Transcript Details
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Innovations in Non Invasive Colorectal Cancer (CRC) Screening

Announcer:
Welcome to ReachMD.

This medical industry feature, titled “Innovations in Non-Invasive Colorectal Cancer Screening” is sponsored by Exact Sciences. This program is intended only for healthcare professionals in the United States.

The presenter for this program is an Exact Sciences Employee.

Your host is Dr. Charles Turck.

Announcer:
The content being presented today focuses on the use of Cologuard® in accordance with its approved labeling.

Information presented today is not clinical, diagnostic, or treatment advice for any particular patient. Providers should use their clinical judgment and experience when deciding how to diagnose or treat patients. Exact Sciences Corporation does not recommend or endorse any particular course of treatment or medical choice.

The presenter for this program is an Exact Sciences Employee.

For additional product information, visit cologuardhcp.com.

Dr. Turck:
Colorectal cancer, or CRC, remains the most preventable yet least prevented form of cancer. Approximately 44 million average-risk patients aged 45 years and older remain eligible for CRC screening.[1] So, what strategies can we use to close this gap in CRC screening?

This is ReachMD, and I’m Dr. Charles Turck. Joining me to discuss how we work to improve CRC screening rates is Dr. Durado Brooks, deputy chief medical officer at Exact Sciences.

Dr. Brooks, welcome to the program.

Dr. Brooks:
Thanks for having me.

Dr. Turck:
Dr. Brooks, let’s begin by focusing on the purpose of screening for colorectal cancers.

Dr. Brooks:
Well, the purpose of screening is not only to detect cancers, but to detect them in earlier stages. Earlier detections associated with improved survival rates.[2] Screening can also help to prevent colorectal cancer by finding adenomatous polyps by finding and removing these lesions, we can keep cancer from occurring.

Now, when colorectal cancer is detected in early stages, stage I or II, the five-year relative survival rate is 90 percent[2] The evolution of a colorectal adenoma to early CRC often takes more than 10 years[3,4], and this is a key time window to detect adenomas and early-stage colorectal cancer.

However, the 5-year relative survival rate drastically drops in later stages. When CRC is diagnosed in stage IV, this rate drops to as

low as 14 percent.[2,5]

As clinicians, we aim to improve our patients' survival by detecting colorectal cancers earlier. In order to accomplish this, we need effective strategies, tools, and systems.

Dr. Turck:
The American Cancer Society and the U.S. Preventive Services Task Force have created recommendations regarding preventive screening. What exactly do those guidelines say about screening for colorectal cancer?

Dr. Brooks:
Well, let's start with the American Cancer Society's guidelines. Due to rising incidents and the higher likelihood of advanced-stage diagnosis among people younger than 50 years, the American Cancer Society in 2018 revised its screening guidelines to include patients 45 years or older with an average risk of colorectal cancer.[6] These patients should undergo regular screening with a choice of either a high sensitivity stool-based test, or a structural or visual exam, depending on patients preference and test availability.[6]

Starting in May 2021, the U.S. Preventive Services Task Force now also recommends screening patients at average risk for colorectal cancer beginning at age 45.[7]

Dr. Turck:
Based on the importance of screening, it seems most patients should be screened, yet they're not. What would you say are the top barriers patients face that might keep them from getting screened?

Dr. Brooks:
Well, when we ask patients directly, several common themes emerge. In a survey of previously screened and unscreened urban and rural patients, one of the most common barriers the patients reported was fear, that impacted about 25% of respondents.[8]

Patients also commonly reported financial challenges, such as a lack of insurance or cost of testing, logistic challenges, like transportation and time, and disgust or discomfort with the prep or procedure.[8] Many of these barriers are related to screening with colonoscopy.[8]

Dr. Turck:
And how do these patient-reported barriers contribute to the overall disease burden?

