

NAVIGATING ACCESS TO CANCER CARE: IDENTIFYING BARRIERS TO PRECISION CANCER MEDICINE

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Objective: Precision medicine is revolutionizing cancer treatment. However, there has been limited investigation of barriers patients endure to access precision cancer medicine. This study aims to report the experiences of underserved patient populations with limited access to genomic testing, clinical trials, and precision cancer treatment.

Methods: A mixed-method study was employed to quantitatively evaluate patients (N=300) seeking precision cancer medicine between January 2014- August 2017. Qualitatively, we conducted semi-structured interviews with eight case managers who navigate the health care and health insurance systems to provide patients with access to precision cancer medicine care. All interviews were analyzed to identify themes.

Results: Within our patient cohort, 69% were diagnosed in stage I of cancer disease. Overall, 27 patients (9%) were denied treatment as a final outcome of their case due to insurance denials, 35 patients (12%) died before gaining access to precision cancer medicine, and 6 patients (2%) received precision cancer medicine through clinical trials. Four broad thematic areas emerged from the qualitative analysis: 1) lack of patient, provider and insurer knowledge of precision cancer medicine; 2) barriers to clinical trial participation; 3) lack of patient health literacy; and 4) barriers to timely access to care.

Conclusion: Our combined analyses suggest that both system-level and patient-level barriers limit patient access to precision cancer medicine options. Additionally, we found that these barriers may exist not only for traditionally underserved patients, but also for resourced and insured patients

INTRODUCTION

Precision cancer medicine is rapidly emerging in the field of oncology. Precision cancer medicine utilizes two main approaches to improve patient health outcomes. The first approach uses genetically targeted therapies to disrupt specific molecules involved in cancer progression.¹ The second approach focuses on improving immunotherapy, which increases the strength of immune responses to cancer.² Researchers are hopeful that precision medicine will benefit more patients by reducing side effects and providing greater effectiveness for certain cancer biomarkers.³ Moreover, the number of personalized medicine clinical trials and approved personalized medicine treatments is expanding rapidly.⁴ These therapies and medications utilize patients' ge-

nostic profile to treat cancer irrespective of the type of cancer or where it is located in the body.⁵ The US Food and Drug Administration (FDA) has also expanded the medical indications associated with a variety of approved personalized medications particularly targeted to cancer care.⁴

Despite these noteworthy advancements in precision cancer medicine, insurance and cost issues have prevented the utilization of these treatments for many patients who need them.⁶⁻⁸ These overwhelming costs may lead to financial toxicity, fostering additional burdens for patients that impact their quality of life and survival rates.⁹⁻¹² Researchers have investigated the impact these expensive personalized medical treatments have on the household of cancer patients. Their findings demonstrate that the skyrocket-

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ing costs of genomic-based cancer therapies have forced patients to empty their lifesavings, choose between paying for their medications or mortgages, and/or utilize friends' and family members' financial resources for their daily necessities.¹⁰⁻¹⁴

Current scientific literature considers the socioeconomic implications of precision cancer medicine on patient, providers, and the health care system. Researchers have evaluated how precision medicine implementation may alter the health delivery model, require additional

accessing precision cancer medicine by examining time to case closing as well as number of contacts between patients and case managers, examine the definition of the "underserved" patient in precision cancer medicine, and detail case managers' role in helping patients actualize these medical treatments in research programs and in clinical care. These aims were achieved through interviews with case managers and retrospective review of cancer patients' experiences.

METHODS

Study Design

We conducted a mixed-methods study. The quantitative analysis included a random sample of 300 patient cases from the Patient Advocate Foundation (PAF) Personalized Medicine CareLine. Eight case managers were interviewed using a semi-structured interview guide, and each interview lasted between 30-60 minutes. All case managers were administered a short demographic questionnaire prior to the interview. This study was determined exempt human subjects research pursuant to §45 CFR 46.104(d)(2) by the National Institutes of Health, Office of IRB Operations (Project Number P194599).

