

Table of Contents

1.	TITLE	2
2.	OVERALL GOAL & OBJECTIVES	2
2.1.	RATIONALE AND BACKGROUND	2
2.2.	MAIN SCIENTIFIC QUESTION	3
2.3.	HYPOTHESES	3
2.4.	AIMS	4
3.	TECHNICAL APPROACH.....	4
3.1.	CURRENT ASSESSMENT OF NEED	4
3.2.	INTERVENTION DESIGN AND METHODS.....	5
3.2.1.	Overall Study Design	5
3.2.2.	Aim 1: Hypothesis, Intervention/Evaluation Design and Statistical Analysis	6
3.2.3.	Aim 2: Hypothesis, Intervention/Evaluation Design and Statistical Analysis	8
3.2.4.	Aim 3: Hypothesis, Intervention/Evaluation Design and Statistical Analysis	10
3.2.5.	Feasibility of Accrual	11
3.2.6.	Anticipated Challenges and Solutions	11
4.	WORKPLAN AND DELIVERABLES SCHEDULE.....	12
4.1.	WORKPLAN	12
4.2.	DELIVERABLES TABLE	12
4.3.	DISSEMINATION PLAN	12
5.	ORGANIZATIONAL DETAIL	13
5.1.	LEADERSHIP AND ORGANIZATIONAL CAPABILITY	13
6.	REFERENCES	16
	APPENDIX A: DELIVERABLES TABLE	19

1. Title

Improving the care of patients with metastatic renal cell carcinoma via a patient and provider intervention program

2. Overall Goal & Objectives

2.1. Rationale and Background: Renal cell carcinoma (RCC) is a relatively rare cancer, comprising only 3.9% of all new cancer cases in the United States, with an estimated incidence of new cancers of the kidney and renal pelvis being 65,150 cases in 2013 and leading to 13,680 deaths.¹ World-wide, RCC is diagnosed in approximately 170,000 individuals each year with over 72,000 deaths.² Due to a lack of a proven screening intervention and an often clinically silent disease course, RCC often presents in an advanced or metastatic state and over half of RCC patients will at some point develop metastatic renal cell carcinoma (mRCC).³ Once metastatic, RCC is resistant to conventional chemotherapy and radiotherapy.⁴ Immunotherapy with high-dose IL-2 or interferon-alpha was for many years considered the standard treatment for patients with mRCC, but resulted in only a modest response rate and is associated with significant toxicity.⁵

Fortunately, over the last decade, advances in translational research have led to a rapid paradigm shift in the management of mRCC patients. With the elucidation of the von Hippel-Lindau/hypoxia-inducible factor (VHL-HIF) and mammalian target of rapamycin (mTOR) pathways in mRCC, seven new drugs have been approved since 2005 and many more are in clinical development.⁶ Currently FDA approved agents include vascular endothelial growth factor (VEGF) receptor tyrosine kinase inhibitors (TKIs) sunitinib, pazopanib, axitinib and sorafenib; the mTOR inhibitors temsirolimus and everolimus, and the anti-VEGF monoclonal antibody bevacizumab.⁷

Due to the above development, the median survival of patients with mRCC is now approaching 30 months (up from less than one year in 2000) and is poised to increase even further with the preliminary, but very promising results of novel immunotherapy approaches.^{8,9} Many patients are now living with metastatic disease for years as they undergo sequential drug treatments, sometimes surgeries (metastasectomies and/or cytoreductive or palliative nephrectomies) and targeted radiation treatments.^{10,11}

Unfortunately, although often better tolerated than conventional cytotoxic chemotherapy, all of the agents approved for mRCC have potential side-effects and most patients experience at least some of those on a chronic basis.¹² Common side effects associated with VEGF TKIs include hypertension, hypothyroidism, gastrointestinal symptoms such as nausea, vomiting or diarrhea and palmar-plantar erythrodysesthesia.¹³ mTOR inhibitors often lead to mucositis or stomatitis, rash, hypercholesterolemia, hyperglycemia and diarrhea.¹³ All of the agents lead to some degree of fatigue.

In addition, five of the seven drugs approved for mRCC are oral agents and this leads to the toxicity often occurring insidiously while the patient is at home, without the treating team necessarily being aware of the patient's symptoms and patients being unclear as to what is important to report to their treatment team. Primary care physicians and subspecialist are often not familiar with these drugs or their side-effect profile and may be unable to help patients manage toxicities. Thus patients often times exclusively rely on their oncology

providers to support them during their treatment. Optimally managing these patients throughout their disease course is a challenge with many nuances that requires a multi-disciplinary approach and experience. Simply following guidelines is difficult, as even the NCCN guidelines are rather non-specific in many areas such as to how to appropriately sequence therapy, when to switch therapy and how to integrate multi-modality therapy into practice.¹⁴ In addition, guidelines may not be updated frequently enough to reflect the rapidly evolving therapeutic landscape and not be able to appropriately differentiate recommendations based on an inherently very heterogeneous group of mRCC patients (e.g., high vs. intermediate vs. low risk patients). Thus, new paradigms are necessary for a multidisciplinary management of these patients who have a form of chronic metastatic disease (interventions such as the creation of patient-centered oncology medical homes are trying to address some of these concerns).

