Official Title: Dialectical Behavioral Therapy Skills Training for Metastatic Lung Cancer Patients

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Please type your Research Abstract here:

The Research Abstract should summarize the main points of your study in one paragraph. The following guidelines may help you:

1. Purpose and objective (1-2 sentences)
2. Study activities and population group (2-4 sentences)
3. Data analysis and risk/safety issues (1-2 sentences)

Metastatic lung cancer patients experience significantly greater psychological distress (i.e., depression, anxiety) compared to other cancers. Psychological distress is as a prognostic indicator for worse clinical outcomes and poorer overall survival in cancer patients. Dialectical behavioral therapy (DBT) is a transdiagnostic, evidence-based psychotherapy that teaches participants a core set of behavioral skills (distress tolerance, emotion regulation, mindfulness, interpersonal effectiveness) to cope more effectively with emotional and physical symptoms. The proposed study seeks to adapt and pilot test DBT skills training for patients with metastatic lung cancer using the ADAPT-ITT framework. Participants will be metastatic lung cancer patients who score >3 on the NCCN distress thermometer. Phase I aims to use focus groups and interviews with key stakeholders (metastatic lung cancer patients (N=20), thoracic oncology providers (N=6), clinicians with expertise in survivorship and behavioral symptom management (N=6)) to determine if and how DBT skills training must be modified for implementation with metastatic lung cancer patients. Adapted material will be reviewed by topical experts in DBT and implementation science to produce a manualized, adapted DBT skills training protocol for metastatic lung cancer patients (DBT-MLC). Phase II aims to pilot test DBT-MLC to assess feasibility, acceptability, and examine pre-to-post intervention outcomes of psychological distress, (i.e., depression and anxiety) fatigue, dyspnea, pain, emotion regulation, tolerance of uncertainty, and DBT coping skill use. Qualitative data from focus groups and interviews will be analyzed using rapid analysis. Quantitative data from Phase II will be analyzed using descriptive statistics and multivariate analyses in SAS or SPSS. The risks to participants are minimal and include psychological distress and breach of confidentiality.

Research Summary

State your primary study objectives

Aim 1: To adapt DBT skills training for patients with metastatic lung cancer (DBT-MLC).

Aim 2: To pilot test and refine the developed DBT-MLC protocol, "LiveWell".

State your secondary study objectives

None - not applicable.

Please select your research summary form:

Standard Research Summary Template

This is the regular (generic) research summary template which is required for all regular applications (unless your protocol fits under the other research summary templates in this category). Use of these instructions is helpful for ensuring that the research summary contains all necessary elements.

Standard Research Summary

Purpose of the Study

- Objectives & hypotheses to be tested

We propose to adapt, pilot test, and refine DBT skills training for patients with metastatic lung cancer. The proposed project consists of two phases. Phase I will entail adaptation of DBT skills training for metastatic

lung cancer patients. We will follow the ADAPT-ITT framework, a step-by-step approach to adapting an intervention for a new target population while maintaining its core elements and spirit. We will enlist stakeholders to evaluate if and how DBT skills training needs to be modified to improve fit with metastatic lung cancer patients. The goal is to produce an adapted DBT skills training that can be implemented with patients with metastatic lung cancer (DBT-MLC). Phase 2 will involve pilot testing and refining the DBT-MLC protocol with the target population.

Aim 1: To adapt DBT skills training for patients with metastatic lung cancer (DBT-MLC). We will conduct focus groups and in-depth interviews with key stakeholders: patients with metastatic lung cancer (N=20, 4-6 groups), thoracic oncology providers (N=6), and clinicians with expertise in survivorship and behavioral symptom management (N=6), to collect input on the format and content of DBT skills training (i.e., delivery, dose, materials). Stakeholder input will inform adaptation to increase relevance and acceptability to patients with metastatic lung cancer. This will inform production of an initial DBT-MLC protocol (i.e., manualized protocol, patient workbook). Topical experts (N=5) with specialization in areas relevant to DBT-MLC (DBT, intervention science) will provide detailed feedback on the developed DBT-MLC protocol. Feedback will be integrated to produce the next iteration of the DBT-MLC protocol. *H1*: The systematic steps of the ADAPT-ITT framework will produce an adapted version of DBT skills training that can be implemented with metastatic lung cancer patients (DBT-MLC).

Aim 2: To pilot test and refine the developed DBT-MLC protocol, "LiveWell". Participants will be metastatic lung cancer patients who score >3 on the NCCN distress thermometer. We will evaluate feasibility, acceptability, examine pre- to post- intervention outcomes, and conduct qualitative exit interviews to collect participants' experience and feedback. We hypothesize that DBT-MLC will demonstrate evidence of: *H1*: feasibility (meet study accrual, >80% completed sessions, <25% attrition); *H2*: acceptability (>80% of participants report satisfaction); *H3*: benefit in the primary outcome of psychological distress (i.e., depression, anxiety); *H4*: benefit on secondary outcomes (fatigue, dyspnea, pain, emotion regulation, tolerance of uncertainty, quality of life, illness acceptance, DBT skill use). *H5*: Information collected in qualitative exit interviews will inform DBT-MLC refinement.

Background & Significance

- Should support the scientific aims of the research

Lung cancer is the second most common cancer in the United States, with an estimated 229,000 individuals diagnosed in 2020.[1] Non-small cell lung cancer (NSCLC) accounts for 84% of lung cancers, and nearly 40% of patients with NSCLC have metastatic disease at diagnosis.[1] Metastatic NSCLC has a historically poor prognosis, with a 5-year survival rate of 6% in 2014.[1] However, median survival has improved markedly over the past several years thanks to advances in treatment, namely the approval of immune checkpoint inhibitors and targeted therapies.[1,2] First-line treatment with pembrolizumab, an immune checkpoint inhibitor, has demonstrated significant survival benefit and durable responses in patients with metastatic NSCLC and high levels of PD-L1 expression.[3] Recent 5-year data from the KEYNOTE trial showed that first-line treatment with pembrolizumab doubled median survival compared to platinum-based chemotherapy (26 vs 13 months), and twice as many patients treated with pembrolizumab were alive at 5 years (32% vs 16%).[3] Targeted therapies have had the most dramatic effect on survival in metastatic NSCLC.[4] Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) positive NSCLC have a median overall survival of 3 and 7 years, respectively, with targeted therapy.[5-7] However, only a subset of patients have these mutations, and there remains uncertainty about which patients will respond to therapies and what the duration of response will be. This can be a source of psychological distress for patients as they try to understand their prognosis and adjust to a terminal diagnosis.