Dr. Brooks:
So, these barriers may lead to lower screening rates, which in turn can lead to worst colorectal cancer outcomes.[7]

For context, after lung cancer, colorectal cancer is the second leading cause of cancer mortality in the United States.[2]

The American Cancer Society estimates that 52,980 people will die from colorectal cancer in 2021,[2] and this year alone, approximately 150,000 new cases of colorectal cancer will be diagnosed in the United States, making colorectal cancer the third most common cancer diagnosis in both men and women.[2]

Dr. Brooks:
Though screening rates have marginally increased, the United States still faces key gaps in colorectal cancer screening. Approximately 44 million average-risk adults in the United States, aged 45 years and older, remain unscreened.[1]

National screening rates for colorectal cancer are still well below the National Colorectal Cancer Roundtable's goal of 80% in every community for patient adherence with colorectal cancer screening among patients age 50 to 75 years.[9] As of 2018, the overall US screening rate was only 67%.[10]

And it's important to note that rates among underserved communities and vulnerable populations are often far lower than this national average.[11]

Dr. Turck:
And as I understand it, Dr. Brooks, national guidelines recommend offering patients informed choices and engaging patients in the decision-making process to improve adherence to CRC screening. So, can you tell us what informed choice means and what options are available for CRC screening?

Dr. Brooks:
Sure. Well, let's start with patient informed choice. For all important healthcare decisions, patients should be aware of their options and

be given a choice.

To arrive at this choice, healthcare providers and patients need to work together to reach the optimal decision. In making an informed choice, a healthcare provider offers options, describes the associated risk and benefits and then in turn the patient plays a key role in the decision-making process by sharing his or her preferences and values.[12]

Both the United States Preventive Services Task Force, or commonly referred to as the USPSTF, and the American Cancer Society, ACS, have issued guidance in this shared decision making as it relates to colorectal cancer screening.[6,7]

The USPSTF states that each colorectal cancer screening option has different implementation considerations that may help with uptake.[7]Implementation considerations include where the screening test is performed, who performs the procedure, the need for pre-procedure bowel prep, the need for anesthesia or sedation during the test, and follow-up procedures for abnormal findings on a screening test. These considerations have implications for how feasible and preferable a given screening test is.[7]Discussing implementation considerations with patients may reveal which screening tests are more likely to be completed by a given person.[7]

Now, the American Cancer Society states that the importance of offering a choice between structural or stool-based testing is included in its guideline and recognition of the role that patient values and preferences and a practical, implementation strategy can improve adherence.[6]

Now, going back to patients informed choices for a moment, patients need to know about all of their screening options for colorectal cancer and be given a choice. These include invasive options, such as colonoscopy, and noninvasive options, including fecal occult blood test, fecal immunochemical test, and another option is multi-target stool DNA testing, also known commercially as Cologuard®. Cologuard® is an effective, noninvasive, at home colorectal cancer screening test that's easy to use for patients.

Dr. Turck:
For those just joining us, this is ReachMD.

I'm Dr. Charles Turck, and today I'm speaking with Dr. Durado Brooks about how we work to improve CRC screening rates.

So, Dr. Brooks, earlier, you listed a few screening options available to patients, but I'd like to zero in on one in particular, and that's Cologuard.

Starting with clinical data, can you tell us about the design for the pivotal study that was published in the *New England Journal of Medicine* in 2014 focusing on this screening option?

Dr. Brooks:
Certainly. This was a prospective, head-to-head, 90-site study of about 10,000 patients age 50 to 84 years who were at average risk for colorectal cancer.[13]

The study was conducted to evaluate the performance of Cologuard® in the detection of colorectal cancer and advanced precancerous lesions, as well as to compare Cologuard® with a commercially available FIT in the detection of both colorectal cancer and advanced precancerous lesions. Colonoscopy was the reference method.[13]

The primary outcome was the ability of Cologuard® to detect colorectal cancer with disease stage determined with the use of the American Joint Committee on Cancer, or AJCC staging system.[13]

The secondary outcome was the performance of Cologuard® for the detection of advanced precancerous lesions, and that included advanced adenomas, and sessile serrated polyps measuring greater than or equal to one cm in diameter.[13]

Dr. Turck:
And what were the findings from the Cologuard pivotal study, with regards to sensitivity and specificity?