Also, communication between patients and physicians is critical to the management of toxicities among mRCC patients receiving these oral agents. As promoted by federal agencies, reporting and monitoring of symptoms and health-related quality of life (HRQOL) has recently shifted from traditional clinical encounter collection to the patients' self-report.^{15,16} In particular, technologies do exist to provide opportunities for electronically collecting patient-reported outcomes,¹⁷ but to our knowledge none have been tested among the outpatient mRCC population.

Given that RCC is a relatively rare disease it is infrequently seen by oncologists, and in particular community oncologists. Simultaneously, most mRCC patients are in fact treated in a community setting as opposed to academic-based cancer centers. An independent assessment and analysis of the needs of medical oncologists in the US in regard to taking care of mRCC patients was conducted by the Annenberg Center for Health Sciences at Eisenhower in collaboration with Clinical Care Options and the AXDEV Group, Inc. This mixed-methods analysis identified at least seven practice performance gaps in the treatment and management of RCC patients by community and academic oncologists.¹⁸ We propose to address those gaps in a large oncology community network via an educational intervention and virtual tumor board for providers and an electronic self-reported assessment portal for patients.

2.2. Main Scientific Question: Can the care of mRCC patients being treated in the community be enhanced by improving and supporting the expertise of community oncology providers to treat mRCC and by empowering mRCC patients to communicate with their treatment team?

2.3. Hypotheses: Management of mRCC patients is challenging for community oncology providers with a great heterogeneity between providers and centers in the application of current guidelines, drug sequencing and dose adjustments, side-effect management techniques, tailoring therapy based on risk stratification and quality of life assessments and collaborative processes between various subspecialists treating mRCC patients.

Simultaneously, navigating mRCC is also challenging for patients who have to deal with chronic physical side-effects due to treatments and psychological uncertainty.

We hypothesize that the use of an education intervention and an ongoing virtual tumor board for clinicians, as well as a self-reported assessment portal for patients will increase providers' knowledge and preparation for decision making in treating mRCC patients and improve patients' quality of life (QOL), cancer related distress and overall disease management.

2.4. Aims: Aim 1 is to develop, implement and evaluate an ongoing educational series of didactic and case-based presentations for oncology providers (MDs, NPs, PAs, RNs) focusing on the primary challenges of treating mRCC: appropriate prognostication and selection of drugs for a given line of therapy, adverse event management, adherence to oral agents, decisions of when to switch or escalate/de-escalate therapy, QOL assessments and appropriate integration of surgical and radiation therapy. Aim 2 is to develop, implement and evaluate a sustainable on-line patient self-reported assessment portal to improve patient-provider communication, patient disease management and QOL and the management of therapy-related side-effects. Aim 3 is to operationalize and implement a virtual tumor board for community oncologists to be able to interact on a regular basis with an academic medical center's genitourinary (GU) experts.

3. Technical Approach

3.1. Current Assessment of Need: The population of target for this initial proposal is a group of medical oncology providers and patients who will be recruited from a large community cancer affiliate program. The primary institution coordinating the project will be Fox Chase Cancer Center (FCCC). FCCC is a founding member of the NCCN and the academic base for the nation's first known community cancer affiliate program, the Fox Chase Cancer Center Partners program (FCCCP). This group of 18 (representing 9 health systems) community cancer programs is located throughout southeastern Pennsylvania and New Jersey and has promoted quality cancer care and research in the community setting for years. The group has published and presented on quality assurance audits of NCCN guidelines in the community setting.^{19,20} There is a close working relationship between FCCC and the various partner sites with patients frequently being referred to FCCC for clinical trials or advanced care. Thus, FCCC is ideally suited to develop and implement educational and quality improvement programs in the community via this already established and close partnership. FCCCP practices are diverse in their patient population, and include urban, suburban, and rural practice populations. They have approximately 60 medical oncologists as well as approximately 30-40 nurse practitioners, physician assistants and registered nurses who routinely take care of RCC patients.

Amongst the FCCC and FCCCP, there were 450 analytic (new to the system without ever having had any treatment for their RCC) cases of RCC in 2012 alone and FCCCP saw approximately 224 of those cases. This comprised 4.11% of total analytic tumor registry cancer cases and thus clearly demonstrates the relative rarity of this disease overall, but at the same time a significant absolute number of newly diagnosed patients in this healthcare system. Furthermore, FCCCP saw 300 analytic RCC cases in 2011 and 232 in 2010, showing a consistent patient pool. Out of these cases at FCCCP ~35/year were de novo metastatic and ~30/year were locally advanced and thus at high risk for short-term metastatic progression. In addition, ~30 non-analytic (primary treatment conducted elsewhere) cases per year were seen at FCCCP sites.

