

Determining and Addressing Adherence to the NCCN Guidelines for Chronic Phase CML

Overall Goal: Test a novel behavior change and education intervention to improve physician adherence to the NCCN guidelines and best practice recommendations for chronic-phase chronic myeloid leukemia (CP-CML) at four oncology practices across Colorado.

The literature on the clinical practice of physicians treating CP-CML suggests several major gaps between identified best practices and the real world practices of physicians. The most significant gap identified in the literature is the lack of appropriate monitoring of the BCR-ABL1 translocation by qPCR in CP-CML. A second major concern identified in the literature is the problem of patient adherence to Tyrosine Kinase Inhibitor (TKI) medications over time. A third concern is a lack of physician knowledge about how to interpret data from BCR-ABL1 when monitoring is conducted correctly and how to make the correct choice of TKI medication based on this information.

This study will address these three concerns using a novel interactive behavior change intervention for physicians and midlevel providers that will be offered in-person to each of the four practices in the study. The primary outcome measure will be the change in the rate of monitoring BCR-ABL1 by qPCR in peripheral blood.

Key Objective 1: Establish a one-year baseline rate of adherence to NCCN guidelines for qPCR monitoring of BCR-ABL1 in the peripheral blood of CP-CML patients treated at four oncology practices across the state of Colorado.

It is hypothesized that the baseline rate of community oncologists and hematologists correctly monitoring BCR-ABL1 by qPCR in their CP-CML patients will be suboptimal. This hypothesis is based on the results of several studies that have indicated a very low rate of appropriate assessment of this vital marker of treatment response.

Key Objective 2: Implement and assess an interactive behavior modification and education intervention designed to improve provider adherence to NCCN guidelines for qPCR monitoring of BCR-ABL1 *and* increase provider knowledge of treatment guidelines about TKI choice and ways providers can address the problem of *patient* adherence to TKI medications.

A second hypothesis is that the interactive educational intervention, that includes routine audit and feedback, will significantly improve physician *behavior* in monitoring BCR-ABL1 in their CP-CML patients. The rate of BCR-ABL1 testing will be tracked over an intervention period of one year and compared to the baseline rate established in Key Objective 1.

This intervention is also hypothesized to create improvement in provider *knowledge* about monitoring guidelines, evidence based techniques that promote patient adherence to TKI medications, and appropriate TKI choice based on mutational analysis and clinical situation. This hypothesis will be assessed using a pre-post test at the time of the physician training. An additional follow up post-test will be conducted at the end of 6 months to determine the lasting effects of the intervention over time. In addition to the quantitative data collected, quantitative

data will be collected about the barriers that providers encounter when attempting to meet the best practice standards and NCCN guidelines described above and will be used to inform problem solving strategies as possible.

Technical Approach

Assessment of Need:

An increasing population

The success of TKI medications in treating CP-CML now means that the overall prevalence of the disease in the population will rise over time, as the vast majority of people with the disease are able to live out a nearly normal lifespan. In the United States, although the annual incidence of CP-CML remains stable at approximately 1/100,000 people, the prevalence of CML is estimated to increase from approximately 70,000 people in 2010 to a plateau of approximately 181,000 by the year 2050.¹⁵ This ongoing increase in the number of people living with CP-CML highlights the importance of correctly addressing the behavioral factors that optimize the long term treatment outcomes for patients. The treatment of CP-CML with TKI's represents the beginning of an era of targeted molecular treatments that require appropriate monitoring of gene markers by physicians and will also require patients to adhere to a daily medication regimen and medical follow-up appointments for monitoring. Behavioral modification and education have been shown to effectively address these concerns.

Summary

The three sections below are summarized briefly here and represent the most salient gaps in practice vs. recommended practice for the care of patients with CP-CML identified in a national needs assessment and the NCCN guidelines.^{1,12} Gap 1: The most significant practice deficit identified nationally for the treatment of CP-CML is the low rate of proper monitoring of BCR-ABL1 by community oncologists (31%). Monitoring of this marker by peripheral blood is vital to assess treatment response and guide treatment decisions. Gap 2: The second major concern identified is the lack of physician and midlevel provider's understanding of how to assess and address patient adherence to their TKI medications. Gap 3: A third major deficit is the physicians appropriate choice of first-line TKI and a lack of knowledge about when to switch TKI's and which TKI represents the best choice in the event of TKI resistance or lack of disease response.

