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SWOG

IMPLEMENTATION OF A PROSPECTIVE FINANCIAL IMPACT ASSESSMENT TOOL IN PATIENTS WITH METASTATIC COLORECTAL CANCER

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**THIS STUDY IS OPEN TO ALL
NCORP COMPONENTS AND SUBCOMPONENTS
(ALLIANCE, ECOG-ACRIN, NRG, SWOG)**

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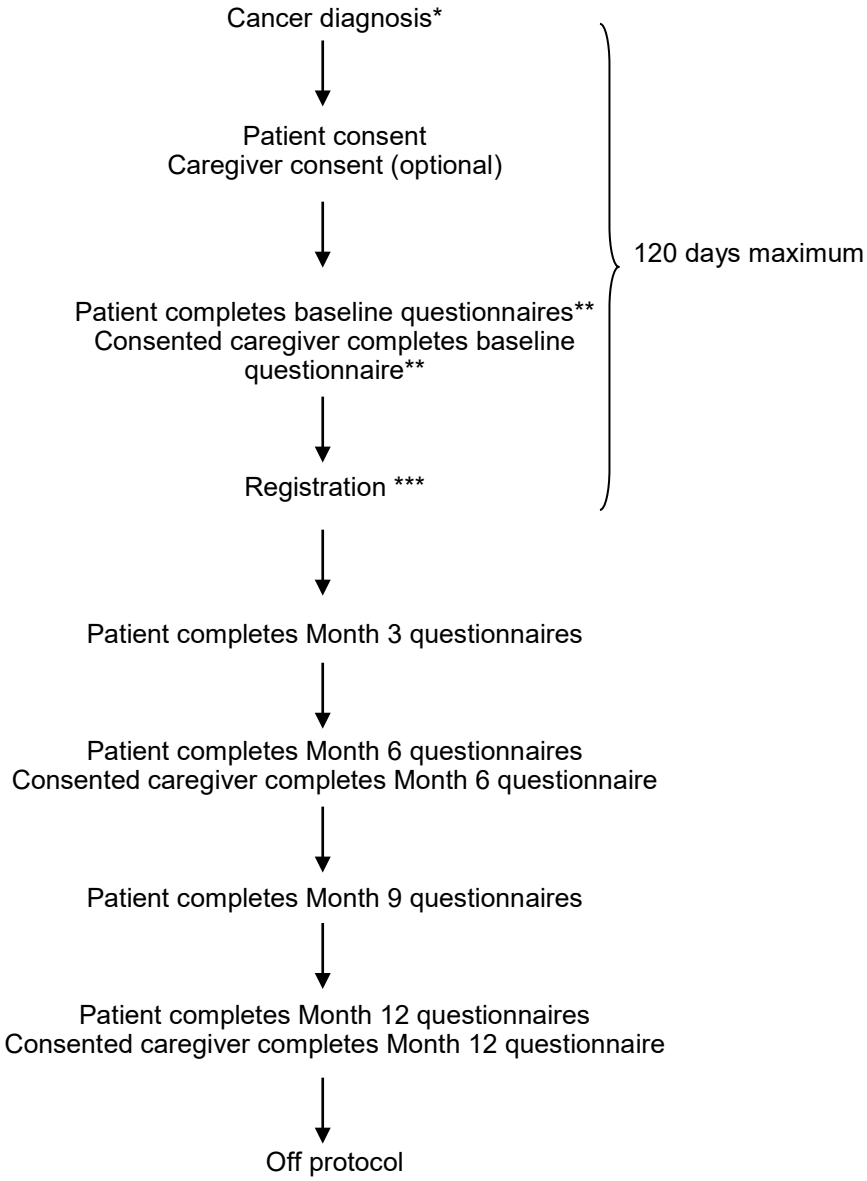
CANCER TRIALS SUPPORT UNIT (CTSU) ADDRESS AND CONTACT INFORMATION

For regulatory requirements:	**For patient enrollments:**	**For study data submission:**
Regulatory documentation must be submitted to the CTSU via the Regulatory Submission Portal: Regulatory Submission Portal (Sign in at www.ctsu.org, and select the Regulatory Submission sub-tab under the Regulatory tab.) Institutions with patients waiting that are unable to use the Portal should alert the CTSU Regulatory Office immediately at 866-651-2878 to receive further information and support. Contact the CTSU Regulatory Help Desk at 866-651-2878 for regulatory assistance.	Please refer to the patient enrollment section of the protocol for instructions on using the Oncology Patient Enrollment Network (OPEN) which can be accessed at https://www.ctsu.org/OPEN_SYSTEM/ or https://OPEN.ctsu.org. Contact the CTSU Help Desk with any OPEN-related questions at ctsucontact@westat.com	Data collection for this study will be done exclusively through Medidata Rave. Please see that data submission section of the protocol for further instructions. Other Tools and Reports: Institutions participating through the CTSU continue to have access to other tools and reports available on the SWOG Workbench via the SWOG website (www.swog.org).
The most current version of the **study protocol and all supporting documents** must be downloaded from the protocol-specific Web page of the CTSU Member Web site located at https://www.ctsu.org. Access to the CTSU members' website is managed through the Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM) registration system and requires user log on with CTEP-IAM username and password.		
For patient eligibility questions and study procedure-related questions contact the SWOG Statistics and Data Management Center by phone or email: 206-652-2267 cancercontrolquestion@crab.org **For study procedure related questions** contact the SWOG Statistics and Data Management Center by phone or e-mail.		
For questions unrelated to patient eligibility, site requirements or data submission contact the CTSU Help Desk by phone or e-mail: CTSU General Information Line: 888-823-5923 ctsucontact@westat.com All calls and correspondence will be triaged to the appropriate CTSU representative.		
The CTSU Web site is located at https://www.ctsu.org		

SCHEMA FOR FLOW OF STUDY



* Patients must have newly diagnosed metastatic colon or rectal cancer (de novo metastatic diagnosis or metastatic recurrence after prior treatment for Stage I-III disease) at registration and be within 120 days after diagnosis.

** Patient and caregiver may complete baseline questionnaires at any time following consent. Questionnaires are to be submitted within 7 days after registration. Caregiver participation is optional.

*** Systemic chemotherapy and/or systemic biologic therapy must be planned to be administered ≤ 30 days after registration or must have been initiated ≤ 60 days prior to registration.

1.0 OBJECTIVES

1.1 Primary Objective(s)

To estimate the incidence of treatment-related major financial hardship over 12 months, among patients with newly diagnosed metastatic colorectal cancer (mCRC) treated at components and subcomponents of the NCI Community Oncology Research Program (NCORP).

1.2 Secondary Objective(s)

a. To describe the association of major financial hardships with mCRC treatment by demographic factors, including age, race, marital status, employment status, and income.

b. To explore whether occurrence of major financial hardship is associated with poorer health-related quality of life over time.

c. To profile the magnitude and timing of treatment-related changes in patients' income, assets, debt, and employment, and to quantify major out-of-pocket expenses during the 12 months following registration.

d. To explore the extent to which health insurance factors (e.g. high copayments, deductibles, premiums, loss/change of insurance plan) are associated with major financial hardship and treatment non-adherence.

e. To determine feasibility of recruiting primary caregivers and measuring caregiver burden and caregivers' perceptions about cancer treatment costs.

f. To determine the feasibility of conducting a prospective-multi-site longitudinal cohort study assessing financial outcomes in patients with mCRC undergoing treatment within the NCORP network.

1.3 Tertiary Objective

To obtain objective measures of expenses, debt and credit through linkage with individual patient credit reports (TransUnion) at enrollment (baseline), at 6 months, and end of follow up (12 months).

2.0 BACKGROUND

Rising Cancer Treatment Costs – Implications for Patients

By 2015, it is expected that 20% of the United States Gross Domestic Product (GDP) will be spent on health care, compared with 5% of GDP in 1965. *(1)* Cancer treatment costs are expected to comprise an increasing percentage of total health care spending due, in large part, to the rapid adoption of expensive new drugs and diagnostics. From a societal standpoint, the economic sustainability of current trends in cancer spending is of increasing concern. However, the impact of rising cancer treatment costs on individual patients remains a largely understudied area in oncology.

Recent reports have demonstrated that cancer patients may be at particular risk for treatment-related financial difficulty. In a recent study using data from the 2001 to 2008 Medical Expenditure Panel Survey, the proportion of non-elderly insured patients reporting high out-of-pocket cost burdens (defined as spending more than 20% of income on health care) was greatest among patients with cancer (13.4%) compared to patients with and without other chronic illness (9.7% and 4.4%, respectively). *(2)* In a 2008 national survey of 930 individuals with various cancer

diagnoses, 25% reported depletion of savings accounts to pay for treatment and 11% reported an inability to pay for basic necessities such as food, heat, or housing as a result of cancer treatment costs. *(3)*

Previous studies that have attempted to describe patient out-of-pocket costs have been small, retrospective, and have not captured the financial impact of routine use of newer, high-cost therapeutics. *(4,5,6,7,8,9,10,11)* Importantly, the degree to which various factors (e.g. age, employment, income, assets, health insurance cost-sharing scheme) predispose certain patients to treatment-related financial hardships are poorly understood. Further, lack of standardized financial assessments in clinical practice limits early detection of treatment-related financial issues. Finally, financial hardships may theoretically contribute to depression, anxiety, and poor treatment tolerance. Yet very little is known about the impact of financial hardships on health-related quality of life.

