Study title: Project PEER: Understanding the lung cancer Patient ExperiEnce in the Real-World setting

ClinicalTrials.gov Identifier: NCT05826756

Cover Letter Date: April 26, 2023

Project PEER: Understanding the lung cancer **P**atient **E**xperi**E**nce in the **R**eal-World setting

WCG IRB

March 31, 2023

PROTOCOL NUMBER:	LUNGevity-2020-01—Version 6
TYPE OF STUDY	Prospective longitudinal online survey with no experimental treatment or intervention
STUDY START DATE: **STUDY END DATE**:	August 15, 2020 Open-ended
SPONSOR:	LUNGevity Foundation 6917 Arlington Road, Suite 352 Bethesda, MD 20814 Phone: 240-454-3100 Fax: 240-497-0034 Email: info@LUNGevity.org

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1.0 PROTOCOL SYNOPSIS

Protocol title: Project PEER: Understanding the lung cancer **P**atient **E**xperi**E**nce in the **R**eal-World setting

Type of study: Prospective online longitudinal survey study with no experimental treatment or intervention

Study period: Open-ended

Objective: To collect longitudinal data that facilitates a more rigorous understanding of the treatment experiences and needs of lung cancer patients—either reported by patients or through their caregivers.

Study population and sample size: Patient with lung cancer and caregivers in the US and internationally who are able to read and answer questions in English

- **Inclusion/exclusion criteria:** Inclusion:
    - Adults with self-reported lung cancer diagnosis or caregiver of someone with a self-reported lung cancer diagnosis (patient has to be alive)
    - Ability to read and answer questions in English
    - Access and ability to use a computer or other internet-connected device
- Exclusion:
    - Younger than 18
    - Healthcare providers and healthcare professionals who provide care to lung cancer patients except for those who are themselves a patient or a caregiver to a loved one.
    - Not able to provide informed consent

Study design: Online longitudinal study; participants will sign up and consent to be part of the study. Participants will receive follow-up emails to inform them of new surveys available to be completed. They will be sent periodic surveys to complete. Participants will complete a baseline survey on their 1) lung cancer experience, 2) lung cancer diagnosis, 3) treatment experience, 4) lung cancer outcomes and symptoms, and 5) demographic characteristics. They will then be asked to complete 11 periodic surveys (one per month) to update the baseline information to help understand their disease and treatment progression. Participants will have the option of accessing aggregate responses at the end of the study. A (de-identified) summary of results will also be made available publicly. No individual results will be presented.

Data management and protection: A two-pronged approach will be used:

1. Self-selected participants who self-identify as being diagnosed with lung cancer or being the caregiver of someone diagnosed with lung cancer and participate through an open link on social media or other digital platforms (**not identified through a clinic**) .
2. Lung cancer patients receiving care at a participating clinic site will be identified by a member of the research clinic staff reviewing their medical records. These patients and their caregivers will be invited to participate in PEER by a member of the research clinic staff. The clinic site **will not** have access to participants survey responses, **and**, LUNGevity Foundation **will not** have access to the clinic site's patient data. Authorized research personnel from LUNGevity Foundation **will only** have access to participants' who consented to participate in Project PEER.

All Private Health Information (PHI) for clinic and non-clinic participants will be encrypted within the EmpiraMed™ PRO Portal™ Software Platform (PRO Portal). Access will be provided only to those authorized research personnel from LUNGevity Foundation and EmpiraMed with a need to access such information and will be provided through secure connections to maintain full Health Insurance Portability and Accountability Act (HIPAA) compliance of PHI. Participants in the study will be assigned a unique study identification number. Study participants will consent to participate in the study. They can fully withdraw their consent to participate in the study at any time for any reason. Additionally, the Principal Investigator may remove study participants from the study if he feels it poses harm to participants or suspects fraud.

Additionally, external researchers may apply to LUNGevity to have limited access to de-identified study data. Any data transfers will occur through protected files and platforms. External researchers will not be able to identify individual responses. Data access to external researchers will be controlled by LUNGevity.

Data will be collected and stored through a survey platform (PRO Portal) that complies with HIPAA and General Data Protection Regulation (GDPR).

Data analysis: All data analysis will be conducted using Excel, SPSS, Stata, R, or another similar software package. Data will be analyzed using frequencies, cross tabulation, and regression analysis. All analyses will include aggregate results and presented as tables, graphs, or charts. No individual-level data comparisons will be made. However, individual level responses will not be presented and any analyses presented will not contain personally identifiable information.

2.0 Study Synopsis

The study objective is to collect longitudinal data to facilitate a more rigorous understanding of the diagnostic and treatment journey of people diagnosed with lung cancer and to identify determinants of treatment heterogeneity. Study data will facilitate a deeper and more scientifically rigorous understanding of the needs and wants of people living with lung cancer and assist with the integration of patient experiences into the development of lung cancer treatments and research. It supports ongoing efforts at the U.S. Food and Drug Administration (FDA) to promote patient-focused drug development (PFDD).[1]

During this study, surveys will be deployed to catalog different components of a patient's diagnostic and treatment journey, along with how a lung cancer diagnosis impacts the quality of life of those living with lung cancer. Study participants will consent and register for the study and complete an initial baseline survey. They will then be followed for 12 months and receive a monthly survey (11 surveys in total). The development of the surveys has been guided by input from patients, clinicians, FDA experts, and incorporates questions from existing PRO measures.

