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PROTOCOL TITLE: Helping Oncology Patients Explore-Genomics (HOPE-Genomics) Web Tool Randomized Clinical Trial

PROTOCOL SHORT TITLE: HOPE-Genomics Tool Clinical Trial

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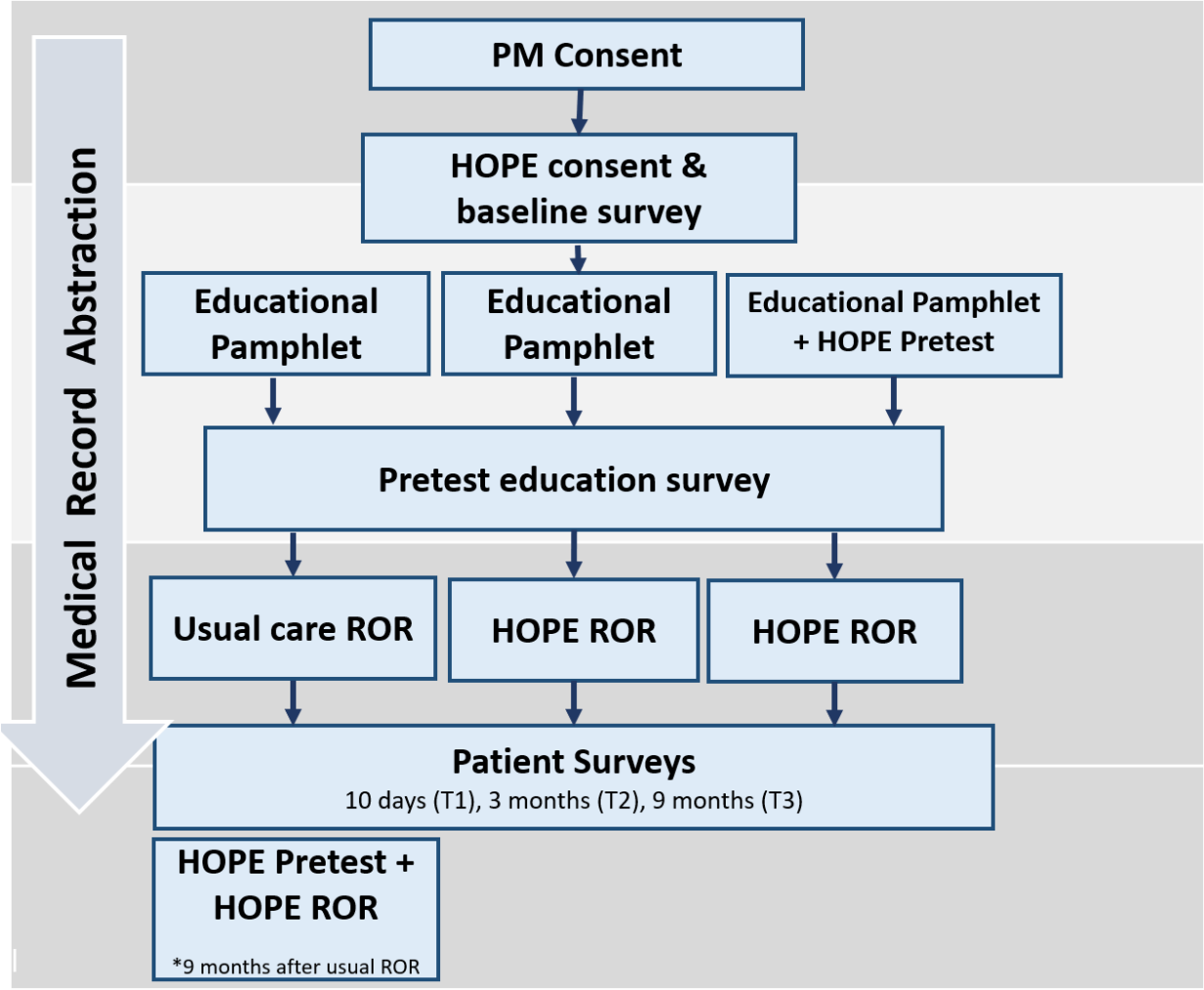
PATIENT PARTICIPANTS



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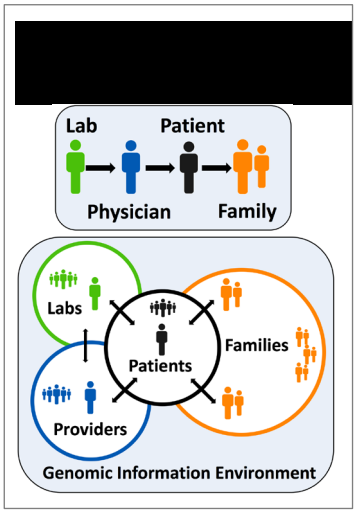
1.0 OBJECTIVES

The introduction of large-scale genomic testing in medicine promises to transform patient care. Cancer is at the leading edge of this revolution and hundreds of thousands of cancer patients receive tumor genomic testing yearly. Understanding how genomic information is conveyed in the context of cancer has broad relevance across the spectrum of human disease. Early evidence reveals that despite rapid adoption of genomic testing in cancer, many patients fail to comprehend basic information about cancer genetics or the defining genomic characteristics of their disease. For example, many breast cancer patients lack knowledge about their own tumor biomarkers and such knowledge deficiencies have been associated with lower adherence to highly effective targeted therapies.[1] Given that better-informed patients can more effectively engage in their care, and that greater knowledge about cancer and one's personal health characteristics is associated with improved cancer-related outcomes, there are significant concerns that patients' genomic knowledge deficits may contribute to poor quality care. In this context there is an urgent need to educate patients about cancer genomics generally, and their sequencing results specifically, in a format that is usable, useful, and that easily integrates into existing clinical workflows.

The goal of our research program is to improve the delivery of high-quality precision cancer medicine. In the current study, we plan to test the efficacy of providing patients with direct access to their sequencing results and information on cancer genomics through a web-based interface, Helping Oncology Patients Explore-Genomics (HOPE-Genomics).

2.0 BACKGROUND AND RATIONALE

We are in the midst of a genomic revolution; more than 250,000 human genomes have been sequenced, generating over a petabase of genomic data. If these data were used correctly, they could save hundreds of thousands of lives each year. However, there is a disconnect between genomic discovery and clinical care. Physicians frequently misinterpret genomic information and patients often don't understand their own test results. To address these care gaps, we have developed tools to help physicians and patients interpret, use, and share genomic data. Our work has been primarily in cancer and we aim to further develop and test tools that overcome gaps in genomic care delivery. Our overarching goal is to optimize the integration of whole-exome and whole-genome sequencing (WES, WGS) into general clinical practice.



The ineffective implementation of genomic discoveries produces a ubiquitous "last mile" problem.[1,2] For example, *BRCA* testing has been guideline-endorsed for 20 years but most patients who could benefit from testing are not sequenced. Moreover, data misinterpretation and poor communication has devastating consequences, including unnecessary organ removal, missed disease prevention opportunities, and premature death. Without rigorous interventions to address these problems, the societal investment of billions of dollars in genomics may yield little real world payoff.[1]

Most attempts to improve genomics-based care have targeted only one clinical factor and have focused on a few genes. Multi-level interventions, ones that target multiple factors, are hypothesized to be more effective.[3] Furthermore, tools are needed to communicate WES/WGS data to physicians and patients, including non-English speakers. Our work will improve care by transforming genomic communication from a traditional model of linear information flow to one that puts patients at the center of communication and enables them to seamlessly connect with providers, labs, and family members (Figure 1).

This proposal builds on our prior research and preliminary data which demonstrates that patients frequently don't know that they have had sequencing or understand the implicaitons of their results, and that many physicians don't understand sequencing information.[4-10] In order to overcome these problems, we developed a patient intervention called HOPE-Genomics. HOPE-Genomics is an interactive, web-based, point-of-care tool that 1) educates patients about genomics, 2) enables direct-to-patient return-of-results, and 3) facilitates sharing of genomic results within families. Based on pilot testing, we have found this interveniton to be highly acceptable to patients and clinicians.

2.1 Specific Aims

In the proposed work we aim to:

- **Aim 1:** Test the efficacy of the HOPE-Genomics intervention in improving patient knowledge of genomics (recall rates)

  Hypothesis: The use of HOPE-Genomics will result in higher rates of patient knowledge (recall rates) of genomics and their personal test results

  Strategy: We will conduct a randomized controlled trial of HOPE-Genomics as an educational tool among patients receiving WES/WGS as a part of their clinical care.

- **Aim 2:** Test the efficacy of the HOPE-Genomics intervention in improving patient receipt of guideline-concordant care

  Hypothesis: The use of HOPE-Genomics, will result in higher rates of uptake of evidence-based genetically-guided care vs. usual care.

  Strategy: We will conduct a randomized controlled trial of HOPE-Genomics among patients who receive WES/WGS as a part of their clinical care.

3.0 PARTICIPANT NUMBER, RECRUITMENT, COHORT CHARACTERISTICS AND EGLIGIBILITY

3.1. Participant Number

We anticipate recruitment and enrollment of approximately 465 patients for this study and assume a 10% overall attrition rate after enrollment. We will recruit from among patients who consent to the COH IRB 07047 Precision Medicine protocol and who have been or had been diagnosed with cancer. For 07047 overall, we estimate approximately 4000 total patients in year 1 of Precision Medicine (beginning CY 2021), 6000 total patients in year 2, and larger numbers yet in subsequent years, demonstrating likely feasibility. Given that patients who consent to 07047 may receive WES (e.g. GEM ExTra), Panel

Testing (e.g. HopeSeq), and/or germline (e.g. Invitae) as part of their care, they will have the genomic testing that is necessary for this education intervention study.

3.2. Duration of Study

Protocol will end when enrollment has reached limit of 465, and all study activities have concluded.

3.3. Recruitment

We will enroll approximately 465 patients from City of Hope Duarte main campus and community locations. Patients will be identified in collaboration with the COH Precision Medicine (PM) team. Dr. Gray, the study PI, is the Deputy Director of the Center for Precision Medicine and works closely with the entire PM team. Patients who have consented to COH IRB 07047, who are having genomic sequencing through 07047, and who have solid tumor diagnoses (see eligibility criteria below) will be eligible to participate. Patients will provide consent to this protocol at the start of their participation in the study and will subsequently be randomized into either the control arm (i.e., Usual Care), the Return of Results arm or the Return of Results plus Pretest Education arm.

In Clinic Recruitment
Potentially eligible patients will be approached by study team members during clinic visits for verbal informed consent. Patients will either be enrolled on site or given a study packet containing an invitation letter, informed consent document, return envelope, and a postcard to denote interest in participating or declination. Patients who do not return the postcard within 2-3 weeks will be contacted by a study team member to reassess interest in participating. Patients will be contacted either by telephone or web-conference or will be contacted at their next COH appointment in person. For patients interested in participating, study staff will schedule a verbal informed consent session by telephone, web-conference, or a patient's next COH appointment in person.

Remote Recruitment
When in-clinic recruitment is not feasible, potentially eligible patients will be contacted by study team members via telephone/email to gauge interest and potentially schedule a verbal consent session. If the patient cannot be reached, participants will be mailed a study information packet containing an invitation letter, informed consent document, return envelope, a postcard to denote interest in participating or declination. Study staff will also email patients to encourage contact. Patients who do not return the postcard within approximately 7-10 days weeks will be contacted by a study team member to reassess interest in participating, either by telephone or web-conference. Study staff will schedule a verbal informed consent session with patients who are interested in participating, either by phone or web-conference.

