually. This supervision provides ongoing professional development for all involved. In addition, the PI participated annually in the IPOS conference (presenting and attending; support provided from this mechanism) and the post-doctoral fellow attended APOS this past March 2023 (support provided by VCU).

How were the results disseminated to communities of interest?

Preliminary results of the phase IIa/b are being presented at both EANO (Rotterdam, Netherlands) and SNO (Vancouver, Canada) in 2023. The PI received a travel award for support to travel, attend, and present these findings. Final results from the project are not yet available.

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

We plan on finalizing all follow-up assessments for those currently enrolled in the phase IIa/b trial. We will also continue the regulatory process for the phase IIc trial. We have met to discuss preliminary accommodations being named – and will implement all final decisions into the phase IIc trial.

4. Impact

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

Nothing to report as first phase is ongoing.

What was the impact on other disciplines?

Nothing to report as first phase is ongoing.

What was the impact on technology transfer?

Nothing to report as first phase is ongoing.

What was the impact on society beyond science and technology?

Nothing to report as first phase is ongoing.

5. Changes / Problems

Changes in approach and reasons for change
We have made two explicit changes that differ from the statement of work. We initially intended to (1) submit this protocol to the McGuire VA IRB and (2) recruit individuals using “opt out letters.” We did not submit this protocol to the McGuire VA but were approved to advertise the study to those individuals receiving relevant treatment at the McGuire VA without this submission. We are not recruiting individuals using “opt-out” letters but instead allowing individuals to self-refer after receiving recruitment materials via email / mail. Both of these aspects of the project are italicized in the table above detail project progress. For our phase IIc, we plan to expand recruitment to social media platforms and trial a video recruitment modality to broaden interest / reach of recruitment.

Actual or anticipated problems or delays and actions or plans to resolve them
This project has experienced significant delays due to the regulatory approval process. As a result, aspects of the project have been delayed until later in the timeline than initially projected. In response to this, we have accelerated recruitment efforts.

We expanded enrollment to N=15 to account for attrition so that we would have a hopeful N=12 completers (as originally targeted).

One program participant enrolled in the study and withdrew after the first session, citing a misunderstanding of what is involved in the intervention. As a result, a concerted effort to explain and re-explain the intent and process of the project has been made with each following participant. We have addressed this issue with the Patient Advocate Advisory Board and integrate further recommendations to pre-empt it from re-occurring in the second project phase.

There was a protocol deviation identified on 2/21/23 (screening omission) - all regulatory paperwork has been documented and submitted to VCU IRB.

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
Nothing to report.

Significant changes in use or care of human subjects
Nothing to report.

Significant changes in use or care of vertebrate animals.
Not applicable.

Significant changes in use of biohazards and/or select agents
Not applicable.

6. Products

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

RedCAP database for Phase IIa/b is currently being used for data entry but will include rich data needed to make adjustments to the intervention for Phase IIc.

7. Participants & Other Collaborating Organizations

What individuals have worked on the project?

Name: Dr. Ashlee Loughan
Project Role: Principal Investigator
Nearest person month worked: 24
Contribution to Project: No change

Name: Giuliana Zarrella
Project Role: Research Assistant / Graduate Student
Nearest person month worked: 12
Contribution to Project: No change

Name: Dr. Autumn Lanoye
Project Role: Co- Investigator
Nearest person month worked: 24
Contribution to Project: No change

Name: Dr. Alexandria Davies
Project Role: Postdoctoral Fellow; Interventionist
Nearest person month worked: 12
Contribution to Project: Dr. Davies has served as an interventionist providing CALM therapy for this trial.

Name: Amber Fox
Project Role: Interventionist
Nearest person month worked: 12
Contribution to Project: Amber Fox has served as an interventionist providing CALM therapy for this trial.

Name: Chris Kleva
Project Role: Interventionist
Nearest person month worked: 12
Contribution to Project: Chris Kleva has served as an interventionist providing CALM therapy for this trial.

Name: Dr. Gary Rodin
Project Role: Co- Investigator
Nearest person month worked: 24
Contribution to Project: No change

Name: Dr. Mark Malkin
Project Role: Co- Investigator
Nearest person month worked: 24
Contribution to Project: No change

Name: Dr. Suzanne Mazzeo
Project Role: Co- Investigator
Nearest person month worked: 24
Contribution to Project: No change

Name: Dr. Dace Svikis
Project Role: Co- Investigator
Nearest person month worked: 24
Contribution to Project: No change

Name: Dr. Leigh Swartz
Project Role: Co- Investigator
Nearest person month worked: 24
Contribution to Project: No change

Name: Leroy Thacker
Project Role: Co- Investigator
Nearest person month worked: 24
Contribution to Project: No change

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

Post-doctoral fellow, Dr. Alexandria Davies, and two graduate students, Amber Fox and Chris Kleva, were added as interventionists on this trial.

Dr. Sarah Braun is no longer an interventionist, but she remains active in the project as an unpaid consultant.

Dr. Malkin (co-I) and Kelcie Willis (interventionist) have left the VCU institution. They remain active in the project as unpaid consultants, as needed.

What other organizations were involved as partners?
There is no formal partnership. Hunter Holmes McGuire VA personnel have allowed us to provide materials to their patients for recruitment.

8. Special Reporting Requirements

Nothing to report.

9. APPENDICES

None attached.