Gap 1: Physician non-adherence to NCCN guidelines for monitoring of BCR-ABL1

The NCCN guidelines currently recommend testing for BCR-ABL1 with qPCR in CP-CML patients every three months after initiating therapy, regardless of treatment response. A recent report by the Annenberg Center for Health Sciences found that only 31% of community physicians and 52% of academic medicine physicians in the U.S. were correctly tracking this vital marker of treatment response in peripheral blood.¹ Most were not adequately using this molecular analysis to track their patient's response to TKI therapy and many were performing unnecessary bone marrow biopsies to conduct monitoring, usually on a suboptimal timeline.¹ CP-CML monitoring was also found to be suboptimal in a recent study with 1,200 CML patients. This study found that 41% of patients on a TKI did not receive qPCR monitoring of BCR-ABL1 within one year of treatment initiation, while 31.9% had 1-2 tests in that year and 27% had 3-4 tests. This study also compared patients in the "no tests" group to patients in the "3-4 tests" group,

and found that the latter group had 37% fewer inpatient admissions for CP-CML related concerns, suggesting that monitoring in accordance with NCCN guidelines for qPCR testing is economically and medically useful.²

Gap 2: Physicians lack knowledge of how to effectively assess and then promote the adherence of their CP-CML patients taking TKI medications.

Patient adherence to oral TKI medication is strongly associated with overall treatment response and likely remains one of the primary factors effecting the loss of Major Molecular Remission (MMR) or lack of response to treatment.^{3,4} The ADAGIO study examined the adherence of patients to imatinib and compared their reported level of adherence to their actual pill consumption. 64% of patients reported perfect adherence to their medication, however only 14% of this group actually achieved perfect adherence. 71% of patients in the study were found to be taking less than the prescribed dosage.³

Poor adherence has a substantial impact on treatment response. In one study, patients with less than or equal to 90% adherence to medication were found to have only a 28.4% rate of MMR to treatment in comparison with a 94.5% rate for those with greater than 90% adherence.⁴ 90% adherence is the equivalent of taking 27/30 doses in a 30 day month.⁵

Gap 3: Community physicians have been shown to lack information about first-line TKI choice, the importance of early and deep molecular response when starting treatment and when to switch TKI medication.

Community oncology physicians may encounter only a few CP-CML patients per year and thus keeping up with current recommendations for TKI selection may be challenging. In a recent needs assessment, 62% of oncologists continued to use imatinib as a first line treatment for their CML patients when second-generation TKI's such as dasatinib and nilotinib have been shown to produce an earlier and deeper molecular molecular response with data and recommendations that show that may be better tolerated.^{1,6,7,8} Providers were also not sufficiently aware that dasatinib and nilotinib were recommended by the NCCN guidelines for patients with high risk disease and were associated with earlier and deeper molecular remission.⁹ There is also evidence that physicians lack the ability to differentiate the appropriate clinical actions when patients become resistant to a first-line TKI. Many were unaware of the need to conduct a mutational analysis and the TKI recommendations for specific mutations. Difficulty interpreting and appropriately determining the meaning of increases on qPCR monitoring using the International Scale has been identified as another concern.¹

Primary Audience of the Intervention:

This intervention will be provided directly to oncologists, hematologists, midlevel providers and other members of care teams directly involved in patient care or treatment decision-making at four practices across the state of Colorado. The intervention will be offered for Continuing Medical Education (CME) credit. These four practices represent a unique opportunity to study adherence to the NCCN recommendations for CP-CML as they treat a large number of patients in a community setting, share a common EMR (EPIC), and have all recently become connected

to the University of Colorado Health System. Each of the four practices have expressed support and enthusiasm for this study.

Direct beneficiaries of this program:

The direct beneficiaries of this intervention include the four practices involved in this study and the CP-CML patients of these practices. The physicians in these practices will benefit from improved knowledge about treatment guidelines and updates about recent developments in the state of science and clinical care for patients with CP-CML. This information will be presented in an interactive fashion that makes use of baseline data from the practices actual monitoring adherence to the NCCN guidelines for BCR-ABL1 by qPCR over the past year. This practice specific data and interactive format (described below) will engage their attention and serve to motivate future behavior change in their practice.

