100 S. Commons, Suite 245
Pittsburgh, PA 15212

Castle ID:

FINAL REPORT

Patient:
Sex:
DOB:
Client:
Provider:
Additional Specimens Tested:

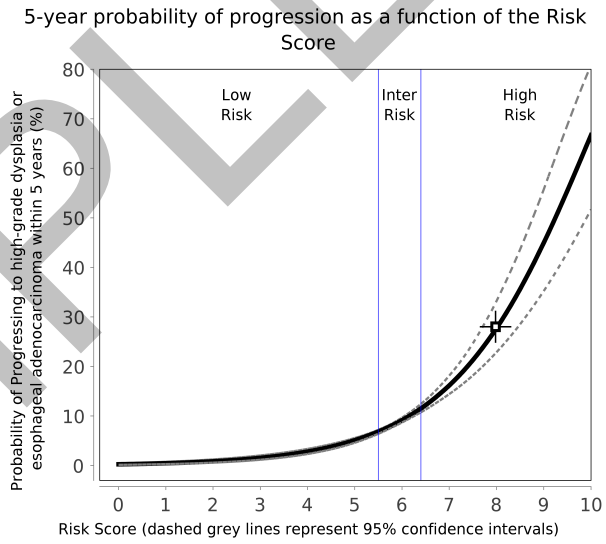
Specimen ID:
Collected:
Received:
Reported:
Specimen Type: FFPE Tissue

TissueCypher Risk Class and Risk Score

Risk Class* **HIGH**

Risk Score **8.0**

5-year Probability of Progression** **28%** (95% C.I. 23,33)



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

** For reference, population-based studies and systematic reviews and meta-analyses have estimated that untreated patients with NDBE, IND and LGD have 5-year rates of progression to a combined endpoint of HGD/EAC of 3.2%, 7.5% and 8.5%, respectively.[1-3]

TissueCypher Barrett's Esophagus Test Description

The test uses whole slide digital images from formalin-fixed paraffin-embedded (FFPE) tissue sections from endoscopic biopsy specimens. Using a proprietary, locked, 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 (HGD) or esophageal adenocarcinoma (EAC) within five years.

The TissueCypher Barrett's Esophagus test 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 morphology.[4]

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Clinical Experience

The TissueCypher Barrett's Esophagus test is indicated for patients diagnosed with non-dysplastic (NDBE), indefinite for dysplasia (IND) or low-grade dysplasia (LGD) Barrett's esophagus. Risk of progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) 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 institutions.[5-11] The test has been shown to detect significantly more patients with BE who progress to HGD/EAC (62.3%) than an expert pathology review diagnosis of LGD (28.3%). The test has also been shown to identify a high-risk subset of patients with NDBE who progress to HGD/EAC at a higher rate (16.7%)[6,7] than published estimates of progression in patients with LGD BE.[3] The clinical utility of the TissueCypher Barrett's Esophagus test to guide risk-aligned management has also been demonstrated.[12,13]

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 prevalence; however, the prevalence of progression of Barrett's esophagus may vary between clinical institutions.[6]

Comparison with Clinicopathologic Risk Factors

This table presents univariate risk of progression to HGD/EAC for patients with specific clinical features, pathology diagnoses or TissueCypher risk results as hazard ratios. Hazard ratio represents the likelihood of HGD/EAC in the group with the risk factor compared to the group without the risk factor (e.g. patients with long segment BE have a progression risk that is 1.5 times greater than patients with short segment BE, and patients with TissueCypher high risk results have a progression risk that is 7.8 times greater than patients with a low risk result).[6]

Multivariate analysis demonstrated that the TissueCypher high- and intermediate-risk results (HR 5.3 and 2.2, respectively) predict progression to HGD/EAC independently of segment length, hiatal hernia, age and sex. An expert review diagnosis of LGD (HR 2.5) was also statistically significant in multivariate analysis.[6]

Risk Factor	Hazard Ratio	P value
Int vs. Low	2.7	<0.0001
High vs. Low	7.8	<0.0001
Segment - Long vs. Short	1.5	0.041
Hiatal Hernia - Present vs. Absent	1.0	0.86
Age (per year)	1.02	0.0098
Sex-Male vs. Female	1.9	0.0055
Expert Review Dx - IND vs. NDBE	1.1	0.739

For additional information about the development and validation of the TissueCypher Barrett's Esophagus test, visit **www.castlebiosciences.com/TCResults**

1. Wani, et al. *Clin Gastroenterol Hepatol* 2011 Mar;9(3):220-7. 2. Krishnamoorthi, et al. *Gastrointest Endosc* 2020. Jan;91(1):3-10.e3. 3. Singh, et al. *Gastrointest Endosc* 2014 Jun;79(6):897-909. 4. Prichard et al. *J Pathol Inform.* 2015 Aug 31;6:48. 5. Iyer et al., *Clin Gastroenterol Hepatol.* 2022 Dec;20(12):2772-2779.e8. 6. Davison, et al. *Gastroenterology.* 2023 May;164(Supplement). 7. Critchley-Thorne, et al. *Cancer Epidemiol Biomarkers Prev.* 2016 Jun;25(6):958-68. 8. Critchley-Thorne, et al. *Cancer Epidemiol Biomarkers Prev.* 2017 Feb;26(2):240-248. 9. Davison, et al. *Am J Gastroenterol.* 2020 Jun;115(6):843-852. 10. Frei, et al. *Clin Transl Gastroenterol.* 2020 Oct;11(10):e00244. 11. Frei, et al. *Am J Gastroenterol.* 2021 Apr;116(4):675-682. 12. Diehl, et al. *Endosc Int Open.* 2021 Mar;9(3):E348-E355. 13. Duits, et al. *Am J Gastroenterol.* 2023 Nov 1;118(11):2025-2032.

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

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.

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