Dr. Brooks:
In regard to sensitivity, the main finding of the trial was that Cologuard® had a higher sensitivity compared with FIT for both colorectal cancer and high-risk precancerous lesion detection.[13] Cologuard® testing identified 92.3% of patients with cancer at any stage versus 73.8% identified by FIT, which means that 7.7%, and 26.2% of patients with cancer at any stage found on colonoscopy tested negative with Cologuard® and FIT, respectively.[13]

In patients with screening relevant cancer, stage I through III, Cologuard® identified 93.3% of patients versus 73.3% identified by FIT.[13]

In patients with colorectal cancer and high-grade dysplasia, Cologuard® identified 83.7% of patients versus 63.5% identified by FIT.[13] In patients with advanced precancerous lesions, Cologuard® identified 42.4% of patients versus 23.8% identified with FIT.[13]

Cologuard® testing detected 13 of 60 screening-relevant cancers that were undetected by FIT, whereas FIT detected one cancer that was undetected by Cologuard®.[13]

Cologuard® testing also detected 22.5% of advanced pre-cancerous lesions that were undetected by FIT, whereas FIT detected 3.8% of such lesions that, were undetected by Cologuard®.[13]

Now let's focus on the specificity of these tests. Of the patients with non-advanced adenomas, non-neoplastic findings, and negative results on colonoscopy, 13.4% of these patients tested falsely positive with Cologuard®, so the specificity of Cologuard® was 86.6% in this population, versus 94.9%, in patients tested with FIT.[13] And of the patients with negative results on colonoscopy, 10.2% tested falsely positive with Cologuard®. So, the specificity of Cologuard® was 89.8% in this population versus 96.4% in patients tested with FIT.[13]

Now, to place these results in a practical clinical context, researchers created a model to extrapolate the results of this study to a reference population of 10,000 people at average risk for colorectal cancer, undergoing screening with Cologuard®.[13]

Based on the pivotal study data, 83.9% of patients would have screened negative using Cologuard® and 16.1% would have screened positive.[13]

Of patients who screened negative, 99.94% would have accurately screened negative for Cologuard®, leaving 0.06%, or about five patients out of 10,000 who would've had a colorectal cancer missed.[13]

Of the patients who screened positive, 3.7% would have been diagnosed with colorectal cancer, 19.9%, would have advanced adenomas, 30.9% would have had nonadvanced adenomas, and 45.4% would have had no findings on diagnostic colonoscopy.[13]

About 23.6% of persons with a positive Cologuard® result would have had colorectal cancer or an advanced precancerous lesion which is defined as an advanced adenoma and/or sessile serrated polyp measuring greater than or equal to one cm, on colonoscopy.[13]

Dr. Turck:
Thank you for that detailed review of Cologuard® sensitivity and specificity. I appreciated how you placed this into clinical context.

Before we wrap up, Dr. Brooks what parting thoughts would you like to leave with our audience about CRC screening and the utilization of Cologuard®?

Dr. Brooks:
Well, I think it's important to note that the US still faces key gaps in colorectal screening. Approximately 44 million average risk adults, age 45 or older remain unscreened.[1]

Common barriers to effective colorectal cancer screening include fear, financial challenges, logistic challenges, such as transportation and time, and disgust or discomfort with the prep or the procedure. And many of these barriers are related to screening with colonoscopy.[8]

Earlier detection is associated with improved survival rates.[2] When colorectal cancer is in stages I and II, the five-year survival rate is 90 percent, but five-year relative survival rates drastically diminish when diagnosed in stage IV, with the survival falling to 14%.[2,5] Several options in colorectal cancer screening exist including Cologuard®.

Cologuard® is an effective, noninvasive, use at home CRC screening option that is easy to use for patients.

Dr. Turck:
Well, considering just how much of an impact early detection can have on our patients, I want to thank my guest, Dr. Durado Brooks, for helping us better understand the various barriers that keep patients from getting screened and how options like Cologuard® can help us address those barriers.

Dr. Brooks, it was great speaking with you today.