Midlevel providers, social workers and nurses at these practices will benefit from knowledge about how to appropriately assess and address the adherence of their patients to TKI medications. Patients with CP-CML who are treated at the practices involved will benefit substantially from any improvements in physician knowledge and changes in appropriate monitoring of BCR-ABL1 given how vital the routine monitoring of this marker is for successful treatment of CP-CML.

Intervention Design and Methods:**Intervention Factors: Creating Lasting Change in Provider Behavior**

Traditional CME presentations delivered in a non-interactive lecture format may not be effective in changing physician practice behaviors.¹⁰ The literature on changing provider behavior suggests several strategies that have been demonstrated to change the practice behavior of medical providers. This intervention has been designed from the ground up to incorporate the most effective strategies for changing physician and provider behavior. These factors are summarized below and are integrated into each of the intervention components described in the paragraphs that follow.

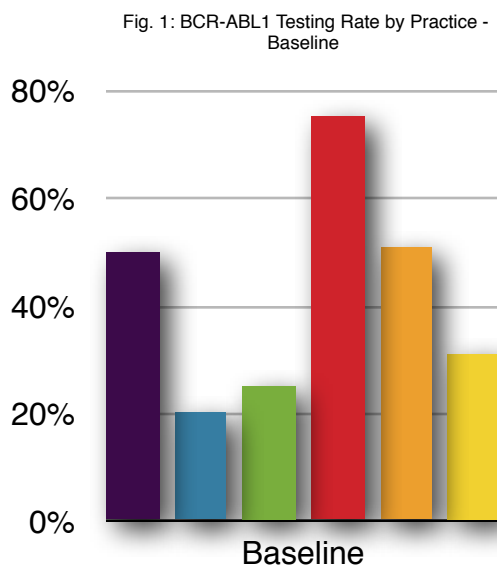
The most studied effective strategy to change provider behavior is the use of audit and feedback.¹¹ Audit and feedback involves establishing a feedback loop between physician behavior and the metric of desired change. In this study, each provider's rate of appropriately assessing BCR-ABL1 by qPCR will be provided at quarterly reporting intervals. The research on interventions to change the behavior of practicing physicians and providers also suggests a strong correlation between presentations that are interactive and those that create desired change in provider behavior.¹² The use of interventions directed at local practice experts and opinion leaders has also been demonstrated to be an effective strategy of changing provider behavior across a practice.¹³ The identification of barriers to desired change has shown mixed results in the very limited literature but appears theoretically justified and may provide useful information to inform the current study. All of these strategies have been integrated into the intervention described in detail below. The intervention addresses the three areas of deficit identified in the needs assessment section above.

Training Oncology Providers:**Part 1: Changing provider behavior to match NCCN guidelines for BCR-ABL1 testing by qPCR.**

An in-person training will be provided to each of the four practice groups in this study. The training will make use of practice specific information about that practices rate of testing for BCR-ABL1 in comparison with the ideal rate per NCCN guidelines. Each physician in the practice will be provided with a card containing their *personal* rate of testing during the baseline period in comparison with the ideal rate of assessment. The ranking of the practice in comparison with the other practices in the study will also be shown with each practice knowing only their own rate and the other practices' rates de-identified: see Figure 1.

This presentation of data about the performance of the individual physician (privately on an index card) and the practice in relation to other practices in the study and the national average, will promote physician engagement with the presentation and motivate future behavior change.

- Practice 1
- Practice 2
- Your Practice
- Practice 4
- National Average: Academic Centers
- National Average: Community Practices



Further motivation for change will be supported by an iterative process of updates on the rate of BCR-ABL1 assessment during the intervention period following the presentation. This will be accomplished by a quarterly email to each provider in the study, which will contain both provider-specific and practice-specific testing rates. This type of audit and feedback intervention has been shown to be an effective strategy for changing physician practice.¹¹

The training will present information about the appropriate interpretation of BCR-ABL1 data by qPCR using the International Standard. Changes in knowledge base of the physicians (for this and many other aspects of information contained in the presentation) will be evaluated using a pre-post test with a follow-up post-test at 6-months after the initial presentation. Also at this time point, a semi-structured qualitative interview to identify and address provider barriers to appropriate assessment

will be implemented, along with another update given to the physician and practices about their rate of BCR-ABL1 assessment.