Study Setting and Participants

This study was conducted with the PAF, a national organization serving the needs of patients who face access and affordability barriers to health care. PAF Case Management services provide financial and social needs navigation at no cost to

patients and generally focus on solving social, financial, and insurance related access barriers. As part of their portfolio of services, PAF runs a Personalized Medicine CareLine that aids patients who are encountering barriers accessing target therapies, immunotherapies, and/or clinical trials recommended by their physicians. These patients are interested in or pursuing additional clinical testing to gain genetic or genomic information needed to access the latest treatments for their diagnosis.²⁵ This study explored the barriers that these patients face and the role of case management in addressing these barriers.

Case Managers

Case managers with expertise in genomic medicine were recruited for in-person interview participation at PAF. We interviewed all case managers with this expertise, and a total of eight case managers met these qualifications. This team of case managers responded to patient requests for assistance through the Personalized Medicine CareLine. All case managers provided written informed consent prior to completing the demographic questionnaire and participating in the semi-structured interviews. In addition to general demographic and professional background questions, we asked case managers about navigating the health care system and their personal experience as case managers.

Patient Cases

The retrospective patient data analysis was conducted for patients who sought PAF services to access precision cancer medicine options

Our study aimed to identify the obstacles that prevent patients from accessing precision cancer medicine...

genomic-based educational opportunities for physicians, and may foster tensions between physicians and patients due to the high out-of-pocket costs.¹⁵⁻²² Scientific literature also investigates the prevalent inequities in cancer prevention, precision oncology treatment and outcomes for racial and ethnic minorities and patients of low socioeconomic status.^{23,24} There is limited analysis on how patients, providers and organizations are maneuvering the health care system to gain access to these treatments.

Our study aimed to identify the obstacles that prevent patients from

from January 2014 to August 2017. PAF provided a random sample of 300 de-identified patient cases for analysis. Patient cases were excluded from our final dataset if they were either: 1) patients who were not receiving assistance on the Personalized Medicine CareLine; and 2) patients who were on the Personalized Medicine CareLine but did not have a full dataset. Data was collected by PAF staff during routine case manager activities and was self-reported by the patient, with specific data elements verified by the patient's medical team. Each case included information about the number of contacts the case manager made to or on behalf of the patient, issues and resolutions of the initiated assistance request, demographics, a brief summary of the case management activities required for case resolution, and how long it took to resolve each individual case. As recipients of PAF case management services, patients provided written consent for their data to be utilized for research purposes. Patient data were transferred through a secure online portal. All non-essential protected health information and personally identifiable information was removed from patient cases prior to transport and each case was issued a unique identifier for tracking purposes.

Analyses

Qualitative Analysis

Interviews were audio-recorded and transcribed verbatim. An initial coding structure was created based on the interview question guide and after a preliminary review of the

transcript data. After initial analysis, the coding structure was amended to include additional themes and trends. Conventional content analysis was utilized to categorize transcript data, described in Shannon and Hsieh.²⁶ NVivo 12 software was used to facilitate thematic analysis. Two coders were tasked with analysis of the case manager transcripts. Codes were compared, and coding discrepancies were resolved through in-person conversations. We ensured inter-rater reliability was maintained and transcript coding had a percentage agreement score of >90%. Descriptive analysis was conducted to identify case manager demographics and professional backgrounds.

Quantitative Analysis

We used descriptive statistics to examine the demographics of our patient population along with the frequency of our two outcomes of interest: 1) time to close a case; and 2) number of contacts between case-managers and a patient case. The first outcome, time to close a case, was calculated by subtracting the date that a patient case was created, "receipt date," from the date the case was closed or resolved, "done date." The second outcome, number of contacts, was determined by the number of interactions (ie, online research, calls to external organizations or medical providers) or any other activities conducted by a case manager on behalf of the patient's case. Demographic variables included OMB race and ethnicity categories (for purposes of analysis the racial and ethnic groups were combined as minority and White

for sufficient sample size), gender, employment status, insurance status, household size, age group, and income group. Multivariable linear regression models were utilized to test the association of our demographic variables as predictors for each of the two outcomes. All analyses were performed using SAS version 9.4.

RESULTS

Most of the patient cohort was White (79%), female (61%), aged 56 to >75 years (68%), and were either employed or retired (61%). There was noteworthy variation in household size and income with approximately 86% having a household size of 0 – 2 individuals (ie, number of individuals living with patient) and 31% making between \$72,000 and \$119,000. Most patients (99%) were insured (Table 1). Within this cohort, the top diagnosed cancers in increasing order, were prostate (5%), endometrial (5%), breast (7%), ovarian (9%) and lung cancer (13%) (Table 2).

