RESULTS FROM A RANDOMIZED CONTROLLED TRIAL: INTRODUCING A PRECISION MEDICINE DIAGNOSTIC TEST INCREASES ADHERENCE TO GUIDELINES IN PATIENTS WITH BARRETT'S ESOPHAGUS

John W Peabody, MD PhD[1,5,6], Jamielyn DC Cruz, MD[1], Divya Ganesan, MS[1], David Paculdo, MPH[1], Rebecca J Critchley-Thorne, PhD[2], Sachin Wani, MD[3], Nicholas J Shaheen, MD MPH[4]

[1]QURE Healthcare, San Francisco, CA, USA; [2]Castle Biosciences, Inc., Pittsburgh, Pennsylvania, USA; [3]University of Colorado Anschutz Medical Center, Aurora, CO, USA, [4]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [5]University of California, San Francisco, CA, USA; [6]University of California, Los Angeles, CA, USA.

ABSTRACT

Introduction: Barrett's esophagus (BE) is a treatable precursor to esophageal adenocarcinoma (EAC). Adherence to BE management guidelines is poor, leading to reduced dysplasia detection and inappropriate treatment. We conducted a randomized controlled study to determine the clinical utility of a test that predicts risk of progression to high grade dysplasia (HGD) or EAC.

Methods: 259 practicing general and interventional gastroenterologists and gastrointestinal surgeons participated in this study. We measured the clinical care for three simulated BE patient types: high-risk clinical profile and high-risk test score [variant A], low-risk clinical profile and high-risk test score [variant B], and high-risk profile and low-risk test score [variant C]. After collecting baseline data on clinical care for the cases, the test was introduced to two intervention groups who viewed its educational materials. In a second round, intervention 1 was given the test results while intervention 2 optionally ordered the results. Their care was compared to controls. Quality of care scores were calculated based on the number of physician responses that matched evidence-based criteria for BE management.

Results: Intervention 1's quality of care scores showed improvement compared to control for all case variants. Intervention 1 outperformed controls in correctly determining risk of HGD/EAC among all case variants ($p<0.01$ for all) and ordering the correct primary management ($p=0.02$). Intervention 2 participants ordered the test results in 21.9% of cases, and those who did performed similarly to, or even outperformed, intervention 1. Those who did not order the test performed similarly to controls ($p>0.10$).

Discussion: This precision medicine test for BE optimized appropriate care for patients at high-risk and low-risk for disease progression to HGD/EAC, particularly for patients with low-risk clinical profiles but high-risk test results. With increased test use, physicians may treat early disease stages more efficiently and accurately and prevent progression to EAC.

CONTACT

Rebecca Critchley-Thorne, Ph.D.
Castle Biosciences, Inc
Email: rthorne@castlebiosciences.com
Phone: +1-412-596-5980
Website: www.castlebiosciences.com

John Peabody, PhD
QURE Healthcare
Email: john.peabody@qurehealthcare.com
Phone: +1-415-321-3388
Website: www.qurehealthcare.com

Introduction

- Gastroenterological societies have established recommended guidelines for management of BE. However, low adherence to these guidelines leads to both overuse of endoscopic surveillance and endoscopic eradication as well as under-use of care leading to reduced detection of dysplasia and esophageal adenocarcinoma (EAC).[1–2]
- The TissueCypher Barrett's Esophagus Assay is a commercially-available, validated test that predicts risk of progression to high-grade dysplasia (HGD) or EAC within 5 years.[3-7]
- This study aimed to assess the ability of this test to improve physicians' ability to assess the risk of developing HGD/EAC in BE patients and improve adherence to guideline-recommended management strategies for patients with BE.

Methodology

- 259 physicians were randomized to 3 arms (Table 1), and given a set of clinical performance and value (CPV) vignettes (Table 2) to evaluate in round 1.
- In round 2, education on TissueCypher was provided to Intervention arms 1 and 2, test results were supplied to Intervention 1, and optionally ordered by Intervention 2.
- A quality-of-care percentage (0-100%) score was generated from the CPVs based on American College of Gastroenterology (ACG)[8] and American Society of Gastrointestinal Endoscopy (ASGE)[9] guidelines.
- A fixed effects difference-in-difference model was used to assess the impact of the test.