Waiver of Documentation of Informed Consent
We have requested a waiver of documentation of informed consent for patient participants in the randomized clinical trial. This portion of the study qualifies for waiver of documentation of informed consent under the criteria established by the Office of Human Research Subjects Protection that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

This randomized clinical trial entails data collection through surveys and data from existing medical records, which fall under these criteria.

Although we will be requesting a waiver of documentation of informed consent, study staff will fully review the information sheet that contains all elements of informed consent with the participant before the participant starts any study activities. During patient recruitment, the study staff will keep additional documentation that information sheet was reviewed with the participant, through OnCore and REDCap systems.

3.4. Cohort Characteristics and Eligibility

3.4.1 Patient Participants

Patients will be eligible if: 1) they are enrolled in COH IRB 07047, 2) have a cancer diagnosis, 3) they are having somatic, germline or paired somatic/germline sequencing, 4) they are fluent in English, 5) they have an ECOG performance status of 0-2, and 6) they are ≥ 18 years old.

Patients will be ineligible if they 1) are unable to provide informed consent.

3.4.2 Cohort Characteristics

In accordance with NIH guidelines, women and members of minority groups and their subpopulations will be included in this protocol. We will aim for the proportion of minority participation in the study to be representative of the patient population seen by our clinics at the City of Hope Cancer. The following percentages of racial and ethnic groups constitute the City of Hope clinic population: 15% Hispanic, 2% African American, 5% Asian, 0.2% American Indian/Alaska Native, 0.2% Native Hawaiian or Other Pacific Islander and 78% are Caucasian.

4.0 STUDY PROCEDURES

4.1. Informed Consent and Baseline Survey

Potentially eligible patients will be approached by study team members for verbal informed consent, either by mail/ email, during clinic visits, or by phone. Patients will receive a study packet that will contain an invitation letter, interest postcard, return envelope, and informed consent document. Patients will be randomized into one of three arms immediately after enrollment. Arm 1 is usual care, Arm 2 is return of results only in the HOPE-Genomics tool, and Arm 3 is return of results plus pretest education in the HOPE-Genomics tool.

Table 1: Outcome and covariate data collection

			Patient surveys			MRA
	Baseline	Pre-edu. survey	T1	T2	T3	
Genetic Care outcomes						
MD recommendations						
Screening, surgery, meds			X	X	X	X
Referrals GC, specialists			X	X	X	X
Cascade testing			X	X	X	X
Patient utilization/behavior						
Screening, surgery, meds			X	X	X	X
Consult GC, specialists			X	X	X	X
Inform family members			X	X	X	
Cascade testing			X	X	X	
Patient-centered outcomes						
Recall of results	X		X	X	X	X
Understanding of results			X	X	X	
Genomic knowledge	X	X	X	X		
Engagement in care			X	X	X	
Information seeking				X		
Psychosocial impact	X		X	X	X	
Follow up outcomes						
HOPE-Genomics usability			X	X		
Satisfaction with MD-patient communication and care			X	X		
Covariates						
Socio-demographics	X					X
Clinical information						X
Other (e.g., health literacy)	X				X	

Medical record abstraction (MRA); Post disclosure: 10 days (T1); 3 months (T2); 9 months (T3); Medications (Meds); Genetic counseling (GC); Physician (MD)

Arm 1 patients will receive a pamphlet (20430 Educational Brochure in iRIS) about WES after they enroll. Their clinician will return their genomics test results in a typical manner, without the assistance of the HOPE-Genomics tool.

Arm 2 patients will receive their genomics test results both from their clinician and from the HOPE-Genomics tool but will only view the tool after their results are available. Arm 3 patients will view the HOPE-Genomics tool (containing educational content) before their sequencing results are available. These patients will also receive their genomics test results both from their clinician and from the HOPE-Genomics tool. After completing all study surveys at 9 months post results disclosure, participants in Arm 1 (usual care), will receive access to the HOPE-Genomics tool, which will contain both the educational information and the personalized genomics results.

4.1.1 Patient Baseline Survey

At time of consent, patients will complete the baseline survey. Baseline survey outcomes are detailed in Table 1. We will follow standard survey methods as outlined by Dillman[2,3] (e.g., contact type and intervals; mail/email/in-person reminders) to ensure high response rates. The survey will be administered in one of the following ways, according to patient preference: (1) mailed to the participant, along with a return envelope, (2) provided electronically and/or by text message via REDCap survey link, or (3) completed over a scheduled phone or Zoom call with a study staff member. For patients who complete the baseline survey via phone or Zoom call, study staff will not assist them in selecting the correct answers for questions pertaining to their understanding of cancer and genetics.

Germline sequencing knowledge will be measured using an adapted version of the UNC Genomics Testing Knowledge Scale[1], a validated 25-item measure developed by Langer and colleagues to evaluate overall understanding of genomics and health. We will also assess patients' knowledge of the implications of WES on 1) personal cancer risk, 2) family cancer risk, and 3) genetics generally.

General cancer genomics knowledge will be assessed using a modified form of a 12-item measure developed by Blanchette and colleagues.[5] The measure assesses three domains of cancer genomic knowledge: 1) general understanding of cancer, 2) how biological changes influence cancer, and 3) the potential implications of genomic testing in cancer. Higher general cancer genomic knowledge has been associated with higher levels of education, higher personal income and patients' perceived ability to provide informed consent for genomic testing.

Knowledge about the use of genetic testing in cancer will be assessed using a 6-item measure developed by Roth, Gray and colleagues for the Lung-MAP study (unpublished). The measure assesses participant's knowledge of why genetic testing is used in cancer care (e.g., to help select a treatment, to predict response to treatment). Eight items have been added in the following content areas: 1) use for cancer staging, 2) use to time cancer onset, 3) use to predict treatment efficacy, 4) use for clinical trials, 5) use to monitor cancer treatment, 6) use to identify a cancer's location, 7) use to determine metastasis, and 8) use to assess cancer risk.

Knowledge about the difference between somatic and germline testing (categorical questions) will be assessed using a 7-item measure developed by Roth, Gray and colleagues for the Lung-MAP study (unpublished). The measure assesses participant's knowledge about 1) germline mutations found every cell of the body and 2) somatic mutations found only in cancer cells.[6] 4 items have been added in the following content areas: 1) finds gene changes that a person was born with, 2) finds gene changes that have happened over a lifetime, 3) finds gene changes that are passed from parent to child, and 5) commonly has health implications for family members.

Understanding of personal genomic knowledge will be assessed through an adapted version of a measure created by Freedman and colleagues[1], which evaluated women's knowledge of their personal cancer ER and HER2 status using a two-item question (3 response options; yes/no/I don't know). Our adapted questions will evaluate patients' recall of genomic testing results and the implications of their results (i.e., harmful and unknown). Patient recall will also be assessed 10 days, 3 months and 9-months following results disclosure with a clinician.

Recall of prior genetic counseling will be assessed with a single question (3 response options; yes/no/I don't know) created by Sheppard and colleagues, which evaluated African American women's experiences with counseling counselling for hereditary breast cancer.[2]

Psychosocial wellbeing/anxiety/depression/stress will be assessed at baseline and at each follow-up timepoint using a 14-item measure from Zigmond's Hospital Anxiety and Depression scale.[3] These questions will assess potential changes in patients' psychosocial wellbeing in response to genetic testing and their experience with cancer throughout the randomized trial.

Socio-demographics will be assessed using questions (including race, ethnicity, marital status, education) from the Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System (BRFSS) questionnaires. The BRFSS questionnaires are health-related telephone surveys that collect state data about U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services.[4] Primary language spoken will be assessed by a 4-item measure developed for CSERII. Sex, gender, and date of birth will be assessed using measures from CSERII.

Other covariate data (e.g., health literacy, numeracy, health status, and primary language spoken) will be assessed using validated measures.

- Health literacy will be assessed by up to 3 single-item health literacy screening questions, as evaluated by Chew and colleagues.[5]
- Numeracy will be assessed by a 3-item version of the Subjective Numeracy Scale (SNS-3), as validated by McNaughton and colleagues.[17]
- Health-related Internet use will be assessed by a an adapted 1-item measure from the National Cancer Institute Health Information National Trends Survey (HINTS).[18,19]
- Health status will be assessed by a validated single item measuring general self-rated health.[18,20,21]
- Patient-reported functional status will be measured by a single item measure developed by Basch and colleagues (patient ECOG-PS). [22]
- Quality of care will be assessed using a single item measure from HINTS.[6]

4.1.2 Patient Follow Up Survey

The follow up surveys will either be mailed to the participant, along with a return envelope, provided electronically and/or by text message via REDCap survey link, or completed via phone or Zoom call with a staff member, according to patient preference. For patients who opt to complete their follow-up surveys via phone or Zoom call, study staff will not assist them in selecting the correct answers for questions pertaining to their understanding of cancer and genetics. Study staff will follow-up with patients once a week within 2–3-week window to encourage completion of the survey. We will attempt to contact non-responders up to five times to encourage survey participation.

Understanding of personal genomic knowledge will be assessed through an adapted version of a measure created by Freedman and colleagues[1], which evaluated women's knowledge of their personal cancer ER and HER2 status using a two-item question (3 response options; yes/no/I don't know). Our adapted questions will evaluate patients' recall of genomic testing results and the implications of their results (i.e., harmful and unknown). Patient recall will be assessed at all survey timepoints (i.e., at baseline, 10 days, 3 months and 9-months following results disclosure with a clinician).

Engagement in care will be assessed by a novel item that queries patients as to whether WES prompted questions to care providers (yes, no, don't know). We will use items adapted for our CSERII study to ask patients if they recall changes to their cancer treatment as a result of their genomic test results. We will also assess engagement via interactive functionality of HOPE-Genomics (see below).Seeking and sharing information about genetic tests will be assessed using two items from the Health Information National Trends Survey (HINTS) 4 that were adapted for our CSERII study.[7]

Satisfaction with physician/patient communication around the results of gene testing will be assessed with a 7-item measure adapted from HINTS 3 & 4. Satisfaction with care will be assessed using a single item measure from Charles and colleagues that was created to evaluate satisfaction with genetic counseling and that was adapted for our CSER1 study.[14] We have also included two novel questions to assess whether patients (1) recalled asking their healthcare providers about their genetic test results and (2) recalled receiving a copy of their genetic test report.

Psychosocial impact of genetic testing and patient uncertainty will be assessed using both the adapted PAGIS Certainty Scale and the FACToR.[23] The FACToR is a 12-item measure developed by CSER1 colleagues at the University of Washington that applies across disease contexts and also includes items related to uncertainty, test-related distress, and positive experiences. Uncertainty about genetic testing results will be assessed using the PAGIS. A 5-item measure by Read and colleagues (Psychological Adaptation to Genetic Information Scale; PAGIS certainty subscale).[8]

Tool usability/usefulness/acceptability will be assessed for patients who view the HOPE-Genomics tool (Arms 2 and 3) approximately 10 days and 3 months after results disclosure. HOPE-Genomics usability/acceptability will be assessed using two instruments. To assess system usability, we will use the System Usability Scale (SUS).[9] The SUS is a 10-item measure that evaluates a variety of aspects of system usability including the perceived complexity of a system and the need for support and training to facilitate use. We will also use an adapted version of the Electronic Self-Report Assessment-Cancer (ESRA-C).[13] The ESRA-C is a 6-item measure that assesses participants' opinions about a web-intervention (e.g., easy and enjoyable, acceptability of time required to navigate, overall satisfaction). The ESRA-C is written at a 5th-grade reading level and is highly reliable (Cronbach alpha 0.76).

