BEHAVIORAL AND SOCIAL SCIENCE RESEARCH
SECTION I

1. Status:
New Submission

♦ Revised electronic IRB Application; IRB# 318-13-EP
Initial electronic submission of an existing expedited IRB approved protocol; IRB#

2. Title of Protocol:
Patient-Defined Treatment Success and Preferences in Stage IV Lung Cancer Patients

3. Responsible Personnel:

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G. Are you a student?
No

4. Funding Source:
Check all that apply and provide the source of the funding.

♦ Grant - Provide Source: Patient-Centered Outcomes Research Institute (PCORI)
Commercial - Provide company name:
Department of Defense
Other - Provide Source:

5. Contract:
Is there a contract or agreement associated with this study?
Yes

6. Funding Agency Deadline for IRB Approval:
♦ Yes 7/1/2013
No

7. Study Sites:
A. Provide the names and locations of all study sites where this research will be conducted under the oversight of the UNMC IRB.
University of Nebraska Medical Center, Omaha, NE, including Village Pointe Cancer Center and Bellevue Cancer Center
Saint Francis Medical Center, Grand Island, NE
Great Plains Regional Medical Center Callahan Cancer Center, North Platte, NE
Southeast Nebraska Cancer Center, Lincoln, NE, including all satellite sites, including, but not limited to the 49th and Pine Lake, Lincoln, NE location

B. Is this a multi-site study?
Yes

Does UNMC, TNMC, CH&MC or UNO serve as the lead site with responsibility for data and/or safety monitoring?
Yes

Provide a list of all sites where this study will be conducted.

1. Avera Cancer Institute, Sioux Falls, SD, including all sites overseen and approved by their IRB
2. Nebraska-Western Iowa (NWI) VA Health Care System, VAMC-Omaha, 4101 Woolworth Avenue; Omaha, NE, including all sites overseen and approved by their IRB
3. Moffitt Cancer Center, also known as H. Lee Moffitt Cancer Center and Research Institute; 12902 Magnolia Drive; Tampa, FL 33612-9416, including all sites overseen and approved by their IRB

4. Saint Luke's Cancer Institute; 4321 Washington Street, Suite 4000; Kansas City, MO 64111 including all sites overseen and approved by their IRB
5. Kansas City VA Medical Center; 4801 Linwood Blvd; Mailstop 151, F1-103; Kansas City, MO 64128 including all sites overseen and approved by their IRB

C. Does this study involve any international sites where the PI will either conduct or supervise the study?
No

8. Principal Investigator Assurance
The PI understands and accepts the following obligations to protect the rights and welfare of research subjects in this study:

- **I certify that I have carefully reviewed this application and all supporting documents. I have determined that the application is accurate, complete and ready for submission to the IRB.**
- **I certify that I, and all listed research personnel, have the necessary qualifications and expertise to conduct this study in a manner which fully protects the rights and welfare of research subjects.**
- **I certify that all listed research personnel will be given a copy of the final IRB approved application and any other relevant study related documents in accordance with their defined responsibilities.**
- **I recognize that as the PI it is my responsibility to ensure that this research and the actions of all research personnel involved in conducting the study will comply fully with the IRB-approved protocol, all applicable federal regulations, state laws, and HRPP policies.**
- **I recognize that it is my responsibility to ensure that valid informed consent/assent has been obtained, as appropriate, from all research subjects or their legally authorized representative (LARs). I will ensure that all research personnel involved in the process of consent/assent are properly trained and are fully aware of their responsibilities relative to the obtainment of informed consent/assent according to applicable federal regulations, state laws, and HRPP policies.**
- **I certify that the minimum amount of protected health information (PHI) or other identifiers necessary will be used and disclosed to conduct this research study**

(if applicable). I will implement reasonable safeguards to protect the PHI/other identifiers at all times.

- **I will promptly inform the IRB of any unanticipated problems involving risk to the subjects or to others, as required within the time frame defined by HRPP policies. I will analyze each reported problem to determine if it impacts the risk-benefit relationship of the study, the safety of the subjects, or informed consent.**

- **I will promptly inform the IRB if I become aware of 1) any complaints from research subjects, LARs, or others about research participation, 2) violations of federal regulations or state law, 3) violations of the HIPAA Rule, or 4) violations of HRPP policies.**

- **I will not initiate any change in protocol without IRB approval except when it is necessary to reduce or eliminate a risk to the subject, in which case the IRB will be notified as soon as possible.**

- **I certify that there are, or will be, adequate resources and facilities to safely initiate, carry out and complete this research at the study sites specified in Section I.7. This includes sufficient staff, funding, space, record keeping capability, and resources necessary to address any unanticipated problems involving risk to the subject or others. If the necessary resources become unavailable I will promptly notify the IRB.**

- **I will promptly inform the IRB of any significant negative change in the risk/benefit relationship of the research as originally presented in the protocol and approved by the IRB.**

- **I understand that continuing review by the IRB is required at least annually in order to maintain approval status. I will maintain IRB approval as long as this study is active.**

- **I certify that I and all other personnel listed in Section I.3A-E of the IRB Application have disclosed all potential financial conflicts of interest as required and are in full compliance with the UNMC Conflict of Interest Policy and HRPP policy. I further certify that all potential financial conflicts of interest are appropriately managed in order to ensure protection of the rights and welfare of subjects.**

- **I will maintain all required research records on file and I recognize that representatives from the IRB, OHRP, HHS, and other Federal Departments or Agencies may inspect these records in accordance with granted authority.**

- **I understand that failure to comply with the Common Rule, applicable Subparts B, C, and D of HHS regulations at 45 CFR 46, the HIPAA Rule, applicable state law, HRPP policies, and the provisions of the IRB-approved protocol may result in suspension or termination of IRB Approval of my research project and/or other administrative or legal actions.**

Islam, KM (Monirul) Monirul - 2016-01-27 12:13:00.000

9. Principal Investigator Financial Interest Disclosure
A. As the PI, I certify that I am in full compliance with UNMC Conflict of Interest Policy #8010 and I declare:
♦ I have no financial interest in this research.
I have a financial interest in this research. I have completed the UNMC Disclosure of Potential Conflict of Interest Form and obtained all required signatures. The original disclosure form is attached to this application.

B. As the PI,
♦ I understand that if there is any change in my financial interest during the course of this research, I will update and submit the UNMC Disclosure of Potential Conflict of Interest Form within five (5) business days from the time the change becomes known.

C. As the PI who is ultimately responsible for the proper conduct of this research, I also certify that:
♦ No Responsible Personnel have a financial interest in this research.
The Responsible Personnel listed below have informed me that they have a financial interest in this research. Each person identified below has completed the UNMC Disclosure of Potential Conflict of Interest Form and obtained all required signatures. The original disclosure form is attached to this application.