Summarized study results will also be posted on LUNGevity's website. External researchers will be able to apply to LUNGevity Foundation to administer additional surveys to study participants. They can also apply to have limited access to de-identified data. The study is an open-ended longitudinal survey study. Protocol updates and amendments will be submitted to the IRB throughout the duration of the project as needed.

3.0 Background

Lung cancer continues to be the number-one cancer killer in the United States and worldwide. It is often discovered at later stages of the disease when decisions must be made rapidly, and these decisions can be extraordinarily difficult. They are dependent, or should be, on the patient's preferences. With a high overall mortality rate, only 19% alive at the 5-year mark, the focus has been on new diagnostics and new therapies to save lives.[2] In the last few years, lung cancer science has progressed at an unprecedented rate: new categories of therapies for patients with lung cancer have become available, including immunotherapies and targeted therapies with companion diagnostics, and the application of existing therapies has been expanding.

This progress is especially apparent in certain driver mutation-specific non-small cell lung cancer (NSCLC) adenocarcinomas, such as EGFR, ALK, ROS1, BRAF, NTRK, RET, and MET for which FDA-approved targeted therapies exist in the first-line setting.[3] These targeted agents provide higher response rates and a superior quality of life compared to traditional chemotherapy. Patients with EGFR- and ALK-positive NSCLC may also have second-line treatment options.[3] The prescribing preferences for different first-line and second-line treatments are currently not known. Furthermore, reasons for treatment discontinuation (adverse events, progression, mechanisms of resistance, etc.) are not well documented beyond a clinical trial context. In addition, how patients experience their disease in terms of symptoms, impacts, outcomes, and quality of life (QoL) throughout their disease progression is unclear.

To enhance understanding of the patients' disease and treatment journey, LUNGevity Foundation has developed a mechanism for patients with lung cancer and their caregivers to enroll in a patient experience study that will collect longitudinal data to facilitate a more rigorous understanding of the diagnostic and treatment journey of people diagnosed with lung cancer and to identify determinants of patient experience heterogeneity.

3.1 LUNGevity Foundation:

LUNGevity, one of the nation's largest lung cancer non-profits, is dedicated to changing outcomes for people with lung cancer through research, education, and support. LUNGevity focuses on research because the link between research spending and improved survival is clear. Survival rates have dramatically improved for colorectal, breast, and prostate cancers over the last several decades in step with the exponential growth in their research spending. The foundation's goal is to accelerate progress for lung cancer in the same way, in order to dramatically improve on the current 19% five-year survival rate.

To date, LUNGevity has funded 133 research projects at 59 institutions in 23 states. LUNGevity research investments focus on early detection, because survival rates rise when lung cancer is detected while still localized. LUNGevity also focuses on more effective treatment approaches—getting the right treatment to the right patient at the right time to help people with lung cancer live longer and better.

LUNGevity also provides a community of empowerment, support, and hope for everyone affected by lung cancer through our extensive educational resources, online peer-to-peer support, and in-person survivorship programs, as well as more than 40 grassroots awareness and fundraising events held from coast to coast each year.

LUNGevity's mission is patient-centric—to provide a voice to the lung cancer patient community.

4.0 Objectives

The study objective is to collect longitudinal data that facilitates a more rigorous understanding of the treatment experiences and needs of patients with lung cancer—either reported by patients or through their caregivers. This research project will catalog different elements of a patient's diagnostic and treatment journey and identify unmet needs of patients with lung cancer. This is an international study with an open-ended timeframe.