Interactive Presentation: utilizing a cell phone-based service to allow live polling

Because interactive presentations have been correlated with desired change in physician behaviors, this presentation will use the presentation software Top Hat or a similar service that allows the presenter to poll the audience with specific questions. Audience members respond using a text-based cell phone message (no smart phone required) and responses are then displayed live on the screen. This type of interactive presentation will engage the audience and also allow the presentation of clinical examples relevant to the information being taught. An example of a question used to poll the audience in this manner would be a multiple choice

question regarding the appropriate frequency of BCR-ABL1 assessment by qPCR that contains answer choices that approximate the correct choice and may also involve the rate of assessment using bone marrow biopsy (a demonstrated gap in practice). These questions will be targeted across the presentation to address the knowledge and practice gaps identified in the needs assessment.

Part 2: Changing Providers Interactions with their Patients to Promote Patient Adherence to TKI Medication

The most effective strategy physicians can use to promote the adherence of their patients to TKI medications is the establishment of an open dialogue and a discussion about adherence to medication regimens *at every visit*.¹⁴ Research and clinical experience demonstrates that oncologists, mid-level providers and nurses often lack the needed training and support to implement these sorts of interventions. This interactive presentation utilizes the same live audience polling of questions described above. An example of a question asked in a live polling format for this part of the presentation can be found in Figure 2.

Examples of specific *evidence-based* techniques taught to the practices will include:

- The difference between an open and a leading question about adherence.
- The use of simple behavioral recommendations with patients such as: tracking, setting a time to take the medication, putting the medication in a standard place and integrating it into a routine
- The importance of normalizing common difficulties with adherence so patients are open about their adherence
- A direct discussion about the financial costs of medication and addressing financial barriers in the patient visit (often with help from social work)
- Ongoing education and discussion about the concept of resistance, the possibility of disease progression and tolerance/reporting about side effects along with the idea that TKI medications are not a cure, they simply maintain the patient when they are taken correctly.
- The importance of direct verification of dose and behavior of patients (patient brings pill bottle to provider visit so that amount of medication can be verified as being taken appropriately- with a pill count if needed)
- Discussions about the planning of refills to accommodate out-of-town travel
- Involvement and education of family members in the adherence of the patient

This training component will also utilize clinical examples that highlight the complexity of patient adherence to TKI medication based on psychological factors associated with the medication being the only visible reminder of disease. Examples will be de-identified but will be based on clinical situations experienced by Dr. Brewer who, as a clinical health psychologist, works with CP-CML patients to promote medication adherence. This example will be given to

Fig. 2

“What is the best example of an open question about adherence during a follow up visit?”
A. So you’re taking your imatinib appropriately, right?
B. How many pills are you taking each day?
C. Are you using a pill box to track your medication?
D. So, you’re taking two pills a day, how has that been going for you?

promote appropriate referral by providers or nurses to social work or psychology services to address adherence in complex situations.

Part 3: Changing provider behavior in regard to initial TKI choice, the importance of early and deep molecular remission and when to switch TKI therapy based on the results of BCR-ABL1 monitoring by qPCR.

Content will be matched to that identified in the NCCN Guidelines and the Annenberg report cited in the needs assessment. Specific areas of content will be presented and then will utilize interactive live audience polling with specific clinical examples to assure interest and attention. Specific areas of content that were identified in the needs assessment include:

- Approved options and recommendations for first-line TKI choice based on disease status
- The importance of early and deep molecular remission (MMR)
- How to interpret BCR-ABL1 by qPCR when conducting appropriate three month monitoring
- When to switch TKI medication
- Identifying TKI resistance and when to conduct a mutational analysis of ABL
- What mutations in ABL may mean and which TKI medications may be most beneficial given specific mutations

As with the above sections, knowledge changes in the participating practices will be tracked at pre-post and 6-month follow up, and a component that serves to identify and address barriers to recommended practice will be implemented.

Follow up emails to providers every three months

During the one year period after the presentation the providers will receive quarterly update emails with their rate of BCR-ABL1 assessment by qPCR, their practices rate, and any updated NCCN guideline or other relevant provider recommendations that may have changed during this time.

Identification of Barriers and Action Items at 6-months

During the 6-month follow-up visit with each practice, a semi-structured interview to identify barriers to implementing the content of the presentation will be conducted. Qualitative data about these barriers will be recorded and action items to resolve barriers may be identified. Action items may include anything from problem-solving patient adherence concerns to implementing specific structures in the EMR across all sites. This represents a unique aspect of this project and will provide an identification of factors preventing optimal treatment of patients with CP-CML at practices around the state. A summary report of these barriers and any practice changes will be produced as a deliverable.