Psychological distress describes the experience of symptoms that can range in severity, from typical challenges with adjustment to illness to diagnosable mood and anxiety disorders. Distress can interfere with an individual's ability to cope with cancer diagnosis, symptoms, and treatment, and has been identified as a prognostic indicator for worse clinical outcomes and poorer overall survival in people with cancer.[8,9] Given this, the International Psycho-oncology Society Standard of Quality Cancer Care has emphasized that distress should be measured as the "6th vital sign", alongside blood pressure, pulse, and respiratory rate.[10-14]

Patients with lung cancer endorse significantly higher rates of psychological distress (44%-61%) compared to other disease types.[15-18] This is likely a product of significant physical and emotional symptom burden from the disease and its treatment. Patients with NSCLC consistently endorse high frequency and intensity

of fatigue, dyspnea, and pain on patient-reported outcome measures,[19] and these symptoms have been associated with distress.[20] Emotionally, patients with metastatic lung cancer experience intense, negative emotions (e.g., fear, sadness) that are normal and justified in the context of adjusting to a cancer diagnosis, undergoing tough and changing medical treatments, modifying important life goals, experiencing effects on relationships with loved ones, and confronting mortality.[21,22] Patients with lung cancer may also experience uniquely difficult emotions (e.g., shame, guilt) due to having a cancer that is stigmatized.[23] Health-related stigma and related negative affect can have significant negative consequences for health-related quality of life and clinical outcomes.[24,25] Finally, patients with metastatic lung cancer must tolerate significant uncertainty about the future, given the complex situation of having a historically poor prognosis cancer, but the potential to respond to new therapeutic agents. Taken together, these challenges contribute to increased psychological distress in lung cancer patients, which is related to worse clinical outcomes and lung cancer-related survival.[9]

Little research has described the application of psychological and behavioral interventions to reduce distress in people with metastatic lung cancer, likely due to nihilism about its benefits.[16] Interventions that have been tested demonstrate mixed findings[23] and have encountered methodological issues (e.g., not screening for baseline distress, variability in interventional approaches and outcome measures) and barriers to implementation (e.g., high symptom burden, poor physical function, challenges attending in-person study visits). As the number of patients living longer with metastatic lung cancer continues to grow, there is a critical need for interventions that provide patients with the skills to manage challenging symptoms, regulate difficult emotions, and live meaningfully with uncertainty about the future.

Dialectical behavioral therapy (DBT) is an evidence-based psychotherapy that is likely to benefit patients with metastatic lung cancer. DBT is unique from other cognitive behavioral approaches in its combination of elements of dialectical thinking (e.g., two seemingly opposing ideas, views or emotions that can both be true at the same time), behavioral therapy, and zen.[26-28] DBT teaches participants a compendium of over 60 skills from across psychology, including strategies to promote acceptance of the present moment (e.g., mindfulness, distress tolerance), as well as strategies to facilitate behavior change (e.g., emotion regulation, interpersonal effectiveness). DBT provides a unifying model to combine these pieces into a coherent, cohesive treatment designed to help people cope more effectively with difficult emotions and symptoms.[28] Traditional full-model DBT includes multiple therapeutic components (i.e., individual therapy, skills training) and is time and resource intensive.[26] However, DBT skills were developed to be transdiagnostic, and DBT skills training has been successfully adapted and demonstrated efficacy in reducing psychological distress in a variety of clinical populations, including people with mood and anxiety, eating, trauma, and substance use disorders.[30-37]

Surprisingly, very few studies have explored DBT skills training in patients with chronic illness, although initial research has suggested benefit.[38-44] To date, DBT skills training has not been evaluated in patients with metastatic lung cancer, who can benefit substantially due to high rates of psychological distress and congruence of skills with patients' physical and emotional symptom needs. However, DBT skills training likely needs to be adapted to increase acceptability and relevance in patients with metastatic lung cancer. Considerations for DBT for this patient population include: 1) delivery, as traditional in-person, group-based treatment poses significant burden (i.e., time, physical, cost) and environmental risk for immunocompromised patients, 2) dose, as typical duration of skills training visits (2.5 hours) and length of treatment (6 months) are not feasible for patients with serious illness, and 3) materials, to increase content relevance (e.g., examples).

The proposed intervention will adapt an evidence**-**based treatment, DBT skills training, to help metastatic lung cancer patients cope more effectively with difficult emotions and symptoms. The adapted intervention will provide patients with training in DBT skills deemed most relevant for patients with metastatic lung cancer. Skills training is expected to decrease psychological distress (depression, anxiety), as well as reduce physical symptom burden (fatigue, dyspnea, pain) and improve emotion regulation and tolerance of uncertainty**.** The proposed project is innovative in its selection of an evidence-based intervention that is theoretically and practically well suited to meet the needs of patients with metastatic lung cancer. The proposed study addresses three significant gaps in the literature.

i. Psychosocial and behavioral symptom management interventions for patients with metastatic lung cancer are few and not often adapted to meet their specific needs. Psychosocial and behavioral symptom management interventions are effective for patients with cancer.[45-48] However, few intervention studies include metastatic lung cancer patients. Evidence-based interventions adapted to meet the specific needs of metastatic lung cancer patients are even fewer.[23] Furthermore, while some symptoms may respond to traditional intervention strategies (e.g., thought challenging, behavior change), others may not. Metastatic lung cancer patients require strategies to change things within their control (e. g., emotions, behavior), and to facilitate acceptance of things outside of their immediate control (e.g., the future). Such strategies can alleviate suffering without invalidating the patients' experience. As therapeutic advances increase the number of patients living with metastatic disease, interventions that meet these needs are warranted.