In terms of accessing treatment in the patient cohort, the average number of case manager contacts with a patient case was 58 contacts (SD 46.2, range [2-257 contacts]). The average number of days from the opening of a patient case to the close of the case was 58 days (SD 54.1, range [0-356 days]). Namely, this indicates that, on average, patients were able to access some form of precision cancer medicine within two months. Clinically, 69% were diagnosed in stage I of cancer disease. Overall, 27 patients (9%) were un-

Table 1. Patient characteristics

Characteristic	%
Sex	
Male	39.3
Female	60.7
Age categories, yrs	
Birth to 18	2.0
19 to 35	4.7
36 to 55	25.7
56 to 75	56.3
Over 75	11.3
Insurance status	
Insured	99.3
Uninsured	.7
Race and/or ethnicity	
White/Caucasian, non-Hispanic	79.4
Black /African American, non-Hispanic	5.1
Asian	5.4
Hispanic/Latino	8.7
Middle Eastern	.4
Native Hawaiian/Other Pacific Islander	1.1
Income	
< \$23,999	20.5
\$24,000 - \$47,999	24.1
\$48,000 - \$71,999	11.4
\$72,000 - \$95,999	21.1
\$96,000 - \$119,999	10.2
≥\$120,000	12.7
Household size	
0	15.3
1	16.3
2	54.0
3	7.7
4	4.7
5 or more	2.0
Employment status	
Employed	20.1
Self-employed	2.9
Homemaker	1.4
Full time student	1.4
Retired	38.0
Disabled	24.7
Unemployed	11.5

able to access treatment as the final outcome of their case due to insurance denials, 35 patients (12%) died before gaining access to treatment, and 6 patients (2%) received precision cancer medicine through clinical trials. Tables 1 and 2 present the demographic and clinical character-

istics of our population, respectively.

We also performed two multivariable regression analyses examining factors associated with amount of time to close a case and the number of contacts between case managers and a patient case. Table 3 examines the factors associated with these two

outcomes. The following factors were observed with increased time to close a case: sex (females vs males, $\beta=.28$, $P=.6$), race (minority vs White, $\beta=.56$, $P=.4$), older age ($\beta=.24$, $P=.6$), higher income ($\beta=.004$, $P=1.0$) and increased household size ($\beta=.21$, $P=.5$). Conversely, the following factors were observed with decreased time to close a case: having insurance ($\beta=-2.45$, $P=.3$), and more advanced cancer stage ($\beta=-.17$, $P=.3$). Despite these trends, none of the variables were statistically significant.

Table 3 also explores factors associated with the number of contacts between case managers and a patient case. The following variables were observed with an increased number of case manager contacts: older age ($\beta=.42$, $P=.2$), higher income ($\beta=.07$, $P=.6$), and increased household size ($\beta=.2$, $P=.4$). The variables detected with decreased number of contacts with case managers were: sex (females vs males ($\beta=-.08$, $P=.9$), race (minorities vs White ($\beta=-.67$, $P=.2$), having insurance coverage ($\beta=-.19$, $P=0.9$) and a more advanced diagnosis stage ($\beta=-.09$, $P=.6$). None of the variables were statistically significant.

Qualitative Interviews

Case Manager Characteristics

A convenience sample of specially trained case managers from the PAF who worked on the Personalized Medicine CareLine were interviewed for the present study. All case managers were administered a short questionnaire prior to the survey to measure general demographics. Most case managers were female (87.5%), White (100%)

with some college education or a bachelor's degree (100%). The average number of years working in case management was seven years.

Based on the semi-structured interviews with the case managers, four broad thematic trends emerged from our study: 1) lack of patient, provider and insurer knowledge of precision cancer medicine; 2) barriers to clinical trial participation; 3) lack of patient health literacy; and 4) barriers to timely access to care (Table 4).