Motivations for sharing genetic test results will be assessed using a modified 9-item measure adapted from our CSERII study and the Development of the Informing Relatives Inventory (IRI) by de Gues and colleagues.[10] Patients will be asked to rank the importance of various reasons for sharing genetic test results on a 5-point scale, from "Not At All Important" to "Very Important." This measure will only be included in the 3-month follow-up survey and will be included as an exploratory measure.

4.2 HOPE-Genomics Tool Details & Security Features

The HOPE-Genomics tool is a web-based, interactive tool that provides personalized genomics results and educational content to patients. The tool was designed with stakeholder feedback and we have collaborated closely with the COH Research Informatics group to build a fully functioning HOPE-Genomics tool on the HL7 SMART on FHIR platform. For this effort, Research Informatics has built a Web-based responsive application that can be accessed through any popular web browser using devices with varying screen sizes, like computers, tablets, and mobile phones.

Securing the application and the patient data is one of the design principles of this platform; application enforces two-factor authentication for its users to login, when a user signs up for an account, he/she will have to provide a phone number during the registration process. Subsequently the user will have to enter a code sent to the phone (number used during registration) along with the password to login to the application. The application backend uses a JSON Web Token mechanism to authenticate every request coming into the server. A secure token is generated upon user login, and token should be attached to every request to the backend API for the request to be successful. Tokens automatically expire after 30 mins of non-usage and forces the user to login again.

The application also offers secure authorization mechanism, application backend authorizes every data request to make sure the user requesting the information is authorized to view the information. The authentication token when generated is assigned to a patient resource, and data related to that patient resource can only be retrieved from the API using the token generated. The application is also hosted within City of Hope firewall keeping it secure from various vulnerabilities. The application is made available on https to enforce end-to-end secure connection between the patient's browser and the application server. The tool also offers some administrative capabilities, this tool provides direct access to all enrolled patients and allows the study team to manage patient's account details. Each patient user is assigned a FHIR ID that cannot be linked or traced back to the patient's MRN. Lastly, no PHI is captured through the HOPE-Genomics platform, as patients are not asked to input any personal information into the application, and it is not directly linked to the electronic medical record. Our informatics team performs cybersecurity scans every week on the entire HOPE-Genomics application to look for any vulnerabilities. They will then assess the severity of any detected vulnerabilities and fix them as needed.

4.3 Tool Access and Patient Pre-Education Survey

After enrollment, all participants will be provided with a hard-copy or electronic educational pamphlet about whole-exome sequencing (WES). Patients in the Return of Results plus Pre-test Education arm will be provided with login and dual-factor authentication instructions and have immediate access to educational content in the tool, with their sequencing results to become available in the tool shortly after their results are available in Epic. Patients in the Return of Results Only arm will not be able to see tool content until their genomic test results are available (e.g., ~2-6 weeks after sample collection). Patients in the Usual Care arm will have access to the tool content after completing all study surveys, approximately ~9 months after their have sequencing results are available.

Approximately 2-3 days after completing the baseline survey, patients in all study arms will complete a pre-test education survey that assesses general genomic knowledge prior to results disclosure. For patients requesting paper versions of the baseline and pre-test surveys, we will mail the pre-test survey 1 week after mailing the baseline. This will ensure that patients who opt for paper surveys can complete the pre-test survey within 2-3 days of completing their baseline survey. As with all study surveys, patients will also have the option of completing the pre-test education survey over a scheduled phone or Zoom call with a study staff member. During the phone or Zoom call, study staff will not assist patients in selecting the correct answers for questions pertaining to their understanding of cancer and genetics. As mentioned above, patients in the Return of Results plus Pre-test Education arm (Arm 3) will view the HOPE-Genomics tool prior to their results disclosure and completion of this survey. The HOPE-Genomics tool will be populated with educational material about genomics, cancer, and other related content, but without the patient's individual test results. We will track Arm 3 patients' tool access through Google Analytics, which is an IT-approved software that monitors user interaction metrics within the HOPE-Genomics platform, specifically button clicks per page, page scrolls, double clicks, and page-viewing duration times. We are utilizing Google Analytics to better understand which features of the tool are most frequently used by patients and identify technical aspects of the tool that need improvement. The version of Google Analytic implemented (GA4) in the HOPE-Genomics platform has a process of data anonymization, so no IP address or other PHI is collected from the participants. In addition, Google Analytics does not gather text data from the HOPE-Genomics platform and therefore has no access to potential PHI within the HOPE-Genomics platform. Additional security features of the HOPE-Genomics platform are discussed in Section 4.2 of this protocol (HOPE-Genomics Tool Details & Security Features). Study staff will call and/or email patients in the Return of Results plus Pre-Test Education arm within approximately 24 hours of receiving their login information to track whether patients interact with the HOPE-Genomics platform and if patients have not accessed the tool, study stuff will encourage and facilitate intervention use. All other patients (Usual Care & Return of Results Only) will only view the WES pamphlet before completing this survey. The HOPE-Genomics educational content will be available to those patients in the Return of Results Only and Usual Care arms but will only be made available after their genomic test results are available in the tool.

To improve patient compliance to study requirements, all patients will be presented with the option to opt-in to receive text message reminders related to study participation and to receive access to unique survey links. Patients will have the option to opt in and opt out of receiving text message reminders at any point during their participation; the decision would not affect their participation in the study. For patients who have agreed to provide their mobile number for text message reminders, this method will be used to supplement electronic communication reminders to encourage and facilitate intervention use. Mobile numbers will be collected solely for the purposes of communicating study-related requirements to patients and will not be used to disclose any PHI nor will they be shared for purposes beyond this study and without patient consent. Information detailed in text message correspondences will reference time points and reminders of which patients will need to:

1. Complete a study procedure (e.g., view HOPE-Genomics platform, complete a survey)
2. Be provided with unique survey links generated by REDCAp (i.e., links for Baseline, Pre-test Education, 10-day Follow-up, 3 Month Follow-up and 9 Month Follow-up surveys).

Patients who have opted to receive reminders through their mobile phone will receive an initial message acknowledging their opt-in. Frequency of follow-up reminders to complete study procedures will be dictated by patient preference (i.e., patients prefer reminders only by text message), study arm assignment, and/or with regards to timeliness of completion of study requirements. Frequency of text messages will mimic the schedule for automated email reminders:

- **Baseline Survey:** every 96 hours
- **Pre-Test Tool Viewing (Arm 3):** 24 hours after login instructions sent
- **Pre-Test Survey:** every 96 hours
- **HOPE Tool Viewing (Arms 2/3):** 5 days after login instructions sent
- **All follow-**up surveys: Every 2 weeks

There will be a total of five time points of which patients will be provided survey links through text message. These time points correspond to the required completion of surveys as follows: Baseline survey, Pre-test Education survey, 10-day Follow-up survey, 3 Month Follow-up survey and 9 Month Follow-up surveys.

4.4 Results Disclosure

We expect results to be available within ~3-14 days of sample acquisition. We will monitor the patients' laboratory data to see when results have been finalized. Lab results and variant interpretations for the HOPE Genomics intervention will be stored in a custom genomic database designed by COH Research Informatics. All results will be validated by study staff before data are input into the HOPE-Genomics tool. All clinicians will receive results through the EHR. Additionally, clinicians with patients in the intervention arm will also be able to view their patients' results through the HOPE-Genomics after individual-level patient data have been entered into HOPE-Genomics. Results will be available to patients in the HOPE-Genomics app approximately 3-14 days after they are available in the EHR.

At this time, we will ask patients in the Return of Results Only intervention arm, (Arm 2) and the Return of Results + Pre-Test Education arm (Arm 3) to log into the HOPE-Genomics tool on their own time. Study staff will provide patients with instructions to create an account and log into the tool using dual-factor authentication. Study staff will track patients' tool access through Google Analytics and call or send automated RedCap reminders to encourage tool use, if necessary. Study staff will track patients' tool access through Google Analytics and call and/or send automated REDCap reminders to encourage tool use, if necessary. In addition, the study staff will be available to help patients access HOPE-Genomics at subsequent clinic/infusion visits or via secure web conference at any point in time following the disclosure of their test results until the end of the study (with coordination with the study team).

Patients in the control arm (Arm 1) will have their results returned in clinic by their provider, with no changes to the clinician's typical delivery method. Patients will be provided an educational pamphlet that generally describes sequencing and will granted access to the HOPE-Genomics tool with their results after completing all follow-up study surveys, approximately 9 months after their results are in the EHR.

As a thank you for their participation, patients will be provided with electronic or physical gift cards totaling $25 throughout study participation. Patients will receive a $5 gift card after completing the 10-day follow-up survey, a $10 gift card after completing the 3-month follow-up survey, and a $10 gift card after completing the 9-month survey. If patients require a separate study-specific visit to view HOPE-Genomics, we will provide them with a valet parking voucher to facilitate in-person study activities.

4.5 Follow up Surveys

4.5.1 10-Day Follow-Up Survey

All patients enrolled in the study will be asked to complete a follow-up survey approximately 10 days after results are released in the EHR. The survey will either be mailed to the participant, provided electronically and/or by text message via REDCap survey link or completed over a scheduled phone or Zoom call with a staff member, according to patient preference. If the survey is mailed, the patient will be provided with a return envelope. Follow-up survey reminders will be similar to those outlined for the baseline survey. The follow-up survey outcomes are detailed in Table 1. For participants of both intervention arms, the survey will also include questions about the usability of HOPE-Genomics. Survey measures will be similar to measures detailed in Section 4.1.1.

Patients in Arm 1 (usual care) will receive a modified survey that does not contain questions that pertain specifically to the HOPE-Genomics tool, like usability.

4.5.2 3 Month Follow-Up Survey

Delivery of the follow-up survey and study materials will follow similar procedures mentioned in Section 4.3.1. The 3 Month follow-up survey outcomes are detailed in Table 1. Survey measures will be similar to measures detailed in Section 4.1.1.

4.5.3 9 Month Follow-Up Survey

Delivery of the follow-up survey and study materials will follow similar procedures mentioned in Section 4.4.1. The 9 Month follow-up survey outcomes are detailed in Table 1. Survey measures will be similar to measures detailed in Section 4.1.1. Participants in the Usual Care Arm will view their results in the HOPE-Genomics tool after completing the 39Month Follow-Up Survey. None of their follow-up surveys will contain questions pertaining to the HOPE-Genomics tool or its usability.

4.6 Medical Record Abstraction

Throughout the study, study staff will perform a limited medical record abstraction of consented participants. Primary outcome data will include high-risk screening, surgery, chemoprevention, targeted therapies, genetic counseling, informing family members, and cascade testing. Covariate data will include sociodemographic information, cancer information, germline and somatic genomic biomarker testing, and dates and types of treatments for cancer. Additional outcomes are detailed in Table 1.