D. I have informed all Responsible Personnel that if there is any change in their financial interests during the course of this study it must be disclosed by submitting or updating the required UNMC Disclosure of Potential Conflict of Interest Form.
Islam, KM (Monirul) Monirul - 2016-01-27 12:13:00.000

11. Scientific/Scholarly Merit and Resource Review Certification

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B. My signature certifies that this application has been reviewed for scientific/scholarly merit and available resources. It has been determined that the application merits consideration by the IRB based upon the following:

- **1) The proposal has an acceptable level of scientific/scholarly merit which justifies the use of human subjects.**
- **2) The proposal has a sound research design in consideration of the stated objectives.**
- **3) The PI has the necessary qualifications and experience to conduct this research.**
- **4) The PI has, or will have, the necessary funding to support this research**
- **5) There is or will be adequate physical space required for the research interventions at all study sites specified in Section I.7. In addition, there is or will be adequate laboratory and clerical support, data storage capability, and any other resources necessary to complete this research.**
- **6) At all study sites specified in Section I.7, there are provisions to respond promptly to unanticipated problems involving risk to the subject or others.**
- **7) I will promptly notify the IRB if the necessary resources to support this research become unavailable.**
- **8) I am not listed as study personnel in Section I of this application.**

Soliman, Amr S - 2013-05-21 13:15:00.000

SECTION II

PROTOCOL ABSTRACT

1. Provide a brief (less than 400 words) abstract of the research protocol. This summary should include: 1) the title of the protocol, 2) a *brief* description of the purpose of the study, 3) eligibility criteria, 4) interventions and evaluations and 5) follow-up.

Title

Patient-defined treatment success and preferences in stage IV lung cancer patients.

Purpose

Our long-term goal is to integrate NSCLC patient treatment preferences into clinical treatment planning.

Our aims are to: (1) Determine whether individual patients' preferences, characteristics, and treatment experiences affect the definition of treatment success; (2) Determine how to best predict real-life patients' treatment choices based on patients' preferences of adverse events; and (3) Determine whether physicians are likely to change their clinical practice after receiving communication of patients' preferences of adverse events.

Eligibility

for patients --

- Diagnosed with advanced, metastatic stage IV NSCLC
- ≥19 years of age
- Willing and able to provide consent
- Eligible to undergo chemotherapy for stage IV NSCLC, to include, but not limited to, those who:
    - decline chemo
    - have not yet started chemo
    - are currently undergoing chemo
    - have completed chemo or progressed to maintenance for stage IV NSCLC
    - elect to have chemo elsewhere (not at one of the study sites)

Phase 1

Conduct focus groups to:

- gather information for the purpose of refining the data collection forms
- collect ideas for recruiting and retaining future study participants
- obtain suggestions for dissemination of the study findings.

Phase 2

- Recruit patients to interview about their level of tolerance or degree of distress for a list of possible side effects to cancer treatment and to indicate their willingness to tolerate adverse side effects in exchange for a survival advantage; and to:
- Ask about their actual experience with side effects from chemotherapy, if appropriate.

Phase 3 (exploratory)

- Explore physicians/clinicians willingness to consider patient preferences in treatment planning and change their clinical practice accordingly.

Follow-up

We will seek to interview patients at three time points: (1) before, (2) during, and (3) after chemotherapy, as appropriate. We will also collect data on time-dependent variables that are likely to lead to changes in patients' preferences, such as medical adverse events experienced in real-life during actual chemotherapy treatment, if any, as well as patients' reported scores regarding their quality of life. If appropriate, we will ask patients to rate and describe their actual experiences with adverse side effects to chemotherapy.

PURPOSE OF THE STUDY AND BACKGROUND

2. Purpose of the Study

What are the specific scientific objectives of the research?

Our study has the following specific aims:

- ***Aim 1:*** Determine whether individual patients preferences, characteristics, and treatment experiences affect the definition of treatment success.

- ***Aim 2:*** Determine how to best predict real-life patients treatment choices based on patients preferences of adverse events.

- ***Aim 3:*** Determine whether physicians are likely to change their oncologic clinical practice after receiving a detailed communication of their patients preferences of adverse events.

3. Background and Rationale

Describe the background of the study. Include a critical evaluation of existing knowledge, and specifically identify the information gaps that the project is intended to fill.

In the U.S. lung cancer is the leading cause of cancer-related deaths[1]. An estimated 226,160 new cases of lung cancer are expected in 2012, accounting for about 14% of cancer diagnoses and 28% of all cancer deaths. Lung cancer is also a major source of health care costs and significant health care services utilization compared to other cancers in the US[2,3]. Most newly diagnosed patients are elderly (the average age at diagnosis is about 70 years). Over 50% of lung cancer patients die within one year of being diagnosed[4]. Forty percent of patients with newly diagnosed non-small cell lung cancer (NSCLC), the most common type of lung cancer, have stage IV disease[5].

Treatment goals are to prolong survival and control disease-related symptoms. There are

four to five commonly used chemotherapy combinations for the treatment of stage IV NSCLC. These drug regimens lead to a similar improvement in survival, but have different toxicity profiles[6]. Thus, as noted by NCI, toxicity profiles are important determinants of treatment choices and treatment success[5].

However, patients preferences regarding treatment adverse events are not systematically considered when choosing a treatment for stage IV NSCLC. There is no clinical guide for patients or physicians on how to integrate patients preferences of adverse events in treatment decisions, although it is well-known that most cancer patients prefer either an active or a shared role in decision making[7,8]. To our knowledge, there are no studies assessing patient preferences in direct relationship to individualized treatment choices at the time of clinical treatment planning for stage IV lung cancer. There has been one cross-sectional survey of patients preferences of medical adverse events, which was sent to participants by mail at variable time points during or sometime after their treatment (with potential for recall bias)[8]. This study had a very low percentage of participation (31%) and high missing/unknown data for some variables (up to16%); it did not link preferences of adverse events to real-life drug choices; it only considered five medical adverse events (most of them common to all drug regimens); it did not evaluate changes in preferences before and after real-life experiences of adverse events; and it did not collect clinical information. Additionally, potential changes in oncologic clinical practice based on patients preferences were not evaluated.

Our study will provide valuable information on patient treatment preferences at the most critical time, *i.e.,* during the clinical treatment planning visit. We will follow-up patients to assess whether patient preferences expressed at the time of treatment planning remain stable over time and with real-life treatment experiences. We will also involve physicians to explore changes in clinical practice when patient preferences are known.

The results of this study will empower patients to actively participate in the care of their malignancy and therefore have the potential to improve their quality of life and decrease caregiver burden during this treatment.

CHARACTERISTICS OF THE SUBJECT POPULATION

4. Accrual

Is this study conducted <u>solely</u> at sites under the oversight of the UNMC IRB (e.g. UNMC, TNMC, CH&MC, UNO)?

No

A. What is the total number of subjects needed to complete the research in order to

achieve the scientific objectives of the research?
Total number of subjects = 450 (overall accrual for entire study).
The 450 will be allocated as follows: Phase 1 (focus groups) = 36 (closed) + Phase 2 (patients) = 354 (currently open) + Phase 3 (physicians) = 60.

B. What is the statistical justification for the total number of subjects needed to complete the multi-site study?
A sample size of accrual up to 450 subjects for all phases, will assure that we have at least the number of participants with enough evaluable data that will produce a 95% confidence interval equal to the sample proportion plus or minus 5% (PASS 2005; NCSS LLC; Kaysville, Utah) so that we can achieve all the study aims. We accrued 36 subjects in Phase 1 (which is now closed to enrollment), and our accrual goal for Phase 2 is now 354 and for Phase 3 is 60 subjects.
We had originally intended to accrue 210 subjects for Phase 2 who would nearly all complete a series of up to 3 interviews for Phase 2, which would enable us to have the statistical power to answer Aims 1 and 2 of the study. However, we see from our preliminary analyses of data collected from the currently-enrolled subjects (many of whom only completed one or two interviews rather than the three that we had planned, for example, because they died or moved away). This means that we will need to aim for more subjects for Phase 2, so that we may be assured of a robust sample size with enough evaluable data to answer our research questions. Therefore, our new accrual goal for Phase 2 is 354.
For Phase 3 (Aim 3) we our new accrual goal is 60 physicians from participating clinical sites for exploratory Aim 3. This will improve our statistical power for answering Aim 3.