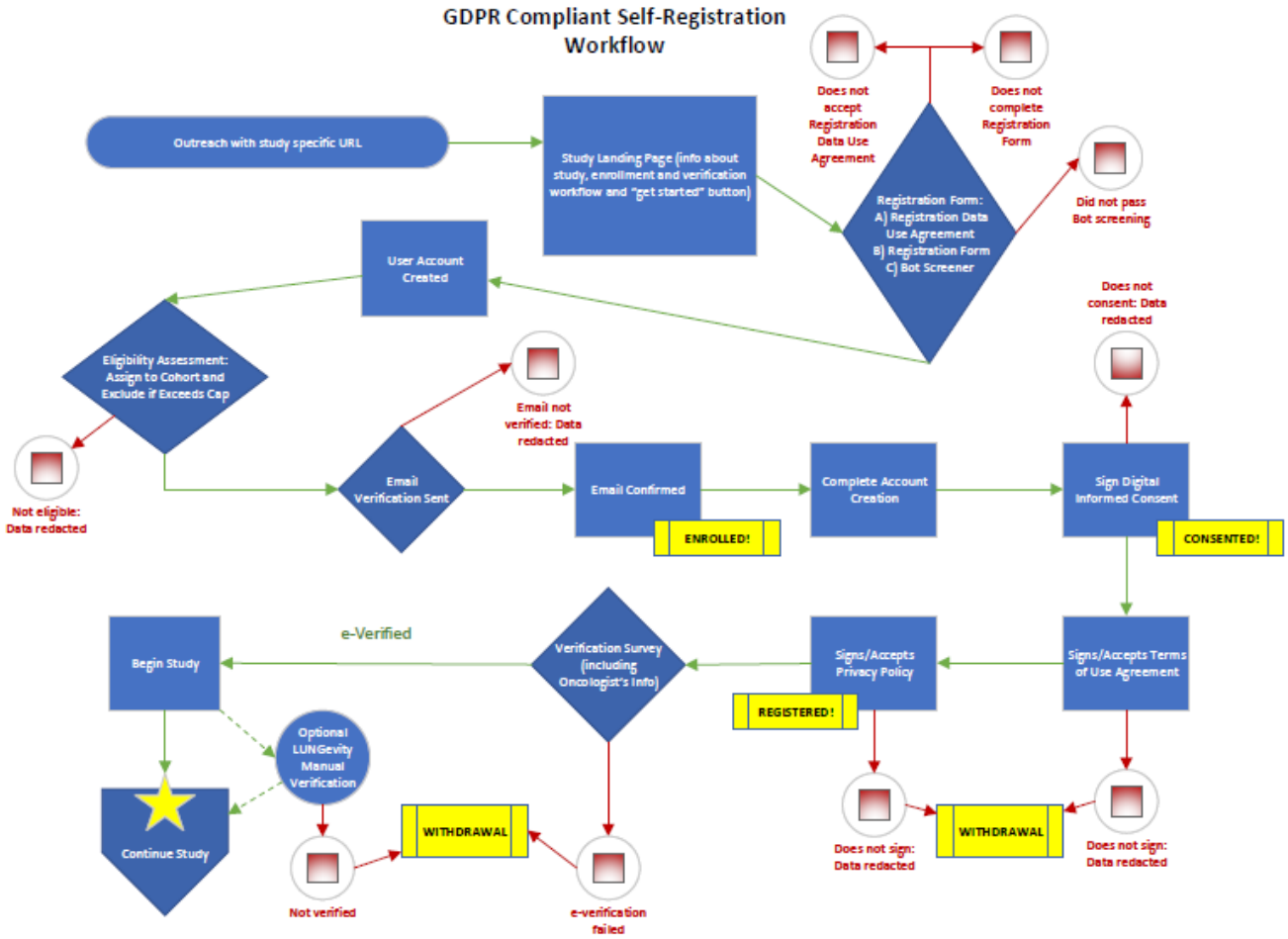
The study will collect data to answer the following questions:

1. What are some of the first-line treatment options prescribed to patients?
2. What are the reasons for treatment change and second- and subsequent-line treatment options (including immunotherapy (I/O) and clinical trials)?
3. What types of biomarker testing practices were utilized to diagnose the cancer and characterize mechanisms of resistance?

4. Are there specific risk factors that can predict the histology of the disease and response to specific treatments?
5. How does a lung cancer diagnosis impact the quality of life of a patient?
6. Which symptoms, impacts, and outcomes do patients with lung cancer experience and how do these change over time (collected through validated patient-reported outcome instruments)?
7. Do patients who have participated in clinical trials have better outcomes than those who have not participated in clinical trials?

5.0 Study Workflow

A GDPR-compliant workflow for the study is shown below.



Briefly,

1. Potential participants will be directed to the study landing page (**Attachment 1**) through various recruitment methods (section 6.3).

2. They will then fill out the Self Registration Form (**Attachment 2**)
3. They will then be asked to read the Registration Data Use Agreement and complete the Registration Form (**Attachment 3**)
4. Following creation of account on the PRO Portal and system determination the cohort maximums have not been met (either within the 1200 patients or 300 caregivers), an email verification (**Attachment 4**) will be sent to potential participants.
5. After account verification, a potential participant will sign the electronic informed consent form (eICF) (**Attachment 5 and 6**)
6. After a potential participant has consented, they will agree to and sign the Terms of Use Agreement and Privacy Policy (**Attachment 7 and 8**)
7. The potential participant will complete a brief survey (**Attachment 9**) to verify that they are a lung cancer patient or caregiver as a means to screen out "fraudsters"
8. At this stage a potential participant is considered a study participant and is able to commence participation.

6.0 Study subjects

6.1 Target population and sample size

Participation in Project PEER is open to adults within the US and internationally who either self-report a lung cancer diagnosis or receive care at a participating clinic site. PEER is also open to any adult caregiver of the above individuals or who self-reports as a caregiver to an individual with a lung cancer diagnosis. There is no limit on the number of participants or countries included in Project PEER. However, LUNGevity anticipates enrolling a minimum of 1,500 patients and caregivers. We hope to enroll around 1,200 patients and 300 caregivers. LUNGevity will be tracking recruitment and may decide to cap enrollment based on participant characteristics.

6.2 Inclusion and Exclusion Criteria

- **Inclusion criteria:**

  - Adults with self-reported lung cancer diagnosis or caregiver of someone with a self-reported lung cancer diagnosis (patient has to be alive)
  - Ability to read and answer questions in English.
  - Access and ability to use a computer or other internet-connected device.