If proven effective, this intervention can be easily be expanded to other centers and also applied to more complex cases in the treatment of Acute Lymphocytic Leukemia (ALL), Acute Myeloid Leukemia (AML) and other cancers that rely on active monitoring of molecular markers and require adjustments of corresponding treatment with TKI medications.

Evaluation Design

Baseline Data Collection

One year of baseline data for BCR-ABL1 assessment by qPCR will be pulled from the EMR of all four medical centers in this study. One of the unique aspects of this study, which allows consistent and accurate data collection, is that four hospitals across the state now have the same EMR which is called EPIC. Many of these hospitals have recently implemented EPIC and each medical center in the study had a different “go live” date for EPIC. The retrospective baseline data collection can begin on the date that the last hospital in the study switched to using EPIC in their oncology clinics. This date is **November 2nd, 2013** for Memorial Hospital in Colorado Springs Colorado. Of note this date is approximately six months from the date of potential funding of this project which is May of 2014- allowing six months of baseline to be collected retrospectively prior to the potential funding of the project.

One year of baseline data is needed to ensure sufficient power and accurately document the baseline rate of BCR-ABL1 assessment in comparison to the testing rate recommended in the NCCN guidelines (every three months or 4 times per year). The *prevalence* (not the incidence) of CML in the population is relatively low and estimated by rough calculations to be about 1,333 patients living with the disease in the state of Colorado for 2014. Six months of retrospective data (before the date of funding) and six months of prospective data (after the date this grant may be funded) will be combined to make this one year baseline. This baseline will be complete six months from the date of funding.

Data Extraction from EPIC (EMR)

Baseline data will consist of diagnostic and billing data, which will be obtained using ICD-9 code for CML (205.10) and data from the EMR of the four medical centers in this study. This information will be de-identified at the patient level, but will identify the practice where the patient was treated and the oncologist or physician treating the patient. Data about BCR-ABL1 monitoring by qPCR will consist of billing data using the CPT codes 81206 and 81207 for this test. BCR-ABL1 assessment by qPCR from peripheral blood will be evaluated against the ideal four time points per year recommended by the NCCN, to determine the baseline rate of each practices adherence to the NCCN guidelines.

Comparison of Baseline Rate to Post-Intervention Rate

Diagnostic and billing data will also be collected following the one-year intervention period using the same process and will be analyzed to assess change in testing rates by physician and by practice. The data analyst will be responsible for data management and analysis and will be supported by additional consultation from the biostatistics core for the University of Colorado Cancer Center.

Preliminary Power Analysis

A preliminary power analysis was conducted using each of the four potential BCR-ABL1 testing data points per year. Table 1. highlights the percentage change in adherence to BCR-ABL1 testing and the corresponding minimum number of possible testing events per year needed to detect that change at the .05 level and 80% power. The second column is presented as a range to account for the possibility of different *baseline* adherence rates.

Table 1 Sample Size Required for 80% Power, $\alpha = 0.05$ or better

Percent Change in Adherence to BCR-ABL1 Testing	Range of Possible Testing Events per Year (4 per patient)
15	120-147
20	72-85
25	49-56
30	36-37
35	26-27

Evaluation of Changes in Provider Knowledge

Pre and post-tests immediately before and after the trainings will document immediate changes in provider knowledge. A follow-up post-test, conducted at 6 months, will document changes in provider knowledge from the intervention. Data from the pre-post and 6-month post tests will be entered into a separate relational database to determine provider changes in knowledge about the content of the presentation and the maintenance of any changes in knowledge at 6-months.

Expected Change in Provider Knowledge and Behavior

Based on prior study of changes in provider knowledge and the difficulty of creating behavior change in medical providers, changes in knowledge are expected to be significantly greater than those found in behavior.¹² The amount of change in physician behavior regarding appropriate assessment of BCR-ABL1 will depend on the baseline assessment rate. The results of several recent national assessments of monitoring that put the rate of appropriate monitoring of this marker at 31% for community and 51% for providers at academic settings, the potential for changes of up to 20-40% improvement in adherence to the NCCN guidelines for appears significant given the intensive use of interactive audit and feedback about physician's rate of assessment of this vital marker of treatment response.

