Study Title: Video Intervention to Address Pre-Test Patient Education for Tumor Genomic Testing

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Objectives:
The primary goal of this project is to evaluate a series of videos to be used for pre-test education of patients who undergo tumor genomic testing (TGT) as part of their clinical care. We aim to test the impact of a concise, animated educational video to be used as a supplement to patient-provider discussion on patient understanding of TGT, including benefits, limitations, and possibility of incidental findings when doing TGT. We will compare results in four patient cohorts: 1) Ohio state University Comprehensive Cancer Center (OSUCCC) metastatic breast cancer patients; 2) OSUCCC lung cancer patients; 3) OSUCCC cancer patients of unspecified type; Bon Secours Mercy Health (BSMH) community cancer center cancer patients of unspecified type. The video addresses critical patient-identified and literature-reported education gaps prior to TGT.

Background and Rationale:

Somatic (tumor) next-generation sequencing (TGT) and cancer care

TGT has become increasingly adopted as part of standard cancer care for many cancers,[1] raising important ethical challenges regarding its use including uncertainty of applicability of results, incidental germline findings, and disparities around tumor genomic testing options.[2,3] It is critical to address these challenges now given the growing reliance on tumor NGS results for treatment-related decision-making in an increasingly large population of patients with cancer.

Patient education and tumor genomic testing

Professional guidelines state that treating oncologists should discuss with patients prior to testing the possibility of incidental germline findings and disease-specific limitations in clinical utility and interpretation of somatic (tumor) next generation sequencing (NGS) results.[5] However, oncologists have varied understanding of genetics and time limitations make it challenging for providers to adequately inform their patients about tumor NGS within the context of routine clinical care. As a result, pre-test education is often incomplete and has significant variability across providers resulting in inequitable care.

These challenges have been echoed by professional organizations and were highlighted by a policy statement released by the American Society of Clinical Oncology (ASCO),[5] which notes: "1) Oncology providers should communicate the potential for incidental/secondary germline information…before conducting somatic mutation profiling and should review potential benefits, limitations, and risks before testing; 2) Providers should carefully ascertain patient preferences regarding the receipt of germline information...This may require referral for additional counseling to help the patient clarify preferences; 3) ASCO supports research to determine how to best deliver pretest education, support patient preferences, and understand outcomes of providing incidental/secondary germline information with somatic testing."

Despite professional organization support, evidence suggests that national guidelines are not widely followed. We previously surveyed medical oncologists at Ohio State (unpublished), with response rate 77.5% (31/40). Providers frequently order tumor NGS: 67.7% obtain tumor NGS on >25% of patients. Providers frequently discuss tumor NGS benefits (87.1% counsel all patients on benefits), yet less frequently discuss limitations (58.0%). The potential of incidental germline findings is rarely discussed: <20% of providers discussed with all and 25.8% discussed with none of their patients. One possible explanation: 61.3% of providers feel they do not have enough time in a routine visit to provide adequate patient counseling. These data reveal marked gaps in patient education prior to tumor NGS among providers for the proposed study population.

Additionally, patients' understanding of genomics remains limited, particularly lower income and minority patients, and most patients are not informed regarding potential incidental germline findings.[6] This is not a trivial problem as incidental germline findings are surprisingly common. Among 1040 patients undergoing MSK-IMPACT tumor-normal NGS assay, 182 had actionable cancer susceptibility germline mutations, including 101 patients who would not have had these mutations detected using clinical guidelines.[7] In another study of 1000 patients of all cancer types, 2.3% patients had previously unrecognized pathogenic germline mutations in 19 cancer-related genes.[6] In our recent prospective decision analysis study,[8] 14/100 patients had alterations identified in BRCA1 (n=4), BRCA2 (n=8), or PALB2 (n=2). Of the patients with these alterations, 6/14 (42.8%) did not have prior knowledge of germline alteration. At our center, we confirm prior data of incidental germline findings in ~5% of patients

undergoing tumor NGS, reinforcing the importance of pre-test education regarding germline alterations prior to tumor NGS.