- **Exclusion criteria:**

  - Younger than 18.
  - Healthcare providers and healthcare professionals who provide care to lung cancer patients except for those who are themselves a patient or a caregiver to a loved one.

- Not able to provide consent.

Participation in Project PEER does not involve a risk of physical harm; therefore, women of childbearing potential will not be tested for pregnancy. The racial, gender, and ethnic characteristics of study participants will reflect demographics of patients with lung cancer who are seeking information regarding their disease and are potentially interested in participation in clinical trials or research studies. No individuals will be excluded from participation in Project PEER based on age (if 18 or older), race, ethnicity, or gender.

6.3 Recruitment

For inclusion in PEER, potential participants will be identified either because of attendance at a participating clinic site, participation in a market research panel, or by self-report. Regardless of how a potential participant is identified, LUNGevity **will not** have access to medical records.

All interested participants will be directed to a study landing page **(Attachment 1**) to learn details about study participation. Those interested in participating will be asked to complete a brief study registration form that includes a data use agreement (**Attachment 3**). After submission of the registration form, the email provided by the participant will be confirmed and an account will be created. At this stage, a participant will be considered enrolled in the study and will proceed with signing the electronic informed consent form (eICF).

The study surveys will be available as an online option only and deployed through the PRO Portal. No pen-and-paper version of the survey will be used. Participation in the study is completely voluntary. Language used for recruitment is provided in **Attachment 10, 11, 27 and 28**.

Self-reporting Participants: Participants that self-report as having lung cancer or as being a caregiver of an individual with lung cancer will be recruited by the various methods listed below:

1. **Closed Facebook pages maintained by LUNGevity Foundation and other lung cancer organizations**: A generic link to the study landing page will be posted on closed Facebook groups maintained exclusively for patients with lung cancer (or their caregivers).

2. **Open Facebook pages and Twitter maintained by LUNGevity Foundation and other lung cancer organizations**: Links to information about the study will be posted on public social media accounts.

3. **Newsletters**: LUNGevity Foundation and other patient advocacy send regular newsletters to their constituents. These newsletters will have a link to the study landing page.

4. **Public Meetings**: Information about Project PEER might be provided at LUNGevity's International Lung Cancer Survivorship Conferences, public meetings for lung cancer patients and caregivers, or other meetings that patients with lung cancer attend.

5. **Lung Cancer Europe**: Information about Project PEER will be distributed to constituents of LuCE.

6. **Market Research Firm (firm)/Specialty Pharmacies**: LUNGevity Foundation will work with a market research firm and specialty pharmacies to recruit patients and caregivers. The firm/specialty pharmacy will recruit these individuals through: a) posting on closed social media pages that the firm/specialty pharmacy maintains, b) eblasts and newsletters sent to individuals in their network, c) passive postings in offices of health care providers in their network, and d) referrals from individuals in their network. Patients and caregivers who learn about Project PEER through the firm/specialty pharmacy will contact a member of the firm/specialty pharmacy staff to learn more about PEER. If the interested participant meets study eligibility criteria, the recruiter will email the person the link to the study website **(Attachment 27 and 28).** The firm/specialty pharmacy **will not** have access to participants survey responses, **and**, LUNGevity **will not** have access to the firm/specialty pharmacy's network data.

7. **Postcards**: Postcards containing information about the study may be distributed through LUNGevity partner sites and clinics (**Attachment 11**).

8. **Trial websites**: LUNGevity will work with websites to include Project PEER as one of the research projects listed on their site. People find these websites by performing internet searches. These websites allow people to learn about research studies by providing study and contact details (which they can use to contact the research team if they choose). The contact details provided on the websites will connect people with a member of the LUNGevity research team, who will confirm study eligibility of the interested participant and email a link to the study website **(Attachment 28).**

All language for the various outreach methods that we will be using is provided in **Attachment 10, 11, 27 and 28**. The links posted will take the participant to a landing page on the LUNGevity website that will provide information about Project PEER and where participants can express interest in joining.

Clinic participants: Lung cancer patients receiving care at a participating clinic site and their caregivers will be recruited into PEER by a member of the research clinic staff. This staff member will review the clinic schedule and medical records (when applicable) to determine potential participants eligibility. For all potentially eligible participants, the staff member will inform them about PEER. For interested individuals, the staff member will walk the potential participant through sign up using the potential participant's phone to take them to the study landing page (i.e., PRO Portal) and have them complete the actions in the above section titled: "All interested participants." The clinic site **will not** have access to participants survey responses, **and**, LUNGevity **will not** have access to the clinic site's patient data.

6.4 Consent

Study participants will sign up for the study and complete surveys through an online platform (PRO Portal). No pen-and-paper version of the surveys in the study will be used. Participation in the study is completely voluntary, and study participants will be recruited through methods described above. Before commencing the baseline survey, all participants will be instructed to read and sign the study eICF during the registration process. Study participants will have the option to download the signed eICF for their own records. There will be two versions of the eICF – one for United States study participants (**Attachment 5**) and one for non-United States participants (**Attachment 6**). This separation has been done to include GDPR-related information in the eICF for non-United States study participants.