Dissemination of Project Outcomes

The outcomes of this project will be published in relevant peer reviewed scientific journals. The information about the efficacy of provider behavior change and changes in provider knowledge as a result of the intervention will also be shared directly with the practices involved in the study. The data from the 6-month process of identification of barriers to effective practice will also be shared along with any practice implementations that may generalize to other practices. Any changes to the process the physicians use in EPIC will be documented for integration into other practices that also utilize EPIC, or similar systems, as an EMR. If effective, this study may be continued or expanded with additional funding. The treatment of CP-CML with TKI medications represents the future cancer treatments in which highly toxic treatments are avoided but patients and their medical providers must engage in appropriate long-term monitoring of treatment response and patients must engage in adherence to the TKI medication over time. If effective, this intervention may be tailored to other populations that require ongoing vigilance of monitoring and adherence to a daily medication regimen.

Specific Deliverables, Dates of Delivery and Estimated Costs per Deliverable

Deliverable	Description of Deliverable	Date Delivered	Estimated Cost
One year baseline data summary	One year baseline data summary for rate of appropriate assessment of BCR-ABL1 in CML patients at four practices across Colorado (6 months pulled from prior to funding start)	11/12/14	\$10,000
Presentation Completed	Interactive presentation slides with live polling capability through software (Top Hat)	12/5/14	\$12,000
Pre and Post test questions developed	Pre and Post test questions developed with biostatistics consultation	12/5/14	\$3,000
Quarterly Email to Provider 1	Contains individualized feedback about current rate of BCR-ABL1 assessment over the last three months and the practices rate overall. Rate must be calculated and sent individually to each provider.	3/5/15	\$1,000
Quarterly Email to Provider 2	Contains individualized feedback about current rate of BCR-ABL1 assessment over the last three months and the practices rate overall. Rate must be calculated and sent individually to each provider.	6/5/15	\$1,000
Summary of 6 month follow-up to identify barriers	Qualitative results of 6 month interview with thought leaders about identification of barriers to implementation of what was learned in the presentation: includes structured interview questions.	7/14/15	\$11,000
Quarterly Email to Provider 3	Contains individualized feedback about current rate of BCR-ABL1 assessment over the last three months and the practices rate overall. Rate must be calculated and sent individually to each provider.	9/5/15	\$1000
Quarterly Email to Provider 4	Contains individualized feedback about current rate of BCR-ABL1 assessment over the last three months and the practices rate overall. Rate must be calculated and sent individually to each provider.	12/5/15	\$1000
Final summary of rate of BCR-ABL1 assessment	Final summary of rate of BCR-ABL1 assessment for each practice and comparison with baseline assessment. This will be distributed to physicians as the fourth quarterly email along with their individual rate of change	4/30/16	\$11,500
Final summary of changes in physician/provider knowledge	Final summary of changes in physician/provider knowledge at three time points (pre, post and 6-month follow up). Summary of qualitative data and problem solving changes implemented also provided.	4/30/16	\$7,000



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February 25th, 2014

Benjamin W. Brewer, Psy.D.
 Assistant Professor
 Director, Clinical Psychology and Counseling Services
 Division of Hematology
 University of Colorado Cancer Center
 1665 Aurora, Court, Suite 4331
 Aurora, Colorado 80045

Dear Ben,

We are pleased to offer this letter of support for the project "**Determining and Addressing Adherence to the NCCN Guidelines for Chronic Phase CML**" based at the University of Colorado, Denver. As Chief and Associate Chief for the Division of Hematology at the University of Colorado, Denver Anschutz Medical Campus we are delighted to see this study go forward, and are very supportive of the project. We fully endorse your efforts and feel that, as a clinical health psychologist who works with CML patients routinely, you will be able to provide a unique approach to this grant that takes into account the behavioral aspects of both physician and patient behaviors that affect adherence to the best practice recommendations for CML.

We are enthusiastic about this projects creation of a database of CML patients that will track BCR/ABL assessment by PCR as it will provide our program with our rate of assessment, which may lead to improvements in our ability to provide appropriate care to our patients. This project also creates a system wide database of CML patients that may prove useful for future research collaboration and an intervention that will likely improve the treatment of patients across Colorado. We are invested in continuing to build a strong relationship between our practice and the other practices involved in this study as we are now unified under common leadership and have recently become part of the same University Health System.

