

FINAL REPORT

Patient: John Doe
Sex: Male
DOB: 01/01/0001
Client: Shown Here
Provider: Shown Here

Specimen ID: Shown Here
Collected: Date
Received: Date
Reported: Date
Specimen Type: Esophageal Pinch Biopsy

TISSUECYPHER® RISK SCORE AND RISK CLASS

*RISK SCORE: **8.0** (range 0 – 10)

RISK CLASS: **HIGH**

5-Year Probability of Progression: **27%** (95% C.I. 22,33)

*If multiple specimens were submitted for testing, the reported result is based on the highest scoring specimen.

CLINICAL EXPERIENCE

This test is indicated for patients diagnosed with non-dysplastic (ND), indefinite for dysplasia (IND) or low grade dysplasia (LGD) Barrett's esophagus. Risk of progression to high grade dysplasia or esophageal adenocarcinoma within five years was determined from a pooled analysis of five multi-institutional clinical performance studies that have been completed and published involving 699 patients with Barrett's esophagus from five institutions¹⁻⁶. The clinical utility has also been demonstrated⁷.

The results provided here are adjunctive to the ordering physician's workup for patients with Barrett's esophagus. The reported 5-year probability of progression was adjusted based on estimated prevalence¹, however, the prevalence of progression of Barrett's esophagus may vary between clinical institutions.

TISSUECYPHER BARRETT'S ESOPHAGUS ASSAY DESCRIPTION

The test uses whole slide digital images from formalin-fixed paraffin-embedded (FFPE) tissue sections from endoscopic biopsy specimens. Using a proprietary artificial intelligence-driven quantitative algorithm, a risk score for progression to high grade dysplasia or esophageal adenocarcinoma is generated from the image analysis results. The risk score ranges from 0-10, with 0 indicating lowest risk and 10 indicating highest risk, and patients are classified as low, intermediate or high-risk for progression to high grade dysplasia or esophageal adenocarcinoma within five years. The risk classes provide predictive power (hazard ratio=7.3, p<0.0001) that is independent of clinical and pathologic features of age, sex, segment length, pathologic diagnosis (ND, IND or LGD) and p53 as a single biomarker².

The TissueCypher Barrett's Esophagus Assay is a multi-analyte assay with algorithmic analysis that uses automated image analysis to objectively quantify the expression and localization of nine biomarkers (p16, p53, alpha-methylacylCoA racemase [AMACR], HER2/neu, Cytokeratin-20 [K20], Cyclooxygenase-2 [COX-2], CD68, Hypoxia-inducible factor 1- α [HIF1A], and CD45RO) in the context of tissue morphology³.

For additional information about the development and validation of the TissueCypher Barrett's Esophagus Assay, visit the Products tab of www.castlebiosciences.com.

This test was developed, and its performance characteristics determined by Castle Biosciences, Inc. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Patent Pending.

Based on my review, the TissueCypher® Barrett's Esophagus Assay batch controls passed quality assessment and the observed biomarker expression patterns are consistent with the results described herein.

Castle Biosciences, Inc. | Sherri Borman, PhD, HCLD, Lab Director

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References

1. Data on file, Castle Biosciences. Data from pooled analysis of TissueCypher's risk stratification performance reported in 5 published clinical validation studies (adjusted for prevalence).
2. Critchley-Thorne et al. Cancer Epidemiol Biomarkers Prev 2016;25(6):958-68. A Tissue Systems Pathology Assay for High-Risk Barrett's Esophagus.
3. Critchley-Thorne et al. Cancer Epidemiol Biomarkers Prev. 2017;26(2):240-248. A Tissue Systems Pathology Test Detects Abnormalities Associated with Prevalent High-Grade Dysplasia and Esophageal Cancer in Barrett's Esophagus.
4. Davison, et al. Am J Gastroenterol 2020;115:843-852. Independent Blinded Validation of a Tissue Systems Pathology Test to Predict Progression in Patients With Barrett's Esophagus.
5. Frei, et al. Clin Transl Gastroenterol 2020;11. Independent Validation of TissueCypher to Predict Future Progression in Non-Dysplastic Barrett's Esophagus: A Spatial-Temporal Analysis.
6. Frei, et al. Am J Gastroenterol 2021;116:675-682. Tissue Systems Pathology Test Objectively Risk Stratifies Barrett's Esophagus Patients With Low-Grade Dysplasia.
7. Diehl, et al. Endosc Int Open. 2021 Mar;9(3):E348-E355. TissueCypher Barrett's esophagus assay impacts clinical decisions in the management of patients with Barrett's esophagus.
8. Prichard et al. J Pathol Inform. 2015 Aug 31;6:48. TissueCypher(™): A systems biology approach to anatomic pathology.

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