The development of more reliable ways to capture economically-motivated treatment non-adherence, financial hardship, and quality of life decrements due to financial stress will be critical in developing interventions to address the financial consequences of cancer treatment and, in turn, improve the lives of cancer patients.

Preliminary Data: Fred Hutchinson Cancer Research Center/ Cancer Surveillance System Study

Investigators at the Fred Hutchinson Cancer Research Center recently conducted a population-based study of treatment-related financial changes in patients with Stage III colorectal cancer (CRC). A multi-dimensional survey was administered to 550 CRC patients diagnosed between 2008 and 2010 identified from the Western Washington Surveillance, Epidemiology, and End Results (SEER) registry. *(12)* The study questionnaire was developed through a series of cognitive interviews conducted at the Seattle Cancer Care Alliance. A total of 284 patients responded to the mailed questionnaire, for an overall response rate of 51.2%. A significant percentage of patients (38%) reported at least one treatment-related financial hardship (defined as: debt accumulation, borrowing money from family/friends, ≥ 20% income decline, selling/refinancing primary home). In a multivariate logistic regression analysis, factors most closely associated with financial hardship were younger age (age < 65) and annual income < $50,000. Treatment non-adherence was similarly associated with younger age and lower income, but was also associated with unemployment, disability, or leave-of-absence from work. A minority of respondents (42%) reported discussing treatment-related expenses with their physicians. Thirty-four patients (12%) reported a total of 45 insurance coverage denials for recommended medications, tests, or procedures. Denials for chemotherapy (capecitabine, in most cases) and supportive medications (e.g. anti-emetics or pain medications) comprised 42% of all coverage denials. While this retrospective study is the first large population-based assessment of treatment-related financial consequences in CRC patients, there were many limitations to this approach. In particular, there was no assessment of baseline pre-diagnosis financial information, timing of financial hardship in relation to diagnosis, and impact of financial hardships on quality of life. In addition, non-response bias may have skewed the observed rate of financial hardship.

Feasibility and Motivation for Proposed Study through the NCI Community Oncology Research Program (NCORP)

The ultimate goal of this research is to measure the association between cancer treatment and financial hardship, using a comprehensive financial impact assessment tool that can be adopted in routine clinical care and alongside cooperative group clinical trials. By developing a system to track treatment-related financial changes over time and by improving our understanding of the major risk factors for financial hardship, we hope to set the stage for the development of interventions to help patients avoid major financial strain. Interventions such as comprehensive financial counseling, advanced planning for patient drug assistance programs, and tools to inform physicians about potential high copayments could help lessen patients' treatment-related financial burden. The NCI Community Oncology Research Program (NCORP) represents a unique mechanism to accrue patients being treated in community clinical settings to cancer care delivery research studies.

Description of Patient Population

This study will focus on patients with mCRC for several reasons. First, patient recruitment is likely to be more feasible in a common malignancy such as CRC compared with a rarer disease. Second, the FDA approval of several new, expensive CRC drugs over the last decade has increased the cumulative lifetime cost of CRC treatment; the degree to which these costs have been shifted to individual patients is poorly understood. *(13)* Finally, as the median survival for metastatic CRC continues to improve, the financial impact of chronic palliative therapy over a longer period of time may be significant.

Inclusion of Women and Minorities

This study was designed to include women and minorities, but was not designed to measure differences of intervention effects. The anticipated accrual in the ethnicity/race and sex categories is shown in the table below. Because several components of the questionnaire have only been validated in English, we will limit enrollment only to patients who can complete the forms in English. Translation of the questionnaire into other languages will require testing and validation in a population of patients who speak the language and is outside the scope of the current study.

Racial Categories	**Ethnic Categories**				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/Alaska Native	1	1	0	0	2
Asian	13	15	0	0	28
Native Hawaiian or Other Pacific Islander	1	1	0	0	2
Black or African American	20	22	0	0	42
White	123	141	17	19	300
More Than One Race	0	0	0	0	0
Total	158	180	17	19	374

3.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration. Any potential eligibility issues should be addressed to the SWOG Statistics and Data Management Center in Seattle at 206/652-2267 or cancercontrolquestion@crab.org prior to registration. NCI policy does not allow for waiver of any eligibility criterion (https://ctep.cancer/gov/protocolDevelopment/policies_deviations.htm).

When calculating time frame for date of diagnosis, the date that the pathological diagnosis was made is considered Day 0. **If Day 30 or 120 falls on a weekend or holiday, the limit may be extended to the next working day.**

3.1 Disease Related Criteria

a. Patients must have newly diagnosed metastatic colon or rectal cancer (mCRC) (de novo metastatic diagnosis) or metastatic recurrence after prior treatment for Stage I-III disease and be ≤ 120 days after diagnosis at time of registration.

b. Systemic chemotherapy and/or systemic biologic therapy must be planned to be administered ≤ 30 days *after* registration OR must have been initiated ≤ 60 days *prior* to registration. Patients who are planning palliative or hospice care only (no chemotherapy or biologic therapy) are not eligible.

3.2 Clinical Criteria

a. Patients must be at least 18 years of age.

3.3 Regulatory Criteria

a. Registering site must be an NCORP site.

NOTE: It is recommended that patients receive medical care for the mCRC at the registering site to ensure accessibility of patient records.

b. Patients must be able to complete questionnaires in English.

c. Patients must provide their full name, primary address in the U.S., birth date and social security number at registration for the purposes of accessing credit report data.

d. Patients must sign and give written informed consent in accordance with institutional and federal guidelines.

e. As a part of the OPEN registration process (see Section 8.0 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

4.0 INTERVENTION

4.1 Setting

This study will be conducted through all NCORP components and subcomponents. Enrollment will be limited to these sites in order to capture the financial impact of treatment in community clinical practices. The infrastructure for charity care and financial counseling may be different in NCORP sites compared with larger comprehensive cancer centers and the financial experiences of patients treated at NCORP sites may be more representative of the financial experiences of all mCRC patients in the United States.

4.2 Screening, Consent and Patient Registration

Eligible patients will be identified by the treating providers who will, together with the clinical research associate (CRA), describe the study and obtain written informed consent from eligible patients and their consenting caregivers (optional). Refer to Section 10.0 for information on caregiver eligibility and administering consent and questionnaires to caregivers. Register the eligible, consented patient to **S1417CD** within 120 days after cancer diagnosis per Section 8.0.

4.3 Administration of Questionnaires to Patients

a. Patients will be assessed at baseline following consent, and at subsequent routine clinical visits (3, 6, 9 and 12 months) following registration. (See Section 5.0 for the list of questionnaires and time points they are to be administered.) Questionnaires will be self-administered and are anticipated to require 30 minutes to one hour to complete at each study time point.

b. Target follow-up assessment dates should be based on the date of registration. A window of ± 21 days is allowed for each assessment to provide more flexibility in scheduling.

c. Patients undergoing treatment for mCRC will generally be seen at the clinic or practice approximately every two weeks. In order to minimize patient burden and streamline patient visits, it is preferable for questionnaires to be given to the patient at the clinical visit immediately prior to the study time point, completed at home and returned at the routine clinical visit coinciding with the study time point; however, the study staff should accommodate the patient's preferences for filling out the questionnaires as described below. Some questionnaires will require detailed financial information so it is recommended that the CRA contact the patient a week before their scheduled visit to remind him/her to bring the appropriate information to the visit to complete the questions on the forms. At time of consent, the patient should be provided with a copy of the forms for reference.

d. The research site should provide the patient with options for completing the questionnaires after the patient has reviewed them. The patient's review may help them decide if they need information they do not have with them at their visit or they may need assistance from a family member or caregiver. The patient may also be more comfortable completing the questionnaire(s) at home. The options for the patient are as follows:

- Complete questionnaires at home. Provide the patient with questionnaires in advance and instructions to return them to the site at the clinical visit corresponding to the study time point (e.g., give patient questionnaires 2 weeks in advance at a routine clinical visit). Review the returned questionnaires for completeness at the clinical visit and clarify answers while the patient is at the clinic. If the patient does not return the completed questionnaires as scheduled, the patient should complete the questionnaires at the clinical visit or schedule a phone contact.

- Complete the questionnaires in the clinic or practice. Due to the sensitive information being asked, when possible, offer the patient a private location to sit and complete the questionnaires. Supply additional paper, pencil and a calculator. One question requests the total amount of owed debts. The patient may need to perform some calculations to answer the question. After completion of the questionnaires, the CRA should immediately review the questionnaires for completeness and confirm the patient answered the questions per the directions on the form and clarify questions with the patient while they are still at the clinic or practice.

- Partially complete the questionnaires in the clinic or practice. If due to illness, time or any reason the patient begins completing the questionnaires in the clinic or practice but then decides he/she cannot finish one or more questionnaire, make a photocopy of the incomplete questionnaire(s), give the patient the copy and keep the original in the patient's research chart. Give the patient a pre-addressed stamped envelope to return the questionnaire(s) by mail to the clinic or practice, but also schedule a phone call with the patient 1 week later. If questionnaire(s) are returned (by mail or in person) within 1 week, use the scheduled phone call to clarify any missing or unclear responses (if applicable). If questionnaire(s) are not returned, use the scheduled phone call to complete the questionnaire(s) by phone interview.