When diagnosed in an advanced or metastatic state, FCCCP patients are not infrequently referred to FCCC for a second opinion. FCCC has both a regional and national reputation for expertise in the management of RCC. According to the FCCC RCC database 256 nephrectomies were performed in 2010, 234 in 2011, 227 in 2012 and 204 in 2013. Over 75 new patients with RCC were seen by GU medical oncology in 2013 and over 43 patients with

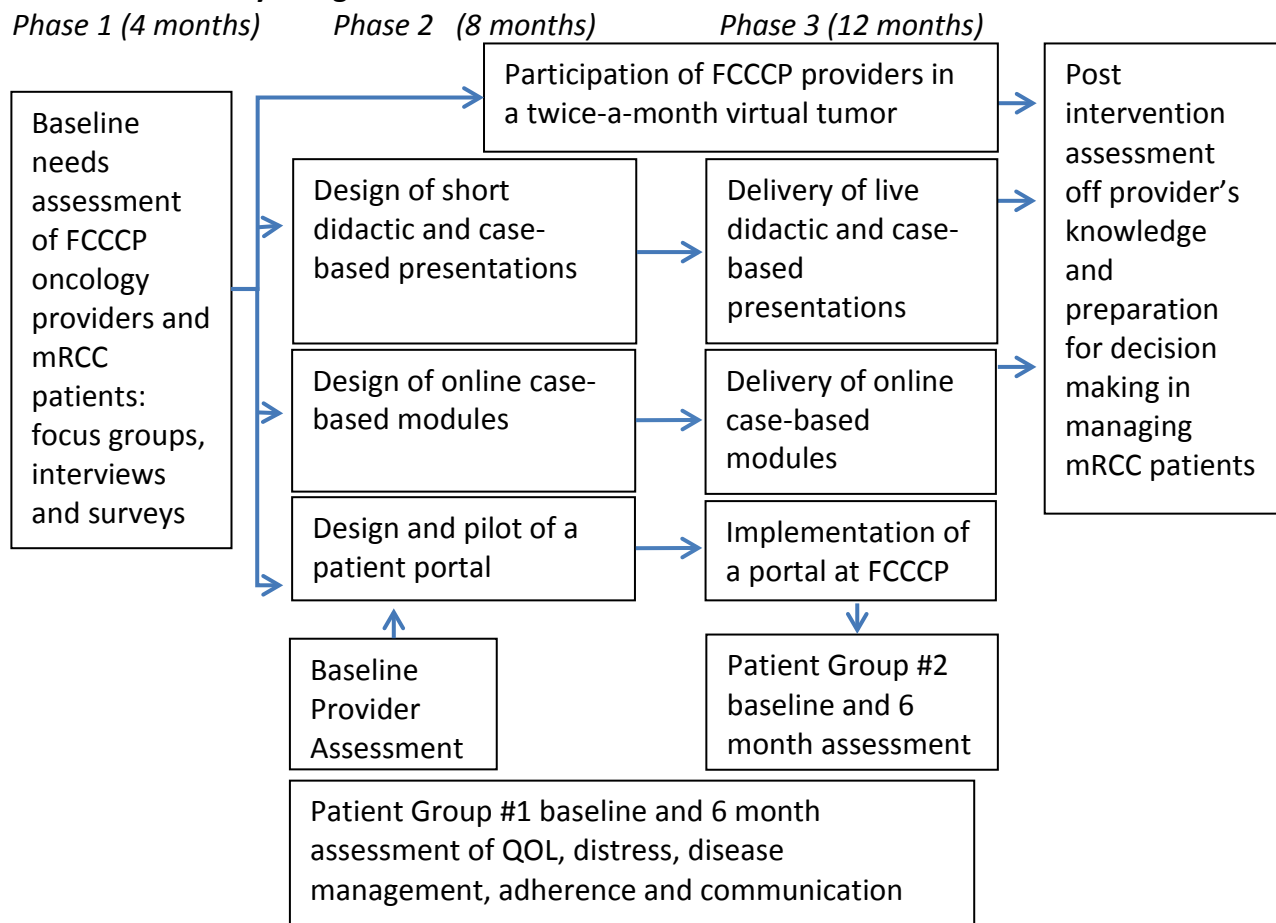
RCC were enrolled on therapeutic clinical trials. The GU team consists of medical oncologists (n=4), urologic oncologists (n=6), radiation oncologists (n=3), pathologists (n=1), nurse practitioner (n=1), physician assistant (n=4), registered nurses (n=3) and nurse navigator (n=1).