ii. DBT skills are well suited to address psychological and physical symptoms in people with cancer, but remain largely unstudied. DBT skills were developed to be transdiagnostic, making them highly relevant across clinical populations. However, little research has examined DBT skills in patients coping with chronic illness. Several studies have evaluated DBT for chronic pain and found improvements in pain catastrophizing and interference, physical functioning, and depressive symptoms.[38,39] Additional studies have demonstrated efficacy of DBT skills to improve medication adherence and self-care behaviors in patients with chronic illness.[40,41] The few studies to date describing DBT in cancer have significant methodologic limitations, including problems with session attendance, study adherence, and questionnaire completion.[42-44] One study evaluated DBT skills training combined with biofeedback training in women with early-stage breast cancer.[42] Participants were taught DBT skills in an 8-session workshop. Narrative analysis identified skills across the four DBT domains that participants found helpful to cope with cancer, including mindfulness (wise mind), distress tolerance (deep breathing, self-soothing), emotion regulation (label emotions, take a pause, exercise) and interpersonal effectiveness (negotiate, saying 'no'). Participants demonstrated reductions in distress and somatization symptoms on quantitative measures and rated the study as highly beneficial. Qualitatively, participants reported receptivity to DBT skills, improvements in coping with cancer-related distress, and appreciation of the group format as a way to share coping strategies with and feel supported by others with a shared experience. This sparse but promising literature indicates a need for further study of DBT in cancer.

iii. DBT skills training has not been adapted for patients with metastatic lung cancer. It is likely that DBT skills training must be adapted to increase acceptability and relevance to patients with metastatic lung cancer.[28] Intervention adaptation balances fidelity to the original intervention with modifications to meet the needs of the new target population and optimize benefit.[49-50] This may include adaptations in delivery, dose, and/or materials (e.g., individual vs. group, in-person vs telehealth, changing the order or length of activities, addition or removal of content, developing customized materials specifically for the primary audience). Research suggests that DBT skills training can be effectively delivered in individual or group formats, and that it can be implemented via telehealth.[28,30,51] Briefer adaptations of skills training have demonstrated efficacy in reducing psychological distress.[30] An abbreviated, telehealth-delivered protocol consisting of skills relevant to managing emotional and physical symptoms may be particularly beneficial for metastatic lung cancer patients.

Adapted DBT skills training has the potential to significantly reduce psychological distress in metastatic lung cancer patients. If adapted DBT skills training for metastatic lung cancer (DBT-MLC) demonstrates initial evidence of feasibility, acceptability, and positive change in pre-to-post intervention outcome measures, the intervention will be tested in a larger randomized controlled trial. Positive findings could encourage researchers to adapt DBT skills training for other cancer and chronic illness populations reporting psychological distress, as well as their caregivers. Findings could also have implications for clinical practice. Patients with metastatic lung cancer who endorse elevated distress during clinic visits could be referred and offered participation in DBT-MLC. Early intervention may reduce the downstream burden of psychological distress (mental and physical health comorbidities, healthcare utilization and costs). Future work could assess the cost-effectiveness of DBT-MLC, and its potential for broader dissemination.

Design & Procedures

- Describe the study, providing details regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

The proposed project will adapt and pilot test DBT skills training for patient with metastatic lung cancer. We utilize the ADAPT-ITT theoretical framework, which details a series of eight sequential steps to modify an existing evidence-based treatment for use in a new target population. Phase 1 will focus on intervention adaptation. Phase 2 will focus on pilot testing the intervention in the new target population. Figure 1 provides an overview of the study design.

Phase 1 (Months 0 to 12): Adaptation of the Intervention

We will enlist stakeholders to evaluate DBT skills training to determine if and how it must be adapted to increase relevance and acceptability to metastatic lung cancer patients. Stakeholders will include metastatic lung cancer patients (N=20), thoracic oncology providers (N=6), and clinicians with expertise in survivorship and behavioral symptom management (N=6). We will conduct focus groups and/or individual

interviews. We plan to conduct patient stakeholder interviews in a small group format (e.g., 4 focus groups of 5 participants) given that skills training is typically delivered in a group format. This will allow us to assess group dynamics as we consider the optimal format for intervention delivery (group vs individual). We chose individual interviews for providers given past challenges with coordinating a shared time and place for multiple busy providers.

Stakeholders will be queried about intervention structure and delivery characteristics (e.g., group vs individual, treatment dose, session length, acceptability of telehealth) as well as content and materials (e. g., relevance of skills, examples, activities). We will inquire about anticipated barriers to attendance and strategies to provide participants with missed content. Patient stakeholder interviews will be approximately 90 minutes and participants will be compensated $30. Provider stakeholder interviews will be approximately 60 minutes and participants will be compensated with a $20 gift card. Stakeholder focus groups and/or interviews may be conducted in-person or remotely via video-conferencing using Zoom for Health. The IRB-approved study team members will use a Duke encrypted laptop for data collection and audio recording of stakeholder interviews using Voice Recorder (10.1805.1201.0) by Microsoft. After focus groups and sessions are completed, audio recordings will be saved to the Duke University Medical Center psychiatry server and deleted from the laptop. All audio recordings will be deleted at the end of the study. Audio recordings will be transcribed verbatim for supervision purposes and for qualitative analysis. Transcription and qualitative analysis will be conducted by Dr. Hyland, who may be assisted by other study key personnel. Demographic and clinical information for patient stakeholders will be extracted via medical record review.

Using the information gleaned from stakeholder interviews, will draft an initial protocol (provider treatment manual, patient materials) for the adapted evidence-based treatment, DBT-MLC. Once the initial protocol has been developed, we will consult with experts in DBT to ensure the protocol remains true to the spirit of the original evidence-based intervention. We will also consult with experts in implementation science to evaluate the potential for adoption and integration of DBT-MLC into healthcare. No individual identifiable participant information will be provided in the protocol sent to topical experts. Feedback from topical experts will be integrated into the adapted DBT-MLC treatment protocol and materials. This will produce a final draft of DBT-MLC for pilot testing.