- Complete questionnaires by phone interview. If the patient is unable to come in for their clinical visits or questionnaires were not completed before or at the clinical visit, questionnaires may be completed by phone interview. Phone interviews should be scheduled within 1 week of the clinical visit corresponding to the study time point. The patient should be given a copy of blank forms (or partially-completed, if applicable) so that the patient may look at a copy of the questionnaires while the staff conducts the interview. The date of the telephone interview is to be noted on the **S1417CD** Cover Sheet for Patient- and Caregiver-Completed Questionnaires. If the phone interview is to complete data on a partially-completed, form, review all the questions with the patient, even those previously completed, in case the patient needs to change a previously answered question. If the phone interview is not completed as scheduled, reschedule to remain within the ± 21-day window for the study time point.

e. As a general reminder, review all completed questionnaires to be sure all of the questions have been answered and, when the patient is directed to mark only one response, that only one answer is marked. If the patient has marked more than one answer per question, ask which answer reflects how the patient is feeling. If the patient has skipped a question, tell the patient that a question was not answered and ask if the patient would like to answer the question. If the patient is unable to answer the question at the time of the visit, site staff are encouraged to retain the questionnaire and contact the patient by phone to obtain outstanding information. If patient does not want to answer a particular question, the CRA will enter "Not answered by the patient" in Medidata RAVE®.

f. Caregivers may assist patients with their questionnaires by administering the questionnaire orally to the patient, helping the patient find information and/or recording the patient's answers. Caregivers cannot answer for the patient. For patients who are too sick to complete the questionnaire (even with assistance from the caregiver) or who are not able to come to a clinical visit (e.g. enrolled in hospice care), the CRA will record on the **S1417CD** Cover Sheet that the patient was too sick to complete the questionnaire.

g. Patients will not receive incentives (e.g. gift cards, monetary compensation) for participation in this study.

h. **S1417CD** Cover Sheet for Patient and Caregiver-Completed Questionnaires

For each time point, the nurse or CRA completes the **S1417CD** Cover Sheet for Patient and Caregiver-Completed Questionnaires. The Cover Sheet is submitted with the set of patient-completed forms at each scheduled assessment. The Cover Sheet is very important for tracking how and when the patient forms were completed. When a patient-completed form is not administered at a scheduled time point, it is important to know why the assessment did not occur; the form includes potential reasons for a patient not completing a form. All issues of noncompliance are noted on the **S1417CD** Cover Sheet.

4.4 Additional Quality Control Procedures:

a. When a patient is registered on **S1417CD**, a calendar should be made with dates of upcoming patient-completed questionnaires noted. A copy of this calendar can be given to the patient with the notation that the questionnaires should be completed. You may wish to photocopy the Study Calendar (Section 5.0), and include the patient's name and specific dates. Alternatively, an editable version of the Study Calendar is available on the **S1417CD** abstract page on the SWOG

website (http://www.swog.org) or CTSU member website (https://www.ctsu.org). A copy of this should be kept in the patient file. If the patient is off the study time point schedule, all attempts should be made to complete the next assessment within the target follow-up assessment schedule per Section 4.3b and 5.0.

b. Anyone involved in the collection of quality of life data in SWOG trials should review the training program available on the SWOG website accessible from three locations. On the SWOG Home Page (prior to member login), in the **QUICKLINKS** section on the bottom right corner of the page, there is a link to the Patient Reported Outcomes Training. The other two locations that the training is available are after SWOG member login on the CRA Workbench. The Training section and the New CRAs! Section both contain access to the Patient Reported Outcomes (PROs) training module. The training program is a narrated set of slides designed to standardize the way quality of life data is collected from patients. Questions regarding the quality of life assessments can be addressed to the SWOG Statistics and Data Management Center (206-652-2267).

4.5 Caregiver Questionnaires

For instructions related to administration of the caregiver questionnaires, please see Section 10.0.

4.6 Credit Reports

The patient's full name, address, birth date, and Social Security number (SSN) will be used by the SWOG Statistics and Data Management Center (SDMC) to request a copy of the patient's credit report at baseline, at 6 months, and at the time the patient goes off protocol (at 12 months or sooner if the patient discontinues participation prior to the 12 month time point) directly from the credit report agency for research purposes. This is considered a "soft pull" and will not have an effect on the patient's credit score. This process will occur automatically at SDMC, and beyond obtaining the patient's name, address, birthdate, and SSN, no further efforts on the part of the site staff or patients is required for this portion of the study. The credit report will remain confidential and will not be shared with the patient, treating institution/study site, insurance companies, or any other entities. Funding for the acquisition of credit reports from TransUnion and the handling of credit reports by SDMC will come from an American Society of Clinical Oncology (ASCO) 2013 Career Development Award (PI Shankaran). Patients are not responsible for any costs related to the credit report.

4.7 Criteria for Removal of Patient from Protocol Participation

a. Patient completes 12 months of study participation.

b. Patient does not receive at least one cycle of chemotherapy within the first 90 days after registration.

c. The patient may withdraw from the study at any time for any reason. (Research staff should only submit the **S1417CD** Off Protocol Notice if the patient refuses both direct and indirect follow-up on the study. If the patient allows for indirect follow-up or is refusing to complete any further patient forms but will allow the site to follow them directly, do not submit the **S1417CD** Off Protocol Notice and continue to submit the site-completed forms at the time points required in Section 9.4b.)

d. Patient death.

4.8 Discontinuation of Study Participation

All reasons for discontinuation of study participation as defined in Section 4.7, including patient death, must be documented on the **S1417CD** Off Protocol Notice and submitted per Section 9.4c.

NOTE: If a patient cannot or refuses to complete the patient questionnaires for a study time point, this is not a criterion for discontinuation of protocol participation. Do not submit the **S1417CD** Off Protocol Notice. Submit the site-completed forms for the time point per Section 9.4b, the **S1417CD** Cover Sheet for Patient- and Caregiver-Completed Questionnaires documenting the reason the questionnaires were not completed at the time point and the **S1417CD** Follow-up Patient Status and Disease Characteristics form at the time point. Administer questionnaires to the patient at the next study time point. See also Section 4.7c for additional follow-up and forms management information.

4.9 Follow-up Period

No further follow-up will be required once the patient completes 12 months of study participation or if the patient discontinues study participation as defined in Sections 4.7b, 4.7c and 4.7d prior to 12 months of participation and the **S1417CD** Off Protocol Notice is submitted.

5.0 STUDY CALENDAR

REQUIRED	Prestudy/ Baseline	Month 3	Month 6	Month 9	Month 12
PATIENT QUESTIONNAIRES					
S1417CD Baseline Questionnaire	X				
S1417CD Financial/Employment Impact Questionnaire		X	X	X	X
S1417CD Insurance Impact Questionnaire		X	X	X	X
S1417CD Quality Of Life Questionnaire	X	X	X	X	X
S1417CD Treatment Perceptions Questionnaire	X	X	X	X	X
CAREGIVER QUESTIONNAIRE					
S1417CD Caregiver Questionnaire √	X		X		X
SITE COMPLETED FORMS					
S1417CD Registration Worksheet (Not submitted)	X				
S1417CD Onstudy Form	X				
S1417CD Follow-Up Patient Status and Disease Characteristics		X	X	X	X
S1417CD Cover Sheet for Patient- and Caregiver- Completed Questionnaires	X	X	X	X	X
S1417CD Off Protocol Notice					XΩ

NOTE: Forms are found on the protocol abstract page on the SWOG website (www.swog.org) or CTSU member website (https://www.ctsu.org).
Forms submission guidelines are found in Section 9.0.

√ For consenting caregivers (optional). See Section 10.0 for administration guidelines.
Ω If patient discontinues study participation earlier than 12 months, submit the **S1417CD** Off Protocol Notice per Section 4.8.

6.0 CRITERIA FOR EVALUATION AND ENDPOINT ANALYSIS

6.1 Primary Endpoint

a. Major Financial Hardship: Defined as one or more of the following during the 12 month study period: debt accumulation of any amount, selling or refinancing home, ≥ 20% income decline, borrowing money of any amount from family/friends.

6.2 Secondary Endpoints

a. Treatment Non-Adherence: Defined as refusing treatment or skipping doses due to cost concerns (e.g., lack of coverage, high co-payment requirement)

b. Health-related Quality of Life (HRQOL): As measured by the EORTC Quality of Life Questionnaire C30 (QLQ-C30) v. 3.0. *(14)* This is a well-validated questionnaire which includes 30 items assessing global quality-of-life, functioning in five domains (physical, role, cognitive, emotional social) and several items assessing specific symptoms (e.g. fatigue, trouble sleeping, pain). Importantly, the QLQ-C30 does include one item assessing the impact of medical treatment on finances. Questionnaire responses will be transformed into a linear score (0 to 100) using the EORTC scoring manual.

c. Out-of-Pocket Expenses: Defined as total out-of-pocket direct medical (e.g., prescriptions, physician visits, deductibles) and non-medical (transportation, meals) expenses in the 3 months prior to each study visit.

d. Credit History (TransUnion): Credit reports are obtained at baseline, 6 months, and when the patient goes off protocol and measure the following: non-mortgage amounts past due on credit cards and bankcards; non-mortgage credit card and bankcard balances; bankruptcies, liens, collections or repossessions.