Based on this expertise, FCCC GU medical oncologists often are asked to provide guidance to FCCCP colleagues informally (internal survey and discussions). Common questions or reasons for referral include: appropriate sequencing of therapy, continuation vs. changing of therapy in the face of modest disease progression, role of cytoreductive surgery and the treatment of non-clear cell mRCC. Thus, there is both an adequate patient and provider volume to support the proposed intervention, a demonstrated need for the intervention and an appropriate GU expertise to conduct the project.

There are two audiences targeted in the proposed intervention: oncology providers who take care of mRCC patients and mRCC patients themselves. By targeting both groups simultaneously we will ensure the highest chance of success for this project which is aimed at improving the care for mRCC patients overall. Previous work has shown successful implementation of educational interventions and telemedicine for community physicians by an academic medical center in areas such as geriatrics and hepatitis C management and we propose to extend this concept to oncology.²¹⁻²³

3.2. Intervention Design and Methods:

3.2.1 Overall Study Design



3.2.2 Aim 1: Hypothesis, Intervention/Evaluation Design and Statistical Analysis

Aim 1: To develop, implement and evaluate an ongoing educational series of didactic and case-based workshops for oncology providers (MDs, NPs, PAs, RNs) focusing on the primary challenges of treating mRCC: appropriate prognostication and selection of drugs for a given line of therapy, adverse event management, adherence to oral agents, decisions of when to switch or escalate/de-escalate therapy, QOL assessments and appropriate integration of surgical and radiation therapy.

Hypothesis: Ongoing educational exchanges between academic GU and community oncology providers will lead to an improvement in provider knowledge and preparation for decision making in treating RCC patients.

Intervention: We will develop, implement and evaluate an ongoing educational series of didactic and case-based presentations for oncology providers at FCCCP community sites. During phase 1 (~4 months), we will conduct small group semi-structured interviews with 5 oncologists as well as 5 non-physician oncology providers (NP, PA or RN) who take care of mRCC patients. Every FCCCP site will have the study IRB approved with a site PI. Every participant will be provided with a \$40 Amazon gift card in appreciation for their time and input. Initial interviews will focus on eliciting knowledge gaps and provider uncertainties in the treatment and management of mRCC patients using both open ended questions as well as specific case based scenarios. The PI has qualitative data collection experience²⁴ and will conduct the interviews, but also work with collaborators at FCCC (Dr. Wen and Dr. Wong) who have had extensive experience in qualitative research techniques, survey development, and needs assessment research.²⁵⁻²⁸ The interviews will be audiotaped, transcribed and analyzed for main themes. Questions and topics will be based both on previously reported areas of need¹⁸ as well as internally developed topics by an expert panel of FCCC dedicated GU providers (see section 3.1. for FCCC GU team description).

Following this first step, using both a literature review and the data gathered during the qualitative interviews, a formal needs assessment survey will be created by the investigators. All oncology providers at all FCCCP sites will be invited to participate. The survey will be conducted using REDCap, a customized, secure, web-enabled information system and relational database which will be utilized for data entry, storage, retrieval, and analysis and with which the study team has extensive experience. All participants will be once again reimbursed with a \$20 Amazon gift card. Finally, the surveys will be analyzed with the goal of tailoring provider interventions to the most salient topics.

During phase 2 (~8 months), the educational content will be prepared and will consist of two PowerPoint presentations and two web based modules, each covering ~4-5 cases. The presentations will be based on the most up to date data and NCCN guidelines. It will be specifically tailored and focused on the assessed needs of the community providers from phase 1. All of the FCCC GU medical oncologists attend and present regularly at major scientific meetings. In addition Dr. Elizabeth Plimack, one of the FCCC GU medical oncologists sits on the NCCN guidelines panel for RCC. The GU expert panel of providers at FCCC will define, refine and help shape the final version of all educational materials. The primary work will be conducted by the PI with the assistance of a project manager. The web based case presentations will be developed by the PI along with FCCC informatics experts with links to the

modules provided to each participating oncology provider. A USB drive of the presentations, cases, NCCN guidelines for RCC and an annotated bibliography of the most relevant articles addressing the aforementioned knowledge gaps will be developed by the PI and provided to each FCCCP oncology provider.

During phase 3, the PI will present the two PowerPoint presentations at two different time points over a one year period at all FCCCP sites and the link to the web based cases will be made available to each participating oncology provider. The educational component will be presented at FCCCP cancer committee meetings and scheduled tumor boards. For providers who cannot attend these meetings, a recording will be created and placed on the USB drive for self-review.

Evaluation Design: All FCCCP providers will be asked to complete assessments at two time points after phase 1. The first evaluation will occur during the first half of phase 2 and serve as a baseline measure. The second assessment will occur after phase 3 and serve as the comparator measure following the educational intervention. Every participant will be provided with a \$40 Amazon gift card after each evaluation. Four assessment tools will be included: 3 surveys and one set of 7-10 scenarios with multiple choice questions following each scenario. All assessments will be administered via REDCap.