Our practice is looking forward to participation in this project and we wholeheartedly support your application.

Sincerely,

Craig T. Jordan, Ph.D.
 Professor, Department of Medicine
 Chief, Division of Hematology
 University of Colorado, Denver

Clay Smith, MD
 Professor, Department of Medicine
 Associate Chief, Division of Hematology
 University of Colorado, Denver

Brewer, B

February 25th, 2014

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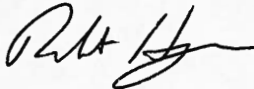
Dear Dr. Brewer:

We are pleased to offer this letter of support for your project "**Determining and Addressing Adherence to the NCCN Guidelines for Chronic Phase CML**" based at the University of Colorado, Denver. We are both hematologic oncologists at Memorial Hospital in Colorado Springs, Colorado. Dr. Hoyer is the oncology service line director for Southern Colorado and Dr. Vishal Rana is the hematologic malignancies lead. Our practice is strongly invested in the long term treatment of patients with CML and we are continually seeking updated information to inform our clinical practice in this area.

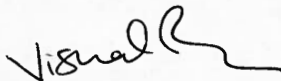
This projects creation of a database that will track BCR/ABL assessment by PCR is also of interest to us as we are interested in knowing more about our practices rate of assessment. This project would also create a system wide database of CML patients that may prove useful for future research. We are invested in continuing to build a strong relationship between our practice and the other practices involved in this study as we are now unified under common leadership and have recently become part of the same University Health System.

Our practice is looking forward to participation in this project and we wholeheartedly endorse the application submitted by Dr. Brewer.

Sincerely,



Robert J. Hoyer, M.D.
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February 25th, 2014

Benjamin W. Brewer, Psy.D.
Assistant Professor
Director, Clinical Psychology and Counseling Services
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University of Colorado Cancer Center
1665 Aurora, Court, Suite 4331
Aurora, Colorado 80045

Dear Dr. Brewer:

I am pleased to offer this letter of support for the project "**Determining and Addressing Adherence to the NCCN Guidelines for Chronic Phase CML**" based at the University of Colorado, Denver. I am the hematologic malignancies lead for St. Mary's Regional Cancer Center based in Grand Junction, Colorado. Our practice is strongly invested in the long term treatment of patients with CML and we are continually seeking updated information to inform our clinical practice in this area.

This project's creation of a database that will track BCR/ABL assessment by PCR is also pertinent to us as we are interested in improving our practice in this area. This project would also create a system wide database of CML patients that may prove useful for future research collaboration. We are invested in continuing to build a strong relationship between our practice and the other practices involved in this study as we are now working with University Hospital to start a bone marrow transplant program that will perform autologous stem cell transplants in Grand Junction and this entails a close working relationship between our centers.

Our practice is looking forward to participation in this project and we wholeheartedly endorse the application submitted by Dr. Brewer.

Sincerely,

A handwritten signature in black ink, appearing to read "Virginia Tjan-Wettstein". The signature is fluid and cursive, with a large loop at the end.

Virginia Tjan-Wettstein, MD
St. Mary's Regional Cancer Center
Grand Junction, Colorado



Colorado Health Medical Group

UNIVERSITY OF COLORADO HEALTH

February 25th, 2014

Benjamin W. Brewer, Psy.D.
Assistant Professor
Director, Clinical Psychology and Counseling Services
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University of Colorado Cancer Center
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Dear Dr. Brewer:

I am pleased to offer this letter of support for the project "Determining and Addressing Adherence to the NCCN Guidelines for Chronic Phase CML" based at the University of Colorado, Denver. I am the hematologic malignancies lead for the Cancer Center of the Rockies based in Fort Collins, Colorado. Our practice is strongly invested in the long term treatment of patients with CML and we are continually seeking updated information to inform our clinical practice in this area.

This projects creation of a database that will track BCR/ABL assessment by PCR is also of interest to us as we are interested in knowing more about our practices rate of assessment. This project would also create a system wide database of CML patients that may prove useful for future research collaboration. We are invested in continuing to build a strong relationship between our practice and the other practices involved in this study as we are now unified under common leadership and have recently become part of the same University Health System.

Our practice is looking forward to participation in this project and we wholeheartedly endorse the application submitted by Dr. Brewer.

Sincerely,

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Cancer Care and Hematology

References

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