6.3 Definition of Primary Caregiver

a. Primary caregiver is defined as a family member or friend who provides the greatest degree of emotional, physical, logistical, and/or financial support in navigating cancer treatment

6.4 Questionnaires

The majority of items in the final financial impact assessment tool were adapted from the a questionnaire used in our previous work that was successfully administered to a population-based sample of patients with stage III colon cancer in the Seattle/Puget Sound region. (15) Several questions were also adapted from the Medical Expenditures Panel Survey (MEPS), a large-scale survey of households, employers, and medical providers on the cost and use of health care in the United States and the University of Michigan's Health and Retirement Study (HRS), a longitudinal panel survey of older adults. *(16)* The EORTC Quality of Life Questionnaire (QLQ C-30), an existing, validated quality of life instrument, will also be used to assess HRQOL. *(17)* Questions measuring caregivers' stress and anxiety related to cancer treatment expenses were adapted from a questionnaire used in the Family and Cancer Therapy Selection (FACTS) Study conducted at the Fred Hutchinson Cancer Research Center as well as the Caregiver Strain Index, an existing validated survey of cancer caregiver burden. Additional questions were obtained from a survey-based study of caregivers performed by Evercare, in collaboration with the National Alliance for Caregiving, entitled "Family Caregivers: What they Spend, What they Sacrifice." *(18)* The final questionnaires focus on different aspects of patients' or caregivers' financial experience:

BASELINE QUESTIONNAIRE: **Baseline patient financial, employment, and insurance characteristics** – education level, annual income, preexisting debt, total assets (including retirement and savings), baseline employment status.

FINANCIAL/EMPLOYMENT IMPACT QUESTIONNAIRE: **Treatment-related financial or employment changes** – accumulation of debt, depletion of assets, inability to pay other bills, changes in income, job loss, borrowing money, selling home.

INSURANCE IMPACT QUESTIONNAIRE: **Treatment-related insurance issues and out-of-pocket expenses** – insurance coverage denials, high copayments, changes in premiums, treatment non-adherence, all treatment-related out-of-pocket expenses.

QUALITY OF LIFE QUESTIONNAIRE: Health-related quality of life – EORTC Quality of Life Questionnaire (QLQ C-30)

TREATMENT PERCEPTIONS QUESTIONNAIRE: Subjective financial burden assessment – which includes questions assessing stress, anxiety, and guilt related to cancer treatment costs as well as prioritization of treatment costs in the list of disease-related concerns.

CAREGIVER QUESTIONNAIRE: (Consented caregiver only.) Assessment of financial changes made to accommodate patient's cancer treatment expenses and subjective caregiver burden assessment (adapted Caregiver Strain Index), which will include questions assessing stress and anxiety related to patient's cancer treatment costs as well as prioritization of treatment costs in the list of disease-related concerns.

6.5 Performance Status:

Patients will be graded according to the Zubrod Performance Status Scale.

POINT DESCRIPTION

0 Fully active, able to carry on all pre-disease performance without restriction.

1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.

2 Ambulatory and capable of self-care but unable to carry out any work activities; up and about more than 50% of waking hours.

3 Capable of limited self-care, confined to bed or chair more than 50% of waking hours.

4 Completely disabled; cannot carry on any self-care; totally confined to bed or chair,

7.0 STATISTICAL CONSIDERATIONS

7.1 Primary Objective

The primary objective is to estimate the incidence of treatment-related major financial hardship (debt, selling/refinancing home, borrowing money from friends/family, ≥ 20% income decline) among evaluable patients with newly diagnosed metastatic colorectal cancer (mCRC) treated at NCORP sites.

Given serial measurements, the primary endpoint is time to first evidence of major financial hardship. Dropout due to death from mCRC will be a significant factor in this study. Recent randomized clinical trial data have reported 1-year survival of around 60% for this population. *(19)* Therefore death represents a substantial competing risk in the detection of financial hardship, which is accounted for in the study design. Both time to first evidence of major financial hardship and death are assumed to exhibit exponential decline. Dropout for reasons other than death (e.g. transferring care to another institution, withdrawal of consent) following enrollment in the study is estimated to be around 10% based on other studies in the literature. *(20,21)* Non-death related dropouts will be censored.

Based on preliminary data, we anticipate that 40% of patients will experience major financial hardship at some point in the first year after diagnosis. Estimates of major financial hardship at 1 year will be derived using cumulative incidence to account for competing risks.

Under this scenario, a sample size of n=320 eligible, evaluable patients will allow us to estimate the confidence interval to within ± 8% (based on the upper bound of the 95% confidence interval using an exact binomial in patients with complete follow-up), if the assumed incidence is at least 40%. Thus this sample size will allow us to estimate the confidence interval to within ± 20% of the assumed incidence (the "relative accuracy"). The relative accuracy will improve with higher incidence as shown in the table below. This estimate is conservative as it is based on the assumption of no information from the 50% of patients estimated to drop out.

Assumed incidence (p)	95% confidence interval about p	Confidence range	Relative accuracy [(95% CI upper bound – p)/p]
20%	14.1% - 27.0%	± 7.0%	± 35.2%
30%	23.0% - 37.7%	± 7.7%	± 25.8%
40%	32.3% - 48.0%	± 8.0%	± 20.1%
50%	42.0% - 58.0%	± 8.0%	± 16.0%

Given non-restrictive eligibility criteria, we anticipate a low rate of ineligibility (5%). In addition, 10% of patients are anticipated not to complete their baseline forms and will be inevaluable. Therefore 374 total patients will be enrolled to obtain 320 eligible, evaluable patients.

The total number of patients experiencing at least one financial hardship at each study interval will be determined. The proportion of patients experiencing multiple financial hardships will also be reported.

7.2 Secondary Objectives

Risk Factors for Financial Hardship

Sample size calculation will be driven by the key secondary objective of this study, which is to assess whether major financial hardship at one year differs by age (< 65 vs. ≥ 65), race (white vs. non-white), marital status (married vs. unmarried), employment status (any employment vs. unemployed), and income (household income < $50,000 / year vs. ≥ $50,000 / year). In particular, we hypothesize that financial hardships are more likely in patients who, at diagnosis, are younger, non-white, unmarried, unemployed, or have lower incomes.

With a series of 5 hypotheses to be tested, we account for multiple comparisons using a conservative Bonferroni alpha = 0.01 two-sided test for each comparison. Three years of accrual with one year of follow-up is anticipated. Based on a two-sample survival design accounting for the competing risk of death (40% deaths at 1 year [hazard rate of 0.51]), n=320 eligible, evaluable patients will give 90% power to detect an absolute difference of 20% (that is, 30% rate at year 1 in good performing group [hazard rate 0.356] vs. 50% in poor performing group [hazard rate of 0.693]) in the proportion of patients with major financial hardship, if a ratio of patients between two groups is 1:1. This corresponds to a hazard ratio of 1.95. Power drops to 83% if the ratio of patients in subgroups is 2:1.

The effect of age, race, marital status, employment status, and income on major financial hardship will be estimated using multivariable Cox regression. The regression will include the 5 covariates of interest plus insurance status, education, and gender. A sample size of 320 eligible patients ensures that the ratio of events to independent predictors will be at least 10:1. *(22,23)*

Major Financial Hardship and HRQOL:

A secondary objective of this study is to assess the relationship between major financial hardship and HRQOL. These factors are likely positively correlated and associated with the same general status of poor prognosis (endogenous factors). Therefore, any analysis that evaluates, from baseline, the association of major financial hardship and HRQOL will find a positive correlation as an artifact of the endogeneity, and adjustment for performance status is unlikely to fully account for this. Therefore we will use landmark analysis to establish major financial hardship as a baseline predictor of HRQOL. In particular, patients will be categorized as having major financial hardship at their 3 month assessment (yes vs. no). We will then use linear regression to assess whether the 3-month assessment of financial hardship predicts the 6-month HRQOL score. HRQOL at 3 months will be included as an adjustment covariate. The 6-month HRQOL score will be based on the EORTC QLQ-C30 questionnaire transformed into a linear score (0 to 100) using the EORTC scoring manual. A difference in mean score of ≥ 10 between time points is considered clinically relevant. In addition, to assess the robustness of potential associations between major financial hardship and HRQOL to large changes in a subset of patients, HRQOL at 6 months will also be categorized as decline vs. no decline and logistic regression performed. This analysis is limited by the fact that patients without 6 months follow-up scores are more likely to be worse prognosis patients that may also be related to predictive factors of interest (that is, age, race, marital status, employment status, and income).

Feasibility

The feasibility of successfully accruing to a prospective-multi-site longitudinal cohort study assessing financial outcomes in patients with metastatic colorectal cancer (mCRC) undergoing treatment within the NCORP network will be examined. The total anticipated accrual time is 3 years. To be conducted in that timeframe, each of the NCORP components (we anticipate 25 NCORP components) will each need to enroll, on average, about 5 patients per year. Accrual will be monitored regularly. Given the open eligibility criteria, we hypothesize that enrollment will be feasible. However accrual will be assessed at 1.5 years after study activation. If monthly average accrual in quarters 5-6 after study registration is < 50% of projected accrual, efforts will be made to increase accrual over the succeeding 6 month period. If after 2 years, monthly accrual remains < 50% of projected accrual, study revision will be considered. In order to address the potential for selection bias, we will compare demographics (age, race, gender, etc.) of the final cohort to the typical patient population seen at the various practice sites.