1. To assess the provider's preparedness to make decisions regarding their mRCC patients the Preparation for Decision Making Scale will be used.²⁹ The scale was originally developed to assess patient's perception of how useful a decision aid or other decision support intervention is in preparing them to communicate with their providers. We will adapt this to evaluate how useful our intervention is for providers as they prepare to speak to and take care of their mRCC patients. It is a 10-item scale with an overall score between 0-100. It has good reliability (0.944).

2. To assess provider's mRCC management, a clinical vignette-based 7-10 scenario questionnaire will be used. It will be developed by the PI with the assistance from co-investigators and assess common challenges faced when treating mRCC. Each case will have 1-2 questions following it with multiple choice answers. The answers will be constructed in a way where at least several answers are incorrect as determined by an expert panel at FCCC. A single score will be generated for each provider by adding all of the incorrect question answers given, with higher scores being worse. The clinical vignettes will test similar concepts and content for the baseline and post-intervention evaluations, but will be framed in a somewhat different presentation in order to both maintain consistency content and avoid participants from answering questions correctly based simply on self-directed question specific research after completing the initial assessment.

3. To further assess provider's mRCC content specific knowledge, a questionnaire asking fact based questions, with correct answers derived from the published literature to avoid any ambiguity or personal bias will be used. The questions will address in Aim 1 and have approximately 15-20 multiple choice questions with a single correct answer. The questionnaire will be scored on a continuous scale with higher values representing a higher score.

4. To assess provider's comfort level in treating mRCC patients, a general survey developed by the investigators will ask ten Likert-based questions about one's perceived knowledge/expertise level/weakness/strengths in treating mRCC patients; desire to take care of

mRCC patients; general comfort level in treating these patients, satisfaction and utility of a virtual tumor board (see Aim 3 below) and provider's current unmet needs in mRCC management.

Statistical Analysis and Endpoints: Degree of improvement in content-specific knowledge, degree of preparation for decision making, proportion of correct answers in the clinical vignettes and overall sense of comfort with taking care of mRCC patients will be the primary endpoint. The analysis will be conducted for both the group overall as well as separately for MDs vs. others (NP, PA, RN). Each endpoint will be treated as continuous for the purposes of analysis, with t-tests, Wilcoxon tests, and regression models used to evaluate the improvement in scores. All tests will be two-sided with 5% type-I error. We will collect responses from approximately 60 MDs at baseline, and we expect good rates of follow-up post intervention. With an anticipated 20% drop-out rate, we expect to collect responses from approximately 48 MDs. This sample size will give us 80% power to detect a standard effect size of 0.41 (0.41 times the standard deviation of the change in scores), a medium effect size.³⁰ We will collect baseline measures from 30 other care providers (NP, PA, RN), and we anticipate approximately 20 of these will be available to give responses post-intervention. We will use non-parametric tests to compare the changes in scores for these care providers vs. MDs.

3.2.3. Aim 2: Hypothesis, Intervention/Evaluation Design and Statistical Analysis

Aim 2: To develop, implement and evaluate a sustainable on-line patient self-reported assessment portal to improve patient-provider communication, patient disease management and QOL and the management of therapy-related side-effects.

Hypothesis: An on-line patient portal will lead to a more prompt reporting and management of side-effects. This will result in an improvement in patients' QOL, cancer related distress and disease management, as well as enhance adherence to oral drugs and improve provider-patient communication.

Intervention: We will develop, implement and evaluate a sustainable on-line patient portal. This will allow the patient and/or their caregivers to input information (e.g., side effects, adherence data, blood pressure readings, HRQOL) and oncology providers to obtain this information in real time. Patients will be asked to log in two times a week to provide information on any new symptoms, their blood pressure readings, blood sugar readings, rash, diarrhea, nausea/vomiting, fatigue, mouth sores and any other bothersome symptoms. Any time a new piece of information is entered, an email and fax will be automatically generated to go to the linked provider for that patient (established at the outset by each center and physician; the assigned provider can be an MD, NP, PA or RN). To facilitate patient care, a provider may designate an office staff member to check the portal as well. The provider will then be able to log into the secure web-site to see the information from the patient. Each patient outcome reported at or above a predetermined threshold will be automatically flagged by color by our portal system to facilitate clinicians' decision making. However, no recommendations will be offered to address any reported outcomes; best practices will be used by the clinicians at each site. Based on the patients' self-reported information, the provider may choose to follow up with the patient over the phone or ask them to come in if deemed necessary. We will work with FCCC informatics personnel to create a platform that will be sustainable at multiple sites. During phase 1 of the study, interviews will be conducted with