If a study participant withdraws their consent, they will not be contacted further and will not be asked to contribute additional data to the study. They will be given the option to share their reason for withdrawal (**Attachment 12**) If invitations when follow-on monthly surveys bounce back or if LUNGevity receives notice that the study participant has passed away, LUNGevity will withdraw the patient. Their existing survey responses will not be removed from the study but any personally identifiable information (PII) will be removed. If a caregiver's patient passes away during the study, the caregiver's participation is complete following the completion of a close-out bereavement survey.

A study FAQ is available for participants once they are registered (**Attachment 13**). Participants will also have access to a Quick Start Guide on the study landing page (**Attachment 14**)

7.0 Study Design and Methods

7.1 Financial Incentives

Study participants will be incentivized minimally to complete all the surveys. It is anticipated that a study participant will receive $20 (in the form of an eGift card) every 3 months – a total annual incentive amount to not exceed $80 for a total of 12 surveys (1 baseline and 11 follow-up surveys). Compensation is dependent on successful completion of all surveys sent out by the research team. The schedule of compensation is based on the number of completed surveys. The PRO Portal awards "Hearts" (which are a particular type of points) for completion of monthly surveys, diary entries, and other information study participants may report directly into the system. Hearts are awarded independent of a participant's specific answers to questions. In addition, the number of hearts a study participant receives will vary depending on the scope of the data collected. Hearts can be redeemed for cash gift cards (called eGifts) which are distributed to them via email. Once every three months, 800 hearts can be redeemed for a $20 eGift that a participant can choose from a selection of popular merchants. Inactivity for 60 days on the PRO Portal will lead to the expiration of 100 hearts. The study-specific rules about accumulation of points and eGift redemption limits can be accessed in the PRO Portal by clicking on the Rewards tab. If a study participant withdraws from the study early, they can still redeem their earned points for eGifts prior to withdrawal; redemption of the points that they have accumulated is not contingent upon study completion. If a participant is removed from the study

by the Principal Investigator for suspected fraudulent involvement, they will not be able to redeem any pending rewards.

7.2 Description of study design for study participants

Patients: Once patients provide informed consent, they will continue with the study baseline survey which can be found in **Attachment 15**. The baseline survey design includes structured questions with response options or ratings on a Likert-type scale, as well as the ability to enter comments and open-ended text for the structured questions. **It is expected to take 45-60 minutes to complete**. The survey has language reminding patients that they may need to check their medical records to complete the survey.

The **baseline survey** for patients is modular and contains the following sections:

- **Module 1** will ask patients about their lung cancer diagnostic journey

- **Module 2** will ask patients questions about how a lung cancer diagnosis has impacted their quality of life, including questions on hospitalizations and experience with their healthcare team.

- **Module 3** will include validated PRO instruments that ask patients about their lung cancer symptoms, impacts, and outcomes.

- **Module 4** will ask patients questions specific to their lung cancer, including questions on biomarker testing and different treatment options

- **Module 5** will ask patients about their demographic characteristics

In addition, for patients who enroll between August 2020 and December 2020, we will have a COVID-19 specific module (which will be displayed between Modules 4 and 5).

There will be 11 additional **follow-on surveys** (one every month after a patient has completed the baseline survey) each lasting approximately 10-15 minutes. Patients will receive an email invitation when these surveys are ready to be filled out (**Attachment 16**). The follow-on surveys are identical for all the 11 months of follow-up.

An additional set of COVID-19 vaccine questions will be inserted to learn about vaccination patterns and hesitancy (**Attachment X of May amendment**). For new enrollees to PEER these items will be included as part of the Patient Baseline Survey. For current PEER participants, the items will be asked as part of their next scheduled monthly questionnaire. If a participant has received the vaccine, no additional vaccine questions will be asked. For participants who have yet to receive the vaccine, they will be asked items 7 – 10 at 6 months and again at 12 months only if they still have not received the vaccine.

Patients will also have the option to provide additional information by logging on to their account and providing information in their eDiary. The eDiary will chart a patient's compliance with

medications with food and weight as well as the option of "checking in". This is completely optional. A screenshot of the eDiary option is included in **Attachments 17A, B, and C**.

The consent process will explicitly discuss the time needed to complete surveys.

Summary of the different PRO instruments to be used in Module 3 for patients is as follows:

1. A PRO-CTCAE side-effect question— Please choose the response below that best describes the severity of your **overall side effects from treatment** over the past week" (where 0 = none and 4 = very severe)
2. SAQ items for **all-comers,** including small cell lung cancer (SCLC) patients to understand how SAQ may be applied to the SCLC population [4]
3. EORTC short-form questions on physical/functional/emotional functioning, fatigue, and pain[5,6]
4. EORTC questionnaire on financial toxicity[7]

Caregivers:

Once caregivers provide informed consent, at the beginning of their participation they will be asked if the patient they care for is deceased or still alive.

If during the caregiver's baseline survey (**Attachment 18**), they report that their patient is deceased, they will be compensated $20 for their time upon completion of their survey. These caregivers will not receive any follow on monthly surveys.

The **baseline survey** (**Attachment 18**) for caregivers is modular and contains the following sections:

- **Module 1** will ask caregivers about their role in caregiving.