Phase 2 (Months 13 to 36): Test and Refine the Intervention.
Data from stakeholder interviews in Phase I has informed the final intervention structure and delivery characteristics (e.g., group vs individual, treatment dose, session length, acceptability of telehealth) as well as content and materials (e.g., relevance of skills, examples, activities). This has produced the adapted DBT-MLC intervention, "LiveWell", which consists of 8 sessions, approximately 45-60 minutes in length, delivered approximately weekly. Stakeholder insights determined that skills training will be done individually (versus in a small group setting). Given the benefits telehealth offers with regard to access and research demonstrating its acceptability and feasibility with cancer patients, the intervention will be delivered remotely. An overview of proposed session content is provided in the Table below. It is anticipated that participation in the intervention will take approximately 12 weeks overall.

Table. Session Topics, Skill Content, and Homework Assignments

We will assess the feasibility, acceptability, and pre-to-post intervention improvement in outcome variables using a single-arm pilot study (N=30). Standardized self-report assessment measures will be administered at baseline, immediately post-intervention, and 1 month follow-up. Participants can complete assessments via hard copy or online via RedCap. All participants will be offered participation in an exit interview to inform DBT-MLC refinement. If necessary and appropriate, patient participants in Phase II of the study may be provided with a device (e.g., tablet computer) to participate in the pilot intervention program. A data plan will be provided if necessary. These will be set with restrictions. Participants will return tablet computers following completion of study activities.

Study personnel will be trained in procedures related to delivering DBT-MLC. Dr. Hyland will attend formal trainings in delivering DBT skills training as part of the fellowship project. She will create a standard operating procedure manual for the delivery of DBT-MLC. Study interventionists will thoroughly review the treatment manual and rehearse intervention delivery by role playing skills training sessions.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

Eligibility criteria for patients. Eligibility criteria for patients were determined in consultation with mentor and thoracic oncologist, Dr. Thomas Stinchcombe, MD, and based on previous psychosocial studies in advanced lung cancer.

Eligibility criteria for patients included in Phase I and Phase II include:
1) be diagnosed with metastatic (AJCC stage IV) non-small cell lung cancer,
2) be undergoing systemic treatment (chemotherapy, targeted therapy, and/or immunotherapy) for lung cancer at DCI,
3) score $\geq$3 on the National Comprehensive Cancer Network Distress Thermometer for distress over the past week (Range: 0-10),
4) be $\geq$ 18 years of age,
5) be able to understand, speak, and read English, and
6) be able to provide informed consent.

Exclusion criteria for patients include:
1) reported or suspected cognitive impairment subsequently informed by a Montreal Cognitive Assessment (MOCA) of <26;
2) presence of untreated serious mental illness (e.g., schizophrenia) indicated by the medical chart, treating oncologist, or other medical provider; or
3) expected survival of 4 months or less.

Eligibility criteria for non-patient stakeholders. Non-patient stakeholders included in Phase I will include individuals with expertise in areas relevant to the intervention, including: thoracic oncology, palliative care, cancer metavivorship (e.g., cancer patients living with metastatic disease), behavioral symptom management, dialectical behavioral therapy, and intervention science. Potential stakeholders will be identified in consultation with the study mentorship team. Examples of such providers may include: healthcare professionals (e.g., oncologist, physician assistant, nurse) working within the Division of Thoracic Oncology at Duke University Medical Center.

Eligibility criteria for non-patient stakeholders included in Phase I include:
1) be $\geq$ 18 years of age,
2) be able to understand, speak, and read English, and
3) be able to provide informed consent.

Subject Recruitment and Compensation

- Describe recruitment procedures, including who will introduce the study to potential subjects. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about approximately how many DUHS subjects will be recruited. If subjects are to be compensated, provide specific prorated amounts to be provided for expenses such as travel and/or lost wages, and/or for inducement to participate.

Recruitment will take place through the Duke Cancer Institute (DCI). Research and clinical care providers at the DCI are in support of recruitment for this study, including Thomas Stinchcombe, MD, thoracic oncologist, and Cheyenne Corbett, PhD, LMFT, Director of DCI Psychosocial Services and the Cancer Patient Support Program. Recruitment procedures will comply with HIPAA regulations.

Non-patient stakeholder recruitment will be facilitated by Kelly Hyland, PhD (F32 awardee) and supported by the mentorship team. For example, Dr. Thomas Stinchcombe, MD, a thoracic oncologist and member of this study's mentoring committee, will invite his colleagues within the Division of Thoracic Oncology to participate in the thoracic oncology provider interviews. Expert stakeholders will be contacted by F32-awardee and study coordinator, Kelly Hyland. Kelly Hyland will also deliver a brief presentation about the study to providers within the Division of Thoracic Oncology as well as to the Duke Cancer Patient Support Group to advertise the study. Time, format, and location for this presentation will be coordinated with Dr. Stinchcombe and other relevant providers.

For patient recruitment, the proposed study will follow the same recruitment procedures used in numerous federally funded projects by our research team in the Duke Pain Prevention and Treatment Research Program (PPTRP). Under a HIPAA waiver, potentially eligible patients will be identified via electronic medical record review. Potential participants will be emailed and/or mailed a letter signed by their treating

oncologist and study PI informing them about the study. The letter will state that a member of the study team may approach them in clinic at their next appointment; patients wishing not to be approached can call a number to opt out of the study. All study team members who are involved in recruitment (Dr. Hyland & research coordinators) will complete the required DOCR Recruitment and Engagement training. Providers will be recruited for the focus groups and interviews directly through study staff. Using a script that is compliant with IRB policies, a member of the study team will describe the study purpose, procedures, risks and benefits, and provide potential participants with an opportunity to ask questions, as well as assess participants' eligibility. Informed consent will be documented by signature on forms approved by the IRB for eligible and interested participants. If a member of the study team is unable to make contact with the participant during a clinic appointment (e.g., due to time constraints, COVID-19 restrictions), the participant will be informed that a member of the study team would like to contact him/her by telephone. In these cases, the eligibility screening and informed consent procedures will occur remotely, via phone and /or videoconferencing. Eligible and interested participants who consent by phone will either: 1) complete an eConsent form via Redcap; or 2) be mailed two written consent forms (one for the participant and one to be returned to the research team via mail). This will be based on participant preference and convenience.