The feasibility of incorporating a caregiver component to the study will also be examined. Caregiver participation is optional. The caregiver component will be considered feasible if the designated caregivers for > 50% of eligible patients complete and submit their baseline and at least one follow-up assessment. We will use means, medians, proportions to describe the participating caregiver population. Our analyses will be largely descriptive. We will look at the proportion of caregivers who experienced changes in employment and expenses (caregiver questionnaire items 11 and 13). We expect that caregivers of patients who experience financial hardship will be more likely to report financial burden. We will therefore investigate the association between patient-reported financial hardship and level of caregiver-reported financial burden. We will compare proportion of caregivers experiencing 'high financial burden' (≥ 3 on Likert scale) for patients who do vs. do not report major financial hardship using two-sample t tests. If our caregiver accrual is very poor (<20%), we will focus on describing the patient population rather than attempting to correlate caregiver and patient responses.

7.3 Other Secondary Endpoints:

The linkage of clinical and financial data with credit histories obtained from TransUnion will allow us to explore additional indicators of financial stress, including high balances

and past due amounts of credit card and bankcards as well as evidence of bankruptcies, liens, and collections or repossessions. These data will also allow us to corroborate self-reports of debt and bankruptcy in order to investigate the reliability of self-reports in estimating financial hardship. Credit reports will be obtained at baseline and at 6 and 12 months after registration. Given the poor 1-year survival for this patient cohort (60%), multiple post-baseline credit reports are requested to limit bias due to missing data related to death.

Other secondary objectives including measurement of out-of-pocket expenses, health insurance changes, changes in assets/income/wealth, measurement of debt and spending by credit report histories, and assessment of patient, caregiver, and bereaved caregiver financial stress will be handled using descriptive statistics (e.g. mean, median, proportions). We will use descriptive statistics to summarize baseline patient characteristics and will compare populations using two-sample means and proportions tests (α level 0.05). Caregiver strain index will be scored based on responses (score range 0 to 26). Mean scores will be compared for caregivers of patients reporting vs. not reporting at least one financial hardship.

7.4 Data and Safety Monitoring Committee

There is no formal data and safety monitoring committee for this study. Monitoring of study conduct and accrual for feasibility will be performed routinely by the Study Coordinator, Study Statistician, and the Disease Committee Chair. Accrual reports are generated weekly.

8.0 REGISTRATION GUIDELINES

8.1 Registration Timing

Registration must be within 120 days after diagnosis of metastatic colorectal cancer. Treatment must start ≤ 30 days after registration or must have been initiated ≤ 60 days prior to registration.

8.2 Investigator/Site Registration

Prior to the recruitment of a patient for this study, investigators must be registered members of a NCTN Group. Each investigator must have an NCI investigator number and must maintain an “active” investigator registration status through the annual submission of a complete investigator registration packet to CTEP.

a. CTEP Investigator Registration Procedures

Food and Drug Administration (FDA) regulations and National Cancer Institute (NCI) policy require all investigators participating in any NCI-sponsored clinical trial to register and to renew their registration annually.

Registration requires the submission of:

- a completed ***Statement of Investigator Form*** (FDA Form 1572) with an original signature
- a current Curriculum Vitae (CV)
- a completed and signed ***Supplemental Investigator Data Form*** (IDF)
- a completed ***Financial Disclosure Form*** (FDF) with an original signature

Fillable PDF forms and additional information can be found on the CTEP website at <http://ctep.cancer.gov/investigatorResources/investigator_registration.htm>.

For questions, please contact the ***CTEP Investigator Registration Help Desk*** by email at <pmbregpend@ctep.nci.nih.gov>.

b. CTEP Associate Registration Procedures

The Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) application is a web-based application intended for use by both Investigators (i.e., all physicians involved in the conduct of NCI-sponsored clinical trials) and Associates (i.e., all staff involved in the conduct of NCI-sponsored clinical trials).

Associates will use the CTEP-IAM application to register (both initial registration and annual re-registration) with CTEP and to obtain a user account.

Investigators will use the CTEP-IAM application to obtain a user account only. (See CTEP Investigator Registration Procedures above for information on registering with CTEP as an Investigator, which must be completed before a CTEP-IAM account can be requested.)

An active CTEP-IAM user account will be needed to access all CTEP and CTSU (Cancer Trials Support Unit) websites and applications, including the CTSU members' website.

Additional information can be found on the CTEP website at <http://ctep.cancer.gov/branches/pmb/associate_registration.htm>. For questions, please contact the ***CTEP Associate Registration Help Desk*** by email at <ctepreghelp@ctep.nci.nih.gov>.

c. CTSU Registration Procedures

This study is supported by the NCI Cancer Trials Support Unit (CTSU), but it is not under the purview of the DCP CIRB.

1. **IRB Approval:**

Each investigator or group of investigators at a clinical site must obtain IRB approval for this protocol and submit IRB approval and supporting documentation to the CTSU Regulatory Office before they can be approved to enroll patients. Assignment of site registration status in the CTSU Regulatory Support System (RSS) uses extensive data to make a determination of whether a site has fulfilled all regulatory criteria including but not limited to: an active Federal Wide Assurance (FWA) number, an active roster affiliation with the Lead Network or a participating organization, a valid IRB approval, and compliance with all protocol specific requirements.

2. **Downloading Site Registration Documents:**

Site registration forms may be downloaded from the **S1417CD** protocol page located on the CTSU members' website.

- Go to https://www.ctsu.org and log in to the members' area using your CTEP-IAM username and password
- Click on the Protocols tab in the upper left of your screen
- Either enter the protocol # in the search field at the top of the protocol tree, or
- Click on the By Lead Organization folder to expand
- Click on the SWOG link to expand, then select trial protocol

S1417CD

- Click on LPO Documents, select the Site Registration documents link, and download and complete the forms provided.

3. **Requirements For S1417CD Site Registration:**

   - CTSU IRB Certification
   - CTSU IRB/Regulatory Approval Transmittal Sheet

4. **Submitting Regulatory Documents:**

   Submit forms and documents to the CTSU Regulatory Office via the Regulatory Submission Portal, where they will be entered and tracked in the CTSU RSS.

   Regulatory Submission Portal: www.ctsu.org (members' area) → Regulatory Tab → Regulatory Submission

   When applicable, original documents should be mailed to:

   CTSU Regulatory Office
   1818 Market Street, Suite 1100
   Philadelphia, PA 19103

   Institutions with patients waiting that are unable to use the Portal should alert the CTSU Regulatory Office immediately at 866-651-2878 in order to receive further instruction and support.

5. **Checking Your Site's Registration Status:**

   You can verify your site registration status on the members' section of the CTSU website.

   - Go to https://www.ctsu.org and log in to the members' area using your CTEP-IAM username and password
   - Click on the Regulatory tab at the top of your screen
   - Click on the Site Registration tab
   - Enter your 5-character CTEP Institution Code and click on Go

   Note: The status given only reflects compliance with IRB documentation and institutional compliance with protocol-specific requirements as outlined by the Lead Network. It does not reflect compliance with protocol requirements for individuals participating on the protocol or the enrolling investigator's status with the NCI or their affiliated networks.

8.3 OPEN Registration Requirements

The individual registering the patient must have completed the appropriate SWOG Registration Worksheet. The completed form must be referred to during the registration but should not be submitted as part of the patient data.

Patient enrollment will be facilitated using the Oncology Patient Enrollment Network (OPEN). OPEN is a web-based registration system available on a 24/7 basis. To access OPEN, the site user must have an active CTEP-IAM account (check at < https://eapps-ctep.nci.nih.gov/iam/index.jsp >) and a 'Registrar' role on either the LPO or participating organization roster.

OPEN will also ask additional questions that are not present on the SWOG Registration Worksheet. The individual registering the patient must be prepared to provide answers to the following questions:

a. Institution CTEP ID

b. Protocol Number

c. Registration Step

d. Treating Investigator

e. Cooperative Group Credit

f. Credit Investigator

g. Patient Name (full name is required for this study)

h. Patient's Date of Birth (required for this study)

i. Patient SSN (SSN is required for this study. Do not enter invalid numbers.)

j. Country of Residence

k. Patient address (required for this study)

l. ZIP Code

m. Gender (select one):
- Female Gender
- Male Gender

n. Ethnicity (select one):
- Hispanic or Latino
- Not Hispanic or Latino
- Unknown

o. Method of Payment (select one):
- Private Insurance
- Medicare
- Medicare and Private Insurance
- Medicaid
- Medicaid and Medicare
- Military or Veterans Sponsored NOS
- Military Sponsored (Including Champus & Tricare)
- Veterans Sponsored
- Self Pay (No Insurance)
- No Means of Payment (No Insurance)
- Other
- Unknown

p. Race (select all that apply):
- American Indian or Alaska Native
- Asian
- Black or African American
- Native Hawaiian or other Pacific Islander
- White
- Unknown

8.4 Registration Procedures

a. All site staff will use OPEN to enroll patients to this study. OPEN is integrated with the CTSU Enterprise System for regulatory and roster data and, at the time of patient registration, initializes the patient in the Rave database. OPEN can be accessed at https://open.ctsu.org or from the OPEN tab on the CTSU members' side of the website at https://www.ctsu.org, or from the OPEN Patient Registration link on the SWOG CRA Workbench.

b. Prior to accessing OPEN site staff should verify the following:

- All eligibility criteria have been met within the protocol stated timeframes and the affirmation of eligibility on the Registration Worksheet has been signed by the registering investigator or another investigator designate. Site staff should refer to Section 3.0 to verify eligibility.