Lack of Patient, Provider and Insurer Knowledge of Precision Cancer Medicine

PATIENT AWARENESS AND EDUCATION

A common concern expressed by case managers was the lack of awareness of genomic testing and precision cancer medicine by patients, physicians and insurance companies. Case managers felt that patients were particularly unacquainted with cancer precision treatment options:

Table 2. Clinical characteristics of patients

Diagnosis stage	%
Stage I	69.0
Stage II	.3
Stage III	3.4
Stage IV	27.3
Treatment status	
Obtained treatment	54.0
Deceased before receiving treatment	11.7
Unable to access treatment	9.0
Top five cancers	
Breast cancer	7.4
Ovarian cancer	9.1
Lung cancer	13.1
Prostate cancer	5.0
Endometrial cancer	5.0
Days to close a case, mean (SD)	58.1 (46.1)

“From the patient’s side, it’s just kind of an overall lack of awareness of what [precision medicine] actually is...on the medical side, we talk about personalized medicine all the time. I don’t think people really have a good grasp of what that means to them on their individual cases...what does

it mean when it comes down to you and trying to face your treatment?” (Case Manager 2)

Case managers also described various conversations where patients were fearful of exploring genomic testing and targeted therapy because their providers never discussed this field of cancer treatment with them:

Table 3. Adjusted multivariable regression models of independent variables and patient outcomes (number of case manager contacts, time to close a case)

Characteristics	Model 1 ^a : time to close a case		Model 2 ^b : number of case manager contacts with a patient case	
	Adjusted β	P	Adjusted β	P
Sex (vs Male)				
Female	.28	.6	-.08	.9
Age	.24	.6	.42	.2
Race (vs White)				
Minority	.56	.4	-.67	.2
Insurance status (vs Uninsured)				
Insured	-2.45	.3	-.19	.9
Income	.004	1.0	.07	.6
Household size	.21	.5	.2	.4
Diagnosis stage	-.17	.3	-.09	.6

a. Model 1: The β coefficients give the estimated amount of time to closing a case for every unit increase (eg, increased age) or between the indicated group and reference group (eg, females vs males).
R-squared for this model= .02; F-statistic=.55, P=.794

b. Model 2: The β coefficients give the estimated number of contacts between case managers and patients for every unit increase (eg, increased age) or between the indicated group and reference group (eg, females vs males).
R-squared for this model= .03; F-statistic=.62, P=.740

Table 4. Themes and subthemes from case manager interviews^a

Themes	Subtheme
Theme 1: Lack of patient, provider, and insurer knowledge of precision medicine-based cancer treatments	Patient awareness and education Provider awareness and education Insurers awareness and education
Theme 2: Barriers to clinical trial participation	High cost of accessing clinical trials Eligibility requirements of clinical trials Lack of provider referral Patient sentiments toward clinical trials
Theme 3: Lack of patient health literacy	Patient insurance literacy Patient genomic literacy
Theme 4: Barriers to timely access to care	Cancer stage and severity Difficulty navigating health care system

a. Supplemental qualitative data available from corresponding author.

“Patients think that they don’t really have an option; that the doctor tells them, “This is what your treatment is.” They don’t really understand that they have the right to go get a second opinion.” (Case Manager 1)

PROVIDER AWARENESS AND EDUCATION

Fears that providers were not discussing genomic medicine with their patients was a concern of case managers. Many informants believed that this lack of knowledge of genomic medicine led to delayed utilization when patients needed it the most. These concerns were compounded by a prevalent issue that, like patients, providers have not been exposed to genomic medicine in their medical training, hindering the use of genomic medicine in their clinical decision making with patients.

INSURERS AWARENESS AND EDUCATION

While case managers agreed that it is imperative to provide educational resources for both patients and

providers regarding genomic medicine, they felt that it was equally critical to inform insurance companies about the benefits of genomic medicine for the patients that they insure. The overwhelming majority of case managers expressed strong opinions that the number one cause of delayed access to genomic medicine was insurers inability to cover off-label medications, or drugs that are not FDA approved for certain conditions, age groups or routes of administration, for patients. Case managers also identified additional barriers preventing patients from receiving genomic and personalized medicine. They believed that many patients were not aware of navigation services, like PAF, nor did they understand the role of case managers in orchestrating their access to medical care.

