TissueCypher
► Barrett's Esophagus ®

Discussion Guide

This discussion guide can be used to assist you in a conversation with your healthcare professional to determine if the TissueCypher Barrett's esophagus test may be right for you.

Are you at risk for developing Barrett's esophagus?

Barrett's esophagus (BE) is caused by chronic acid reflux that may or may not be associated with heartburn. While BE can develop in anyone, the following elevated risk factors for BE are outlined by the American Gastroenterology Association (AGA), which suggests endoscopic screening (commonly called "endoscopy" or "EGD") for patients with three or more factors.[1,2,3]

☐ Frequent reflux symptoms

☐ Caucasian race

☐ Male

☐ Age over 50

☐ Overweight

☐ Use of tobacco products

☐ Family history of BE or esophagus cancer

☐ Diabetes

☐ Sleep apnea

Have you already been diagnosed with Barrett's esophagus?

If yes, you are likely aware that BE isn't cancer, but it is a precancerous condition. If your BE turns into cancer, the survival rate is only around 20%.[4]

The good news is that only 1 in 40 patients[5] with BE will progress to cancer within 5 years. The other good news is that there are highly effective ways to treat BE if your case is determined to be high risk.

The TissueCypher Barrett's Esophagus test is designed to predict your personal risk of progression to cancer. The test has been used by 2,000+ clinicians across the U.S. to help guide surveillance and treatment decisions related to BE.

Do I have Barrett's esophagus that has been confirmed by pathology?

☐ No
☐ Yes, non-dysplastic
☐ Yes, indefinite for dysplasia
☐ Yes, low-grade dysplasia
☐ Other: _____

Learn more about BE diagnosis, risk, and treatment
info.castlebiosciences.com/BE

Print this guide and have a conversation with your healthcare professional about how a personal risk assessment with TissueCypher can help guide your BE management.

![TissueCypher Barrett's Esophagus]

The TissueCypher Barrett's Esophagus test is designed to **predict** your personal risk of progression to cancer. The test analyzes biopsies taken during an endoscopy, and it uses a locked and validated artificial intelligence algorithm to predict your personal risk of progression to cancer.

You are eligible for testing if your BE is described as "non-dysplastic," "indefinite for dysplasia," or "low-grade dysplasia." The results can be used to help guide critical surveillance and treatment decisions.

What will a TissueCypher report tell me?

The **risk classification** tells you which category you are in based on your predicted risk of progression:

HIGH RISK

INTERMEDIATE RISK

LOW RISK

The **risk score** is your risk on a scale of 0-10. The lower the number, the lower your risk of progression

0.0-10.0

A **5-year probability of progression** is your percent likelihood of progressing toward cancer within 5 years of your biopsy

0.20-67%

How could TissueCypher affect my BE care?

Knowing your individual risk of developing cancer of the esophagus can help your healthcare professional create a plan of care that is right for you, ranging from periodic surveillance to endoscopic eradication therapy.

Your TissueCypher risk score, pathology report, overall health, age, health habits, family history, and risk tolerance are all important in determining the right plan of care for you.

Low risk
Less aggressive options

High risk
More aggressive options

Castle Biosciences is committed to providing high-quality molecular testing to all patients.

We do not want financial concerns to be a barrier to you accessing critical healthcare information. We will work with all insurance providers, including Medicare, Medicaid, commercial insurers, and Veterans Affairs (VA), to secure payment coverage for our testing. For those who may need additional assistance with their Castle test, we offer a comprehensive patient assistance program.

The next page provides information your healthcare professional may want to know regarding how to order the test and interpret results.

Information for healthcare professionals

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Molecular testing with TissueCypher provides an independent risk factor that can be used to help affirm long-interval surveillance for patients at low risk of progression. For patients at high risk of progression, care can be escalated to short-interval surveillance or endoscopic eradication therapy (EET).

How extensively has TissueCypher been studied?

- TissueCypher's performance has been published in **14+ peer-reviewed validation and utility studies.**

- Analysis performed at Mayo Clinic shows TissueCypher is a **stronger predictor of progression** than any clinical or pathologic risk factor.[6]

- TissueCypher's performance earned recognition from Medicare as an **Advanced Diagnostic Laboratory Test** (ADLT), which is granted to tests that provide new clinical diagnostic information that cannot be obtained from any other test or combination of tests.

TissueCypher is an easy-to-order, send-out test that can be performed with new or existing, standard BE pinch biopsies up to 2 years after an endoscopy.

Here is what is needed for your order:

- ☐ Faxable requisition form (or you can be set up to order online)
- ☐ Pathology report confirming Barrett's esophagus
- ☐ Endoscopy report (if needed to confirm BE)

Learn more at
info.castlebiosciences.com/learnTC

TissueCypher's-guided management for Barrett's esophagus

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LOW Risk Class   **HIGH/INT Risk Class**

LOW Risk Class		HIGH/INT Risk Class	
Non-dysplastic BE	**Indefinite or low-grade dysplasia**	**Non-dysplastic BE**	**Indefinite or low-grade dysplasia**
Consider surveillance in 3-5 years	Consider surveillance in 1 year	Rule out prevalent dysplasia/EAC; consider EET or surveillance in 1 year	**IND:** rule out prevalent dysplasia/EAC and consider EET; **LGD:** EET[8]

References:
1. Spechler S. et al. *N Engl J Med.* 2014. 2. Evans JA et al. *Gastrointestinal Endoscopy.* 2012. 3. Muthusamy et al. *Clin Gastroenterol Hepatol.* 2022. 4. American Cancer Society. Cancer Facts & Figures 2023. 5. Shaheen NJ. et al. *Gastroenterol.* 2000. 6. Iyer et al. *Clin Gastroenterol Hepatol.* 2022. 7. Villa NA. et al. *J Clin Gastroenterol.* 2024. 8. Rubenstein JH, et al. *Gastroenterology.* 2024.

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