C. How many subjects will be consented at sites under the oversight of the UNMC IRB?
For the record, Phase 1 closed with 36 subjects total from all sites.

354 subjects for Phase 2 will be consented under the oversight of the UNMC IRB and participating clinical sites.. 60 subjects will be consented for Phase 3.

Please note that because we have added, and may continue to add new clinical sites, we no longer have accrual goals assigned by site. We work as a team to contribute as many eligible and willing subjects as possible to the overall total goal for each phase.

5. Gender of the Subjects
A. Are there any enrollment restrictions based on gender?
No

6. Age Range of Subjects
A. What is the age range of the adult subjects?

We will recruit adult patients ≥ 19 years of age, patients advocates, and physicians/nurses (patients' advocates, physicians/nurses for focus group; physicians also for Aim #3).

B. What is the rationale for selecting this age range?
Lung cancer is a disease of older age and it rarely affects children.The average age at diagnosis of lung cancer patients in Nebraska is 70.3 years (NE cancer registry. DHHS; 2010). SEER data reported the average age of the National lung cancer patients at diagnosis is 70 years. The average age of our samples (preliminary data from study sites) is comparable to the average ages of the lung cancer patients of Nebraska, SD, and the National lung cancer patients.

C. Will children (18 years of age or younger) be included in this research?
No

What is the justification for excluding children from participating in this research?
♦ Research is irrelevant to children.
Knowledge being sought in the research is already available for children or will be obtained from another ongoing study.
A separate study in children is warranted and preferable.
Insufficient data are available in adults to judge the potential risk in children.
Other. Explain.

7. Race and Ethnicity
Are there any subject enrollment restrictions based upon race or ethnic origin?
No

8. Vulnerable Subjects
A. Will any of the following vulnerable populations be allowed to participate in this research? Check all that apply.
Pregnant individuals
Prisoners
Children
Decisionally-impaired persons
♦ None

B. Will any of the following vulnerable populations (Students of the investigator, Employees of the investigator, Educationally disadvantaged individuals, Socially or economically disadvantaged individuals, Individuals with a stigmatizing illness or condition, or Other) be <u>specifically</u> recruited for enrollment in this research?

No

9. Inclusion Criteria
What are the specific inclusion criteria?
Inclusion criteria for patients:

- Willing and able to provide consent
- Age ≥19 years
- Diagnosed with stage IV NSCLC
- Able to understand spoken English
- Eligible to undergo chemotherapy for stage IV NSCLC, to include, but not limited to, those who:
    - decline chemo
    - have not yet started chemo
    - are currently undergoing chemo
    - have completed chemo or progressed to maintenance for stage IV NSCLC within the last 30 days
    - elect to have chemo elsewhere (not at one of the study sites)

Inclusion criteria for physicians:

- Age ≥ 19 years
- Willing and able to provide consent
- Has cared for lung cancer patients for at least one year prior to the study

Eligibility criteria for nurses:

- Age ≥ 19 years
- Oncology nurse at one of the four participating cancer centers
- Have been involved in treating lung cancer patients prior to the beginning of our study
- Willing and able to provide consent

Eligibility criteria for patient advocates:

- Age ≥ 19 years of age
- Willing and able to provide consent
- Have been directly involved in a lung cancer patients' treatment
- Spouses and adult children of lung cancer patients OR
- Staff members and volunteers of American Cancer Society of Nebraska

10. Exclusion Criteria
What are the specific exclusion criteria?
Exclusion criteria for patients:

- Age < 19 years
- Not willing and/or able to provide consent
- Not able to understand spoken English

Exclusion Criteria for Physicians:

- Not willing and able to provide consent
- Have not cared for oncology patients for at least one year prior to the study

Exclusion Criteria for nurses:

- Newly employed oncology nurses at the four cancer centers who have not been treating lung cancer patients prior to the beginning of our study.
- Not willing and able to provide consent

Exclusion Criteria for Patients Advocates:

- Age < age 19
- Persons who have not been directly involved in a lung cancer patients' treatment.
- Not willing and able to provide consent

METHODS AND PROCEDURES

11. Methods and Procedures Applied to Human Subjects
A. Describe sequentially all procedures, interventions, evaluations and tests.
There are three phases of this research project:

- Phase 1: Focus Groups
- Phase 2: Questionnaires/Interviews
- Phase 3: Intervention

Phase 1
During Phase 1 of the research, we will conduct four focus groups:

- One group will be comprised of 10 patients or their advocates from the Stage IV lung cancer population already served who will be identified by nurse coordinators at each of two cancer centers.

- The second group will be comprised of 10 oncology nurses and/or physicians at each of two cancer centers.

The focus groups participants will be recruited from the four participating centers, but the focus groups will be held in two centers (St. Francis Medical Center for Nebraska centers and Avera for the South Dakota centers).

The purpose of the focus groups will be to gain input to:

- Refine the Phase 2 questionnaire,
- Generate ideas for the recruitment of study participants
- Generate ideas for the retention of study participants
- Disseminate the study findings regarding patient-centered care of patients with the Stage IV lung cancer.

Recruitment

The study nurse coordinators at the participating sites will identify:

- Eligible lung cancer patients using medical records. The nurse coordinator will contact the potential participants to discuss the study.

- All oncology nurses and physicians by reviewing of current patient medical records as well as from hospital personnel lists, personal knowledge and experience at the cancer center.

- Patient advocates from cancer centers as well as from the staff & volunteers list of the American Cancer Society, Nebraska.

The nurse coordinator will invite them for participate the focus groups. The study nurse coordinators will provide this list to the site investigators who will provide consent form to all participants to participate in the study.

Conduct of the Focus Groups

Subjects that choose to participate in the focus group will be directed to the time and place for the focus group. It is anticipated that the session will last approximately 2 hours (refreshments and introductions followed by the focus group discussion).

The sessions will be conducted and audiotaped by a trained focus group facilitator using generally accepted focus group methodology. Usually that individual will be the PI for the study. The focus group themes and specific suggestions will be determined by the PI and Co-Investigators collectively. **See the attached document,* ***Focus Group Questions to Lead Discussion and Guide Facilitators****, for stimulus questions that facilitators plan to ask group participants.*

The audiotapes will be maintained for the duration of the study. They will be transcribed by one or more persons not involved in conducting the focus groups.

Phase 1 results will be used to refine the drafted questionnaire so that the questions asked of study subjects in Phase 2 are most appropriate based on what the focus group key

informants said. (For the questionnaire, see the attached document: *Patient-Defined Treatment Success and Preferences in Stage IV Lung Cancer Patients Questionnaire.*)

The following description of Phase 2 and 3 is for informational purposes. The conduct of Phase 2 and 3 is contingent upon the results of Phase 1. Phase 2 and 3 can run concurrently. Therefore, once Phase 1 is complete, the final questionnaire developed and the final intervention is designed, a Request for Change must be submitted for IRB review and approval prior to initiation of these phases. The description of Phase 2 and 3 will be expanded to provide more information about what will occur during this phase, as well as provide the appropriate consent form(s).