- **Module 2** will ask caregivers questions about their patient's lung cancer diagnostic experience

- **Module 3** will include caregiver-specific questions on quality of life and coping mechanisms as a caregiver (including the CarGOQoL instrument[8,9] and the Enriched Social Support Instrument[10])

- **Module 4** will ask caregivers questions specific to their lung cancer, including questions on biomarker testing and different treatment options

- **Module 5** will ask caregivers about their demographic characteristics

Caregivers whose patients are alive at the time of study initiation and who have completed the baseline survey will also be asked at the start of each follow-on survey if the patient they provide care for is still alive. There will be 11 additional **follow-on surveys** (one every month after a

caregiver has completed the baseline survey) each lasting approximately 10-15 minutes. Participants will receive an email invitation when these surveys are ready to be filled out (**Attachment 19** and **Attachment 20**).

An additional set of COVID-19 vaccine questions will be inserted to learn about vaccination patterns and hesitancy (**Attachment X of May amendment**). For new enrollees to PEER these items will be included as part of the Caregiver Baseline Survey. For current PEER participants, the items will be asked as part of their next scheduled monthly questionnaire. If a participant has received the vaccine, no additional vaccine questions will be asked. For participants who have yet to receive the vaccine, they will be asked items 7 – 10 at 6 months and again at 12 months only if they still have not received the vaccine.

If the patient has passed away during the duration of the study, the caregiver will be directed to the close-out bereavement survey (**Attachment 21**).[11,12] They will be compensated for their time based on the number of follow-on surveys completed. For example, a caregiver who has completed 6 of the 12 surveys will be compensated $40 in total.

The following table summarizes the three potential possibilities of caregiver participation.

Type of Caregiver	Participation
Patient deceased at time of study commencement	Will only finish baseline survey (Attachment 18)
Patient is alive during follow-up	Will finish baseline (Attachment 18) and monthly surveys (Attachment 19 and 20)
Patient passes away during the follow-up period	Will have the option to complete bereavement survey (Attachment 21), in addition to completing baseline baseline survey (Attachment 18) at study commencement

7.3 Reminders

All participants will receive **standard** email reminders for activities, such as password changes and reminders when surveys are available (**Attachment 22**).

7.4 Participant-facing results

Aggregate summary results of the study will be posted on the LUNGevity website and will be periodically updated as participants join the study and complete more follow-on surveys.

The study is an open-ended longitudinal survey study. Protocol extensions will be submitted as needed throughout the duration of the study.

7.5 Study risks

All participants: Recruitment and participation in the study itself does not put potential study participants at risk.

Self-report participants *not* from a market research firm, specialty pharmacy, or trial website**:** There are no privacy concerns associated with recruitment given that all recruitment will be conducted through online means and not use any touch-points with patients or their caregivers.

Self-report participants from a market research firm, specialty pharmacy, or trial website: There is minimal risk for privacy concerns. Since: 1) these participants will be recruited by staff that have completed the appropriate training for the conduct of research and will recruit participants according to this training. 2) The market research firm, specialty pharmacy, and trial website **will not** have access to participants survey responses. 3) LUNGevity **will not** have access to the market research firm, specialty pharmacy, and trial website network data.

Clinic participants: For patients and caregivers recruited at a clinic site, there is minimal risk for privacy concerns. Since: 1) these participants will be recruited by clinic staff that have completed the appropriate training for the conduct of research and will recruit participants according to this training. 2) The clinic site **will not** have access to participants survey responses. 3) LUNGevity **will not** have access to the clinic site's patient data.

All study participants will be provided a link that directs them to the study surveys. Responses will be confidential and only analyzed in aggregate, and personally identifiable information will not be shared with outside parties.

As with all electronic data capture systems, there is a potential risk of breach of confidentiality of personal and medical information and the associated privacy of study participants. Such risks will be minimized by (1) storing personal identifiable information (e.g., subject names) in tables separate from other study information; (2) limiting direct access to information contained within the study to trained LUNGevity and EmpiraMed research personnel; (3) de-identifying any shared data; and (4) the use of a secure, compliant, well-established, and proven software application (PRO Portal).

7.6 Withdrawal or removal from study

Withdrawal: If a study participant wishes to withdraw from the study, they may do so by emailing the Principal Investigator or by accessing the Forms and Privacy Settings section of their personal profile and selecting "withdraw". They can still redeem their earned points for eGifts before their account becomes inactive; redemption of the points that they have accumulated is not contingent upon study completion. Their email address and other identifiable information will be removed from the database and they will no longer be asked to provide additional data to the

study. Data that have already been collected will not be removed from the study. Study participants will be given the option to provide a reason for their withdrawal in the PRO Portal. (**Attachment 12**)

Removal: The Principal Investigator may remove a study participant from the study under the following circumstances:

- LUNGevity Foundation or IRB cancels the study
- The Principal Investigator thinks that removing a study participant from the study is in their best interests
- A study participant is not responding to the surveys or not following directions given for the study. In this case, an email to the study participant notifying them of their non-compliance will be sent to the registered email address (**Attachment 4**)
- The Principal Investigator suspects fraudulent participation in the study (**Attachment 23**)