Barriers to Clinical Trial Participation

ENROLLING IN CLINICAL TRIALS

Case managers indicated that a number of patients sought participation in clinical trials to ac-

cess the genomic-based treatment options that were not offered or covered by their insurance. One case manager described the financial barriers that some patients faced trying to enroll in precision cancer medicine clinical trials:

“I have a patient that is trying to get in a clinical trial. But they’re having some difficulty with their insurance because the clinical trial’s out of network. And he has a very rare cancer.” (Case Manager 5)

Many case managers stressed that patients commonly faced difficulties in enrolling in clinical trials. Some of these obstacles included clinical trial eligibility restrictions, financial burdens to participate such as inability to take off from work or transportation concerns, and lack of provider referral to utilize clinical trials for treatment.

PATIENT SENTIMENTS TOWARD CLINICAL TRIALS

Case managers described situations where patients did not feel comfortable participating in clinical trials. Case managers felt that some of patients’ beliefs of clinical trials were connected to lack of genomic and health literacy:

“I’m not going to be your guinea pig,” That’s the first thing we hear. “I’m not taking some medication nobody knows anything about.” This stuff has a stigma from however many years ago. One of the things we have talked about

..., is just trying to get the education out there about clinical trials.” (Case Manager 1)

Many case managers emphasized that barriers to access clinical trials were not specific to one racial group, income level or geographical region. Case managers emphasized that middle income or insured patients could face these challenges in their odyssey to access to clinical trials.

Patient Health Literacy

PATIENT INSURANCE LITERACY

A salient system-level barrier to health care navigation was the lack of patient knowledge of their own health care plans and the ever-evolving health care systems in the United States.

Case managers also voiced concerns that limited insurance literacy was particularly pertinent for patients of low socioeconomic status and individuals whose first language was not English. All case managers, however, emphasized the need for population-wide education on maneuvering health insurance and the health system.

PATIENT GENOMIC LITERACY

All case managers discussed the need to provide some form of education on genomics for patients. Unlike insurance literacy, case managers felt that patients' limited understanding of medical and genomic jargon had clear implications on their ability to understand how genomics is utilized in their clinical care:

“We'll explain the difference between what the results mean, and that they may have a particular mutation that may be found in breast cancer ...I think that is helpful for them to understand why they're having a test and what it's going to be used for, what does that mean as far as their treatment goes... [having an] opportunity to either re-educate or give them the confidence to know what's happening.” (Case Manager 6)

Case managers expressed that patients commonly misunderstand genomic testing results. Subsequently, patients are unable to fully participate in decision-making regarding their medical treatment.

Barriers to Timely Access to Care

CANCER STAGE AND SEVERITY

For patients suffering from chronic and debilitating illnesses, case managers stated that another well-defined barrier is their battle against time. In some instances, patients had to fulfill their daily responsibilities while also combating the clinical complications of cancer. Particularly in advanced stage cancers, gaining access to precision-based cancer medicine is a matter of life or death in many cases.

DIFFICULTY NAVIGATING HEALTH CARE SYSTEM

Case managers felt navigating the health care system and helping patients obtain treatment takes an increasing amount of time that many patients do not have. Informants

suggested that patients will only access genomic medicine if there are system-level changes and alterations in provider decision-making to reduce the amount of time that it takes to provide patients with the medical care that they need.

DISCUSSION

Precision cancer medicine is at the forefront of the integration of personalized medicine in health care. These novel therapies allow patients to receive medical treatments that are tailored to their genetic makeup and tumor characterization.²⁷ There is limited research on the obstacles that deter cancer patients from receiving these personalized treatments. Furthermore, we lack an accurate depiction of the patients that face barriers to access precision cancer medicine.

Our study was designed to elucidate the barriers that patients face in accessing precision cancer medicine.²⁸ Our goal was to share the unique narrative of case managers and focus on how they navigate the healthcare system to help patients receive these therapies and participate in clinical trials.²⁹ Our qualitative results indicate that patients, providers, and insurers lack familiarity with precision cancer medicine which prevent proper utilization by patients.

Our findings also suggest that challenges remain in accessing clinical trials that investigate precision cancer medicine. Case managers believe that systemic barriers, such as high cost of treatment and access to precision-based cancer medicine, dissuade patients who have been

economically marginalized as well as under-resourced patients from utilizing these treatments. However, these barriers span beyond cancer patients who are traditionally viewed as underserved. Issues of access are increasingly apparent for patients who are middle income and educated. Current research lacks acknowledgment of the evolving profile of what it means to be underserved in terms of access to precision oncology. It is paramount to recognize that these barriers will impact a significant

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number of cancer patients from all socioeconomic backgrounds, educational levels, and geographic regions.