With previous versions of the protocol, we submitted changes based on Phase 1 Focus Group findings and expanded on Phase 2 and 3 descriptions as promised in the above paragraph. Three areas were most affected by Focus Group findings. These were: (1) which data elements to collect, (2) how best to present them to the patient, and (3) the process and methods used to collect them. The Aims and Research Questions remain the same.

Phase 2

Phase 2 has three defined time periods in which participants interaction with the research team is planned:

- Time Zero (T0=Interview #1), baseline, is after a patient is newly diagnosed with Stage IV lung cancer and ideally before they have had the initial treatment planning visit with their physician. However, it must be prior to their first chemotherapy treatment;

- Time One (T1=Interview #2) is after the patient has had at least one chemotherapy treatment.

- Time Two (T2=Interview #3) occurs at the end of, or shortly after the conclusion of first line chemotherapy.

At each of the three times the participating patient/subject will be asked IRB approved questions, adapted to reflect the time period involved.

The results of Phase 2 will be used to contribute to the theoretical construction of the range of typical patient preference choices. This information will be used in Phase 3 to address the following question regarding physicians patient-centeredness in their treatment decision-making in Phase 3: *"Do physicians change their treatment choices if they are given information about patient preferences of drugs and/or drug side effects?*"

In version 6 (dated 3-28-2014) of this protocol we made changes in the eligibility criteria and relevant changes in the data collection schedule and have added Interview #1-A to be used for subjects who decline chemotherapy. Because of the characteristics of the study population (advanced lung cancer that carries a high mortality rate) and with increased availability of palliative-care-only as an option and upon the recommendation of research staff from the four cancer centers and the Core Group Advisory Committee, the eligibility criteria have been changed to enlarge the pool of potential subjects while retaining the ability to accomplish the aims.

This has resulted in a change in study design such that it is now a **stratified**, repeated measures design, whereas originally it was a straight-forward repeated measures design in which all subjects were to be enrolled during the treatment planning process. Now subjects may enroll at any point: before, during, or after chemotherapy and the data analysis will be stratified according to where in the treatment series the subjects are at the time they are interviewed.

The data collection for baseline and tracking and for the three interviews (Interview #1 (before), Interview #2 (during), and Interview #3 (after)) remains the same and Interview #1-A has been added for those who decline chemotherapy. All enrollees will have all relevant baseline and tracking data collected as previously planned and described. The following schedule for the interviews will be used, based on where in the treatment series the subjects (patients) are when they enroll and on their personal treatment plan:

- decline chemo (Interview #1-A only; unless they change their minds and choose to accept chemo while enrollment is still open, in that case they will be administered Interviews #1, #2, and #3 as appropriate)
- have not yet started chemo for Stage IV NSCLC (Interviews #1, #2, and #3)
- are currently undergoing chemo (Interviews #2 and #3)
- have completed chemo or progressed to maintenance for stage IV NSCLC within the last 30 days (Interview #3)
- elect to have chemo elsewhere not at one of the study sites (Interview #1 only; unless they change their minds and choose to have or continue chemo at a study site, in that case they will then be administered Interviews #2 and/or #3, depending on where in the treatment series they are)

Please note that Interview #1-A is the same as Interview #1 except for wording changes that make sense for someone who is declining chemotherapy treatment and the addition of the question: **Please share with us some of your reasons why you would rather not do chemotherapy at this time? (List as many as you would like.)**

Phase 3
With this version of the protocol we are applying for approval to begin the next phase of the study. Phase 3 involves recruiting physicians from participating cancer centers, randomly placing them in intervention versus control groups and asking them theoretical questions about what their treatment plan would be for patients **before** and **after** being given knowledge of common patient preference patterns.

The intervention group of physicians will receive actionable information about patient preferences learned from Phase 2 of the study to inform them as they are making their treatment plans **after** being given patient preference information. The control group will receive common adverse side effect complaints that are not actionable, such as nausea and vomiting. That is, the control group will not receive patient-centered preference information to guide them in making their **after** treatment choices.

For Phase 3 a researchcoordinator will recruit and receive verbal consent of physicians at clinical sites; and then will conduct a brief scripted interview in which they will ask physician subjects the 11 multiple choice questions: 6 core content questions and 5 demographic questions that have been assigned to that physician by the coordinating center's randomization of cases versus controls. The interviewer will mark the subject's answers on the questionnaire supplied and take brief notes, if the subject wishes to comment. These data will be submitted via REDCap or other secure andconfidentialmeans to the UNMC coordinating center.

B. Identify all procedures, interventions, evaluations and tests that are performed <u>solely</u> for research purposes.
All procedures, interventions, and evaluations in this study are solely for the purposes of research.

C. Identify all procedures, interventions, evaluations and tests that are performed more frequently than they would be if the subject was not participating in the research.
All procedures, interventions, and evaluations in this study are solely for the purposes of research; therefore, none of the usual care clinical procedures, interventions, evaluations, and tests will be performed more frequently than usual.

D. Describe briefly the statistical methods used to analyze the data.
Given the characteristics of the study population (advanced lung cancer that carries a high mortality rate), and with increased availability of palliative-care-only as an option and upon the recommendation of research staff from the four cancer centers and the Core Group Advisory Committee, the eligibility criteria have been changed in version 6 (dated 3-28-2014) to enlarge the pool of potential subjects while retaining the ability to accomplish

the research aims and answer the research questions. This has resulted in a refinement of the study design and plans for data analysis for Phase II, such that it is now a **stratified**, repeated measures design, whereas originally it was a straight-forward repeated measures design in which all subjects were to be enrolled during the treatment planning process. Now subjects may enroll at any point: before, during, or after chemotherapy and the data analysis will be stratified according to where in the treatment series the subjects are at the time they are interviewed. Therefore, the plans for data analysis include the addition of further analysis appropriate to stratification.

We planned our analysis according to research questions associated with specific aims of the study:

Question 1.1 (Compare definition of treatment success by patients characteristics)

- Primary analysis: We will estimate the proportion (95% CI) of lung cancer patients for whom PCAE change the definition of success (in reference to length of survival). We will then compare patients definition of success by specific patients characteristics (particularly rural/urban residence, gender, age, FACT-TOI scores, and comorbid conditions). The primary characteristics of interest are residence, age and gender. We will use logistic regression for these analyses, with definition of success as the binary dependent variable and patients characteristics and center as the independent variables.

- Secondary exploratory analyses: Among patients for whom the definition of success depends on PCAE (i.e. survival alone does not equal survival with PCAE) we will determine which specific PCAE affect patients definition of success. We will report the most common PCAE and proportion of patients reporting them.

- We will also compare patients characteristics and treatment choices (based on preferred PCAE) among patients who complete first line treatment vs. those who do not. For this analysis we will use logistic regression.

Question 1.2 (Compare patients definition of treatment success before and after real-life treatment)

- Primary analysis: We will first estimate the proportion of individuals for whom the definition of treatment success changed during the primary time period of interest (T0-T1; i.e., before and after the first chemotherapy dose). We will then compare changes in the definition of treatment success (in relation to a survival advantage) by subgroups. The primary comparisons will be by residence, gender and age subgroups. Other independent variables will include FACT-TOI, common comorbidities, cancer center, treatment & adverse events. For this analysis we will

use logistic regression.