FCCCP providers (~10) to elicit their attitudes and suggestions regarding patient's use of a portal that uses email communication to provide information to the providers. These interviews will be incorporated into the interviews being conducted for phase 1 of Aim 1 to improve feasibility and to decrease undue time burden on the providers. Concurrently, focus groups (n=10) will be conducted with mRCCC patients at FCCCP sites and FCCC to elicit their opinions and preferences on a patient portal, as well as the most important issues to them when dealing with mRCC. Every patient participant will be provided with a \$40 Amazon gift card in appreciation for their time and input. Based on these evaluations, during phase 2, a web-based, secure portal will be developed in collaboration with FCCC informatics department. During the development process, user and usability testing sessions with both providers and patients will be conducted to iteratively refine and improve the functionalities of the portal and to ensure the readability of the assessment. The portal will be designed as a one way communication avenue for patients or their caregivers. Since electronic medical records (EMRs) vary among different practices, the portal will not be integrated into any specific EMR and therefore can be reproduced and disseminated on a large scale at other sites.

Evaluation Design: Evaluations will occur during phase 2 and phase 3 for a control group who will not be exposed to the web portal (patient group #1) and during phase 3 for the intervention group (patient group #2) who will be exposed to the web portal. Basic inclusion criteria for patients in both groups will be mRCC on active treatment either on or off a clinical trial. The first group will be enrolled throughout phase 2, before any portal or educational intervention for providers is made available and will serve as the control group. The second group will be approached and enrolled during the one year period of phase 3 after pilot testing and once the portal is operationalized. The patients will be asked to participate by using the portal to communicate with their providers. For process evaluation data, we will also collect patient's satisfaction with the portal, their objective usage of the portal and the frequencies of clinician's follow-ups based on the portal flagged assessment (evaluation to be done via the portal by the patient). Both groups will be asked to complete an initial assessment and then a second assessment at month 6. Comparisons between the two groups will focus on the change in outcomes over a 6 month period in the standard-of-care group vs. the intervention group. 50 mRCC patients at FCCCP sites will be recruited to each group and asked to complete five surveys (20% expected loss to follow-up with a final sample size of 40 in each group). We will assess age, race, marital status, education, occupation, employment status, income, residence location, and comorbid conditions. During the study, we will conduct medical record review to assess: date of diagnosis, stage, previous cancer surgery (dates, types), chemotherapy administered (dates, agents, doses), other treatments and supportive care mediations if any. Evaluation surveys will be administered via the portal and mail. Patients will receive a \$20 gift card for each completed assessment. The surveys will be as follows:

1. To assess medication adherence, the Morisky 8-Item Medication Adherence Scale adjusted for oncology will be used.³¹ The PI has extensive experience in studying adherence to oral anticancer drugs and in particular in RCC.^{24,32-34}
2. To assess QOL, the FACT-Kidney Symptom Index-15 will be used.³⁵ This is a widely used scale in RCC and has excellent psychometric properties. It is scored 0-60 with higher scores reflecting a better QOL.

3. To assess cancer-related distress two instruments will be used. First, the NCCN's endorsed distress measurement screening tool will be used.³⁶⁻³⁸ This tool measures distress by use of a single item thermometer rating scale scored 0-10 and has an optimal cut-off of 4, where scores greater than or equal to 4 indicate significant distress. The purpose of this tool is to quickly and effectively identify distress in cancer patients. Second, the Impact of Events Scale will be used.³⁹ This is a 15 item instrument that measures responses to potentially stressful life events. There are two subscales that measure intrusive thinking and periods of avoidance. Higher scores indicate greater distress. Scores range from 0-75.

4. To assess patient perception of their disease management and patient-provider communication, the Effective Consumer Scale will be used (EC-17).^{40,41} This scale measures how effective people are at dealing with their chronic condition and making decisions about their health care. The EC-17 consists of 17 items measuring the main skills and behaviors people need to effectively manage their healthcare such as how to use health information, how to clarify priorities, communication with others, how to negotiate own role and take control and how to decide and take action. The scale is scored 0 to 100 where 100 is the best possible score.

Statistical Analysis and Endpoints: We will assess 0 to 6 month changes in self-reported QOL, disease management perception and communication, medication adherence and cancer related distress before and after implementation of the intervention, and we hypothesize improved outcomes in the group of patients surveyed after implementation of the patient portal. All measures will be considered as continuous, and we will use t-tests and regression models to assess differences. In secondary analyses, we will also examine outcomes in the subgroup of patients who actively used the portal (group #2), and compare their results to patients surveyed prior to the portal launch (group #1), matching on important factors such as age and drug treatment type. With an anticipated sample size of 40 in both groups (50 recruited with anticipated 20% lost to follow-up between baseline and 6 month assessment), we will have 80% power to detect a standard effect size of 0.63 for the change in each measure (0.63 times the standard deviation of the 0 to 6 month differences), using a two-sided test with 5% type-I error.