Patients generally utilized case management services to find resources and help manage health and social care prior to, during, and after their medical treatments.³⁰ The barriers to precision cancer medicine highlight the importance of case management to resolve insurance coverage issues, identify drug discount programs, and assist with other social needs. This study is the first, to our knowledge,

that details the role of case management while providing a snapshot of how case managers navigate challenges of access to precision oncology and the US health care system. The qualitative interviews with the case managers confirmed the study findings that the majority of the patients seeking assistance in access to precision cancer medicine are insured and have incomes above the poverty level. This study highlights that it is difficult for patients with resources (insurance and employment) to gain access to precision cancer medicine. Case managers commonly felt that patients, providers, and insurers were unaware of their role in the navigation process, and this ultimately prolonged the time between patient and treatment.

We believe that our qualitative data provided a nuanced perspective that complements our quantitative findings. Future study is needed to understand the experiences of those underinsured and living below the poverty level and the multifactorial barriers in their access to precision cancer medicine. Future research should also evaluate the impact of case management services in other disease populations to highlight their role as navigators of patient medical and social care. There are considerable barriers between novel drug development and delivery of precision cancer medicine, and it is critical that case management is recognized as a service to support health care access for patients.

Study Limitations

The empirical results reported should be considered in light of the limitations of the study. Quan-

titatively, our study trends indicated that females, minorities, low income, uninsured, and older age were more likely to have additional delays to access precision cancer medicine. However, these findings were not statistically significant. Possible contributors could be small sample sizes, particularly from certain racial and ethnic minority groups, as well as uninsured patients. Additionally, as a retrospective analysis, the researchers were not able to control for exposure and outcome assessment and relied on others for accurate recordkeeping, thus, resulting in some missing information. Our findings nevertheless make important contributions to the growing scientific literature on access to precision oncology. Finally, there are inherent limitations associated with qualitative analysis including, generalizability and the potential subjectivity in coding the data. The limitation in generalizability may also be attributed to the lack of racial and gender diversity among our case managers, in other words, the viewpoints of non-White and non-female participants were not included in this study. To reduce potential subjectivity in data coding, we aimed to combat this by double coding all transcripts and ensured that interrater reliability was obtained. Future work should aim to interview case-managers from various backgrounds as well as investigate additional demographic variables such as zip code, insurance type, access to technology and patient literacy levels to evaluate the effects on accessing precision cancer medicine.

CONCLUSION

A multifactorial response to the causes of these barriers should be employed to improve access to precision cancer medicine. At the forefront is the need for educational opportunities for patients, providers, and insurers to gain information about precision cancer medicine and technologies. Patients can only benefit from life-saving precision cancer medicine if there is clinical willingness to refer patients to appropriate clinical trials. It is of equal importance that the scientific, medical, health care, and advocacy communities join forces to develop best policies to reduce the barriers that patients face to gain access to precision cancer medicine. As testing technologies and therapeutics for precision cancer medicine continue to evolve, researchers, clinicians, and patients must continue to investigate the integration of genomics and precision medicine to improve the quality and longevity of life for patients with cancer and other diseases.

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COMPLIANCE WITH ETHICAL STANDARDS

Research involving human participants and informed consent: The NIH institutional review board reviewed and approved

this protocol. The study was approved as a low-risk, expedited study. Informed consent was required for the case-managers and was obtained verbally before the start of the interview. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all participants included in the study.

CONFLICT OF INTEREST

No conflicts of interest to report.

AUTHOR CONTRIBUTIONS

Research concept and design: Cooper, Bonham; Acquisition of data: Cooper, Bonham, Gallagher; Data analysis and interpretation: Cooper, Abdallah, Angove, Gallagher, Bonham; Manuscript draft: Cooper, Abdallah, Angove, Gallagher, Bonham; Statistical expertise: Abdallah; Acquisition of funding: Bonham; Administrative: Abdallah, Bonham, Gallagher; Supervision: Bonham

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Barriers to Precision-Based Cancer Medicine - Cooper et al

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