- Secondary exploratory analyses: For participants who changed their definition of success, we will report the proportion (95% CI) of individuals who tolerated PCAE more, less or differently. We will repeat the analyses for the secondary time period (T0-T2). We will compare any mismatch (yes/no) between patients preferred treatment and actual treatment received, among patients who dropped out after at least one dose and those who completed the full planned treatment cycle (i.e. reached T2). For this analysis we will use exact logistic regression.

Question 2.1 (Compare preferred list of PCAE to a real-life drug choice)

- Primary analysis: In order to determine the best way to predict a patients real-life drug choice from a list of PCAE, we will build a generalized logits model using patients PCAE preference ranking as the multinomial dependent variable and PCAE as the ordinal independent variables (full model). PCAE with a similar distribution pattern(s) across drug regimens will be grouped together.We will also build a clinical model in which the independent variable is an easy to calculate summary score, such as the mean PCAE score for a drug. We will then compare differences in goodness of fit between the full and clinical models using the Akaike information criterion (AIC). We will also output predicted values from each model to compare % accuracy (i.e., the % of drug choices correctly predicted by the models) and test differences in the proportion of correct predictions obtained from the two models using a McNemars test.

- Secondary exploratory analyses: We will assess model performance by patients characteristics (residence, gender and age)

Question 3.1 (Compare changes in physicians real-life drug choices after communication of patient-centered adverse side effects (PCAE))

- Primary exploratory analysis: We will analyze changes in physicians treatment choices measured before and after knowing patients preferences of drug-specific PCAE compared to a control arm, which receive non-discriminatory patient preferences. Physicians treatment choices after knowing patient preferences will be categorized as "more aligned" or "not more aligned" based on how closely they match patients drug preferences. We will then report the proportion of physicians in each arm who became more aligned versus not more aligned. A higher proportion of alignment when PCAE are known will suggest a good expected performance of our tool(s) in a clinical setting.

CONFIDENTIALITY AND PRIVACY

12. Confidentiality and Privacy
A. Will research data be stored:
1) On a secure server at UNMC/TNMC/CH&MC/UNO?
Yes

2) On a local hard drive?
No

3) On a portable computer?
No

4) On a flash drive?
No

5) In a database accessible through the internet?
No

6) In hard copy?
Yes

a) Will the hard copy be stored at UNMC/TNMC/CH&MC/UNO during the conduct of the study (i.e. not the long term storage location)?
Yes

b) Will the hard copy be stored off campus during the conduct of the study (i.e. not the long term storage location)?
Yes

i) Where?
Under UNMC IRB Oversight:

1. UNMC affiliated clinical sites
2. Saint Francis Medical Center, Grand Island, NE
3. Great Plains Regional Medical Center Callahan Cancer Center, North Platte, NE
4. Southeast Nebraska Cancer Center, Lincoln, NE

Not Under UNMC IRB Oversight -- each of these sites has their own IRB that oversees them and their respective affiliated sites:

1. Avera Cancer Institute, Sioux Falls, SD
2. NWI-VA, Omaha, NE
3. Moffitt Cancer Center, Tampa, FL

4. VAMC, Kansas City, MO
5. Saint Luke's Cancer Center, Kansas City, MO

ii) Explain why the data has to be stored off campus.
Each participating cancer center is required by their clinical research regulatory body to keep a copy of CRFs.

c) Describe the physical methods to protect the hard copies (e.g. locked file cabinet or locked briefcase).
We will store in locked area accessible only to authorized research personnel.

d) Will hard copies ever be transported from one site to another site (on or off campus)?
No

7) Other?
No

B. Will any of the following subject identifiers be obtained from records and/or directly from the subject or their LAR and maintained (at any time) in association with the research data?
Yes

1) Indicate the subject identifiers that will be recorded:
♦ Name
♦ Postal address information: street address, city, county, precinct, ZIP code
♦ All elements of dates (except year) related to an individual (e.g. birth, admission, discharge)
♦ Telephone numbers
♦ Fax numbers
♦ Electronic mail addresses
Social Security numbers
♦ Medical Record numbers
Health plan beneficiary numbers
Account numbers
Certificate/license numbers
Vehicle identifiers and serial numbers, including license plate numbers
Device identifiers and serial numbers
Web Universal Resource Locators (URLs)

Internet Protocol (IP) address numbers
Biometric identifiers, including finger and voice prints
Full face photographic images [and any comparable images]
No identifiers will be maintained

2) Will a unique subject identifying number, characteristic or code be used to protect the confidentiality of the data? This includes codes assigned by the investigator to link data to other identifiers like the subject's name or medical record number.
Yes

a) Where will the key, that links the unique subject identification code to the subject s name or other identifier, be stored?
The key that links the subject to the data will be stored at the clinic site with the site investigator, who has ethical access to patients' record. He, with the assistance of the site study coordinator, will establish a place to keep the key that links unique patients to the study data in locked office space accessible only to authorized study personnel.

We will not collect any personal identifiers from patients' advocate, nurses, and physicians who participate in the focus groups. Upon completion of the study, all data will be maintained in a locked office under the control of the site investigators; after seven years of the completion of the study, the site investigator will assure the destruction by shredding of any paper documents and any electronic data files are erased per all applicable policies.

3) What is the justification for recording the specific identifiers listed above?
The purpose of saving these data is to ensure that participants are not duplicated. Also, we will need to follow up patients at T1 (after first chemotherapy does) and T2 (at the end of the full chemotherapy cycle) for their preferences of PCAE to evaluate question 1.2 of specific aim 1 and specific aims 2 & 3.

4) How long will the subject identifiers be maintained in association with the research data?
We plan to complete data collection from participants in three and a half years after starting the study. We will also validate the data including missing data nearly simultaneously with the data collection. Once we complete the data validation for the study and have completed data collection and analyses of the study data, we will no longer require the subject identifiers.

5) How will the research data be archived or destroyed when the data is no longer required?

We will create a final research database, which will not contain any patient identifiers. The data will be password protected, housed on the COPH "U" drive, and available only to approved study personnel.

Any hard copy of survey data will be locked in office space of UNMC COPH personnel and accessible only to approved study personnel.

The clinical sites will destroy the key in the similar fashion that they destroy all other confidential information after the final analyses of the data with specific direction from the study PI.

6) Will research data that contain subject identifiers be disclosed to any other investigators at UNMC, TNMC, UNO or CH&MC who is not listed in Section I of this application?
No

7) Will research data that contain subject identifiers be disclosed to any investigators outside of UNMC, TNMC, UNO or CH&MC?
No

8) Will research data that contain subject identifiers be disclosed to any commercial sponsor or contract research organization (CRO)?
No

9) Will research data that contain subject identifiers be disclosed to any other external organization or entity?
No

C. What provisions will be in place to protect the subject's privacy? Check all that apply.
♦ Obtaining consent in a private conference room or area
♦ Ensuring that only personnel listed on the IRB application Section I.3(A-E) are present during the consent process
♦ Ensuring that the fewest number of individuals possible are aware of the subject's participation in the research.
♦ Ensuring that the research activities are performed in as private of a place as possible
Other. Explain.

D. Does this research involve data banking at UNMC, TNMC, UNO or CH&MC for future

research that is not related to this study?
No

E. Does this research involve data banking by an outside organization (e.g. NCI Cooperative Group, pharmaceutical company) for future, unspecified research that are not integral to the current research?
No

RISK/BENEFIT ASSESSMENT

13. Potential Risks
What are the potential risks associated with each research procedure, intervention, evaluation and/or test? If data are available, estimate the probability that a given harm may occur and its potential reversibility.
The primary risks associated with the research are psychological distress of the patient/subjects and loss of confidentiality.