3.2.4. Aim 3: Hypothesis, Intervention/Evaluation Design and Statistical Analysis

Aim 3: To operationalize and implement a virtual tumor board for community oncologists to be able to interact on a regular basis with an academic medical center's GU experts.

Hypothesis: A twice-a-month live tumor board with FCCC GU medical, surgical and radiation oncology experts will increase the expertise of community oncology providers in managing mRCC patients.

Intervention: We will adapt our ongoing multidisciplinary GU tumor board to allow FCCCP providers to participate remotely. Currently, the GU tumor board at FCCC meets at least twice a month to discuss challenging cases. The members include experts from FCCC medical oncology, urologic oncology, radiation oncology as well as pathology and radiology. There has been literature to suggest that there is benefit in regard to oncologic outcomes for patients, cost-effectiveness in regard to coordination of care and an improvement in the recruitment to clinical trials with the use of multidisciplinary tumor boards.^{42,43} In GU oncology in particular, a prospective cohort study of 269 patients presented at a tumor board over a year at an

academic medical center showed that for the 94 RCC cases presented, a change in diagnosis occurred in 17% and a change in treatment in 36%.⁴⁴ Given the often times complex nature of mRCC cases and the rapidly evolving treatment paradigms, a multidisciplinary tumor board is often one of the best ways to learn new information, gain new insights into the management of RCC patients and improve the care of mRCC patients. FCCC GU tumor boards are already equipped with audio-visual equipment to allow remote log in and participation. FCCCCP providers will be invited to present their own cases as well as participate in the discussion of FCCC cases. This will foster collaboration, learning and patient referral for clinical trials.

Evaluation Design: The virtual tumor board will begin during the second half of phase 2 (after the baseline provider evaluation) and continue throughout phase 2 and 3 to allow for maximal opportunities for participation. The evaluation design (surveys) will be the same as for Aim 1 as this aim will further serve to increase the provider's knowledge, expertise and comfort with managing mRCC patients.

Statistical Analysis and Endpoints: See Aim 1.

3.2.5. Feasibility of Accrual

As noted in Section 3.1., FCCC and FCCCCP is the country's oldest affiliation program and have a long and strong relationship. The FCCCCP includes 18 sites in Pennsylvania and New Jersey. Investigators at FCCC and FCCCCP, including co-PIs on this grant (Denlinger and Wong) have had funded grants and conducted and published research through the FCCCCP/FCCC partnership. Given the large number of available therapies for mRCC and the rapidly changing treatment environment, participation in this research endeavor is desirable for FCCCCP sites and FCCC. We anticipate up to 18 sites will participate in the proposed project and will be able to provide eligible patients and providers at all required study points. Again, as noted in Section 3, in 2012 FCCCCP saw 224 new analytic cases of RCC, 300 in 2011 and 232 in 2010; approximately 35 cases per year were de novo metastatic and approximately 30 cases per year were locally advanced and thus at high risk for short-term metastatic progression. In addition, ~30 non-analytic RCC cases per year were seen at FCCCCP sites (primary treatment conducted elsewhere).

Given the increasing overall survival of mRCC patients, this then leads to an estimated eligible pool of 75-100 mRCC patients at any given point in time at FCCCCP sites that would be able to participate in this study. From a provider standpoint, there are approximately 60 medical oncologists practicing within the FCCCCP programs and 30-40 nurse practitioners, physician assistants, and registered nurses who would be eligible to participate.

Furthermore, previous work on educational interventions (interventions geared toward cancer survivorship care) within the FCCCCP done by co-investigator Denlinger (NCCN grant 48506-01) were very well received and attended not only by study-enrolled providers, but in many sites support staff and other health care providers. In fact, some of the educational lectures were CME certified and attended by the whole hospital or health system oncology staff. Thus, there is precedent that these educational presentations are an effective way to disseminate information to the FCCCCP practices and often reach out to additional personnel beyond those involved in the study but who may be involved in patient care.

3.2.6. Anticipated Challenges and Solutions

1. Heterogeneous group of practices: we will do a baseline assessment and tailor our educational intervention accordingly. 2. Building a patient portal to be used across distinct

sites: will leverage FCCC IT group that has experience in programming and hosting both the FCCC website as well as a multi-institutional patient websites.^{45,46} This portal will be extensively pilot tested before roll out. One of the co-investigators, Dr. Wen, is an expert in the development and operationalization of a patient web-portal. 3. Connecting distinct practices with FCCC for a twice-a-month tumor board: engage our urologic oncology, radiation oncology, pathology and radiology colleagues with whom we work closely and have excellent collaborative relationships. This conference already has the capability of remote access. If demand is high, the PI will coordinate an additional monthly session with FCCCP partner hospitals. 4. Patient and provider recruitment: account for dropout in the statistical analysis; provide monetary incentives for participation; minimal risk to participants; actively engage colleagues at FCCCP sites who are historically very motivated to participate with FCCC led projects.