For those who decline participation, information will immediately be deleted from our records including their address and telephone number. However, we will retain their name and MRN so that we do not contact a person who has already declined participation. This will allow us to respect the wishes of the patients who do not want to be involved. We will delete the patient's name and MRN upon completion of enrollment. We will retain demographic information and basic medical information on patients who decline in order to see if we are systematically under including certain subgroups of the study population, which would limit our ability to generalize findings. This information will always be kept separate from direct identifiers. If a patient is not eligible or if he/she decides he/she is not/no longer interested in participating, the patient will be provided with psychosocial resources offered through DCI, if needed. Participants will be told they can discontinue participation at any time with no impact to their medical care. Additionally, Duke patients with metastatic lung cancer are able to contact the study staff if they are interested in participating in this study. Participants will be compensated $30 for participating in the focus group. Non-patient stakeholders who participate in interviews will be compensated with a $20 Starbucks giftcard. Participants recruited into the single-arm pilot will be compensated $40 for completing each of the three study assessments (i.e., baseline, post-intervention, 1-month follow-up, maximum compensation of $120). We will conduct qualitative exit interviews with pilot participants to inform DBT-MLC intervention refinement. All participants will be offered the opportunity to participate in a qualitative exit interview after completing the post-intervention assessment. Qualitative exit interviews will follow similar procedures to the stakeholder interviews and participants will be compensated $30.

Consent Process

- Complete the consent section in the iRIS Submission Form.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

Only subjects who have capacity to give legally effective consent will be included in this study.

Study Interventions

- If not already presented in #4 above, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i.e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

The primary (psychological distress) and secondary outcome measures (fatigue, dyspnea, pain, emotion regulation, tolerance of uncertainty, DBT skills use) will be collected at all three assessment time points. We selected brief measures to reduce patient burden. It is estimated that assessments will take approximately 20-30 minutes to complete.

a. Sociodemographic, clinical, and lifestyle variables. Baseline assessment will include relevant sociod emographic variables (e.g., age, race, ethnicity, employment, education). Clinical information (e.g., date of cancer diagnosis, date(s) and type(s) of treatment) will be collected via medical record review. Participants will self-report lifestyle characteristics (e.g., cigarette smoking, alcohol consumption).
b. Feasibility. Treatment feasibility will be assessed through analysis of study process data, including study accrual (goal met in the allotted time frame), session attendance ($\geq$80%), and treatment attrition ($\leq$ 25%). Reasons for missed sessions and study discontinuation will be collected.
c. Acceptability. Acceptability will be assessed post-intervention using the 8-item Client Satisfaction Questionnaire (CSQ). The scale includes eight items assessing participants' level of satisfaction with treatment, with response options ranging from 1 (quite dissatisfied) to 4 (very satisfied). Acceptability will be demonstrated by 80% of participants reporting intervention satisfaction on the CSQ. Intervention engagement will be assessed on an ongoing basis and recorded in RedCap (i.e., homework completion).
d. Pre- to Post-Intervention Outcomes.
Psychological Distress. Distress will be measured using the PROMIS Depression (8 items) and Anxiety (8 items) Short Form Scales. Participants are asked to rate how frequently they experienced each symptom over the past 7 days on a 5-point scale ranging from 1 (never) to 5 (always), with higher scores indicating greater distress (i.e., more depression or anxiety). PROMIS measures of distress have demonstrated reliability and validity in cancer samples as well as sensitivity to change in patients participating in psychological interventions.
Physical Symptoms. *Fatigue.*
Fatigue (i.e., severity and interference) will be assessed using the Fatigue Symptom Inventory (FSI), which was developed for and validated in cancer patients. The FSI consists of four items assessing fatigue severity (worse, least, average, current) and seven items assessing fatigue interference over the past week. Items are rated on an 11-point scale, ranging from 0 (no fatigue/interference) to 10 (worst fatigue imaginable/completely interferes). The FSI has demonstrated excellent reliability and validity in cancer populations.
Dyspnea. Breathlessness will be assessed using the Modified Medical Research Council Dyspnea Scale (MMRCDS). The MMRCDS is self-report measure of perceived respiratory disability. Items are rated on a 5-point scale, ranging from 0 to 4, with higher scores indicating worse dyspnea. The MMRCDS has demonstrated good reliability and validity in lung cancer samples.
Pain. Pain (i.e., severity and interference) will be assessed using the Brief Pain Inventory-Short Form (BPI-SF) The BPI-SF consists of 4 items assessing pain severity (worst, least, average, current) and seven items assessing pain interference over the past week. The BPI-SF includes an 11-point scale, with options ranging from 0 (no pain/interference) to 10 (worst pain imaginable/completely interferes). The BPI-SF has demonstrated good reliability and validity in cancer samples.
Emotion Regulation. The Difficulties in Emotion Regulation Scale (DERS-18) will be used to assess emotion regulation and dysregulation. The DERS-18 consists of 18 items assessing 6 facets of emotion regulation (awareness, clarity, goals, impulse, nonacceptance, strategies). Items are rated on a scale of 1 (almost never, 0-10%) to almost always (5, 91-100%), with higher scores indicating more difficulty with emotion regulation. The DERS has been used in cancer samples and has demonstrated evidence of internal consistency and clinical and predictive utility in adults with emotional distress.
Tolerance of Uncertainty. The Intolerance of Uncertainty Scale (IUS) will be used to measure emotional, cognitive, and behavioral reactions to uncertainty situations. Participants indicate how characteristic 27 items are of them on a scale ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me), with higher scores indicating greater intolerance of uncertainty. The IUS has demonstrated evidence of excellent reliability and validity in cancer samples.
Quality of Life. The Functional Assessment of Cancer Therapy - Lung Cancer version (FACT-L) will be used to assess quality of life across 5 domains (physical, emotional, social, functional, lung cancer-specific concerns).
Illness Acceptance. The Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE) scale - Peaceful Acceptance of Illness sub scale will be used to assess illness acceptance.
DBT Skill Use. The DBT Ways of Coping Checklist (DBT-WCCL) – DBT Skills Subscale (DSS) will be used to assess patient-reported frequency of skill use to manage difficult situations. To avoid response bias, DBT language and the names of skills are avoided in the scale and general descriptions are used. Items are rated on a 0-3 scale, indicating if the coping strategy was never, rarely, sometimes, or regularly used in the past month when faced with a stressor. Items that are not aligned with skills that are included in DBT-MLC following study adaptation procedures (Phase 1) will be removed. The DSS has demonstrated evidence of reliability and validity, including criterion validity to accurately measure DBT skill use, in studies of patients undergoing DBT treatment.
e. Qualitative Exit Interviews. We will conduct qualitative exit interviews with pilot participants to inform DBT-MLC intervention refinement. All participants will be offered the opportunity to participate in a qualitative exit interview after completing the post-intervention assessment. Qualitative exit interviews will follow similar procedures to the stakeholder interviews.