7.7 Detection of possible fraudulent participation

The research team is committed to ensuring the integrity of the data collected, both to respect authentic participants from the lung cancer community and to maintain the rigor and robustness of the data collected. To achieve this, they have taken every precaution to deter fraudulent participation in Project PEER, such as:

- Use of CAPTCHA at the time of participant registration
- Use of a short verification survey (**Attachment 9**) to confirm whether a participant is a person with lung cancer or a caregiver to a person with lung cancer
- Pacing of study participation incentives every 3 months whereby a participant will receive an incentive after completing 3 surveys broken into 4 periods (totally 12 surveys). This is described in detail in Section 7.1

In addition to these precautions, we will flag participants who have registered with duplicate emails and/or duplicate usernames as fraudsters. In the event that a participant is identified to have duplicate accounts, they will receive the fraudulent participant email (**Attachment 23**) and have the opportunity to rectify the misidentification. A participant will be flagged as fraudulent only if they fail to respond to the fraudulent participation email within 7 days of receiving the email. We will also be doing period data quality controls before each incentive is paid out (after completion of survey # 3, 6, 9, and 12):

- Step 1: For all participants, we will be tracking their responses over time and checking for inconsistencies such as **a large selection of "I do not know" for different questions within the same survey** and **variations in data collected through each monthly survey**. For example, baseline and monthly surveys administered to both patients and caregivers have common questions. Variations, such as fluctuation in treatment-related and patient or caregiver experience data, will be easily identified during data quality control.
- Step 2: For those participants where such variations and/or inconsistencies are identified, we will look at survey para data to identify whether the participants identified in Step 1

finished the survey really quickly – defined as time taken to complete the survey that is two standard deviations lower than the mean completion time. This time limit has been decided based on previously published research.[13] The PRO portal allows researchers to access survey para data (**mean survey completion time** for all participants and **individual participant completion time** for each survey). It is important to note that different survey para data time limit values will be used for patients and caregivers, given the different lengths of the surveys.

- Step 3: In the event that a participant is identified through Step 2, they will receive the fraudulent participant email (**Attachment 23**) and have the opportunity to rectify the misidentification. A participant will be flagged as fraudulent only if they fail to respond to the fraudulent participation email within 7 days of receiving the email.

Given all the precautions we have taken, we do not anticipate many fraudulent participants. In the event that a participant is suspected of being fraudulent, we will deal with each situation on a case-by-case basis based on their survey responses and the survey para data.

8.0 Data analysis

All data analysis will be conducted using Excel, SPSS, Stata, R, or another similar software. Data will be analyzed using frequencies, cross tabulation, time-series, and regression analysis. All analyses will include aggregate results and presented as tables, graphs, or charts. No individual-level data comparisons will be made. Participants will have access to their individual responses, but individual-level responses will not be shared and will not contain personally identifiable information.

Study results will be disseminated at international conferences through presentations and posters, and as manuscripts in peer-reviewed journals. Aggregate summary results of the study will be posted on the LUNGevity website and will be periodically updated as participants join the study and complete more follow-on surveys. Findings will be disseminated to stakeholders, such as patients, caregivers, doctors and other healthcare providers, regulatory agencies, and pharmaceutical companies.

Data collected from patients and caregivers will be analyzed separately. As noted above, caregivers will be providing anonymous patient-level data in modules 2 and 4 and in the monthly surveys. Patient-level data provided through caregivers will be used to categorize caregivers (for example, caregivers of non-small cell lung cancer versus small cell lung cancer, caregivers whose patients are receiving chemotherapy versus targeted therapy, etc.) to understand how patient-level factors impact caregiver experience.

9.0 Data management and protection

9.1 Data management

Study participants are informed that their personally identifiable information, including name and contact information, will not be made public or shared with any outside parties, and they

are informed how their de-identified data may be used. Identifiable information will be stored separately from study data.

Only authorized LUNGevity Foundation and affiliate research staff from EmpiraMed will have access to all data collected through the survey. Responses will be held in strict confidence and will be used only for the purposes of this research study. The results will be reported in aggregate form only and such that individuals cannot be identified. There will be no individual participant-level data analysis. All subsets of study participants for analysis (e.g., breakouts by type of cancer, age, etc.) will be based on answers to survey questions voluntarily given by participants and will be anonymous, as these answers will not be tied to any personally identifying information about the participant.

If a study participant requests to be removed from the study, their email address and other identifiable information will be removed from the database and they will no longer be asked to provide additional data to the study. If LUNGevity learns that a patient has died, their personally identifiable information will be deleted from the database. Information of caregivers of patients who have died will also be removed from the study, and they will not be contacted further. Existing data cannot be removed from the study

9.2 Data Storage, Security, and Confidentiality

A state-of-the-art web-based, patient registry platform (EmpiraMed, Maynard, MA) will be used for data capture. LUNGevity will track participant enrollment based on entered data via the secure web portal. This data will be used to track enrollment as needed (1,200 patients and 300 caregivers).

