908P

Evaluation of Anxiety, Distress and Satisfaction Using a Multi-Cancer Early Detection (MCED) Test

ESMO 2022
September 11, 2022
Paris

Deborah Schrag,[1] Tomasz M. Beer,[2] Charles H. McDonnell, III,[3] Lincoln Nadauld,[4] Christina A. Dilaveri,[5] Eric A. Klein,[6] Robert Reid,[7] Catherine R. Marinac,[8] Karen C. Chung,[9] Margarita Lopatin,[9] Eric T. Fung,[9] Donald L. Patrick[10]
[1]Memorial Sloan Kettering Cancer Center, New York City, NY; [2]OHSU Knight Cancer Institute, Portland, OR; [3]Sutter Health, Sacramento, CA; [4]Intermountain Healthcare, St. George, UT; [5]Mayo Clinic, Rochester, MN; [6]Cleveland Clinic, Cleveland, OH; [7]US Oncology Research, VA Cancer Specialists
[8]Dana-Farber Cancer Institute, Boston, MA; [9]GRAIL, LLC, a subsidiary of Illumina, Inc.*, Menlo Park, CA; [10]University of Washington, Seattle, WA

INTRODUCTION

- Circulating cell-free DNA (cfDNA) sequencing enables the detection of multiple cancer types with a single blood test[1,2]
- A targeted methylation-based cfDNA technology detected cancer signal across more than 50 types of cancer and predicted cancer signal origin with approximately 90% accuracy[3]
- PATHFINDER (NCT04241796) is a prospective study in adults ≥50 years of age that evaluates diagnostic steps following a detected signal from a MCED test and participant reported outcomes; see Proffered Paper #9030 for summary of main outcomes
- Because participating in cancer screening might affect psychosocial status such as anxiety, depression, distress, and worry,[4] PATHFINDER surveyed participants before and after testing to better understand the effects of MCED testing

OBJECTIVE

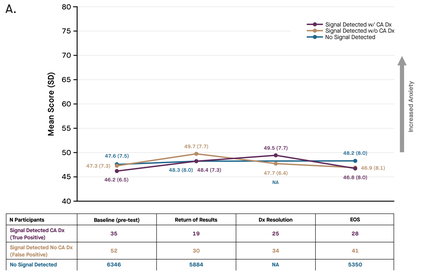
- Evaluate aspects of psychosocial status with participant-reported outcomes before and after MCED testing and to evaluate satisfaction with the MCED testing experience

KEY RESULTS: LOW NEGATIVE PSYCHOLOGICAL EFFECT WITH MCED TEST RESULTS WITH SMALL AND TRANSIENT INCREASE IN ANXIETY IN SIGNAL DETECTED PARTICIPANTS

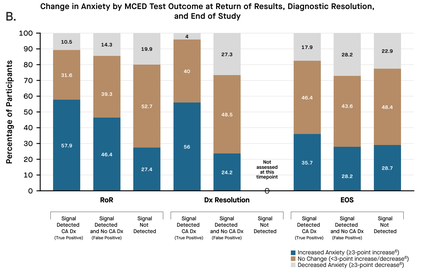
General Anxiety (PROMIS)

- Mean general anxiety scores increased in all groups following Return of Results (RoR), remained increased at diagnostic resolution (in cancer confirmed group), and trended towards baseline by 12-month end of study assessment (**Figure 1A**)
- All groups reported mean general anxiety levels lower than that of adults in the US evaluated in the era of COVID (June-August 2020)[5]
- Responder analyses (**Figure 1B**)
  - The **signal detected and confirmed cancer diagnosis** outcome group had the highest percentage of participants with a clinically meaningful *increase* (at least a 3-point change on PROMIS-Anxiety)[6] in general anxiety (57.9% and 56% at RoR and diagnostic resolution, respectively) which decreased by end of study (35.7%)
  - The **signal detected and no confirmed cancer diagnosis** outcome group demonstrated a clinically meaningful *increase* in general anxiety in 46.4% of participants at RoR which decreased to 24.2% at diagnostic resolution and 28.2% by end of study
  - The **no signal detected** outcome group had the lowest percentage of participants with a clinically meaningful *increase* in general anxiety (27.4%) at RoR, with little change in this proportion by end of study (28.7%)

Figure 1. General anxiety by MCED test outcome (PROMIS Anxiety 4)



N Participants	Baseline (pre-test)	Return of Results	Dx Resolution	EOS
Signal Detected CA Dx (True Positive)	35	19	25	28
Signal Detected No CA Dx (False Positive)	52	30	34	41
No Signal Detected	6346	5884	NA	5350

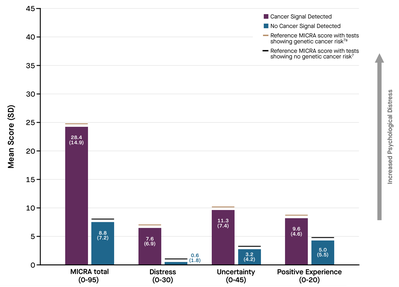


CA, cancer; Dx, diagnosis; EOS, end of study; MCED, multi-cancer early detection; PROMIS, Patient Reported Outcome Measurement Information System; RoR, return of results; SD, standard deviation.