- All patients have signed an appropriate consent form and HIPAA authorization form (if applicable).

- The study site is listed as "approved" in the CTSU RSS.

c. Access requirements for OPEN:

- Site staff will need to be registered with CTEP and have a valid and active CTEP-IAM account. This is the same account (user ID and password) used for the CTSU members' web site. Additional information about obtaining a CTEP-IAM account can be found at http://ctep.cancer.gov/branches/pmb/associate_registration.htm.
  Questions should be directed to the CTEP Associate Registration Help Desk by e-mail at ctepreghelp@ctep.nci.nih.gov.

- To perform registrations, the site user must have been assigned the 'Registrar' role on the SWOG roster:

  1 If you are a SWOG member, to perform registrations on SWOG protocols you must have an equivalent 'Registrar' role on the SWOG roster. Role assignments are handled through SWOG.

Note: The OPEN system will provide the site with a printable confirmation of registration and treatment information. Please print this confirmation for your records.

d. Further instructional information is provided on the OPEN tab of the CTSU members' side of the CTSU website at https://www.ctsu.org or at https://open.ctsu.org. For any additional questions contact the CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com.

8.5 Exceptions to SWOG registration policies will not be permitted.

a. Patients must meet all eligibility requirements.

b. Institutions must be identified as approved for registration.

c. Registrations may not be cancelled.

9.0 DATA SUBMISSION SCHEDULE

9.1 Data Submission Requirements

Data must be submitted according to the protocol requirements for **ALL** patients registered, including patients deemed to be ineligible. Patients for whom documentation is inadequate to determine eligibility will generally be deemed ineligible. If the caregiver consented, submit the Caregiver Questionnaire under the patient's SWOG ID number in Rave®.

9.2 Master Forms

Master forms can be found on the protocol abstract page on the SWOG website (www.swog.org) as well as the **S1417CD** page of the CTSU members' website (www.ctsu.org) and (with the exception of the sample consent form and the Registration Worksheet) must be submitted on-line via the Web; see Section 9.3 for details.

9.3 Data Submission Procedures

a. Data collection for this study will be done exclusively through the Medidata Rave® clinical data management system. Access to the trial in Rave is granted through the iMedidata application to all persons with the appropriate roles assigned in Regulatory Support System (RSS). To access Rave via iMedidata, you must have an active CTEP-IAM account (check at https://eapps-ctep.nci.nih.gov/iam/index.jsp) and the appropriate Rave role (Rave CRA, Read-Only, Site Investigator) on either the LPO or participating organization roster at the enrolling site.

Upon initial site registration approval for the study in RSS, all persons with Rave roles assigned on the appropriate roster will be sent a study invitation e-mail from iMedidata. To accept the invitation, site users must log into the Select Login (https://login.imedidata.com/selectlogin) using their CTEP-IAM user name and password, and click on the "accept" link in the upper right-corner of the iMedidata page. Please note, site users will not be able to access the study in Rave until all required Medidata and study specific trainings are completed. Trainings will be in the form of electronic learnings (eLearnings), and can be accessed by clicking on the link in the upper right pane of the iMedidata screen.

Users that have not previously activated their iMedidata/Rave account at the time of initial registration approval for the study in RSS will also receive a separate invitation from iMedidata to activate their account. Account activation instructions are located on the CTSU website, Rave tab under the Rave resource materials (Medidata Account Activation and Study Invitation Acceptance). Additional information on iMedidata/Rave is available on the CTSU members' website under the Rave tab at www.ctsu.org/RAVE/ or by contacting the CTSU help Desk at 888/823-5923 or by e-mail at ctsucontact@westat.com.

b. You may also access Rave® via the SWOG CRA Workbench via the SWOG website (www.swog.org).

For difficulties with the CRA Workbench, please email technicalquestion@crab.org.

9.4 Data Submission Timeline

a. WITHIN 7 DAYS AFTER REGISTRATION:

Submit the following site completed form:

S1417CD Onstudy Form

S1417CD Cover Sheet for Patient and Caregiver-Completed Questionnaires

Submit the following patient-completed questionnaires:

S1417CD Baseline Questionnaire

S1417CD Quality Of Life Questionnaire

S1417CD Treatment Perceptions Questionnaire

Submit the following caregiver-completed questionnaire:

S1417CD Caregiver Questionnaire (if caregiver consented)

b. WITHIN 7 DAYS AFTER PATIENT COMPLETES QUESTIONNAIRE* AT MONTHS 3, 6, 9 AND 12 STUDY TIMEPOINTS:

* **A +/- 21-day window is permitted for administration of patient and caregiver follow-up questionnaires. See Sections 4.3b and 10.2b.**

Submit the following site-completed forms:

S1417CD Follow-Up Patient Status and Disease Characteristics

S1417CD Cover Sheet for Patient and Caregiver-Completed Questionnaires

NOTE: If a patient cannot or refuses to complete forms at a specific time point, the site-completed forms must still be submitted. Refer to Sections 4.7c and 4.8.

Submit the following patient-completed forms:

S1417CD Financial/Employment Impact Questionnaire
S1417CD Insurance Impact Questionnaire

S1417CD Quality Of Life Questionnaire

S1417CD Treatment Perceptions Questionnaire

Submit the following caregiver-completed form:

S1417CD Caregiver Questionnaire *(at months 6 and 12 only, if caregiver consented)*

c. WITHIN 7 DAYS AFTER PATIENT DISCONTINUES PROTOCOL PARTICIPATION:

Submit the following patient-completed form:

S1417CD Off Protocol Notice

NOTE: The **S1417CD** Off Protocol Notice is submitted to reflect the patient's participation status only. If the consented caregiver discontinues study

participation prior to the patient's completion of 12 months of study participation, refer to Section 10.3 for instructions for reporting caregiver discontinuation on the **S1417CD** Cover Sheet for Patient and Caregiver-Completed Questionnaires.

10.0 SPECIAL INSTRUCTIONS

Instructions for Sites Related to Caregivers

10.1 Caregiver Eligibility and Consent

a. The caregiver must be a family member or friend who provides the greatest degree of emotional, physical, logistical, and/or financial support in navigating cancer treatment.

b. Caregiver participation is optional; however, the caregiver must provide separate written informed consent if they choose to participate.

c. The caregiver must be present during the patient consent process at the time the study is explained to the patient and the caregiver must provide consent at the same time the patient consents for the study.

d. Caregiver participation status is required at the time of patient registration.

e. The same caregiver must be retained throughout the study. If the caregiver discontinues participation, a new caregiver may not be recruited to complete the Caregiver Questionnaire(s).

10.2 Administration of Questionnaires to Caregivers

a. Caregivers will be asked to fill out the **S1417CD** Caregiver Questionnaire at baseline (following consent), and subsequently at 6 and 12 months following patient registration. The questionnaire will be self-administered and is anticipated to require a total of 30 minutes to complete at each study time point, by phone or by mail. The caregiver should be asked to complete the Caregiver Questionnaire even if the patient does not complete the patient questionnaires at the time point. Upon patient death, the caregiver's participation will discontinue and no further Caregiver Questionnaires are required.

b. It is preferable for the caregiver to complete the Caregiver Questionnaire during the patient's routine clinical visits coinciding with the appropriate study time point; however, the study staff should defer to the caregiver's preferences for completing the questionnaires. Questionnaires may be done at home and mailed back to the research staff. Target follow-up assessments should be based on the date of patient registration. A window of ± 21 days is allowed for each assessment to provide more flexibility in scheduling.

c. If the caregiver prefers to mail it back, the research site will provide a pre-addressed stamped envelope. If the caregiver prefers to answer the questionnaire over the phone, research staff will make arrangements for a phone interview. When responses are obtained via phone interview, it is important that the caregiver is looking at a copy of the questionnaire while the staff conducts the interview. The date of the telephone interview is to be recorded on the Caregiver Questionnaire.

d. It is very important to review the completed questionnaire with the caregiver during the clinic visit or over the phone to be sure all of the questions have been answered and, when the caregiver is directed to mark only one response, that

only one answer is marked. If the caregiver has marked more than one answer per question, ask them which answer reflects how he/she is feeling. If the caregiver has skipped a question, bring it to their attention and ask if they would like to answer the question. If the caregiver does not want to answer a particular question, the CRA will enter "Not answered by the caregiver" in Medidata RAVE®.

10.3 Criteria for Removal for Consented Caregiver from Study Participation

a. Caregiver completes 12 months of study participation.

b. Patient death.

c. Patient removed from protocol participation (see Section 4.7).

d. The caregiver may withdraw from the study at any time for any reason. The patient will continue participation even if the consented caregiver discontinues study participation.