4. Workplan, Deliverables and Dissemination schedule and strategies

4.1. Workplan: The workplan for this project spans a two year period. Please refer to Appendix A for a schedule of deliverables and to section 3 for details of the interventions. As noted above, we plan to develop a series of live and online didactic and case-based workshops addressing the challenges of treating mRCC, an on-line patient self-reported assessment portal and a virtual-tumor board. Working with colleagues at FCCC and FCCCP, the PI will take primary responsibility for the implementation and completion of each of the phases of the project. During phase 1 the full protocol will be written and submitted to the IRB for approval. Simultaneously a project manager will be hired and trained. We will then proceed to semi-structured interviews with providers and patients and finally complete an online survey of the providers. During phase 2, we will conduct the first (group #1) patient evaluation to be used as a baseline measure for the outcomes evaluation. The patients will answer surveys at month 0 and 6. We will also conduct a baseline measure of the providers and then start the piloting of the virtual tumor board. We will devote the majority of the 8 months to the design of educational materials for the providers and the design and pilot of the patient portal and use the 8 months to work out any logistical issues related to it. During phase 3 we will spend the bulk of the time (approximately 12 months) implementing the interventions. This will be done by the PI and the research assistant with the support of the co-investigators and the GU team at FCCC. The educational initiatives will be delivered, the patient portal will be open and patient group #2 will be enrolled. The patients will once again undergo a baseline assessment and then a second assessment at month 6. At the end of phase 3, a second evaluation of providers will occur and the study will end. Data will be analyzed with the assistance of the study statistician, Dr. Handorf, and the results prepared for presentation and publication.

4.2. Deliverables Table: See Appendix A.

4.3. Dissemination Plan: Dissemination will occur immediately to the FCCCP sites. FCCC has three Partner affiliates that are part of a broader consortium under the NCCN Affiliate Research Consortium (ARC). This is a group of community oncology sites who like FCCCP have close associations with academic partners. The goal is to foster research at the community level and FCCC is one of 5 academic sites throughout NCCN whose partner sites are now part of ARC. Thus, if this intervention is shown to be effective, it can easily be scaled up via the ARC to community sites affiliated with the other 4 academic medical centers (University of Alabama at

Birmingham, Fred Hutchinson Cancer Research Center; Moffitt Cancer Center; University of Colorado Cancer Center). Furthermore, all of the interventions proposed are relatively inexpensive and sustainable. Participation in a tumor board via remote connection is virtually free once established; a web portal once established can also continue to function with minimal upkeep; educational interventions will need to be updated as new information comes in, but that can be a sustained program between FCCC's GU team and FCCCP program powered by a collaborative effort from faculty and GU dedicated fellows.

5. Organizational Detail

5.1. Leadership and Organizational Capability

There are two main institutions involved: Fox Chase Cancer Center and Fox Chase Cancer Center Partners. FCCC is the lead institution where the PI and the co-investigators work out of. The leadership at FCCC will consist of the PI and a group of co-investigators that bring together overlapping, but also distinct areas of expertise to make sure the project is successfully completed. The PI is a GU medical oncologist at FCCC with expertise in adherence to oral anticancer medications.^{24,32-34} He has conducted research specifically in adherence to oral agents in mRCC showing that up to 35% of patients were not perfectly adherent.^{24,32} He is leading a quality improvement initiative within medical oncology and is focused on improving health outcomes for mRCC patients. The PI is strongly supported by the institution and the FCCC GU group to conduct this research and will have the necessary time protection and resources available to complete this project (see letter of support from chairman of Medical Oncology). The co-investigators have substantial relevant expertise which will be leveraged.

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Appendix A: Deliverables Table

Task	Year 1			Year 2		
	4m	4m	4m	4m	4m	4m
Phase 1						
Protocol Development	■					
Full IRB Submission and Approval	■					
Research Assistant Hiring & Training	■					
Semi-structured interviews with providers	■					
Semi-structured interviews with patients	■					
Needs assessment survey of providers	■					
Phase 2						
Baseline assessment of patient group #1		■	■			
Baseline evaluation of providers		■				
Piloting of a virtual tumor board			■			
Design of live educational materials for providers		■	■			
Design of web-based educational materials for providers		■	■			
Design of a patient portal		■	■			
Pilot of a patient portal		■	■			
6 month assessment of patient group #1			■	■	■	
Phase 3						
Delivery of Educational Content to Providers				■	■	■
Implementation of web portal				■	■	■
Continuation of Virtual Tumor Board				■	■	■
Baseline assessment of patient group #2				■		
6 month assessment of patient group #2						■
End of study survey assessment of providers						■
Data Analysis						■
Presentation of work at ASCO Quality of Care Symposium or GU ASCO						■
Manuscript Preparation						■