Our prior data also show that results of TGT can impact patients' outlook regarding likelihood of treatment success. In a published study that enrolled 100 participants with MBC, we found that patients whose treatment did not change based on tumor NGS had a significant decrease in confidence of treatment success (p=0.001).[8] Patients were overly optimistic: almost half believed tumor NGS would guide therapy while only 11.5% switched therapy based on tumor NGS,[8] similar to prior work.[9,10] The validated Trust in Physician/Provider Scale (TPS) – to be used in this study – was administered successfully, and notably, TPS did not significantly correlate with depression, anxiety, or self-efficacy, suggesting that this metric is not likely to be confounded by other patient psychological features. We demonstrate capacity to successfully complete prospective tumor NGS in the context of a clinical trial with completion multiple validated survey instruments.

Video interventions to address gaps in patient education around genetic/genomic testing

Effective communication is critical for patient-centered care but is complicated by low health literacy in the general population.[11] Genetic information in particular presents a challenge given complexity of the subject matter and gaps in understanding for patients[12] and providers.[13] In a previous study, we developed a 2-minute animated video to be used by patients to communicate their own germline BRCA mutation result to at-risk relatives (video available at [14]). We studied effectiveness of video message in a healthy unselected cohort to mimic the scenario of a relative (who was previously unaware of the family's genetic testing) receiving this information via video. Of 373 participants who viewed the video and completed pre-/post-viewing questionnaires, we saw a significant increase in video content-specific recall ($p<0.0001$) in all demographic categories and a positive association between intolerance for uncertainty and intent to pursue action related to cascade genetic testing ($p<.05$).[15]

The implementation of a video intervention that aids in educating patients about the utility and possible outcomes of tumor genetic testing in accordance with professional organization recommendations is feasible. With MSK-IMPACT, patients who desire germline DNA results receive pre-test genetic counseling via an IRB-approved video. (Hyman, 2015) Recently presented at ASCO 2020, Bradbury et al. show that a web-based video intervention increased patient understanding but did not significantly reduce anxiety, depression, or cancer-specific distress. (Bradbury, 2020)

Study communication aid: A video to address pre-test patient education for tumor genomic testing

To address ongoing gaps, we are developing a video intervention to address pre-test patient education for tumor genomic testing, accomplished through a previous protocol, "Assessment of and addressing the needs of diverse patient populations undergoing tumor next generation sequencing (NGS) as part of oncology care," (OSU IRB # 2021B0077). Through a series of focus groups or interview discussions, we identified patient-reported education gaps and concerns prior to tumor NGS testing by engaging diverse populations (sex, gender, race, ethnicity (if provided), age, insurance status/sociodemographic, cancer type).

Based on focus group data, ASCO-recommendations for pre-test education, and expert input from Cancer Genetics and Communications faculty, a concise animated video using plain language is in process, designed by OSU investigators and produced by Mills James Productions.. This video will be adapted into three separate educational videos for distinct patient populations: 1. Metastatic breast cancer-specific; 2. lung cancer-specific and 3. Tumor agnostic for delivery prior to tumor NGS. The rationale for the inclusion of three separate cohorts is to make possible a comparison of results between the groups. Clinically, the utility of tumor NGS in the breast cancer population and the lung cancer population differs, with a greater number of genomic alterations identifying potential therapies in lung cancer, and it's possible that the results in these cohorts will diverge. The information contained in the videos is identical with the exception of two sentences within which breast- and lung-specific information about the likelihood of treatment change based on tumor NGS is given. It's possible that these targeted statements will have no impact on the study outcomes, which is why we will test a tumor agnostic video in an unselected cancer population.

Objectives:

Primary Objective: To assess change in patient knowledge about tumor NGS following exposure to the video.

Hypothesis: Exposure to a brief educational video will increase patient knowledge about tumor NGS.

Secondary Objectives:

Secondary objectives include to assess changes following exposure to the video, including:
1) Genomic knowledge via the validated 10 true/false question survey (% correct out of 10);
2) 11-item Trust in Physician Survey (TPS) as a single TPS score;
3) Comparison of results in distinct patient cohorts: 1) Metastatic breast cancer; 2) lung cancer; 3) cancer of unspecified type; 4) cancer of unspecified type at community cancer centers

Hypotheses: Change in patient understanding about tumor NGS and trust in provider will vary based on baseline/demographic characteristics but also cohort/cancer type.