Dr. Brooks:
Thanks for the opportunity.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck.

Let's take a moment to review some important risk information.

ReachMD Announcer:

Cologuard Indications for use
Cologuard is intended for the qualitative detection of colorectal neoplasia associated DNA markers and for the presence of occult hemoglobin in human stool. A positive result may indicate the presence of colorectal cancer (CRC) or advanced adenoma (AA) and should be followed by diagnostic colonoscopy. Cologuard® is indicated to screen adults of either sex, 45 years or older, who are at typical average risk for CRC. Cologuard® is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals

Cologuard Contraindications

- Cologuard® is intended for use with patients, age 45 years and older, at average risk who are typical candidates for CRC screening. Cologuard® was not clinically evaluated for the following types of patients:
  - Patients with a history of colorectal cancer, adenomas, or other related cancers.
  - Patients who have had a positive result from another colorectal cancer screening method within the last 6 months.
  - Patients who have been diagnosed with a condition that is associated with high risk of colorectal cancer. These include but are not limited to:
    - Inflammatory Bowel Disease (IBD)
    - Chronic ulcerative colitis (CUC)
    - Chron's disease
    - Familial adenomatous polyposis (FAP)
    - Family history of colorectal cancer
- Patients who have been diagnosed with a relevant familial (hereditary) cancer syndrome, such as Hereditary non-polyposis colorectal cancer syndrome (HNPCC or Lynch Syndrome), Peutz-Jeghers Syndrome, MYH-Associated Polyposis (MAP), Gardner's syndrome, Turcot's (or Crail's) syndrome, Cowden's syndrome, Juvenile Polyposis, Cronkhite-Canada syndrome, Neurofibromatosis, or Familial Hyperplastic Polyposis.

Warnings and Precautions
The performance of Cologuard® has been established in a cross-sectional study (i.e., single point in time). Programmatic performance of Cologuard® (i.e., benefits and risks with repeated testing over an established period of time) has not been studied. Performance has not been evaluated in adults who have been previously tested with Cologuard®. Non-inferiority or superiority of Cologuard® programmatic sensitivity as compared to other recommended screening methods for CRC and AA has not been established.

The clinical validation study was conducted in patients 50 years of age and older. ACS Guidelines recommend screening begin at age 45. Cologuard® performance in patients ages 45-49 was estimated by sub-group analysis of near-age groups.

CRC screening guideline recommendations vary for persons over the age of 75. The decision to screen persons over the age of 75 should be made on an individualized basis in consultation with a healthcare provider. Cologuard® test results should be interpreted with caution in older patients as the rate of false positive results increases with age.

A negative Cologuard® test result does not guarantee absence of cancer or advanced adenoma. Patients with a negative Cologuard® test result should be advised to continue participating in a colorectal cancer screening program with another recommended screening method. The screening interval for this follow-up has not been established.

Cologuard® may produce false negative or false positive results. A false positive result occurs when Cologuard® produces a positive result, even though a colonoscopy will not find cancer or precancerous polyps. A false negative result occurs when Cologuard® does not detect a precancerous polyp or colorectal cancer even when a colonoscopy identifies the positive result.

Patients should not provide a sample for Cologuard® if they have diarrhea or if they have blood in their urine or stool (e.g., from bleeding hemorrhoids, bleeding cuts or wounds on their hands, rectal bleeding, or menstruation).

To ensure the integrity of the sample, the laboratory must receive the patient specimen within 72 hours of collection. Initiate the return process within a day of collecting your sample to allow enough delivery time. Refer to the shipping instructions provided in this box, or ask your prescriber, for more information.

Patients should be advised of the caution listed in the Cologuard® Patient Guide. Patients should NOT drink the preservative liquid.

The risks related to using the Cologuard® Collection Kit are low, with no serious adverse events reported among people in a clinical trial. Patients should be careful when opening and closing the lids to avoid the risk of hand strain.

ReachMD Announcer:
This program was sponsored by Exact Sciences. If you missed any part of this discussion, visit reachmd.com/industryfeature. This is ReachMD. Be Part of the Knowledge.