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant individuals, imprisoned persons or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

Risks
Participation poses minimal risk to participants. No adverse events are anticipated. Participation in all phases of the study is voluntary and participants can withdraw at any time. The risks associated with all phases of this study are minimal and rare. First, participation in either a focus group, interview, or a psychological treatment intervention is associated with few negative side effects. The focus groups, intervention sessions, assessments and exit interviews will cover topics including cancer diagnosis and treatments, symptoms of psychological distress (i.e., depression and anxiety), physical symptom burden (i. e., fatigue, dyspnea, pain), as well as emotion regulation, tolerance of uncertainty, and DBT skill use. Although some participants may find certain questions or topics to be upsetting, heightened awareness of existing psychosocial and practical needs may be the first step in resolving these concerns. All of these topics may involve participants providing sensitive and personal information. Participants may feel embarrassed or uncomfortable with disclosing this information. All efforts will be made to remain sensitive to participant's needs, HIPAA requirements, and confidentiality procedures.

Participants will be fully informed about the study during the informed consent process and instructed to decline to answer any question or to discuss any issues they find troubling. If a participant reports significant distress during study participation, Dr. Somers (licensed clinical psychologists) will be consulted. Participants who report suicidality will be managed following the Suicide Prevention Plan included in "Other Study Documents". If the participant requires additional treatment, appropriate referrals will be made. The study team has extensive experience conducting psychosocial intervention trials with cancer patients and have not encountered significant psychological distress caused by study participation. Moreover, cancer patients and their family caregivers often report benefits from participating in psychosocial research. Thus, the risk of psychological distress is modest and the safeguards should be adequate.

In a group setting, such as in a focus group or treatment group, there is risk of disclosure of personal information by another participant. Groups will be instructed to maintain participants' confidentiality at the onset of the group, and participants will be asked not to share what goes on during the group. Additional efforts will be employed to maintain confidentiality. Two password-protected databases will be used to ensure confidentiality of participant information and data by keeping identifying information separate from research records. The first database, used for tracking and recruitment, will house the contact information of individuals who may be eligible for the study as well as participants who have agreed and those who have declined to participate. No medically sensitive information or outcome data will be stored in this database, and all identifiable data of non-participants (e.g., names) will be deleted. All study data will be stored in a separate, password-protected database. Participants will be assigned separate subject numbers, and data will be stored in the database under the subject number.

The IRB-approved study team members will use a Duke encrypted laptop for data collection and recording of stakeholder interviews and study sessions. After focus groups and sessions are completed, audio recordings will be saved to the Duke University Medical Center psychiatry server and deleted from the laptop. All audio recordings will be deleted at the end of the study. Deidentified transcripts of focus groups and exit interviews will be stored in separate password protected files. Both databases and transcripts will be kept on the Duke University Medical Center psychiatry server housed behind the DUMC firewall. If necessary, paper copies of assessment packets will be filed by subject number and housed in a locked cabinet in a locked office in the PPTRP offices. Only Dr. Hyland, her sponsor (Dr. Somers), and mentors affiliated with the project will have access to the research records. To ensure that there are no changes in potential risk during the study, and that confidentiality is maintained, a Data and Safety Monitoring Plan (see below) will be implemented.

Study tablets may be used for data collection (through REDCap). If necessary and appropriate, patient participants in Phase II of the study may be provided with a device (e.g., tablet computer) to participate in the pilot intervention program. A data plan will be provided if necessary. These will be set with restrictions. Specifically, the following steps will be taken: 1) Duke Mobile Device Manager (MDM) will be installed on all devices; 2) Study staff will keep the operating system on the most current version (Settings>General>Software Update); 3) We will enable encryption on the device (Settings>Passcode) and verify that data protection is enabled, set "require passcode" to immediately, and enable erase data to "automatically erase the device" after 10 failed passcode attempts; 4) We will set Auto-Lock. 4) Study

staff will use Restrictions to restrict any unnecessary access including changing account settings (Settings>General>Restrictions); 5) We will reset devices between use for different participants (Settings>General>Reset>Erase All Content and Settings); and 6) At end of device life, we will send the device to Duke Procurement Surplus & Salvage for secure destruction.

Alternative options to participating in the current study include choosing not to participate. Participants may choose to seek alternative psychosocial treatment through the Cancer Patient Support Program at DCI, or in another clinic at Duke or in the community. Benefits of receiving psychological services outside of the study may also include reduced psychological distress. However, the proposed DBT-MLC is specifically designed to be relevant and acceptable to patients with metastatic lung cancer, and therefore may represent a better fit for the needs of these patients compared to traditional therapeutic approaches.

The risks to non-patient stakeholders are minimal and primarily include psychological distress and breach of confidentiality. Non-patient stakeholders will be asked to evaluate the DBT-MLC protocol by reviewing session handouts outlining educational content and dialectical behavioral therapy strategies to address emotional (e.g., anxiety, depression) and behavioral symptoms (e.g., pain, fatigue, dyspnea). Providers will also be asked about preferences for intervention structure (i.e., individual delivery, session length etc.) and delivery modality (i.e., in-person, telephone, or videoconference), and to describe potential barriers to attendance. These questions are unlikely to cause psychological distress, however, providers will be reminded that they can decline to answer any question or to discuss any issues they find troubling. Breach of confidentiality is another possible risk. This is clearly stated in the consent form. All efforts will be made to maintain confidentiality. Participants' data and research records will be carefully stored. All study personnel will be required to complete courses and ongoing training in protecting participant confidentiality.