14. Risk Classification
What is the overall risk classification of the research?
♦ Minimal risk
Greater than minimal risk

15. Minimization of Risk
A. Will the research utilize procedures that would already be performed on the subjects even if they chose not to participate in the research?
No

B. Describe how the subjects of the research will be monitored by the investigators and other research personnel to ensure their safety.
All participants will be consented. The informed consent form explains that the participants are able to cease participation at any time during the study. This will be reiterated by the investigators and approved study personnel as appropriate throughout the course of the study. Furthermore, the study is considered to be minimal risk as there are no drugs, surgery or any other form of invasive intervention involved in this study. Data confidentiality and patient safety will be included in meeting agendas. All study personnel will be encouraged to discuss any concern on data safety issues. Site investigators who are also patients' care givers will monitor patients psychological status and take appropriate action. Otherwise, there are no assumed threats to a participant's safety in their involvement with the study.

C. Describe the process by which the PI will be informed and how the PI, in turn, will inform other research staff about events concerning subject safety (including (a) interim results; (b) unanticipated problems involving risks to subjects or others; (c) noncompliance; (d) complaints).

1) At UNMC/TNMC/CH&MC and/or UNO (check all that apply)

Not applicable. The PI is the only person listed in Section I of the IRB Application.

♦ By email or campus mail (for events which do not constitute immediate subject safety hazards)

♦ By phone

♦ By in-person meeting

Other. Explain.

2) At external study sites under the oversight of the UNMC IRB as applicable (check all that apply)

♦ By email or mail (for events which do not constitute immediate subject safety hazards)

♦ By phone

♦ By in-person meeting or teleconference

Other. Explain.

Not applicable - there are no external sites.

D. Describe the auditing plan for research conducted:

1) Within the Organization (UNMC, TNMC, UNO or CH&MC), identify who will conduct the audits and specify the audit frequency.

Auditing will be completed through a retrospective review of compliance with the study protocol. The PI will develop and implement the audit prior to the publication of any study outcomes.

2) At external study sites under the oversight of the UNMC IRB, identify who will conduct the audits and specify the audit frequency.

For the external site, the PI will develop and implement the audit prior to the publication of any study outcomes.

E. Describe the data monitoring plan:

1) Who will perform the ongoing data and safety analysis?

Although a Data Safety Monitoring Plan (DSMP) is not required for this minimum risk study, we will establish an Oversight Committee/Core Group Advisory Committee that will meet at least annually to provide input on data and subjects safety, research activities and study progress. We will also provide annual reports to the UNMC Scientific Review Committee (SRC) and IRB.

2) What is the frequency of data analysis?
Basic frequency analysis will be done in every month during data collection to monitor study progress. There will be required analysis for reports (quarterly and annual reports). We will prepare manuscripts and presentations in national, regional, and local scientific meetings. This will require data analysis. After total subject accrual, a final data analysis will take place at the end of the study period.

F. Describe the specific criteria by which the investigator would withdraw individual subjects from the research.
If a participant should request to not be a part of the study after participation has begun, they will be removed from further participation. This can be done at any point of the study. (See adult informed consent.) No other instances of withdrawal are anticipated.

G. Describe the specific criteria for halting or early termination of the study.
None anticipated

16. Potential Benefits to the Subject
Are there potential benefits to the subjects that may reasonably be expected from participation in the research?
No

17. Potential Benefits to Society
What are the anticipated benefits (i.e., value) to society that may reasonably be expected to result from this research?
We will gain valuable knowledge about the patients definition of treatment success and their preferences of treatment for stage IV lung cancer. The study will provide a unique opportunity to understand whether physicians will utilize patients preferences of treatment when patients express their choices of PCAEs they would like to avoid as unwanted side effects of drugs used for the treatment of stage IV lung cancer. Traditionally, treatment success for stage IV lung cancer is measured by survival only. Given the similar survival by any combination of chemotherapy for stage IV lung cancer, understanding patients definition of treatment success is very important. We will use findings from this study to plan similar approaches in other cancer populations.

18. Alternatives to Participation
Are there any reasonably available alternatives in the non-research context which would have the potential for providing the same benefits to subjects?
♦ Not applicable. There are no direct benefits to subjects; the alternative is to not participate in the research.

Yes. Describe:
No. Explain:

FINANCIAL OBLIGATIONS AND COMPENSATION

19. Financial Obligations of the Subject
Are there any financial obligations that the subject will incur as a result of participating in the study (e.g. travel expenses, meals, supplies)?
No

20. Compensation to the Subject for Participation
Will the subject receive any compensation for participation?
Yes

Describe the form of compensation, dollar amount (if applicable) and the prorated compensation plan (if applicable).
Each study participant in Phases 1 and 2 will receive a $20 honorarium per completed interview or focus group they attend.

This includes participants of focus groups in Phase 1 (patients, patients' advocate, nurses, and physicians); however, due to the findings in the focus group phase, physicians in Phase 3 will not be offered this compensation.

Patients in Phase 2 will receive $20 for each interview completed during Phase 2.

PRIOR REVIEW

21. Prior IRB Review
A. Has this study (or one substantially similar) been previously submitted to the UNMC IRB (or the Joint Pediatric IRB) and then withdrawn by the investigator for any reason?
No

B. To the best of your knowledge, has this study (or one substantially similar) been considered by another IRB and not granted approval?
No

SUBJECT IDENTIFICATION & RECRUITMENT

22. Method of Subject Identification and Recruitment

A. Will prospective subjects be identified through initial contact by the investigator?
Yes

1) Identified through (Check all that apply):
Previous research participants
Investigator maintained databases or registries
School records
Support groups
♦ Other. Explain. For Phase 2 identification and recruitment of patients/subjects, site investigators will work with coordinators to identify eligible patients from the medical record and the knowledge of the physicians/clinicians who are caring for the patient. In some instances, the patient's (potential subject's) physician/clinician (an authorized member of the approved IRB protocol) will approach the patient in person and invite them to consider participating in the study. In other instances the subject may be identified and recruited by research staff via tele-med or telephone. The alternate to in-person recruitment and data collection is offered particularly for the convenience and inclusion of patients in rural areas or with other barriers to overcome in order to be included. Each site co-investigator will be responsible for assuring that the identification and recruitment of subjects at their cancer center follows applicable rules, regulations, and practices acceptable for patient identification and recruitment in minimal risk research such as this. Phase 3 physicians are identified as those oncologists working on this research at each of the clinical sites and will be recruited by site coordinators also on this research.

2) Describe how the research staff has ethical access to the potential subjects.
The site investigators and nurse coordinators have a treatment relationship with their patients.