5.0 DATA AND SAFETY MONITORING AND UNANTICIPATED PROBLEMS

5.1 Definition of Risk Level

This is a low risk study, as defined in the City of Hope Institutional Data and Safety Monitoring Plan (DSMP), because it involves minimal risk, as the risks of harm anticipated are not greater than those ordinally encountered during daily life or during the performance of routine psychological tests in a

healthy person. This study involves the administration of surveys before and after an educational intervention, which will be integrated into the patient's usual course of clinical care. The study Principal Investigator is responsible for monitoring protocol conduct and reporting all reportable events to the City of Hope (COH) Data and Safety Monitoring Committee (DSMC) and Institutional Review Board (IRB) in accordance with the City of Hope Institutional Deviation policy, and Clinical Research Adverse Event and Unanticipated Problem policy.

5.2 Unanticipated Problems (UP) Involving Risks to Subjects or Others

An unanticipated problem is any incident, experience or outcome that **meets all three** of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given the following: a) the research procedures that are described in the protocol-related documents such as the IRB approved research protocol, informed consent document or Investigator Brochure (IB); and b) the characteristics of the subject population being studied; **AND**
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcomes may have been caused by the procedures involved in the research); **AND**
- Suggests that the research places participants or others at greater risk of harm (including physical, psychological, economic, or social harm) than previously known or recognized.

Any UP that occurs during the study conduct will be reported to the DSMC and IRB in accordance with the City of Hope's Institutional policy using the electronic submission system, iRIS.

6.0 DATA ANALYSIS

As noted in Section 4.0, we are administering the survey items in order to help with item reduction for the trial. We will generate descriptive statistics (e.g., distributions, means) in order to evaluate for ceiling and floor effects. An amended survey will be submitted prior to administration.

Primary outcome (i.e., patient knowledge, recall rates) will be assessed at the 10-day post-disclosure timepoint.

We will be using MRA and survey data to evaluate if participants received contextual guideline-concordant care. This will involve review of receipt of prophylactic surgery, chemoprevention, targeted therapy for germline mutations, consultation with genetic counseling/ genetic specialists, informing family members, and family member cascade testing. To generate concordance scores for patients already on active therapy, patients will be asked about their current and/or planned cancer treatment at baseline and at each follow-up timepoint in the study (i.e., chemotherapy, radiation therapy, cancer-directed surgery, hormone therapy, immunotherapy, and targeted therapy). Patients will be considered as being contextually guideline-concordant if they receive at least 75% of the recommend guidelines. In sensitivity analyses, we will vary the cutoff for guideline- concordance between 50% and 100%. Survey data will also be used to evaluate usability of the HOPE-Genomics application, the psychosocial impact of using the tool, engagement in care, genetic knowledge, and understanding of genomic test results

6.1 Sample Size and Accrual Rate:

We plan to anchor our cohort on patients with somatic testing. We expect to accrue 465 patients: 155 per each arm. We assume that there will be a 10% attrition rate among accrued patients, leaving us with a final analytical sample of 390 patients. For the first 3 months, we assume that 17 patients are enrolled each month, during which time we will evaluate and optimize study processes. After this we will increase monthly accrual to 35 patients. We expect to be complete with accrual in 16 months. Patient participation will be approximately 7 months consisting of baseline pre-testing followed by genetic testing/results disclosure and then post-testing. The estimated total study time including analysis will be 26 months.

6.2 Statistical Analysis Plan:

The study data will consist of three main areas:

1) patient knowledge testing and clinical care recommendations via survey-based questions
2) patient demographic information collected via the electronic medical record (EMR); and
3) patient clinical and treatment information collected via the EMR.

This information will be used to evaluate outcomes, predictors and adjust for covariates.

6.2.1 Primary Outcome

In Aim 1, recall rates of personal genomic results at the 10-day post-disclosure timepoint for Arms 2 and 3 of the study will be pooled together so that the main comparison is a two-sample test of proportions between patients under usual care (Arm 1) vs. patients with any exposure to the HOPE-Genomics tool (Arms 2/3). Pilot studies indicate that a recall rate for patients with an actionable somatic finding are approximately 39% under usual care. An analytical sample of 390, assuming a 39% recall rate under usual care (Arm 1: n = 130) with a 15% improvement using the tool (Arms 2/3: n = 260), will be sufficient to detect a difference in proportions with 80% power and alpha = 0.05 (two-sided with no adjustment for multiplicity). Rates of recall will be analyzed using a two group Chi-Square test of equal proportions, and logistic regression when controlling for covariates such as age and education level. The overall fit of the model will be examined using Hosmer-Lemeshow goodness-of-fit test and ROC curves. If any normality issues arise, non-parametric techniques such as the Mann-Whitney test will be deployed. Recall rates will be defined as the number of participants who correctly recall somatic test results, which will be assessed in the second question of the 10-day post-disclosure survey.

6.2.2 Secondary Outcome

In Aim 2, we will assess the effect of the intervention on the proportion of patients with contextual NCCN guideline-concordant care. This approach is modeled after analyses used by Dr. Robert Green et al. in the MedSeq CSER1 project.[25,26] Operationalization of contextual guideline concordant care: In the primary analysis, we will assess the uptake of contextualized guideline-concordant care taking into account clinically relevant, patient specific circumstances. We will use clinical characteristics from the

EHR to assign each patient to clinical category for which there are discrete NCCN recommendations. Using patient self-reported baseline/T1 and EHR data, following sequencing disclosure, we will create a summary genetically guided care variable ranging from 0-100%. The denominator consists of the total number of contextual guideline-concordant interventions/behaviors possible during a 12-month period following results disclosure for any given patient given his/her germline findings, family history, and clinical characteristics. The numerator consists of the total number of patient-adopted guideline concordant intervention/behaviors completed during a 12-month period following results disclosure. For a patient found to have a pathogenic germline/actionable somatic variant, we will assign benchmarks of genetically guided care derived from evidence based clinical practice guidelines (i.e. NCCN, United States Preventive Services Task Force, or medical society based clinical guidelines). We convene a weekly POTB meeting where a panel of medical geneticists, cancer geneticists, genetic counselors, genetic nurse practitioners, oncologists, gastroenterologists, cardiologist, and hepatologist review cases and develop multidisciplinary contextualized guideline concordant recommendations (chaired by Dr. McDonnell).

In the secondary analyses, we will define guideline concordant as meeting ≥75% of recommended guidelines. In sensitivity analyses, we will vary the cutoff for guideline concordance between 50% and 100%.

We will test if the use of HOPE-Genomics will result in higher rates of uptake of evidence-based genetically guided care (e.g., patient receipt of guideline concordant care, cascade testing) than usual care: Our primary goal will be to assess whether or not the uptake of contextual guideline-concordant care differs between the two arms. The primary objective is to test the null hypothesis of no intervention effect on the outcome. We expect that patients in the intervention arm will have higher rate of uptake of contextual guideline-guided care than patients in the control arm. A two-sided Type I error of 0.05 will be used for all statistical tests. We will consider two-sided p-value less than 0.05 as a statistically significant. Patients will be considered concordant (Y=1) if they undergo a predetermined percentage of genetically guided care and discordant (Y=0) otherwise. Using an intention-to-treat analysis, the proportion of concordant patients will be modeled using the logisitic regression approach for binary outcome (PROC LOGISTIC in SAS [Cary, N.C.]). We will use compound symmetry and unstructured working correlation matrix to account for correlation between patients within the same physician. The odds ratio of the concordant patients between the intervention and control arms will be calculated using the group coefficient in the Logistic model. The significance of the coefficient will be tested to determine treatment group difference. In addition, we will use Kauermann and Carroll (KC) correction for robust SEs if the number of physicians is small.[11] To evaluate the success of randomization, we will test the differences in characteristics of physicians and patients between the two arms. The Logistic model will include statistically significant characteristics as covariates. Logistic will also be used to model the percentage of the rate of uptake of the genetically guided care per patient, treated as a binomial variable, and include the within-physician correlation, to test for treatment group difference.

6.2.3 Exploratory Outcomes

Recall rates at 3-month: Recall rates of personal genomic results at the 3-month post-disclosure timepoint for Arms 2 and 3 of the study will be pooled together so that the main comparison is a two-

sample test of proportions between patients under usual care (Arm 1) vs. patients with any exposure to the HOPE-Genomics tool (Arms 2/3). Rates of recall will be analyzed using a two group Chi-Square test of equal proportions, and logistic regression when controlling for covariates such as age and education level. The overall fit of the model will be examined using Hosmer-Lemeshow goodness-of-fit test and ROC curves. If any normality issues arise, non-parametric techniques such as the Mann-Whitney test will be deployed.

Concordance Score: We will also use linear regression to conduct sensitivity analysis and test if the use of HOPE-Genomics will result in higher rates of uptake of evidence-based genetically-guided care (e.g., patient receipt of guideline concordant care, cascade testing) than usual care. The created summary concordance score of genetically-guided care variable ranging from 0-100% will be used to as numeric outcome. The null hypothesis is that the concordance score is not different between arms. We will consider two-sided p-value less than 0.05 as a statistically significant.

Test-related distress: We hypothesize that patients who view HOPE-Genomics will have lower test-related distress than patients in the usual care group: Patients will be assessed at 3 post-disclosure time points (T1-T3) using the PAGIS Certainty Scale and the FACToR. Some patients may have little test-related distress, whereas others may score higher (e.g., if testing reveals cancer or non-cancer related disease risk). Test-related distress is thought to decrease with time from the disclosure visit. We will summarize test-related distress at each time point, as well as change score. We will examine baseline characteristics to evaluate the potential for bias. In addition to complete case analysis, sensitivity analyses (e.g., using weighted methods) may occur to evaluate bias. We will use clustered Wilcoxon test for mean score comparison between groups at each time point. In addition, mean change in score from T1 to T3 will be modeled using GEE model adjusting for patient characteristics. We will use Autoregressive (AR1) and compound symmetry working correlation matrix to account for repeated measurement correlation and within-physician correlation. The significance of the coefficient will be tested to determine difference between two groups.

General genomic knowledge: We hypothesize that patients in the Return of Results plus Pre-test Education (Arm 3) arm will have better general genomic knowledge than the Return of Results only and Usual Care arms (Arms 1/2). To examine this, we will compare the pre/post test scores between the intervention group (Arm 3) and the control groups (Arms 1/2) The pre/post test scores will be calculated by taking the difference in score between pre/post tests and then comparing the mean differences with an independent T-test between control groups (Arms 1/2) versus the exclusive exposure to the HOPE-Genomics tool educational content (Arm 3). We also hypothesize that Arm 3 will have better knowledge of the difference between germline and somatic testing, as measured in the modified Lung-MAP instrument, which has been adapted and implemented in our survey. We will test this difference as above, testing the mean difference in scores of the modified Lung-MAP instrument across Arms 1 and 2 vs Arm 3.

Genetically-guided care: In exploratory analyses related to Aim 2 (i.e. receipt of contextual guideline-concordant care), we will also operationalize the secondary outcome in an additional way: Categories of genetically-guided care: We will evaluate patients' receipt of 1) treatment recommended by provider based on sequencing (any/none), 2) patients' sharing of sequencing results with family members (any/none), and 3) patients' consultation with genetic counseling/ recommended specialist (any/none).

HOPE-Genomics tool usage: Finally, in order to understand how patients and physicians use HOPE-Genomics and to determine whether refinements are required prior to dissemination, we will analyze the web-log of user visits (e.g., number of viewing sessions, page views and use of interactive elements).

7.0 MONITORING AND PERSONEL RESPONSIBLE FOR MONITORING

The Principal Investigator, collaborators, and study staff will work closely to ensure adequate monitoring of the study. The Principal Investigator is responsible for monitoring protocol conduct and reporting to the COH DSMB any adverse events related to study procedures.