Exploratory Objective (only at patients enrolled at OSUCCC): Assess whether therapies prescribed as a result of tumor NGS achieved clinically favorable result through chart review.

Research Design:

Study Population

In this proposal, we will use a single IRB protocol to prospectively enroll patients with cancer undergoing clinical tumor NGS as part of standard-of-care disease management in fourclinical cohorts: Cohort 1. Metastatic breast cancer (MBC; n=50). Cohort 2: lung cancer (LC; n=50); Cohort 3. cancer patients of any tumor type (OC; n=50); Cohort 4, cancer patients of any tumor type at Bon Secours Mercy Health community cancer sites (BSMH, n=50).

At Ohio State, we manage >700 LC and >500 MBC patients annually, demonstrating sufficient patient volume to accrue. After enrollment but before video viewing (T1), a participant will complete the first study questionnaire, which assesses personal characteristics, tumor NGS-specific knowledge, genomic literacy/knowledge, tolerance for uncertainty, patient-provider trust, and attitudes about the information received and testing to be performed. Immediately following video viewing, participants will complete a post-counseling questionnaire (T2), which re-assesses the same knowledge components, patient-provider trust, and attitudes about the information received and testing to be performed. Participants will be asked to complete a post-genomic testing questionnaire (T3) after their tumor NGS result is available. When possible, this will occur during the clinic visit at which this is discussed and if not possible, the participant will be contacted after this clinical encounter takes place. T3 questionnaire will mirror the T2 questionnaire.

Eligibility criteria

Inclusion Criteria. Patients must have biopsy-confirmed cancer, be ≥18 years of age, and be undergoing clinical tumor or circulating tumor DNA NGS. This will be gender- and race-inclusive: we will include all races and ethnicities and both women and men, including male breast cancer patients (~1% of all breast cancers[16]). Exclusion Criteria: We will have both English- and Spanish video versions but in this initial study will exclude patients who are not English- or Spanish-speaking.

Study procedures

Eligible participants may be identified for invitation to participate in a video intervention session by study personnel, through provider nomination, or self-nomination (see flyer for oncology waiting areas). Study personnel will review clinic schedules on a weekly basis and maintain an accrual log to facilitate identification of eligible patients. Once eligible patients are identified and the study is introduced to them by their physician or his/her designee (e.g. nurse), study personnel will discuss the risks and benefits of the study with the subject. Recruitment will take place during the patient's regular clinic visit after patient has been informed by their provider that tumor NGS has been recommended. Once contact is established, study personnel will ask questions to assess eligibility.

Informed Consent Process

Subjects will have the option to complete the informed consent process on a secure electronic tablet or on paper. During the in-person consent process, patients will be consented by a member of the key study personnel who will oversee the use of the tablet and the completion of the live electronic signatures. Alternatively, a member of the key study personnel may oversee the completion of the paper format consent.

Electronic consenting
The participant consent encounter will be conducted using a REDCap-based electronic consent form. The consent form has been developed in REDCap, a secure, web-based, HIPAA-compliant, data collection platform with a user management system allowing project owners to grant and control varying levels of access to data collection instruments and data (e.g. read only, de-identified-only data views) for other users.

Subjects' signatures (and initials) may be obtained using a computer mouse or their finger in the appropriate fields on the consent form(s). The signature will also include the subject's typed/printed name and the date (and time where required). Upon completion of the consent, patients will receive a copy of the consent documents via:
- A hard copy of the completed consent form(s) that has been printed or copied in clinic
- An emailed copy of the completed consent form(s) which is sent to the subject's chosen email address

Survey measures

We will collect individual characteristics at T1 and four validated survey approaches at T1, T2, and T3. Surveys will be administered electronically in clinic on iPads reserved for the study. If a participant requires paper questionnaires or to complete the questionnaires outside of the clinical setting, accommodations will be made.

Incentives

All respondents to surveys will be offered a $10 gift card upon completion of each online survey. In total, each participant can receive up to $30 in incentive gift cards.