Benefits
There are several potential benefits of study participation. All participants will have the opportunity to discuss their emotional and physical symptoms with an interested interviewer, and potentially with others facing a similar situation. Providers and patients who participate in interviews and/or focus groups may learn skills that can help to reduce patient distress and improve emotional and behavioral symptom management. Participants in the pilot study will receive an evidence-based treatment aimed at reducing psychological distress at no cost. The benefits to society could include increased knowledge of the emotional and physical symptom burden of patients with metastatic lung cancer, as well as information about whether participating in an adapted DBT-MLC protocol can reduce psychological distress (i.e., depression, anxiety) improve physical symptoms (fatigue, dyspnea, pain), as well as improve emotion regulation and intolerance of uncertainty.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

There is no cost to the study subjects.

Data Analysis & Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.

Data management and attrition. Participant identifying information will be stored in a secure study database. It will not be stored with questionnaire data to protect patient confidentiality. We anticipate approximately 26% attrition from baseline to immediately post-intervention based on previous supportive care interventions in people with cancer.[90] Therefore, we will recruit approximately 38 participants to obtain full data from 30 participants. Reasons for withdrawal will be collected when possible. Data will be checked on an ongoing basis for completeness. If data are determined to be missing systematically, we will consider statistical approaches to manage data missingness (i.e., data imputation methods). Dr. Hyland will work with statistical experts to determine the most appropriate methods for handling missing data. **ii.**

Statistical Power. Phase 1 will include 4-6 focus groups of approximately 5 patient stakeholders each (N=20), and individual interviews with thoracic oncology providers (N=6) and palliative care, survivorship and behavioral symptom management experts (N=6). Assuming the same potential rate of attrition for focus groups due to scheduling conflicts, illness, etc., we will recruit up to 26 participants to get focus group data from 20 participants (assuming 26% attrition). For Phase 2, we will recruit up to 38 participants to get complete data on approximately 30 participants (assuming 26% attrition). These numbers were calculated based off of relevant literature and work that has been previously successfully completed in this setting.[64,90] Literature suggests that 2-3 focus groups are necessary to reveal 80% of qualitative themes.

Analytic Plan.
Aim 1: Adapt Intervention. In-depth interviews and focus groups will be transcribed verbatim using QSR NVivo software. Data analyses will be based on a grounded theory approach, which has been used in the development of other psychosocial interventions for patients with cancer.[92] Kelly will complete several workshops on analyzing qualitative data (see Training Plan). Additionally, the PI and members of the mentoring team have experience with qualitative data analyses. Dr. Somers is a member of the Cancer Control and Population Sciences Program at DUMC, which has a shared resource of qualitative analytic experts. Experts will be consulted as necessary to ensure appropriate handling and conducting of qualitative analyses.
iv. Aim 2: Test and Refine Intervention. Descriptive statistics (frequencies, mean, median, standard deviation) will be used to examine feasibility (i.e., $\geq$80% of sessions completed, attrition $\leq$25%) and acceptability (i.e., $\geq$80% participants report satisfaction on CSQ). Paired sample t-tests will be run to quantify the degree of change over time for the primary and secondary intervention outcomes. Effect sizes will be computed using Cohen's *d*. Unconditional latent growth models will be used to assess main time effects across baseline, immediately post-treatment and 1 month post-treatment. Time will be coded as the number of weeks since the baseline assessment. Control variables and their interactions with time will be included in conditional models. Analyses will be conducted using an intent-to-treat approach to include all available data (N=up to 38). Exit interviews will be coded and analyzed using methods similar to those described under Aim 1. Themes and feedback that are uncovered through exit interviews will be used to inform intervention refinement.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

The proposed study carries minimal risk. The protocol does not use an investigational drug, procedure, or device. Data obtained from participants will include information from medical chart review, stakeholder interviews and focus groups, and self-report inventories. The study team considers the management of participant information and data as a key priority. Best practices for confidentiality and data management will be observed. Two password protected databases will be used for this study to ensure confidentiality.

First, a tracking database will be used for recruitment and follow-up. This data will house information related to tracking the participants in the study, such as phone numbers and addresses. No medically sensitive or outcome data will be stored in this database. This database will also track nonparticipants (i. e., those who have declined participation) only to the barest minimum to ensure that they are not contacted again about participation. At the end of the study, all identifiable data of non-participants such as their names will be deleted. Tracking data on participants will be retained for the usual required period. Second, all study data will be stored in a separate password protected database without any personal identifiers. Data in this database will be derived from patients' direct input into the electronic patient reported outcomes system, Redcap, which is an online survey system; data entered into this system is stored on a secure server housed behind the DUMC firewall. Only a unique study identification number will link the electronic data to the study data file. The tracking data and study data will be stored in a file on a secure DUMC psychiatry server which can only be accessed by necessary members of the research team. Access to the Duke network requires a password protected, 128-bit encrypted virtual private network connection provided by Cisco systems. If necessary, all paper research records (e.g., completed paper questionnaires) will be kept in a locked file cabinet. Only Dr. Somers (PI), Kelly Hyland (F32-awardee and study coordinator), and study members with approved affiliation to the project will have access to the research records. Additionally, individuals participating in focus groups will be instructed to maintain participants' confidentiality at the onset of the group. Participants will be asked not to talk about other participants' comments outside of the group.