HIPAA privacy rules and HIPAA security rules mandate that covered entities have in place appropriate policies and procedures to protect the confidentiality and security of protected health information. EmpiraMed complies with all HIPAA regulations. Furthermore, EmpiraMed complies with the General Data Protection Regulation (EU) 2016/679 ("GDPR"). GDPR is a regulation in EU law on data protection and privacy for all individuals within the European Union (EU) and the European Economic Area (EEA). It also addresses the export of personal data outside the EU and EEA areas.

In compliance with these regulations, the database security features of EmpiraMed's PRO Portal target multiple levels including the data element (e.g., restricted access to fields), user (e.g., password authentication access), application (e.g., role-based access to features, access audit trails), and hosting services (e.g., firewall, secure sockets layer). Taken together, these features ensure access control, audit control, data integrity, user authentication, and transmission security. The research project will be set up in EmpiraMed's PRO Portal to ensure exported datasets are de-identified as defined in the HIPAA privacy regulation [45 C.F.R. §164.514 (b)(2)].

All server requests are transmitted over SSL. All servers have several layers of data and access protection: (1) A dedicated, managed router firewall, (2) A redundant array of independent

disk [RAID] Level 5 is used to ensure that data will not be lost if a hard drive fails between back-ups, (3) A system level back-up is performed nightly and retained for 2 weeks and is stored in the data center, (4) a database level back-up is performed every 6 hours and retained for 2 months and is stored at the data center.

Participant medical information will be stored electronically within the database. The database design is such that participant identifiable information is kept in data tables separate from the medical information.

Access to patient and caregiver information will be restricted to trained research staff from LUNGevity Foundation and EmpiraMed.

Participant information will be stored for an indefinite period of time. If a participant requests to be removed from the study, their email address and other identifiable information will be removed from the database and they will no longer be asked to provide additional data to the study. Existing data will remain in the study database.

9.3 Availability of de-identified data to third-party researchers

External researchers who are interested in analyzing Project PEER data may check the survey and variables collected in the study, which will be posted on the website. The posted survey will not include any consent language.

If a researcher expresses a desire to interrogate the data, they will provide a short proposal to LUNGevity Foundation, clearing stating:

a. What is the research question?

b. How does the research question impact lung cancer?

c. What survey fields/questions are relevant to the research question?

Following approval by LUNGevity and members of LUNGevity's Survivor Advisory Council, the researchers will have access to limited, de-identified data in the form of an Excel csv or an SPSS-compatible file with only specified data fields along with a data dictionary. The transfer of the data file will be made through a password-protected Dropbox Business account maintained by LUNGevity Foundation or a password-protected Excel csv file sent via encrypted email. Two emails will be sent — one with the Excel file and a follow-up email with the password. The data will be made available free of cost. Any identifying information such as age (continuous variable) will be categorized before data sharing.

10.0 Premature closeout of study or study discontinuation

In case LUNGevity Foundation decides to discontinue the study, the Principal Investigator will inform the IRB formally to close the study and also send emails to all registered participants informing them of study closeout.

11.0 Attachments

Attachment 1_LUNGevity Peer _Landing Page
Attachment 2_LUNGevity PEER (LC2)_Participant Self-Registration Intake Form
Attachment 3_LUNGevity_Registration Data Use Agreement
Attachment 4_LUNGevity PEER (LC2)_Custom Email Content
Attachment 5_LUNGevity PEER (LC2) eICF
Attachment 6_LUNGevity PEER (LC2) eICF_EU
Attachment 7_LUNGevity_Privacy Policy
Attachment 8_LUNGevity_Terms of Use Agreement
Attachment 9_LUNGevity PEER (LC2)_PARTICIPANT VERIFICATION survey
Attachment 10_LUNGevity_Project PEER Recruitment Language
Attachment 11_LUNGevity_PEER_PostcardRecruitment_July 8_2020
Attachment 12_LUNGevity PEER (LC2)_Study Withdrawal Reasons
Attachment 13_LUNGevity PEER (LC2)_FAQ
Attachment 14_LUNGevity (LC2) Quick Start Guide
Attachment 15_LUNGevity BASELINE PATIENT survey
Attachment 16_LUNGevity MONTHLY PATIENT survey
Attachment 17A_LUNGevity_LC2 Medication with Food
Attachment 17B_LUNGevity (LC2) eDiary Check-in Screenshots
Attachment 17C_LUNGevity (LC2) eDiary Weight Screenshots
Attachment 18_LUNGevity BASELINE CAREGIVER survey
Attachment 19_LUNGevity CAREGIVER MONTHLY Months 2_4_6_8_10 survey
Attachment 20_LUNGevity CAREGIVER MONTHLY Months 3_5_7_9_11_12 survey
Attachment 21_LUNGevity CAREGIVER Bereavement survey
Attachment 22_LUNGevity PEER (LC2)_Standard Emails
Attachment 23_LUNGevity_Fraudulent Participation email draft
Attachment 24_LUNGevity e-Blast
Attachment 25_LUNGevity Clinic Site Recruitment Script
Attachment 26_LUNGevity Clinic Site Informational Card
Attachment 27_LUNGevity Participant Outreach_ Market Research Firm
Attachment 28_LUNGevity Non-clinic site recruitment script

12.0 REFERENCES

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