Data Analysis

Our primary endpoint will be message-specific knowledge/recall accuracy, measured as number correct out of 10 questions. Based on preliminary data, with each cohort of 50 patients, we will have 90% power to detect an effect size of 0.47 in change of recall accuracy from pre- (immediately prior) to post- (immediately after) video intervention, using a two-sided Wilcoxon signed-rank test with alpha of 0.05. Secondary endpoints include change in patient 1) genomic knowledge via the validated 10 true/false question survey (% correct out of 10)[22]; 2) 11-item Trust in Physician Survey (TPS) as a single TPS score.[21] All secondary outcomes will be summarized using descriptive statistics and compared pre-/post-video using Wilcoxon signed-rank test. For comparisons of MBC and LC, endpoints will include 1) baseline and pre-/post-video intervention change in genomic knowledge/understanding in MBC versus LC patients; 2) baseline and pre-/post-video intervention change in trust in physician/provider. The baseline and the change from pre- to post-video intervention in the secondary outcomes will be compared between MBC and LC patients using Wilcoxon rank sum test.

Sample Size Justification

Power calculations were based on the primary outcome of message-specific knowledge/recall accuracy. Assuming an effect size of 0.47 in change of recall accuracy from pre- (immediately prior) to post- (immediately after) video intervention, using a two-sided Wilcoxon signed-rank test with alpha of 0.05, then a sample size of 50 patients per group has 90% power to detect a difference. We will enroll a maximum of 75 participants per cohort (total maximum 300 participants) to allow for participant drop out. In the context of COVID, there is potential that T3 surveys response rate will be impacted, thus expanded maximum enrollment facilitates full cohorts for all timepoints.

Data Safety and Monitoring Plan

There is no data safety monitoring board for this minimal risk study. RedCap will assign a code number to each participant for the purposes of linking their data across surveys.

This study will utilize REDCap (Research Electronic Data Capture), a software toolset and workflow methodology for electronic collection and management of clinical and research data, to collect and store data. The Ohio State Center for Clinical and Translational Science (CCTS) Research Informatics Services will be used as a central location for data processing and management. REDCap provides a secure, web-based application that provides an intuitive data manipulation interface, custom reporting capabilities, audit trail functionality, real-time data monitoring/querying of participant records, and variations of data exporting/importing. REDCap is hosted by OSUWMC IT in the Ackerman Datacenter (640 Ackerman Road; Room 345)

REDCap instance is located on an internal OSUWMC network. Remote access to this network can be obtained over an encrypted VPN tunnel (AnyConnect). This VPN uses Protocol: DTLS and Cipher: RSA_AES_128_SHA1. Background checks are performed on all staff that are on the network or obtaining VPN access. Guest User accounts will be provided for the key personnel of BSMH that will be administering the survey at community cancer centers.

We will store any exported data on a secure, password protected server in the Division of Human Genetics. For patients enrolled at OSUCCC, the personally identifiable private information involved in the research includes patient name, medical record number, sex, cancer diagnosis, diagnostic tests ordered and the dates of such tests, treatment and outcome for 5 years post tumor genomic test result reporting. IHIS patient charts will be the source of all information utilized.

For patients enrolled at BSMH, the personally identifiable private health information, PHI, involved in the researchincludes patient name, MRN, cancer diagnosis, the specific NGS test ordered because it varies across cancer types, date of its order, as well as information regarding their next appointment: day, date, time and location to facilitate the research encounter. This information will be collected by the study personnel per a partial HIPPA waiver as part of screening procedures. PHI will be maintained in Microsoft 365's Onedrive. Paper documentation regarding research participation will be stored in locked cabinets within locked offices.

Potential Risks and Benefits

While some participants may not view this as a benefit, some participants may benefit from improved understanding of tumor genomic testing which may be valuable to certain participants. They could help society through improvements to cancer care based on results of the study.

There are no perceived physical or health risks related to participation in this study. However, there is a theoretical risk that topics that may arise from the questionnaires or video viewing could cause an emotional response in recipients, but this is not beyond what is expected in everyday life as it pertains to tumor genomic testing. There is a small risk of release of medical data that is not intended. This could affect insurability or employability.

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