Table 1: Physician Cohorts

Arm	Physicians (n)	Round 1	Round 2
Control	90	No Test results	No Test Results
Intervention 1	91	No Test results	Test results supplied
Intervention 2	78	No Test results	Test results ordered optionally

Table 2. Clinical Performance and Value (CPV) vignettes

Clinical Performance and Value (CPV) vignettes		
	Clinical Factors Risk	TissueCypher Risk Class
Case A	High	High
Case B	Low	High
Case C	High	Low

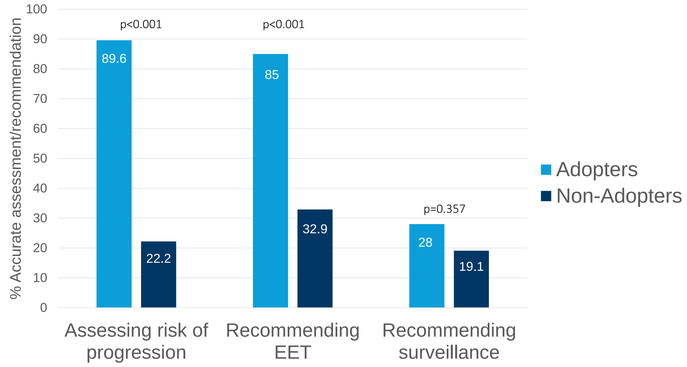
Results

Table 3. Physicians who received the TissueCypher test results performed better than the control group in determining patient risk

Accuracy of Assessing a BE Patient's Risk of Progression to HGD/EAC				
	Arm	Round 1	Round 2	Difference in Difference
Case A	Control	28.30%	26.10%	–
	Intervention 1	19.40%	77.50%	+60.2%, p<0.001
	Intervention 2	27.6%	40.90%	+15.5%, p=0.176
Case B	Control	12.00%	8.30%	–
	Intervention 1	10.20%	72.20%	+65.6%, p<0.001
	Intervention 2	9.4%	25.30%	+19.6%, p=0.020
Case C	Control	19.60%	25.60%	–
	Intervention 1	30.50%	69.10%	+32.6%, p=0.008
	Intervention 2	25.6%	45.20%	+13.6%, p=0.286

- Physicians in intervention group 2 ordered the test results in 21.9% of their cases
- Those who ordered the test performed similarly to or better than intervention 1, and those who did not order the test performed similarly to the control group.

Figure 1. TissueCypher adopters in Intervention 2 were significantly more likely to accurately assess a patient's risk of progression and recommend EET when appropriate.



Discussion

- Quality-of-care scores improved significantly across all patient cases after physicians were given the TissueCypher test results.
- Quality of care was significantly increased for variant B cases (patients presented at a clinically lower risk, but the test indicated a high risk of progression).
- Directional improvements in quality of care due to use of the test were also observed for variant A cases (patients' risk factors and/or endoscopic findings placed them at a higher risk for progression that was confirmed by the test) and variant C cases (patients presented at a clinically higher risk but the test showed a lower risk of progression).

Conclusions

- The improvement in quality of care when TissueCypher was used indicates that the test has the potential to significantly optimize current surveillance programs, and also to reduce management variability.
- Additionally, the test results can assist in preventing under-surveillance for high-risk patients and avoid excessive surveillance and/or invasive treatment for those at low risk.
- Overall, the findings of this study demonstrated the significant impact and clinical utility of the TissueCypher Barrett's Esophagus test to improve risk assessment for all clinical variants evaluated in this study.

References

1. Roumans CAM, et al. Endoscopy 2020; 52: 17–28.
2. Wani S, et al. The American Journal of Gastroenterology 2019; 114: 1256-1264.
3. Critchley-Thorne et al., Cancer Epidemiol Biomarkers Prev. 2016 Jun;25(6):958-968.
4. Critchley-Thorne et al., Cancer Epidemiol Biomarkers Prev. 2017 Feb;26(2):240-248.
5. Davison et al., Am J Gastroenterol. 2020 Jun;115(6):843-852.
6. Frei et al., Clin Transl Gastroenterol. 2020 Oct;11(10):e00244.
7. Frei et al., Am J Gastroenterol. 2021 Apr;116(4):675-682.
8. Shaheen N, et al., Am J Gastroenterol. 2016 Jan;111(1):30-50; quiz 51.
9. Qumseya et al., Gastrointest Endosc. 2019 Sep;90(3):335-359.e2.

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