Impact of Cancer Detection Assessment (Adapted MICRA)

- MICRA scores in those administered the MCED test were comparable to those reported by Culver et al[7] with genetic cancer test results (**Figure 2**):
  - Mean scores in "cancer signal detected" participants are similar to that of individuals with increased genetic risk of cancer via genetic testing (brown reference lines based on Culver et al in **Figure 2**)[7]
  - Mean scores in "no cancer signal detected" participants are similar to that of individuals with no increased genetic risk via genetic testing (black reference lines based on Culver et al in **Figure 2**)[7]
  - Reference lines are provided for broad context and not a direct comparison, as the participant populations between Culver et al and this study vary

Figure 2. Impact of MCED test results by signal detection status (Adapted MICRA)



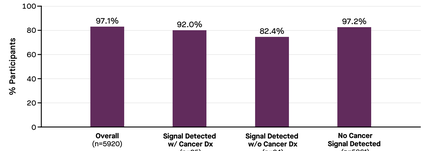
N Participants	Distress	Uncertainty	Positive Experience	Total
Signal Detected	50	50	50	50
No Signal Detected	5864	5865	5865	5864

[a]Genetic cancer risk defined as patients with high risk pathogenic variants
MCED, multi-cancer early detection; MICRA, Multidimensional Impact of Cancer Risk Assessment; SD, standard deviation

MCED Test Satisfaction

- Satisfaction reported by participants following MCED testing was 83.3(16.9) on a 100-point scale. Risk cohorts had similar findings (82.8 [17.1] for participants at elevated and 83.9 [16.5] for those with no additional cancer risk)
- High satisfaction with the MCED test was reported across participant outcome groups (i.e., cancer signal detected with cancer diagnosis at resolution, cancer signal detected with no cancer diagnosis at resolution, cancer signal not detected)
  - Highest satisfaction was reported by participants with no cancer signal detected (mean score=83.4 [16.7]) followed by those with a confirmed cancer diagnosis following MCED testing cancer signal detected with cancer diagnosed (true positive; mean score=79.6 [23.9])
  - Lowest satisfaction was reported by in participants with cancer signal detected but no confirmed cancer diagnosis (false positive; mean score=74.3 [27.6])
- **Figure 3** depicts participants responding satisfied, very satisfied, or extremely satisfied to the following question: "Taking all things into account, how satisfied or dissatisfied are you with the multi-cancer early detection test?"
  - A high level of satisfaction (97.1%) with MCED testing was found across participant groups, including true positives (92%), false positives (82.3%), and no cancer signal detected (97.2%)

Figure 3. Query Responses: "Taking All Things Into Account, How Satisfied or Dissatisfied Are You with the Multi-Cancer Early Detection Test"



Dx, diagnosis; SD, standard deviation

CONCLUSIONS

- Overall mean general anxiety scores were low at baseline and did not change substantially at the end of study (12 month) assessment
  - At end of study, the proportion of participants who were false positives with *clinically meaningful increase* in general anxiety was similar to those with no signal detected
  - The proportion of participants with *clinically meaningful increase* in general anxiety was highest in the those who were true positives
- Levels of distress and uncertainty following MCED test disclosure were low; these were increased for participants who had a signal detected test result compared to no signal detected test result
  - Levels of distress and uncertainty following disclosure of MCED test results in signal detected or no signal detected participants are similar to findings reported for those with genetic tests indicating increased cancer risk or no increase in cancer risk, respectively
- High rates of satisfaction were reported with MCED testing irrespective of MCED test result
- MCED testing is a new screening approach and data on psychosocial impact with this method are limited; further research will help confirm the important findings of this study and the potential role of supportive counseling

References

1. Thierry AR et al. *Cancer Metastasis Rev.* 2016;35(3):347-376.
2. Corcoran RB et al. *N Engl J Med.* 2018;379(18):1754-1765.
3. Klein EA et al. *Ann Oncol.* 2021. 2020; 31(6):745-759
4. Kim A et al. *BMC Cancer.* 2022;22(1):223.
5. Ding K et al. *Int J Environ Res Pub Health.* 2021; 18(5):2686.
6. Kroenke K et al. *J Clin Epidemiol.* 2019; 115:116-124.
7. Culver JO et al. *Cancer.* 2021;127(8):1275-1285.
8. www.healthmeasures.net/images/PROMIS/manuals/PROMIS_Anxiety_Scoring_Manual.pdf
9. Atkinson MJ et al. *Health Qual Life Outcomes.* 2004; 2:12.
10. Cella D et al. *Health Psychol.* 2002;21:564-72.