NOTE: If the patient is alive cannot or refuses to complete questionnaires at a study time point, but remains on protocol, the caregiver will continue to complete the Caregiver Questionnaire at the study time points.

e. If the Caregiver Questionnaire is not completed at a time point, document the reason on the S1417CD Cover Sheet for Patient and Caregiver-Completed Questionnaires for that time point. If the caregiver discontinues study participation prior to 12 months, document the reason on all cover sheet submissions for the remaining time points the patient continues study participation.

11.0 ETHICAL AND REGULATORY CONSIDERATIONS

The following must be observed to comply with Food and Drug Administration regulations for the conduct and monitoring of clinical investigations; they also represent sound research practice:

Informed Consent

The principles of informed consent are described by Federal Regulatory Guidelines (Federal Register Vol. 46, No. 17, January 27, 1981, part 50) and the Office for Protection from Research Risks Reports: Protection of Human Subjects (Code of Federal Regulations 45 CFR 46). They must be followed to comply with FDA regulations for the conduct and monitoring of clinical investigations.

Institutional Review

This study must be approved by an appropriate institutional review committee as defined by Federal Regulatory Guidelines (Ref. Federal Register Vol. 46, No. 17, January 27, 1981, part 56) and the Office for Protection from Research Risks Reports: Protection of Human Subjects (Code of Federal Regulations 45 CFR 46).

Monitoring

This study will be monitored by the Clinical Data Update System (CDUS) Version 3.0. Cumulative CDUS data will be submitted quarterly to CTEP by electronic means. Reports are due January 31, April 30, July 31 and October 31.

Adverse Experiences

There is no SAE Reporting for this study.

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Informed Consent Model for S1417

*NOTES FOR LOCAL INSTITUTION INFORMED CONSENT AUTHORS:

This model informed consent form has been reviewed by the DCTD/NCI and is the official consent document for this study. Local IRB changes to this document are allowed. (Institutions should attempt to use sections of this document that are in bold type in their entirety.) Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making deletions or more substantive modifications to the risks or alternatives sections, they may be justified in writing by the investigator and approved by the IRB. Under these circumstances, the revised language, justification and a copy of the IRB minutes must be forwarded to the SWOG Operations Office for approval before a patient may be registered to this study.

Please particularly note that the questions related to banking of specimens for future study are in bolded type and may not be changed in any way without prior approval from the SWOG Operations Office.

Readability Statistics:	
Flesch Reading Ease	56.1 (targeted above 55)
Flesch-Kincaid Grade Level	9.5 (targeted below 8.5)

- Instructions and examples for informed consent authors are in *[italics]*.
- A blank line, _____, indicates that the local investigator should provide the appropriate information before the document is reviewed with the prospective research participant.
- The term "study doctor" has been used throughout the model because the local investigator for a cancer treatment trial is a physician. If this model is used for a trial in which the local investigator is not a physician, another appropriate term should be used instead of "study doctor".
- The dates of protocol updates in the header and in the text of the consent is for reference to this model only and should not be included in the informed consent form given to the prospective research participant.
- The local informed consent must state which parties may inspect the research records. This includes the NCI, the drug manufacturer for investigational studies, any companies or grantors that are providing study support (these will be listed in the protocol's model informed consent form) and SWOG.

  "SWOG" must be listed as one of the parties that may inspect the research records in all protocol consent forms for which patient registration is being credited to SWOG. This includes consent forms for studies where all patients are registered directly through the SWOG Data Operations Office, all intergroup studies for

which the registration is being credited to SWOG (whether the registration is through the SWOG Data Operations Office or directly through the other group), as well as consent forms for studies where patients are registered via CTSU and the registration is credited to SWOG.

- When changes to the protocol require revision of the informed consent document, the IRB should have a system that identifies the revised consent document, in order to preclude continued use of the older version and to identify file copies. An appropriate method to identify the current version of the consent is for the IRB to stamp the final copy of the consent document with the approval date. The stamped consent document is then photocopied for use. Other systems of identifying the current version of the consent such as adding a version or approval date are allowed as long as it is possible to determine during an audit that the patient signed the most current version of the consent form.

*NOTES FOR LOCAL INVESTIGATORS:

- The goal of the informed consent process is to provide people with sufficient information for making informed choices about participating in research. The consent form provides a summary of the study, of the individual's rights as a study participant, and documents their willingness to participate. The consent form is, however, only one piece of an ongoing exchange of information between the investigator and study participant. For more information about informed consent, review the "Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials" prepared by the Comprehensive Working Group on Informed Consent in Cancer Clinical Trials for the National Cancer Institute. The Web site address for this document is http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/

- A blank line, "_____", indicates that the local investigator should provide the appropriate information before submitting to the IRB.

*These notes for investigators are instructional and should not be included in the consent form sent to IRBs.

Consent Form

Study Title for Study Participants:
Impact of Cancer on Finances

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
S1417, "Implementation of a Prospective Financial Impact Assessment Tool in Patients with Metastatic Colorectal Cancer".

Why is this study being done?

Studies have shown that cancer patients may be at high risk for financial problems because of the cost of treatment. These financial problems can be stressful and sometimes might cause patients to avoid or refuse treatment. We want to measure how often financial problems happen in patients with colorectal cancer, using questionnaires that collect information about finances and quality of life. In order to get a full picture of the financial impact of colorectal cancer, we also want to collect credit reports for all patients in this study.

You have been asked to participate in this study because you have colorectal cancer. This research does not involve medical treatment. Our findings will hopefully help us to better understand the financial impact of cancer and come up with ways to help patients avoid financial problems during treatment. Your participation is very important to this study.

There will be about 374 people taking part in this study.

What is the usual approach to use of medical information for research?

Hospitals or doctor's offices usually use a "Release of Medical Information" form to get medical information from patients. For this study, we are using a consent form that describes what type of information we want from your medical records. Your signing the consent form gives us permission to use this information from your medical records along with your answers to the questionnaires for research.

What are my other choices if I do not take part in this study?

Your decision to participate (or not to participate) in this research study will NOT affect your cancer treatment. If you decide not to take part in this research study, you have other choices. For example:

- You can get treatment for your cancer without being on a study
- You may choose to take part in a different study, if one is available

How long will I be in this study?

You will be in the study for 12 months.

What is involved?

If you agree to take part in the study, you agree to answer questionnaires at the following times:

- on the day you agree to be in the study (baseline)
- 3 months after entering the study
- 6 months after entering the study
- 9 months after entering the study
- 12 months after entering the study

It may take between 30 and 60 minutes to answer each questionnaire. You will have the option to fill out the questionnaires during the clinic visit, at home, or over the phone. If you fill out the questionnaire at home, you can either mail it back to the research staff using a pre-addressed stamped envelope that we will provide, or you can bring it with you the next time you come into clinic for an appointment. The research staff will work with you to find the easiest option for you.

We will obtain the following information, directly from you (through questionnaires) or from your medical record.

- Basic information about you (e.g., gender and race) and your cancer (e.g., names of chemotherapy drugs you will receive) from the medical record.
- Information about your health insurance and finances (e.g., household income, home value, assets) from the questionnaire.
- Information about your physical and emotional health from the questionnaire.
- Information about changes in health insurance or finances after cancer (for instance changes in work, income, expenses).
- Your full name, social security number, address and date of birth in order to obtain your credit report. (This will be obtained from both the questionnaire and medical record.)

A company has been contracted to give us your credit reports for research purposes at the time you agree to participate in this study, at 6 months, and again at the time your study participation has ended at 12 months (or sooner, if you come off study earlier for any reason). *(11/21/17)* You will need to provide your full name, date of birth, address and social security number in order for us to get your credit report. Your social security number will only be seen by research staff who will enter your number into the database, however, it will not be used for any other purpose besides obtaining credit reports. *(Revised 6/20/16)* The credit reports will remain private and will not be shared with you, the treating institution/research office, insurance companies or any other parties.

You will also be asked to identify a primary caregiver (the family member or friend who provides the most support to you during your cancer treatment).

Your caregiver will also be asked to fill out a questionnaire at the time you agree to participate in the study, and again 6 months and 12 months. The caregiver questionnaires will ask for their point of view about treatment, finances and caregiver duties. The primary caregivers' participation is optional; you can still take part in the study even if your primary caregiver says "no" to filling out the questionnaires.

What extra tests and procedures will I have if I take part in this study?

No extra testing or procedures are needed for participation in this study.

What are the possible risks of taking part in this study?

You may feel uncomfortable being asked about your finances or physical and emotional health.

We have procedures in place to protect your personal information and we will do our best to make sure that the personal information used for this study will be kept private. However, we cannot guarantee total privacy. Your financial information (answers to the questionnaires and credit reports) will not be disclosed and cannot be required to be given out by law. If information from this study is published or presented at scientific meetings, your name and other personal information will **not** be used.

To help make sure your information remains private, study staff will use a secure electronic submission program (*Meditata Rave*) approved by the National Cancer Institute (NCI) to send us your information. All data collected during this study will be kept in a password protected, secure, firewalled (blocks unauthorized access) database at the SWOG Statistical and Data Management Center (SDMC). Personal information including your name, address, and social security number will be used for the purpose of obtaining your credit report. Your personal information and credit report will be sent to the SWOG SDMC via a secure, coded (*encrypted*) transmission. A minimum number of authorized staff will be given access to this data. Specific information will be pulled from the credit reports and included in the study database. Your personal information including your name, address, and social security number will not be shared with investigators who are analyzing the data or reporting results. The pulling of your credit report for this study will not affect your credit score.