B. Will prospective subjects make the initial contact with the research personnel to inquire about the study?
Yes

Identified through (Check all that apply):
♦ Referral by individuals specifically for the research
Flier
Newspaper advertisement
Television spot
Radio announcement
♦ Word of mouth
♦ Other. Explain. Study information at the clinic site

INFORMED CONSENT/ASSENT

23. Waiver or Alteration of Informed Consent
Is a waiver or alteration of consent requested for either 1) all of the subjects or 2) a subset of subjects?
No

24. Waiver of a signed consent form
Is a waiver of the requirement to obtain a signed consent form requested?
Yes

25. Capacity to Consent
A. At the time of initial consent, will all subjects have the capacity to give informed consent?
Yes

B. Is there a reasonable likelihood that some subjects may lose the capacity to continue to provide informed consent during the course of the study?
No

26. Process of Informed Consent for Competent Adult Subjects
A. When will the prospective subject be approached relative to their actual participation in the study?
Phase 2
After potential subjects are identified as meeting eligibility criteria and have been invited to consider participating in the study, prospective subjects will be approached -- in-person or by tele-med or telephone -- by an authorized research staff person to explain the study and assure that all their questions are answered and that they have been provided with written study materials, including, "The Rights of Research Subjects," "What Do I Need to Know Before Being in a Research Study?" and the Informed Consent.

For tele-med and telephone informed consent and participation situations, potential subjects will be provided with consent forms and interview materials prior to tele-med/telephone consent or participation. These will be sent to them by mail, fax, or email or by any means designated as preferred by the potential subject. An extra copy of the informed consent will provided to the subject to keep for his/her records. A tele-med/telephone call will be scheduled for after the subject has received the consent document and has had time to review it. Minimum participants in the call are the individual being invited to participate in the study and a research team member authorized to obtain consent for this study. After the subject has been given the opportunity to have each element of the consent explained and

has no further questions, and has given evidence of comprehension of their rights as a research subject and agrees to participate, they will be instructed to sign, date, and return the consent form to the investigator/designee by mail, fax or a scanned copy via email.

No study participation will be done until after the signed consent form is received by the investigator/designee who will sign and date the document and add a note on the form that explains the lapse in time between signature (for example, received in mail 1/30/15 or telephone consent obtained 10/27/15). In addition to other documentation requirements mentioned elsewhere, tele-med/telephone documentation of the consent will include: (1) rationale for use of tele-consent (2) date and time of tele-consent, and identification of all personnel involved in obtaining and documenting consent.

Tele-participation is provided for the convenience of the subject in the non-clinical portions of this study because it allows subjects who may wish to participate to do so, in spite of barriers such as (but not limited to) weather-related travel conditions, safety concerns, or distance impediments. Also, this study involves obtainment of data from medical records and from subjects via interviews/questionnaires, which can be safely done by tele-med, telephone, mail, or other tele-participation.

A subjects first actual participation in the study may occur any time after completion of the consent and signing of the Adult Informed Consent (IC) form, if it is an in-person situation. In cases of a telemed/telephone consent situation, participation would occur after research staff receives the subjects signed consent, ordinarily a day or two after it is mailed and at such a time or manner of return as is convenient for the subject. In either situation, participation will be arranged at the convenience of the subject.

<u>Phase 3</u>
Physician oncologists on this research are eligible to participate in Phase 3. Because the research in Phase 3 presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context, a waiver of written informed consent will allow research coordinator staff to approach physicians at their respective clinical sites -- at a mutually convenient time. Research coordinator staff will use the narrative consent form to obtain verbal consent or refusal of the potential subject to participate in Phase 3. There is no need for undue hurry or pressure and potential subjects will be given contact information so they can have any questions or concerns addressed to their satisfaction prior to consenting to have the brief scripted interview with the research coordinator.

B. Where will informed consent be obtained, and how will the environment be conducive to discussion and thoughtful consideration?

Phase 2. Informed consent will be obtained in a private room, such as, where patients meet their clinicians, or if by telmed/telephone in an environment of the subject's choosing. If at the clinical site, research staff will be careful to arrange for informed consent to be obtained in an environment that is conducive to discussion and thoughtful consideration, such as a room that is private and isolated from other patients and clinic staff, one that provides optimal privacy.
Phase 3. The informed consent will be obtained in an environment of the subject's choosing, that is also agreed-to as appropriate by the research coordinator obtaining the verbal consent.

C. Who will be involved in the process of consent and what are their responsibilities?
Phase 2. Prospective subjects will be recruited from participating cancer treatment centers by authorized study personnel. A study coordinator or other authorized research staff will meet either in-person or by tele-med or telephone with prospective subjects, review the overall study and discuss the study risks and benefits, and answer any questions and consent the patient. The site investigator will be responsible to provide answers to any additional questions not able to be answered by other research staff. Only when potential participants are fully satisfied with the information and completely understand the informed consent will they be asked to sign the consent form.

Phase 3. Similar to Phase 2 except that, since the site investigator is the subject being consented, they are responsible for contacting either the IRB or the overall PI if they have questions or concerns about participating and only when they (the physician, potential participants are fully satisfied and completely understand will they be asked to give their verbal consent.

D. How much time will be allotted to the process of consent?
There is no rush or urgency to push patients to make a decision to sign IC (in the case of Phase 2) or give their verbal consent (in the case of Phase 3) in haste. Only after participants are fully satisfied with the information and completely understand the informed consent will they be asked to sign the consent form (Phase 2) or give their verbal consent (Phase 3).

E. How will the process of consent be structured for subjects who are likely to be more vulnerable to coercion or undue influence?
Voluntary participation will be emphasized to prevent worry of the participants and their thinking that services may be altered because of their participation in the study. Additionally, voluntary participation will be emphasized in any interactions with the patients during informed consent process and throughout the study. We will not include any vulnerable patients in this study but if such a situation arises (e.g., educationally or economically

disadvantaged or other indication of vulnerability), patients will be encouraged to consult family, friends and/or patients advocates to help their decision concerning participation in the study.

F. Will non-English speaking subjects be enrolled in this research??
No

Provide justification for why non-English speaking subjects will be excluded.
More than 90% of lung cancer patients at the study sites are White and most of the remainder are African Americans and Native Americans.

G. How will it be determined that the subject understood the information presented?
Subjects will be asked if they have any further questions and, if appropriate, they will be asked to summarize all elements of the IC in order to evaluate their understanding. Should the subject repeat information incorrectly, they will be corrected by the research team member obtaining consent.

H. Will there be a formal process of on-going re-consent (over and above re-consent associated with changes in protocol)?
No

27. Documentation of Consent and Assent
List who will sign the consent form as the "Person Obtaining Consent".
Awais, Ahmed

Bauer, Linda K

Berg, Alan Richard

Clements, Lindsay

Copur, Sitki

DeVilla, Maria

Dunder, Steven Gary

Einspahr, Sarah

Fetrick, Ann

Ganti, Apar Kishor Prakash Rao

Gauchan, Dron

Green, Nathan B

Gulzow, Mary

Hadenfeldt, Rebecca Kathryn

Islam, Km Monirul

Kessinger, Margaret Anne

Kezeor, Jami Suzanne

Klinetobe, Kimberly M.

Knox, Stacey

Kosmacek, Lisa

Markley, Shelia M

Marr, Alissa Sue

Mayo, Sarah Lynn

McDonald, Monica Lee

McHam, Scott

Nelson, Deborah

Peterson, Cary

Ramaekers, Ryan Christopher

Riley, Bronson

Ryan, June E

Schriner, Megan Elizabeth

Scott, Jennifer R

Silos, Johnna

Thomson, Maureen A

Toombs, Candice

Usasz, Katherine

Vaziri, Irfan A

28. Consent Forms and Study Information Sheets
Indicate the type of consent forms, assent forms, and study information sheets to be used in this research. Check all that apply:
♦ Adult consent form
Legally authorized representative (LAR) consent form
Parental/Guardian consent form
Youth Study Information Sheet
Child Study Information Sheet
Adult Study Information Sheet (decisionally-impaired)
Addendum consent form
Other. Explain.