Disclosures

KC, ML, and ETF are current employees of GRAIL, Inc. with equity in the company. All financial relationships disclosed at abstract submission. In addition to consulting with GRAIL, Inc (TMB, DLP, EAK), financial disclosures related to stock ownership are: TMB (Arvinas Salarius, Pharmaceuticals), CHM (Sutter Medical Group), LN (Citizen Corporation, Clarifi, Guidance Genomics), and DS (Merck, family member).

Acknowledgements

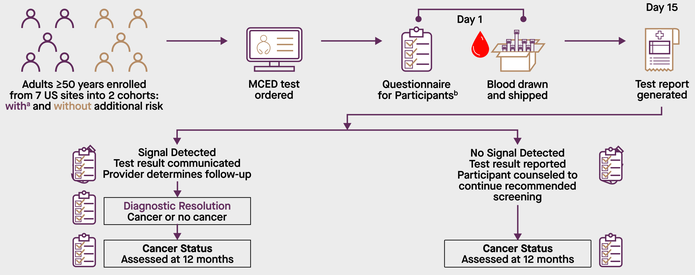
Funded by GRAIL, LLC, a subsidiary of Illumina Inc.* Writing, editorial, and graphic assistance provided by Prescott Medical Communications Group (Chicago, IL). *GRAIL, LLC, is currently held separate from Illumina Inc. under the terms of the Interim Measures Order of the European Commission dated 29 October 2021.

METHODS

Study Design

- PATHFINDER (NCT04241796) is a prospective, multi-center study that enrolled 6662 participants from 7 clinical institutions in the United States between Dec 2019 and Dec 2020 (**Figure S1**)
  - PROs were not all assessed at every timepoint; assessment schedule varied dependent on specific PRO questionnaire and MCED test result (**Figure S1** and **Table S1**)

Figure S1. PATHFINDER Study Design



MCED, multi-cancer early detection; US, United States
[a]Previous history of cancer, smoking, and genetic risk; [b]Schedule of participant reported outcomes varied among assessments

SUPPORTING DATA

- Participants were highly educated, and most were White, non-Hispanic and compliant with single cancer screening options.
- Patient disposition (outcome groups):
  - Signal detected: 92
    - Confirmed cancer diagnosis: 35
    - No cancer diagnosis: 56
    - Resolution not achieved: 1
  - Signal not detected: 6529

Table S1. PRO Assessments

Instrument	Assessment	Details	Timing: Participant Group	Pre-Test: All	Post RoR: Signal Detected	Post RoR: No Signal Detected	At Diagnostic Resolution: Signal Detected	EOS: All
PROMIS	General distress and anxiety	Converted from total raw score into a T-score (standardized T-score with a mean of 50 and a standard deviation of 10) for each participant (higher scores = greater anxiety; PROMIS Scoring manual;[8] ≥3-pointchange represents the minimally important difference)[6]	40.3–81.6	×	×	×	×	×
MICRA	Original instrument[9] developed to assess impact of genetic testing results was adapted to assess the specific impact of MCED test result disclosure	Distress subscale (higher score = greater distress)	0–30					
		Uncertainty subscale (higher score = greater uncertainty)	0–45		×	×		
		Positive experience (positive experience subscale reverse scored, higher scores = lower positive experiences)	0–20					
		Total score (higher score = greater negative overall impact)	0–95					
Satisfaction with MCED test	Test satisfaction	3-item questionnaire adapted from the Treatment Satisfaction Questionnaire for Medication[10] (higher score = greater satisfaction) *1. Overall, how confident are you that this MCED test is a good thing for you?* *2. How certain are you that the good things about the MCED test outweigh the bad things?* *3. Taking all things into account, how satisfied or dissatisfied are you with the MCED test?*	0–100			×	×	

MICRA, Multidimensional Impact of Cancer Risk Assessment (Adapted MICRA); PROMIS, Patient Reported Outcome Measurement Information System (PROMIS) Anxiety (4-item short form)
Pre-test (baseline): includes assessments completed prior to MCED test result availability
Post RoR, Return of results: ≤ 2 months (or 61 days) from PRO questionnaire administration (in signal detected cases, includes assessments completed prior to diagnostic resolution)
At diagnostic resolution: ≤ 3 months (or 91 days) from PRO questionnaire administration
EOS, End of study