8.0 HUMAN SUBJECT ISSUES

We will take measures to protect patients, including the exclusion of patients who are too ill to participate in the study. Dr. Gray, the Co-Investigators and the Collaborating Investigators are experienced working with patients with cancer and have undergone training designed to ensure the adequate protection of human subjects.

8.1 Potential Risks to Participation

This study involves the completion of study-related surveys and the viewing of a computer-based educational too. No invasive procedures are involved and hence the physical, psychological and social risks to participants are minimized. The risks and discomforts of this study are minimal and may be associated with answering potentially sensitive questions on surveys. Data will be retrieved from existing medical records and laboratory results as per the research protocol needs for identifying patient outcomes and populating the educational intervention. Patient confidentiality will be strictly maintained and a breach in confidentiality is not anticipated and will be mitigated by following procedures detailed in Section 5, “Data and Safety Monitoring, Unanticipated Problems, and Protocol Compliance.” In creating a patient-facing application that discloses genetic test results, this study involves the transfer and storage of PHI (patient name, date of birth, medical record number, biological sex, cancer type, ordering provider, and genetic test results) from a password-protected database in REDCAp to the HOPE-Genomics platform. As mentioned in Section 4.2, each participant is assigned a unique FHIR ID that cannot be linked or traced back to any patient PHI. Only team members with appropriate administrative rights have access to participants’ FHIR IDs and corresponding MRNs. Further, no PHI is shared between the HOPE-Genomics platform and Google Analytics, which is purely used for collecting basic user engagement metrics (i.e., number of page clicks, time spent on a page in the tool).

Our informatics team performs cybersecurity scans every week on the entire HOPE-Genomics application to look for any vulnerabilities. Any detected vulnerabilities are assessed and fixed as needed.

8.2 Potential Benefits to Participation

The patients may not directly benefit from study participation. However, the data gained through this study stands to potentially improve their genomic knowledge and quality of patient-centered care. In addition, it may improve education and care quality for future patients.

8.3 Potential Benefits to Others

Information from this study is expected to contribute to the understanding of how to optimally return genomics results to cancer patients and to better communicate important genomics concepts to patients. This information may be especially important as rates of genomic testing increase without proportional increases in clinicians to return these results.

8.4 Alternatives to Participation

Patients can choose not to participate, and this will not impact their medical care at City of Hope in any way.

8.5 Informed Consent

The PI or IRB-approved named designate will explain the nature, duration, purpose of the study, potential risks, alternatives and potential benefits, and all other information contained in the informed consent document. In addition, they will review the experimental subject's bill of rights and the HIPAA research authorization form. Research subjects will be informed that they may withdraw from the study at any time and for any reason without prejudice, including as applicable, their current or future care or employment at COH or any other relationship they have with COH. Research subjects will be afforded sufficient time to consider whether or not to participate in the research.

8.6 Registration into Clinical Trails On-Line system

All participants of this study will be registered into OnCore at COH for this trial.

8.7 Participant Withdrawal from Research

At any time after signing the informed consent document, participants may elect to withdraw from participation in this protocol as follows: A participant may (1) withdraw from future study activities but permit clinical data collection to continue, (2) withdraw from future study activities and disallow the collection of clinical data, (3) remain amenable to study activities but disallow retention of PHI data, or (4) elect to withdraw completely from the study whereby all data will no longer be made available for research. Participant withdrawal, including the nature of withdrawal, will be documented in the Master List which will be kept in a password-protected file, accessible only by authorized study staff using secure COH computers. The request to withdraw from studies will also be documented in the patient's medical record via Epic. If they do not wish to participate but are interested in exploring other options such as talking with their care team or a social worker, we will provide appropriate referrals.

8.8 Financial Obligations and Compensation

In the event of physical injury to a research participant resulting from research procedures, appropriate medical treatment will be available at the COH to the injured research participant, however, there are no plans to provide financial compensation. Such an event is extremely unlikely given the nature of the study activities.

The research participant will receive $25 for taking part in this study. For patients who choose to have an on-site study visit, we will also cover the cost of valet parking.

8.9 Confidentiality

The records related to subject identity will be kept in separate research files and will be accessible only to Principal Investigator and authorized study staff. Any information allowing identification of the subjects will not be included in any published report or any computerized records. Data will be presented as aggregate or group data. The principal investigator and study staff will be the only ones having access to the collected data. The results will not be available to insurance carriers or employers.

The confidentiality of each participant will be rigorously maintained using existing City of Hope standards. HIPAA and state/federal government regulations for protecting patient privacy and security will be strictly observed. Researchers and staff who are not authorized to see PHI will be blocked from viewing PHI following HIPAA guidelines using role-based access controls. For example, unauthorized web app developers will not be allowed to view PHI.

No patient or subject identifiable information will be given to third parties, including family members, unless that subject has given written or witnessed consent to do so. The results of research studies may be published but subjects will not be identified in any publication.

9.0 DEVIATIONS

A deviation is a divergence from a specific element of a protocol and that occurred without prior IRB approval. Deviations from the approved protocol should be avoided, except when necessary to eliminate an immediate hazard to a research participant. A Corrective and Preventative Action (CAPA) plan should be developed by the study staff and implemented promptly to avoid similar issues in the future. All deviations from the protocol must be documented in study source documents and promptly reported to the DSMC and IRB.

9.1 Reporting Deviations

Investigators may deviate from the protocol to eliminate immediate hazards for the protection, safety, and well-being of the study subjects without prior IRB approval. For any such deviation, the PI will notify the DSMC and IRB, within 5 calendar days of its occurrence by electronic submission of a Deviation Notice via iRIS.

9.2 Single Subject Exception (SSE) Amendment Request

Deviations from the written protocol that are not done to eliminate an immediate hazard(s) for the protection, safety and well-being of study subjects but may increase risk and/or alter the protocol integrity require prior IRB approval. The deviation is submitted as a Single Subject Exception (SSE) amendment request. An IRB approved SSE does not need to be submitted as a protocol deviation to the DSMC. The SSE should be submitted according to the IRB guidelines and COH Institutional Deviation Policy and submitted via iRIS. A deviation that is not an SSE (i.e., discovered

after the occurrence) must be reported to the COH DSMC and IRB according to the COH Institutional Deviation Policy and submitted via iRIS.

The main risk to participants is the potential loss of confidentiality. Participants will be assigned a unique study identification number that will be stored separately from personal identifiers. Study materials will be marked with these numbers but no other identifying information. All data will be stored on password-protected computers. Access to data containing personal identifiers will be secured with a password filing system and will be restricted to authorized study staff. All study cabinets and computer databases will be secured in offices that are locked when not in use. No data regarding individuals' responses will be provided to any third party or to study participants. Any paper records will be kept in locked file cabinets for 1 year after paper publication and then destroyed.

Another risk of this study is that participants may feel upset when answering study-related questions. If they feel upset during the surveys, they can stop participating at any time or choose not to answer any question for any reason. As noted in section 7.0, if the participant feels upset and would like referral for psychological counseling, the principal investigator will provide them with a referral to a mental health professional/social worker at City of Hope as appropriate.

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11.0 APPENDICES

Appendix A: Physician Patient-Specific Recruitment Letter

Helping Oncology Patients Explore- Genomics (HOPE- Genomics) Web Tool Randomized Clinical Trial

[DATE]

Dear Dr. [PHYSICIAN LAST NAME],

We are writing to you because your patient, [PATIENT NAME, MRN], is eligible for participation in the HOPE-Genomics research study involving a web-based, patient-facing genomic education tool.

Please let us know if this is incorrect, or if you do not feel that this patient would be a good fit for our research study. We plan to otherwise approach your patient at a future clinic appointment or via email/mail/phone if we do not hear back from you over the next 24 hours. Please refer to the bottom of this email for the eligibility criteria of this study.

IF YOU DO NOT WISH FOR US TO CONTACT THIS PATIENT, PLEASE LET US KNOW. We will otherwise proceed with approaching him/her.

Note: If your patient enrolls in the study, your patient will have access to the HOPE-Genomics tool with HIS/HER genomic test results approximately 3 days after the results become available in EPIC.

For more information or questions about the study please contact the study Principal Investigator, Stacy W. Gray, MD, AM, or the Clinical Research Coordinator, Marilan Luong at 310-218-1539.

We look forward to hearing from you!

Thanks so much,

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

[INSERT PATIENT NAME] is eligible because [HE/SHE]:

- Is receiving somatic, germline or paired somatic/germline sequencing through COH IRB 07047
- Has a cancer diagnosis
- Has an ECOG performance status of 0-2, and
- Is fluent in English

Appendix B: Patient Invitation Letter

[DATE]

Dear [PATIENT NAME],

This is the HOPE-Genomics Team at City of Hope. You may have received a phone call from [consenter] about participating in our study, involving new ways to teach patients about cancer and genomic testing at City of Hope. You have been selected to participate in our study because you have or had been diagnosed with cancer and are undergoing initial genomic testing.

In this study, we will be testing the effectiveness of a web-based, genomic education web-app. The goal of this work is to understand the best ways to communicate genomic findings to patients. In this study, we will be asking patients to fill out a short 10-minute survey about cancer, genetics, and what they understand about their cancer. We will then follow up with you at 4 additional time points in the next 9 months and ask you to complete a survey at those times. The surveys will ask about your reactions to viewing the web-app, receiving your genomic test, your knowledge about cancer and genetics, and any changes to your medical care that may have resulted from your test. All patient participants will receive a $25 gift card as a “thank you” for their participation.

We would like to make sure that cancer patients understand this type of information because doctors and patients often use this information to help find the right cancer care. Your participation in this study would be completely voluntary and there is no obligation to participate. Entry into this study will not involve any treatment. The study is confidential and your responses to survey questions will not be passed along to your medical provider or anyone outside of the study team.

[FOR PAPER INVITATION:] If you are interested, please let us know by completing the enclosed interest postcard and mailing it back to us. We will then send you an online survey link or a paper survey with a return envelope. If you are not interested in participating, please let us know by mailing back the enclosed interest postcard with your response.

[FOR REMOTE RECRUITMENT:] If you are interested, please email HOPEGenomics@coh.org or call [INSERT CRA’s COH PHONE NUMBER] to complete consent over the phone.

If you have any questions about this research study, please call the Principal Investigator, Stacy W. Gray at 626-218-8662, or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you so much,

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road

Duarte, CA 91010

Appendix C: Patient Invitation Phone Script

Hello, my name is [CRA NAME] and I am a clinical research assistant at City of Hope. Is there a [(Mr. Ms) PATIENT NAME] here?

Hi [(Mr. Ms) PATIENT NAME] You may recall recently consenting to receive genetic testing through City of Hope's Precision Medicine Program. Does that sound familiar?

IF YES: I am part of a research team in the genetics department at City of Hope and I am reaching out to you because my team and I are hoping that you will be willing to participate in a research study in which we are looking at new ways to show genomic information to City of Hope patients that will hopefully better explain what their genetic test results mean. We'd like to tell you more about the study and next steps. Is this a good time to talk?

[IF NO: thank them and schedule a time to call back]

IF YES: You were selected to participate in our study because you have/had been diagnosed with cancer and are having genomic testing through the City of Hope Precision Medicine program . In the current study, we are evaluating new ways of showing genomic information to City of Hope patients. We want patients like you to be able to access their test results in a patient-friendly way, so we have developed a web-based cancer tool, called HOPE-Genomics, which educates patients about their genomic test results and provides patient and their family with helpful resources. In this study, we want to show patients this tool and then get their feedback through five short surveys over the span of 12 months. Each survey takes at least 15-30 minutes to complete. This study does not involve any treatment for you; it is purely feedback-based. Although we cannot pay you for participating in the study, we would like to reimburse you for your time with three gift cards totaling $25 over the span of the study. Your participation in this study would be completely voluntary and there is no obligation to participate. Is this something you would be interested in?