All participants in the study will continue their medical care during the course of the study and will be informed that choosing to participate in the study will in no way impact the treatment they receive at the DCI and DUMC. All participants will continue to be monitored by their physicians at the DCI throughout the course of the study. If a health concern is identified during contact with study staff, the patients' treating oncologist will be contacted, and appropriate referrals for medical treatment will be provided to patients. Dr. Somers (PI), Kelly Hyland (F32-awardee and study coordinator) will continuously monitor and tabulate adverse events. An adverse event is any untoward medical event occurring during the clinical evaluation, which is causally related to the study protocol. A serious adverse event is defined as any event which results in death, is immediately life threatening, results in persistent or significant disability/incapacity, results in patient hospitalization, or is serious for any other reason representing significant hazard. For each event, the investigator will provide the onset, duration, intensity, treatment required, outcome, and action taken. Given the study population (i.e., patients with metastatic lung cancer), it is possible that some participants will be hospitalized and/or die while enrolled. Adverse events due to advancement of lung cancer will not be reported, as these are unrelated to participation in this supportive behavioral intervention. If an unexpected frequency of Grade III or IV events occur, depending on their nature, action appropriate to the nature and frequency of these adverse events will be taken. This may require a protocol amendment, dose de-escalation, or potentially closure of the study. Dr. Somers (PI), Kelly Hyland (F32-awardee and study coordinator) will also continuously monitor the conduct, data, and safety of this study to ensure that:

- Risk/benefit ratio is not altered to the detriment of the subjects;
- Appropriate internal monitoring of AEs and outcomes is done;
- Over-accrual does not occur;
- Under-accrual is addressed with appropriate amendments or actions;
- Data are being appropriately collected in a reasonably timely manner.

All interactions with study participants will be conducted under the direction of licensed clinical psychologists (Drs. Somers, Porter, and Neacsiu). Audio and video recordings of patient interactions (focus groups, treatment sessions) will also be obtained and reviewed with Drs. Somers, Porter, and Neacsiu to ensure that Kelly is providing effective and ethical treatment. Kelly has experience working with distressed patients with chronic disease in clinical research contexts. Kelly will be carefully trained to monitor participants' psychological status and report to Drs. Somers Porter, and Neacsiu if a participant shows signs of experiencing high levels of physical and emotional distress that need to be addressed outside of the context of this study. If this is determined to be the case, Kelly will work directly with Drs. Somers, Porter, and Neacsiu and make recommendations for the participant to move forward in a way that is in the best interest of the participant. Drs. Somers, Porter and Neacsiu are practicing licensed clinical psychologists and supervise psychology trainees (i.e., advanced graduate students, clinical psychology interns). Dr. Somers is integrated into the psychosocial care program at the DCI (i.e., Duke Cancer Patient Support Program) and the community. Dr. Somers has experience referring cancer patients and other individuals who are highly distressed to appropriate psychosocial or psychiatric care. She will use the same resources when making referrals for extremely distressed participants in this study. Likewise, Dr. Porter is a provider on the Duke Palliative Care service within the Duke Department of Psychiatry and Behavioral Sciences, where she provides psychological treatment for chronically ill patients. Dr. Neacsiu is an expert in the treatment of highly distressed, difficult-to-treat cases where there are multiple comorbidities combining psychological and medical problems using DBT.

Likewise, Dr. Somers (PI) and Kelly Hyland (F32-awardee and study coordinator) will appoint two data safety officers. One data safety officer will be a MD within the Duke University Medical Center (DUMC) who is not associated with this study. The appointed MD officer will have experience with clinical research and trials, and will have a thorough understanding of adverse events. The other safety data officer will be a DUMC senior investigator who has expertise in psychological treatment and behavioral symptom management, and will have an annual responsibility to evaluate our current methods of assessment and intervention to identify any problems. All adverse events will be reported to the data safety officers in real time.

This study will also be monitored institutionally by the Duke Cancer Institute (DCI). DCI Protocol Review and Monitoring systems (PRMS) review of this protocol begins with an initial review by the Cancer Protocol Committee (CPC). CPC new protocol review focuses on scientific relevance, study design, adequacy of biostatistical input, protocol prioritization, feasibility of completing the study within a reasonable time frame and risk assessment of the trial. The PI will abide by CPC assessment of the level of risk, which will determine the intensity of subsequent DCI monitoring. CPC also conducts annual scientific progress reviews on protocols that are open to enrollment and focus on protocol prioritization, accrual and scientific progress. These reviews are conducted at the time of IRB annual renewals and documentation of all CPC reviews will be maintained in eIRB/iRIS systems.

A determination for the degree of monitoring conducted by the DCI monitoring team is made at the time of initial CPC approval to commensurate with the type and level of intervention, phase, endpoints, degree of risk, size and complexity of the protocol. A formal, independent monitoring will be conducted by the DCI monitoring team according to the risk level and monitoring plan assigned by the CPC until the study is closed to enrollment or subjects are no longer receiving study drug or other interventions that are more

than minimal risk. Additional monitoring may be prompted by findings from monitoring visits, unexpected frequency of serious and/or unexpected toxicities, or other concerns. Monitoring visits may also be initiated upon request by DUHS and DCI Leadership, CPC, SOC, a sponsor, an investigator, or the IRB.

The DCI monitoring team reviews the adequacy of informed consent, enrollment of eligible patients, implementation of protocol-specified procedures and treatment, adequacy of data collection, and appropriateness of adverse event monitoring and reporting. The DCI monitoring team presents final monitoring reports to the DCI Safety Oversight Committee (SOC) highlighting safety concerns and unresolved issues. The SOC, at a convened meeting, assigns an overall rating of satisfactory, marginal, or unsatisfactory to reflect the overall quality of data, regulatory, consent, eligibility, study conduct and AE reporting. Corrective action plans (CAPs) are developed, implemented, and evaluated as indicated. The SOC will notify the sponsor-investigator and DUHS IRB when significant safety concerns are identified.

The SOC in concert with DCI monitoring team conducts data and safety monitoring for DUHS sponsor investigator phase I and II, therapeutic interventional oncology studies that do not have an independent DSMB. These reviews occur at a minimum annually and more frequently for the high risk studies. The SOC safety reviews include review of safety data, enrollment status, stopping rules if applicable, accrual, toxicities, reference literature, and interim analyses as provided by the sponsor-investigator. The SOC, at a convened meeting, assigns a rating of satisfactory when adequate accrual with lack of excessive toxicity is present.

Privacy, Data Storage & Confidentiality

- Complete the Privacy and Confidentiality section of the iRIS submission form.