29. Information Purposely Withheld
Will any information be purposely withheld from the subject during the research or after completion of the research?
Yes

A. What specific information will be withheld?
For Phase 3 only, in order for the subject's answers to be as valid as possible, it is necessary to blind the interviewers and subjects as to whether the subjects are cases or controls.The fewer people who know who is a case and who is a control, both during and

after, the higher the likelihood that subjects will be able to give unbiased answers and the higher the likelihood of analyses being interpreted correctly.

B. What is the justification for this non-disclosure?
Phase 3 is a situation n which cases will be given discriminatory patient preference data whereas controls will not. If physician subjects know that they are cases versus controls it may affect their answers in such a way as to make the test results biased or invalid.

C. Will information that has been withheld eventually be shared with the subject?
No

25. Information Purposely Withheld
Provide justification.
It is advisable that neither subjects nor interviewers ever know for certain who is or was a case or who is or was a control because this could lead unpleasant feelings about one's clinical judgement.The fewer people who know who is a case and who is a control, both during and after, the higher the likelihood that subjects will be able to give unbiased answers that they feel good about and the higher the likelihood of analyses being interpreted correctly and discussed wisely in reporting.

RESOURCES

30. Describe the resources available to safely conduct this study at each study site specified in Section I.7.
All research team members have been or will be trained on Human Subjects Protection and PHI confidentiality according to the federal DHHS regulations, and the Office of Human Research Protections (OHRP) guidance. All team members are familiar with and currently apply these OHRP policy and regulatory guidance materials to ensure that they conduct ethical research that is in compliance with the regulations. The study is fully funded by the Patient-Centered Outcomes Research Institute (PCORI). All participating cancer centers are well organized for clinical services to patients with stage IV lung cancer with adequate rooms and spaces for informed consent process and interviewing for CRFs data collection for this study. The study does not require any laboratory testing. Each participating cancer site has adequate clinical and support staff. In fact, the site PI is covered by alternate oncologists during his leave of absence and vacation time. All site PIs are experienced in cancer clinical trials and each cancer center has its internal review committee. All cancer center sites are equipped with computers, internal server and tele-communication systems to facilitate this research. No other additional resources are necessary from the cancer centers other than support from their leadership, which we have received as evidenced by their letters of support.

LITERATURE REVIEW

31. References

Provide a full listing of the key references cited in the background (Section II.3). The references should clearly support the stated purpose of the study.

1. American Cancer Society. Cancer Facts & Figures 2012. 2012.

2. American Cancer Society. Cancer facts and figures 2012. 2012.

3. Goodwin PJ, Shepherd FA. Economic issues in lung cancer: a review. J Clin Oncol. 1998; **16**(12): 3900-12.

4. Kutikova L, Bowman L, Chang S, Long SR, Obasaju C, Crown WH. The economic burden of lung cancer and the associated costs of treatment failure in the United States. Lung Cancer. 2005; **50**(2): 143-54.

5. National Cancer Institute. Non-Small Cell Lung Cancer Treatment. 2012[cited; Available from: http://www.cancer.gov/cancertopics/pdq/treatment/non-small-cell-lung/healthprofessional/page11

6. National Cancer Institute. SEER Data, 1973-2008.2010 [cited; Available from: http://seer.cancer.gov/data/

7. Shekelle P,Mahar, A. Treatment of Metastatic Non-Small Cell Lung Cancer: A Systematic Review of Comparative Effectiveness and Cost Effectiveness. 2012.

8. Bruera E, WilleyJS, Palmer JL, Rosales M. Treatment decisions for breast carcinoma: patient preferences and physician perceptions. Cancer. 2002; **94**(7): 2076-80.

9. South Dakota Department of Health 2009 [cited;Available from: http://getscreened.sd.gov/documents/Lung2009.pdf

10. Galea S, Tracy M. Participation rates in epidemiologic studies. Ann Epidemiol. 2007; **17**(9): 643-53.

11. Huchcroft SA, Snodgrass T. Cancer patients who refuse treatment. Cancer Causes Control. 1993;**4**(3): 179-85.

SECTION III

SUBMISSION DEADLINE

A. Full Board Review:
The IRB meets twice monthly, on the first and third Thursday of the month, with the exception of January and July when the IRB meets only on the third Thursday of the month. No more than 15 applications (i.e., initial review of a new study, re-review of a tabled study) will be reviewed at each meeting. All reviews are performed on a first-come first-served basis. The IRB meeting schedule and deadline dates can be found on the IRB website at www.unmc.edu/irb.

B. Expedited Review
Applications that qualify for expedited review have no submission deadline and can be reviewed independent of the IRB meeting schedule. Please call the Office of Regulatory Affairs for assistance in determining if your study meets the requirements for expedited review.

SUBMISSION CHECKLIST

Check all that apply.
Subject recruitment material
Performance site approval for all non-UNMC, TNMC, UNO and CH&MC sites
Copy of all questionnaires, surveys, assessment tools, and other relevant materials
Detailed protocol
Grant Application
IRB Review Fee Form for all commercially sponsored research projects.
UNMC Disclosure of Potential Conflict of Interest Form for the Principal Investigator if a financial interest has been declared in Section I.10.
UNMC Disclosure of Potential Conflict of Interest Form for any responsible personnel with a financial interest declared in Section I.10.
Other
♦ No attachments

ADDITIONAL REVIEW REQUIREMENTS

Final IRB approval and release of studies is contingent upon approval by the following UNMC committees or departments. Check the appropriate boxes:
♦ **UNMC Eppley Cancer Center Scientific Review Committee (SRC):** Review by the SRC is required for all protocols involving cancer patients.

Sponsored Programs Administration (SPA)/Office of Regulatory Affairs: For commercial sponsored studies, the consent form and contract will be compared for consistency. Final IRB approval and release is contingent upon completion of a signed contract for all commercially sponsored research.

Conflict of Interest Committee (COIC) All responsible personnel listed in I.3A-E of the IRB application (i.e., PI, Secondary Investigator, Participating Personnel, and Coordinator(s)) must disclose **any** financial interest in the research (see Section I.10 of this application). Data and Administrative Personnel are exempt. The COIC will review any financial interest which is classified as significant.

Other Review

No Additional Reviews Required

ADDENDUM M
Waiver of Requirement to Obtain Signed Consent

Title of Protocol
Patient-Defined Treatment Success and Preferences in Stage IV Lung Cancer Patients

Principal Investigator
Islam, KM Monirul - COPH Epidemiology - 402-559-8283 - kmislam@unmc.edu

1. Are you requesting a waiver of signed consent under 45 CFR 46.117(c)(1) where there is risk associated with a breach of confidentiality?
No

2. Are you requesting a waiver of signed consent under 45 CFR 46.117(c)(2); 21 CFR 56.109(c) where the research is no more than minimal risk and written consent is normally not required outside the research context?
Yes

A. Are you requesting a waiver of written (signed) informed consent for all subjects or just a subset of subjects?
All subjects
♦ A subset of subjects

Describe the characteristics of these subjects.
The subset of subjects for which we are requesting a waiver of signed IC are those eligible to participate in Phase 3: Physicians at clinical sites participating in Phase 2.

B. Does the research present no more than minimal risk of harm to subjects and involve no procedures for which written consent is normally required outside of the research context?
Yes