[If Yes go to **3a**]

[IF NO: thank them for their time and end call]

IF YES: Great! In order to participate, we need to go over the study details and receive your verbal consent for participation. Is this a good time to complete the consent? It should take 10-15 minutes. [IF YES: complete verbal consent with patient and let them know about next steps; IF NO: thank them and schedule a time to call back.]

Appendix D: Patient Reminder Letter

[DATE]

Dear [Patient Name],

This is the HOPE-Genomics Team at City of Hope. A few weeks ago, we contacted you inviting you to participate in a research study involving new ways to teach patients about cancer and genomic testing at The City of Hope Comprehensive Cancer Center. We are contacting you because we have not received a response regarding your interest in participating in this study.

In this study, we will be testing the effectiveness of a genomic education web-app. The goal of this work is to understand the best ways to communicate genomic findings to patients. In this study, we will be asking patients to fill out a 25-minute survey about cancer, genetics, and what they understand about their cancer. We will then follow up with you at 4 additional time points in the next 9 months and ask you to complete a survey at those times. The surveys will ask about your reactions to viewing the tool, receiving your genomic test, your knowledge about cancer and genetics, and any changes to your medical care that may have resulted from your test. All patient participants will receive a $25 gift card as a “thank you” for their participation.

We would like to make sure that cancer patients understand this type of information because doctors and patients often use this information to help find the right cancer care. Your participation in this study would be completely voluntary and there is no obligation to participate. Entry into this study will not involve any treatment. The study is confidential and your responses to survey questions will not be passed along to your medical provider or anyone outside of the study team.

[FOR PAPER INVITATION:] If you are interested, please let us know by mailing back the enclosed postcard. Alternatively, you can also email HOPEGenomics@coh.org or call [CRA’S COH PHONE NUMBER] to complete consent over the phone. We will then send you an online survey link or a paper survey with a return envelope. If you are not interested in participating, please let us know by responding to this email or mailing back the enclosed interest postcard with your response.

[FOR REMOTE RECRUITMENT/EMAIL:] If you are interested, please email HOPEGenomics@coh.org or call [CRA’S COH PHONE NUMBER] to complete consent over the phone. We will then send you an online survey link or a paper survey with a return envelope.

If you are not interested, please let us know. If you have any questions about this research study, please call the Principal Investigator, Stacy Wang Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539.

You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you so much,

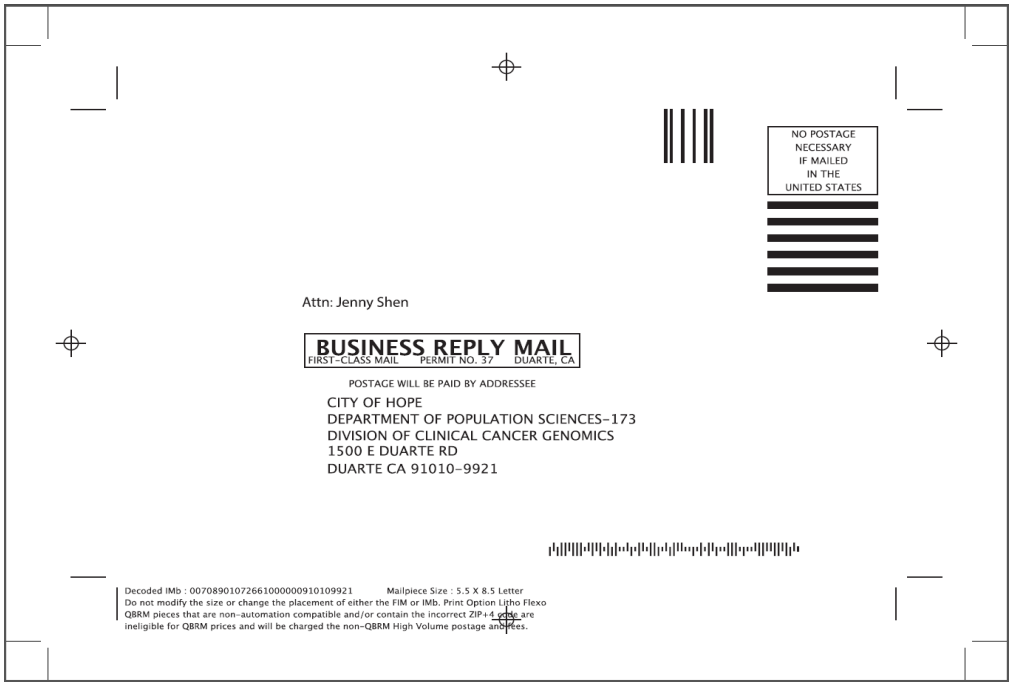
The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano

Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

Appendix E: Patient Interest Postcard

Front of postcard:



Back of postcard:

Study ID: _____

If you are not interested in participating, please check off the box below and mail this postcard back. Thank you!

I have received and reviewed the information related to the HOPE study.

☐ I am interested in participating. Please contact me to discuss the study.

☐ I am not interested in participating. Please remove my name from the contact list.

Appendix F: Patient Verbal Consent Phone Script

Hello, my name is [CRA NAME] and I am a clinical research assistant at City of Hope. Is there a [(Mr. Ms) PATIENT NAME] here?

Hi [(Mr. Ms) PATIENT NAME], is now a good time to talk?

[IF NO: *schedule a time to talk to patient*]

[IF YES] I am reaching out to you today because you recently expressed an interest in participating in our HOPE-Genomics study, which explores new ways of teaching patients about their cancer and genomic testing at City of Hope. Does this sound familiar?

[IF NO] That's okay, I can provide you with a quick summary.

You received information about the study in an email, in the mail, by phone, or from a clinical research assistant during one of your clinic visits. As previously explained, we are looking at new patient-friendly ways of showing genomic information to patients at City of Hope that will hopefully better explain what their genetic test results means. One of these methods is a web-based cancer tool we have developed for patients, called HOPE-Genomics, which educates patients about their genomic test results and provides patients with helpful resources. We will be asking patients to complete five short surveys about their knowledge of cancer and genomic testing over the span of twelve months. Does this sound familiar?

[IF STILL NO] thank them and end the call.

Start here if right after phone invitation script: [IF YES]

Great. First, thank you so much for expressing interest in participating in our study. I am contacting you today to briefly go over what your participation would entail in this study, your rights as a research participant in this study, answer any questions you may have, and then document your consent to participate. We will also talk about next steps in the study, if you decide to participate. If you have any questions along the way, feel free to stop me. I will also be (emailing/mailing) you the complete consent form after our conversation, which will elaborate further on everything we discuss today. Do you have any questions for me before we begin?

[IF YES, answer questions before moving on]

> If you agree to participate in this study, you will be randomly placed into 1 of 3 study groups. Randomization means that you will be put into a group by chance, like pulling a number out of a hat. Depending on the group you are randomly placed into, you will view the HOPE-Genomics tool at different time intervals during your participation in this study. Regardless of which group you are placed in, you will participate in:

- 5 brief surveys within the next 12 months. Each survey will take at least 15-30 minutes to complete. These surveys will ask you questions about cancer, genomics, and what you understand about your cancer and genomic testing results. Although we would love for you to complete the survey in full, we do understand that some questions may be difficult for you to answer. If so, you have the option to skip questions you are not comfortable answering and/or you do not know the answer to by selecting the “do not know” option.
    - Please keep in mind that although you are considered to be "on-study" for 12 months, this does not mean we will require your active engagement each month. I will go into more detail of when you will be asked to actively participate and will provide you with a calendar so that you can better understand when those time points will be.
- You will be asked to use an online cancer tool we have developed. Depending on the group you are placed into, you may be asked to use the tool one time or two times. This may occur at any time during the 12-month span of the study. Our study team will provide you with login information so you can view the tool’s education and resources on your own time.
- We are also asking your permission to review your medical records so that we can learn about your health, the care you are receiving at COH, and about the genomic testing that you have had, if any.

As I mentioned before, we truly appreciate the time and feedback you will be giving to this study, so we will be providing you with three gift cards totaling $25 over the span of the study. You will receive a $5 gift card after completing your third survey, a $10 gift card after completing your fourth survey, and another $10 gift card after completing your fifth survey.

I would like to remind you that your participation in this research study is completely voluntary. You are free to withdraw your consent for participation at any time without penalty. Choosing not to participate will not affect your ability to receive care at City of Hope.

You may benefit directly from participation in this study by learning more about cancer genomics, your genomic testing results and an understanding of the genetic make-up of your cancer and normal cells. In addition, patients in the future may potentially benefits from the knowledge gained from your participation.

All information learned from this study will be kept confidential and secured in the principal investigator’s office. We do not share any of your information with outside parties or third parties. If, despite our best efforts, identifying information about you is released, it could negatively impact you. However, this risk is small.

I know I just shared a lot of information with you. To summarize, you will be completing 5 surveys over the span of 12 months and will be viewing the online tool at designated times. Do you have any questions or concerns regarding the tasks you are being asked to complete over the next 12 months?

Do you think you have the time to participate in this study? There is no pressure to say “yes.”

For documentation purposes, Do you consent to participate in the HOPE-Genomics Study?

[IF NO] Thank them for their time and participation thus far. Rest assured that all the information they provided for this study will be removed.

[IF YES] Great! Thank you so much for joining our study. As a next step in participation, we will be sending you a brief initial survey that will ask you a little about yourself, if you have had genomic testing in the past, and about genomics in general. We can email you a link to complete the survey electronically, or we can provide you with a hard copy of the survey. Which is more convenient for you?

[IF EMAIL] Great. Can you please confirm your email address with me?

[TEXT MESSAGING] Additionally, you have the option to receive updates related to study participation and to receive survey links via text message (standard text messaging rates will apply). Your decision to receive text message notifications is entirely voluntary. If you decide to receive text messages, you may decide at any time that you no longer want to receive them and may cancel by contacting the HOPE-Genomics study team. Your decision to use the service will not affect your ability to take part in this study.

Texting over mobile phones does carry security risks because text messages are not encrypted. This means that information you receive by text message could be intercepted or viewed by an unintended recipient or by your mobile phone provider or carrier. To minimize risks, the messages will not identify you individually and will not include any reference to your course of care at City of Hope. We will not disclose your mobile phone number to anyone outside of this study without your prior permission and consent. If you decide to opt-in for the text message reminders, you may receive:

- Reminder messages to complete a study procedure (e.g., viewing the platform or completing a survey) (up to 5 messages per study activity)
- Messages with unique survey links (up to 5 messages, total)

The cost of messages will vary depending on your mobile carrier and on your per message transaction cost. You can consult your mobile carrier regarding your per message transaction cost.

Would you like to opt-in to receive text message reminders at this time? You can also make the decision later on by contacting our research team. Please take as much time as you like to decide. [Record answer if given: Yes/No]

[IF YES] Can you please confirm the mobile phone number you would like to receive the reminder messages at?

[IF HARD COPY]: Sounds good. Because mailing can cause delays in the study, we would be happy to meet you at an upcoming clinic visit to provide you with a hard copy directly. Or we can schedule a time to complete the survey over the phone together and then mail you a hard copy of the survey for your records. Are either of those options convenient for you?”