What are the possible benefits of taking part in this study?

The information you provide will help us to better understand the financial impact of cancer and come up with ways to help other patients like yourself avoid financial problems during treatment.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

There are no costs for participating in the study. You do not have to pay for credit reports. We will coordinate our research with your other medical appointments so that you do not need to make separate trips to the clinic for this study. The research staff will provide a stamped envelope if you choose to return questionnaires by mail. If you choose to do the questionnaire over the phone, the study staff will call you so that you do not incur long distance phone charges (if this applies to you).

What happens if I am injured or hurt because I took part in this study?

There will be little risk of being injured on this study since it does not involve medical treatment.

Who will see my study information?

Your privacy is very important to us and the researchers will make every effort to protect it. Researchers will do their best to make sure that any information that is released will not identify you. Some of your health information from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your medical records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor, SWOG.

- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The National Cancer Institute in the U.S.
- Qualified representative(s) of the NCI Community Oncology Research Program (NCORP) Research Base with whom your institution is affiliated (Alliance, ECOG-ACRIN, NRG). *(1/24/17)*

The organizations that will look at the financial records are:

- The study sponsor, SWOG
- TransUnion (the company doing the credit reports).

[Note to Local Investigators: The NCI has recommended that HIPAA regulations be addressed by the local institution. The regulations may or may not be included in the informed consent form depending on local institutional policy.]

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this study will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

Future Contact

Sometimes researchers working with SWOG may have another research idea that relates to people who were on a SWOG study. In some cases, to carry out the new research, we would need to contact participants in a particular study. You can agree or not agree to future contact by circling "yes or no"

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

YES NO

My Signature Agreeing to Take Part in the Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in this study.

Participant's (or legally authorized representative's) signature_____

Date of signature_____

Signature of researcher obtaining consent _____

Date of signature _____

Informed Consent Model for S1417
CONSENT FOR PRIMARY CAREGIVER

*NOTES FOR LOCAL INSTITUTION INFORMED CONSENT AUTHORS:

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Please particularly note that the questions related to banking of specimens for future study are in bolded type and may not be changed in any way without prior approval from the SWOG Operations Office.

Readability Statistics:		
Flesch Reading Ease	57.1	(targeted above 55)
Flesch-Kincaid Grade Level	9.3	(targeted below 8.5)

- Instructions and examples for informed consent authors are in *[italics]*.
- A blank line, _____, indicates that the local investigator should provide the appropriate information before the document is reviewed with the prospective research participant.
- The term "study doctor" has been used throughout the model because the local investigator for a cancer treatment trial is a physician. If this model is used for a trial in which the local investigator is not a physician, another appropriate term should be used instead of "study doctor".
- The dates of protocol updates in the header and in the text of the consent is for reference to this model only and should not be included in the informed consent form given to the prospective research participant.
- The local informed consent must state which parties may inspect the research records. This includes the NCI, the drug manufacturer for investigational studies, any companies or grantors that are providing study support (these will be listed in the protocol's model informed consent form) and SWOG.

"SWOG" must be listed as one of the parties that may inspect the research records in all protocol consent forms for which patient registration is being credited to SWOG. This includes consent forms for studies where all patients are registered directly through the SWOG Data Operations Office, all intergroup studies for which the registration is being credited to SWOG (whether the registration is through the SWOG Data Operations Office or directly through the other group), as well as consent forms for studies where patients are registered via CTSU and the registration is credited to SWOG.

- When changes to the protocol require revision of the informed consent document, the IRB should have a system that identifies the revised consent document, in order to preclude continued use of the older version and to identify file copies. An appropriate method to identify the current version of the consent is for the IRB to stamp the final copy of the consent document with the approval date. The stamped consent document is then photocopied for use. Other systems of identifying the current version of the consent such as adding a version or approval date are allowed as long as it is possible to determine during an audit that the patient signed the most current version of the consent form.

*NOTES FOR LOCAL INVESTIGATORS:

- The goal of the informed consent process is to provide people with sufficient information for making informed choices about participating in research. The consent form provides a summary of the study, of the individual's rights as a study participant, and documents their willingness to participate. The consent form is, however, only one piece of an ongoing exchange of information between the investigator and study participant. For more information about informed consent, review the "Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials" prepared by the Comprehensive Working Group on Informed Consent in Cancer Clinical Trials for the National Cancer Institute. The Web site address for this document is http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/

- A blank line, "_____", indicates that the local investigator should provide the appropriate information before submitting to the IRB.

*These notes for investigators are instructional and should not be included in the consent form sent to IRBs.

Consent Form for Primary Caregiver

Study Title for Study Participants:
Impact of Cancer on Finances

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
S1417, "Implementation of a Prospective Financial Impact Assessment Tool in Patients with Metastatic Colorectal Cancer".

Why is this study being done?

Studies have shown that cancer patients may be at high risk for financial problems because of the cost of treatment. These financial problems can be stressful and sometimes might cause patients to avoid or refuse treatment. We want to measure how often financial problems happen in patients with colorectal cancer, using questionnaires that collect information about finances and quality of life. In order to get a full picture of the financial impact of colorectal cancer, we also want to collect credit reports for all patients in this study.

You have been asked to participate because ____*patient name*_____ has identified you as their primary caregiver. ____*patient name*_____ is participating in a **non-**treatment research study. As the primary caregiver, you will be asked to fill out a questionnaire that will capture your point of view about treatment, finances and caregiver duties. We also want to find out about caregivers in general therefore some of the questions may be about how you are related to the patient, your gender, age, race, etc. Our findings will hopefully give us a better understanding of the financial burden of cancer and help us develop ways to lessen the burden. Your participation is very important to this study.

There will be about 374 patients with metastatic colorectal cancer taking part in the study. We hope to capture an equal number of caregivers, though patients may still participate in the study even if their designated caregiver chooses not to.

What is the usual approach to use of medical information for research?

Hospitals and doctor's offices usually use a "Release of Medical Information" form to gather medical information from patients. Since the information we are requesting from you as a caregiver will not be in the patient's medical chart, we are using this consent form to inform you of the study and to get your permission to use the information you provide as part of the research data.

What are my other choices if I do not take part in this study?

Participation in this study is optional.

How long will I be in this study?

You will be in the study for 12 months. Participation ends if you discontinue being the caregiver for the patient or choose to no longer participate.

What is involved?

If you agree to take part in the study, you agree to answer a questionnaire at each of the following times:

- at the time you and the patient agrees to be in the study (baseline)
- 6 months after the patient enters the study
- 12 months after the patient enters the study

It may take between 30 and 60 minutes to answer each questionnaire. You may fill out the questionnaires during the patient's clinic visit, at home, or over the phone. If you fill out the questionnaire at home, you can either mail it back to the research staff using a pre-addressed stamped envelope that we will provide, or you can bring it with you the next time you come to the clinic for the patient's appointment. The study staff will work with you to find the easiest option for you.

We will obtain the following information, directly from you (through questionnaires) and it will be included as part of the research data:

- Basic information about you, changes to your financial status, quality of life, your point of view on aspects of your dependent's cancer treatment.

What risks can I expect from taking part in this study?

You may feel uncomfortable being asked about your finances or physical and emotional health.

We have procedures in place to protect your personal information and we will do our best to make sure that the personal information used for this study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will **not** be used.

To help make sure your information is private, your doctor or nurse will go to a secure data submission program sponsored by the National Cancer Institute (NCI) to send us your information. We can then go to the same secure program and get your information to include it with the information from all of the other patients taking part in the study.

What are the possible benefits of taking part in this study?

We hope to be able to use these questionnaires in the future to reliably capture financial hardship information in cancer patients and their caregivers.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study staff know as soon as possible. If you stop, you can decide whether or not to let the study staff continue to provide your information to the organization running the study.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you or to the patient. You will not lose any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

There are no costs to you associated with this study. The research staff will provide a stamped envelope if you choose to return questionnaires by mail. If you choose to do the questionnaire over the phone, the study staff will call you so that you do not incur long distance phone charges (if this applies to you).

What happens if I am injured or hurt because I took part in this study?

There will be little risk of being injured on this study as it does not involve medical treatment.

Who will see my personal information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your name or contact information will not be put in the database because this information will not be obtained from you. Your questionnaire responses will be entered under the participating patient's ID.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor, SWOG.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.
- Qualified representative(s) of the NCI Community Oncology Research Program (NCORP) Research Base with whom your institution is affiliated (Alliance, ECOG-ACRIN, NRG). *(1/24/17)*

[Note to Local Investigators: The NCI has recommended that HIPAA regulations be addressed by the local institution. The regulations may or may not be included in the informed consent form depending on local institutional policy.]

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this study will be available on http://www.ClinicalTrials.gov**, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.**

Who can answer my questions about this study?

You can talk to the study doctor or study site staff about any questions or concerns you have about this study. Contact the study doctor or research staff _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

My Signature Agreeing to Take Part in the Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in this study.

Primary Caregiver (Participant's) signature_____

Date of signature_____

Signature of researcher obtaining consent _____

Date of signature _____