I will send you the survey right after this meeting. We ask that you please complete the first survey at your earliest convenience, ideally within the next two days. As I mentioned earlier, I will be emailing/mailing the complete consent form to you after our meeting which goes into greater detail on what we discussed today. You don’t need to sign it. It is just for your records and reference. I will also

be sending you a calendar outlining when you can expect to look at the HOPE Genomics tool and complete surveys over the next 12 months. If at any point there are any life events, such as vacations or medical treatment that will impede you from completing study activities, please let me know so we can best accommodate to your schedule. You can expect a few calls from me over the next few weeks to check in with you. Is there an ideal time that you would like me to call? [Make note of time]

Do you have any last-minute questions for me? If any additional questions arise, feel free to reach out to our team at any time. Our contact information is in the consent form, and I will also include it in the follow-up email after this meeting.

Appendix G: Patient Script to Setup Access to HOPE-Genomics tool – RoR + Intervention Arm

Dear [PATIENT NAME],

This is the HOPE-Genomics Team from City of Hope. You may remember speaking with [consenter] about your participation in the HOPE-Genomics study, involving a web-based education tool for patients with genetic testing at City of Hope. Thank you for completing your first survey for the study!

At this time, we would like to invite you to log into and view the HOPE-Genomics before your results are ready. The tool contains helpful information, including a video, that explains the details of genomic testing and its implications for your health. You may log into the tool by clicking the following link: **https://hopegenomics.coh.org/login**.

Once you have viewed the tool, we will send you a follow-up survey. We have also attached instructions on how to access the tool.

If you have any problems accessing the tool, we can accommodate in-person visits at City of Hope Duarte campus or remote visits using web conferencing (i.e. Zoom). Please call [INSERT CRA's PHONE NUMBER] or email us at HOPEGenomics@coh.org if you would like to schedule an appointment to speak with study staff.

If you have any additional questions about this research study, please call the Principal Investigator, Stacy Wang Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you for all your help with our research at City of Hope, and we look forward to hearing from you!

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

Appendix H: Patient Script to Invite Viewing of Tool w/ Results – Either Intervention Arm

Dear [PATIENT NAME],

This is the HOPE-Genomics Team at City of Hope. You may remember speaking with [consenter] about your participation in the HOPE-Genomics study, involving a web-based education tool for patients with genetic testing at City of Hope. Thank you for completing your first two surveys for the study!

At this time, we would like to invite you to log into the tool to view your genetic test results. You may log into the tool by clicking the following link: https://hopegenomics.coh.org/login.

Once you have viewed the tool, we will send you a follow-up survey. We have also attached instructions for viewing the tool.

If you have any problems accessing the tool, we can accommodate in-person visits at City of Hope Duarte campus or remote visits using web conferencing (i.e. Zoom). Please call [INSERT CRA'S PHONE NUMBER] or email us at HOPEGenomics@coh.org if you would like to schedule an appointment to speak with study staff.

If you have any additional questions about this research study, please call the Principal Investigator, Stacy Wang Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you for all your help with our research at City of Hope, and we look forward to hearing from you!

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

Appendix I: Baseline Survey Invitation Letter

Dear [PATIENT NAME],

This is the HOPE-Genomics Team at City of Hope. You may remember speaking with [consenter] recently about your participation in the HOPE-Genomics study. Thank you for your willingness to participate in our research study involving new ways to teach patients about cancer and genetics. It was a pleasure speaking with you!

As we discussed, the first step in the study is to complete a survey about yourself, your cancer care, and your understanding of genetics. This survey takes at least 15-30 minutes to complete. Please complete the following survey, using the provided study ID: [INSERT REDCAP STUDY ID].

[For REDCap]. You can access the baseline survey at this link: [LINK]

[PAPER ONLY]. Please complete the attached baseline survey and mail it back to us in the enclosed self-addressed return envelope.

We have attached two documents to this letter: (1) a pamphlet with information about genomic testing, and (2) an information sheet with further details about the HOPE-Genomics study.

Participation in this study will not involve any treatment. The study is confidential and your responses to survey questions will not be passed along to your medical provider or anyone outside of the study team.

If you have any questions about this research study, please call [CONSENTER'S NAME] at [INSERT CONSENTER'S PHONE NUMBER], or the Principal Investigator, Stacy W. Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you so much,

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

Appendix J: Pre-Test Survey Invitation Letter

Dear [PATIENT NAME],

This is the HOPE-Genomics team at City of Hope. You may remember speaking with [consenter] recently about your participation in the HOPE-Genomics study. Thank you for completing your first survey!

In preparation for your genomic testing, you may have received education materials and/or resources about cancer and genomic testing. The next step in the study is to complete a survey about your knowledge of genetics. The survey should take approximately 10 minutes. Please complete the following survey, using the provided study ID: [INSERT REDCAP STUDY ID].

[For REDCap]. You can access the pre-test survey at this link: [LINK]

[PAPER ONLY]. Please complete the attached survey and mail it back to us in the enclosed self-addressed return envelope.

Participation in this study will not involve any treatment. The study is confidential and your responses to survey questions will not be passed along to your medical provider or anyone outside of the study team.

If you have any questions about this research study, please call [CONSENTER'S NAME] at [INSERT CONSENTER'S PHONE NUMBER], or the Principal Investigator, Stacy W. Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you so much,

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

Appendix K: Follow-Up Survey Invitation Letter (10 day/3 month/9 month for Intervention Arms)

Dear [PATIENT NAME],

This is the HOPE-Genomics team at City of Hope. You may remember speaking with [consenter] recently about your participation in the HOPE-Genomics study. Thank you for viewing your genomic test results in the HOPE-Genomics tool for patients at City of Hope!

To help us make this tool the best it can be, we would love to hear your thoughts. There will be 3 follow-up surveys, approximately 10 days, 3 months, & 9 months after receiving your genomic test results. This is the [SURVEY NAME]. This survey will ask you about cancer, genetics, and what you understand about your genetic testing results and cancer. The survey may also ask you about your experience viewing your test results in the HOPE-Genomics tool. Some of the questions may look familiar from an earlier survey. We would like you to complete this survey as well.

[For REDCap]. You can access the [SURVEY NAME] online by using this link: [LINK]. Please complete the survey, using the provided study ID: [INSERT STUDY ID].

[PAPER ONLY]. Please complete the attached survey and mail it back to us in the enclosed self-addressed return envelope.

After completing this survey, you will be provided with a INSERT 5/$10] gift card as a thank you for your time and feedback.

Participation in this study will not involve any treatment. The study is confidential and your responses to survey questions will not be passed along to your medical provider or anyone outside of the study team.

If you have any questions about this research study, please call [CONSENTER'S NAME] at [INSERT CONSENTER'S PHONE NUMBER], or the Principal Investigator, Stacy W. Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you so much,

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
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Department of Population Sciences

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1500 E. Duarte Road
Duarte, CA 91010

Appendix L: 10-Day Follow-Up Survey Invitation Letter (10 day/3 month/9 month for Usual Care Arm)

Dear [PATIENT NAME],

This is the HOPE-Genomics Team from City of Hope. We are reaching out to you because you recently received your genomic test results from your healthcare provider at the City of Hope Comprehensive Cancer Center. Thank you very much for expressing interest in providing feedback about your experience through a follow-up survey!

We would love to hear your thoughts on receiving your genomic test results. There will be 3 follow-up surveys, approximately 2 weeks, 3 months, & 9 months after receiving your genomic test results. This is the [SURVEY NAME]. This survey will ask you about cancer, genetics, and what you understand about your genetic testing results and cancer. Some of the questions may look familiar from an earlier survey. We would like you to complete this survey as well.

[For REDCap]. You can access the 10-day follow-up survey by clicking this link. [LINK]. Please complete the survey, using the provided study ID: [INSERT STUDY ID].

[PAPER ONLY]. Please complete the attached survey at your earliest convenience and mail it back to us in the enclosed self-addressed return envelope.

After completing this survey, you will be provided with a INSERT 5/$10] gift card as a thank you for your time and feedback.

Participation in this study will not involve any treatment. The study is confidential and your responses to survey questions will not be passed along to your medical provider or anyone outside of the study team.

If you have any questions about this research study, please call [CONSENTER'S NAME] at [INSERT CONSENTER'S PHONE NUMBER], or the Principal Investigator, Stacy W. Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you so much,

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
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Department of Population Sciences

City of Hope Comprehensive Cancer Center
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Duarte, CA 91010

Appendix M: Patient Script Inviting Remote Tool Viewing w/ Test Results

Hello, my name is [YOUR NAME] and I am a clinical research assistant at City of Hope is there a [(Mr. Ms) PATIENT NAME] here?

Hi Mr/Ms. [PATIENT NAME]. I am reaching out to you because you recently agreed to participate in our HOPE-Genomics study, in which patients are receiving and reviewing their genetic test results through our HOPE-Genomics App or website. Does this sound familiar?

[IF NO] That's okay, I can provide you with a quick summary.

For this study you were approached by me or another clinical research assistant either in clinic or via phone to be consented in a study, that your physician or genetic counselor may have mentioned to you in your appointment. For this study we are testing our HOPE-Genomics app or website with patients to help patients review their genetic test results. After this initial consent, you may have completed a survey about cancer and genetics at the clinic or chosen to complete it at home on paper or through a survey link. Does this sound familiar?

[IF STILL NO] thank them and end the call.

[IF YES] Great. First, thank you very much for participating in our study. I am contacting you because the next phase of your participation in the study is to review your genetic tests results via our tool. Did you receive your login information via email?

[IF NO] That's okay, I can provide you with that information now.

[PROVIDE LOGIN INFORMATION]

[IF YES]

Have you had an opportunity to view the tool?

[IF NO]

Are you having any trouble accessing the tool?

[IF YES]

We would be happy to assist you troubleshoot this issue now. Do you have a few minutes to do so now?

[IF NO]

I would be happy to schedule an appointment to discuss this in the next few days. Unfortunately, we have had some recent procedural changes at our institution due to COVID-19, which limit our ability to meet with patients in person. As such, we are primarily meeting with patients via web conference (i.e. Zoom) or phone. Would you like to schedule a time to meet with one of our study staff?

[IF YES]

Great! Thank you so much for accommodating us. [SCHEDULE TIME]

[IF NO] Thank them for the participation thus far and let them know that unfortunately we cannot continue with the study unless they have access to the tool. Rest assured that all the information you provided for this study will be removed.

If you have any questions about this research study, please call me at [INSERT CRA'S PHONE NUMBER], or the Principal Investigator, Stacy Wang Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Appendix N: Patient Incentive Letter

[DATE]

Dear Mr./Ms. [LAST NAME],

This is the HOPE-Genomics Team from City of Hope. We are writing to you because you recently received your genomic testing results and completed a follow-up survey as part of our research study at the City of Hope Comprehensive Cancer Center. Thank you so much for participating – your feedback has been very helpful thus far!

Enclosed, please find your [INSERT $ AMOUNT] gift card as a thank you for your participation so far.

If you have any questions about this research study, please call [CONSENTER'S NAME] at [INSERT CONSENTER'S PHONE NUMBER], or the Principal Investigator, Stacy W. Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you very much again for your participation!

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

Appendix O: Patient Knowledge Answers & Genomic Information Letter

[DATE]

Dear [Patient Name],

This is the HOPE-Genomics Team at City of Hope. We are writing to you because you recently participated in our research study at The City of Hope. In the research study we are developing ways to teach patients about cancer and genomic testing. For this study, you completed a short survey about cancer and genetics. Thank you so much for participating – your responses have been very helpful!

On your survey, you indicated that you would like to receive information on cancer genomic testing, as well as the correct answers to the survey questions about genetics. In the enclosed package, we are including both an information sheet that has resources and links for cancer genomic testing, as well as a copy of the correct answers for the genetics questions from the survey.

If you have any questions about this research study, please call [CONSENTER'S NAME] at [INSERT CONSENTER'S PHONE NUMBER], or the Principal Investigator, Stacy W. Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you very much again for your participation!

The HOPE-Genomics Team
Dr. Stacy Gray, Marilan Luong, Madeline Currey, Sarah Labib, and Vanessa Lozano
Division of Clinical Cancer Genomics
Medical Oncology and Therapeutics Research
Department of Population Sciences

City of Hope Comprehensive Cancer Center
1500 E. Duarte Road
Duarte, CA 91010

Information on Cancer Genomic Testing

What is cancer genomic testing?
Genomic testing is the process of looking closely at your genes. Genes are the instructions to make everything in our bodies work. Some genes can tell us how tall we will be or our eye color. Other genes help us fight cancers. Genes are made up of an instructional code, called "DNA".

Your doctor might order cancer genomic testing from two places (and sometimes, both!):

1. **Cancer cells (i.e. DNA from a tumor)**. These usually come from a biopsy sample. Looking at genes from your cancer cells can help your medical team find more options, and/or understand the prognosis (forecast or likely course of your cancer).

2. **Normal cells (i.e. DNA from non-cancer cells).** These usually come from a blood sample or cheek cells. Testing these can clarify if your family members may be at higher risk for cancer, and help you and your care team figure out how to potentially reduce cancer risk for yourself and your family members.

When testing either cancer or normal cells, it is possible it may not find helpful information, and at times may not work. It is up to you and your care team to decide if testing is right for you, and what types of testing might be helpful.

The following are general questions about cancer and genetics	
1. Cancer is uncontrolled cell growth.	True
2. All cancers are aggressive.	False
3. Cancer is caused by a combination of inheritance, environmental, and lifestyle factors.	True
4. Hereditary (inherited within families) forms of cancer are common.	False
5. Any genetic change within a cell will give rise to cancer.	False
6. Cancers are usually caused by a change to a single gene.	False
7. All cancers have the same gene changes.	False

The following questions ask about how genetic testing can be used in cancer care. **In general, genetic testing can be used to…**	
8. Confirm a cancer diagnosis (tell where in the body a cancer started)	True
9. Find out the cancer "stage" (for example, stage I or stage IV)	False
10. Help select a cancer treatment	True
11. Determine exactly when a person will develop cancer.	False
12. Help predict if a cancer treatment will work.	True

13. Help select a research study (clinical trial)	True
14. Help to confirm if a cancer treatment is working.	True
15. Find out where cancer is located in the body (for example, in the lung or colon)	False
16. Help predict if a person has a better or worse than average outlook (prognosis) than other patients who have the same type of cancer	True
17. Find out if the cancer has spread beyond where it started in the body	False
18. Find out if a person's family members might have an increased risk of developing cancer	True
19. Help predict the chances that the cancer will come back after treatment	True
20. Find out if a person has an increased risk of developing cancer	True
21. Find out if a person (and possibly their family members) have a higher risk of developing a health condition **other than cancer** (for example heart disease or high cholesterol).	True

The following questions ask about your understanding of the differences between genetic testing in CANCER CELLS and NORMAL CELLS.

22. Finds gene changes that a patient was born with	Normal Cells
23. Finds gene changes that have happened over a patient's lifetime	Cancer Cells
24. Can be used to help select a cancer treatment for a patient	Both
25. Can reveal information about a patient's risk of developing cancer in the future	Both
26. Finds gene changes that are NOT inherited and that cannot be passed from parents to children	Cancer Cells
27. Can reveal results that have unknown health implications	Both
28. Commonly can suggest health risks for a patient's family members	Normal Cells

Genes	29. Genes are made of DNA	True
	30. Genes affect health by influencing the proteins our bodies make	True
	31. All of a person's genetic information is called his or her genome.	True
	32. A person's genes change completely every 7 years.*	False
	33. The DNA in a gene is made of four building blocks (A, C, T, and G).	True

	34. Everyone has about 20,000 to 25,000 genes.	True
Genes and health	35. Gene variants can have positive effects, harmful effects, or no effects on health.	True
	36. Most gene variants will affect a person's health.*	False
	37. Everyone who has a harmful gene variant will eventually have symptoms.*	False
	38. Some gene variants have a large effect on health while others have a small effect.	True
	39. Some gene variants decrease the chance of developing a disorder.	True
	40. Two unrelated people with the same genetic variant will always have the same symptoms.*	False
How genes are inherited in families	41. Genetic disorders are always inherited from a parent.*	False
	42. If only one person in the family has a disorder it can't be genetic.*	False
	43. Everyone has a chance for having a child with a genetic disorder.	True
	44. A girl inherits most of her genes from her mother while a boy inherits most of his genes from his father.*	False
	45. A mother and daughter who look alike are more genetically similar than a mother and daughter who do not look alike.*	False
	46. If a parent has a harmful gene variant, all of his or her children will inherit it.*	False
	47. If one of your parents has a gene variant, your brother or sister may also have it.	True
Whole Exome Sequencing	48. Whole exome sequencing can find variants in many genes at once.	True
	49. Whole exome sequencing will find variants that cannot be interpreted at the present time.	True
	50. Whole exome sequencing could find that you have a high risk for a disorder even if you do not have symptoms.	True
	51. Your whole exome sequencing may not find the cause of your disorder even if it is genetic.	True
	52. The gene variants that whole exome sequencing can find today could have different meanings in the future as scientists learn more about how genes work.	True
	53. Whole exome sequencing will not find any variants in people who are healthy.	False

Resources

Cancer Genomics

What is Cancer Genomics? (NIH):
https://cancergenome.nih.gov/cancergenomics/whatisgenomics/whatis

- Has video explaining genetic basis of cancer

- Has links to Cancer Genomics Overview and Research

American Cancer Society Genetics and Cancer: https://www.cancer.org/cancer/cancer-causes/genetics.html

Medical Genetics 101: http://www.ashg.org/education/medical_genetics.shtml

General Support

Genetic Counseling

- National Society of Genetic Counselors: http://www.nsgc.org/page/aboutgeneticcounselors
- Find a Cancer Genetics Clinician (NIH): https://www.cancer.gov/about-cancer/causes-prevention/genetics/directory
- KinTalk: http://kintalk.org/
- My Family Health Portrait: https://familyhistory.hhs.gov/FHH/html/index.html

Cancer Therapy Evaluation Program (NIH): https://ctep.cancer.gov/default.htm

My Cancer Genome: https://www.mycancergenome.org/

CancerCare: https://www.cancercare.org/

ASCO Resources (fact sheets, planning, caregiving): https://www.asco.org/practice-guidelines/resources-patients

ACS Resources (diagnoses, treatment options): https://www.cancer.org/treatment.html

Appendix P: HOPE-Genomics Survey Script (Via Phone or Zoom)

Hello, my name is [CRA NAME] and I am a clinical research assistant with the HOPE-Genomics Team at City of Hope. Is there a [(Mr. Ms) PATIENT NAME] here?

Hi [(Mr. Ms) PATIENT NAME], I am reaching out to you today because you recently expressed an interest in completing your [INSERT SURVEY NAME] over [PHONE/ZOOM]. Is now still a good time to meet?

[IF NO: *schedule another time to talk to patient*]

[IF YES] Wonderful. Before we begin, I would like to mention a few points about the survey. We estimate that this will take approximately [INSERT TIME VALUE] to complete together.

The purpose of this survey is to get your feedback about your cancer care at City of Hope and what you understand about genomics. I am going to read the survey verbatim and record all the responses you provide. These responses will be kept confidential and identified only by a number. Please keep in mind that you are free to not answer any question in this survey, for any reason. As we go through the survey, please let me know if you have any questions or need clarification. This survey does include general questions about genetics and cancer. For these questions, please keep in mind that I cannot assist you selecting the correct answers.

Do you have any questions before we begin?

[AFTER ANSWERING ANY QUESTIONS]: *Proceed to read IRB-approved survey verbatim.*

Appendix Q: HOPE-Genomics Withdrawal Email Template

Dear Mr./Ms./Dr. [PATIENT'S NAME],

Thank you for letting us know about your decision to withdraw from the HOPE-Genomics study! We completely understand, and truly appreciate your interest in our study.

To document withdrawal and protect your personal information, City of Hope requires you to complete the attached withdrawal form at your earliest convenience. I have attached the form to this email, and I will also mail you a physical copy of the form with a return envelope.

You can either mail or scan the completed form back to us or schedule a time to complete the form with us over the telephone. Please let us know what is most convenient for you so we can facilitate the withdrawal process as soon as possible.

If you have any questions about completing the withdrawal form, please email HOPEGenomics@coh.org, or call the Principal Investigator, Stacy W. Gray at 626-218-8662 or the Clinical Research Coordinator, Marilan Luong at 310-218-1539. You can also reach the Institutional Review Board at City of Hope by calling 626-216-2700.

Thank you very much again for your participation!

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Appendix R: Patient Survey Link Text Message Script (Baseline/Pre-study/10 day/3 month/9 month for Intervention Arms)

Dear **[Insert Patient Name]**

This is the HOPE-Genomics Team from City of Hope.

This is a reminder to complete the **[Title of Survey]** at your earliest convenience**.**

You can access the survey by clicking this link **[insert link]** and entering the provided study ID: **[Insert patient study ID number].**

Appendix S: Setup Access to HOPE-Genomics toll – RoR + Intervention Arm Text Message Script

Dear **[Insert Patient Name]**

This is the HOPE-Genomics Team from City of Hope.

We would like to invite you to log into and view the HOPE-Genomics before your results are ready. The tool contains helpful information that explains the details of genomic testing and its implications for your health.

You may log into the tool by clicking the following link: https://hopegenomics.coh.org/login.

Once you have viewed the tool, we will send you a follow-up survey.

Appendix T: Patient Reminder to View HOPE-Genomics with Genetic Test Results Text Message Script

Dear **[Insert Patient Name]**

This is the HOPE-Genomics Team at City of Hope.

We would like to remind you to log into the HOPE-Genomics tool to view your genetic test results.

You may log in by clicking the following link: https://hopegenomics.coh.org/login.

Appendix U: Text-Message Opt-in for Previously Consented Subjects - Template for Email and Mailer

Dear **[Insert Patient Name]**

This is the HOPE-Genomics Team from City of Hope.

You are receiving this letter as a participant on the study, HOPE- Genomics Web Tool Randomized Clinical Trial**.**

We are writing to inform you of an update to the study's consent form. As part of this update, we have included an optional opt-in for patients who would like to receive text message reminders about study related tasks and to receive survey links directly to their mobile. Messages will not contain any information regarding course of care at City of Hope. Standard message and data rates may apply based on your mobile carrier.

Signing up for text message reminders is optional. Your decision will not risk and/or change your participation on this study.

If you would like to receive text message reminders, please email us at hopegenomics@coh.org. A member of the HOPE-Genomics Team will reach out to you by phone to provide more information.

Thank you for your willingness to participate in our research study involving new ways to teach patients about cancer and genetics!

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