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Taking Acid-Reducing Medicine With Aspirin Offers Moderate Benefits in Patients With Barrett's Esophagus

Summary includes updated data not in the abstract

ASCO Perspective



"The risk of esophageal cancer weighs on patients with Barrett's esophagus. For these patients, this regimen reduces serious complications of acid reflux disease and the risk of dying from all causes, including esophageal cancer, and with little to no side effects. It's an approach that people with Barrett's should consider and discuss with their doctors," said ASCO Expert Andrew Epstein, MD.

CHICAGO – Findings from an updated analysis from a randomized phase III trial show that taking a high dose of the acid-reducing medicine esomeprazole (Nexium[®]) with low dose aspirin for at least seven years can moderately reduce the risk of developing high grade dysplasia (a pre-cancerous lesion) or esophageal cancer, or delay death from any cause in people with Barrett's esophagus.

The authors estimate that development of these outcomes could be delayed by using these simple, over-the-counter medicines. Esophageal cancer is an uncommon cancer, but very difficult to screen for and treat – less than 1 in 5 (19%) of patients survive 5 years after diagnosis.

The findings will be featured in a press briefing today and presented at the [2018 American Society of Clinical Oncology \(ASCO\) Annual Meeting](#).

"Based on these data, we believe people with heartburn should talk with their doctor about their risk of Barrett's esophagus, but they should not self-medicate with these medications," said lead study author Janusz Jankowski, MD, PhD, Deputy Vice Chancellor, Royal College of Surgeons, Ireland and Consultant Clinical Adviser, National Institutes for Health and Care Excellence, UK. "We hope that the National Institute for Health and Care Excellence in the UK and national bodies in other countries will consider our findings when developing guidelines for esophageal cancer prevention."

About Esophageal Cancer and Barrett's Esophagus

Related Information

- [Read the full abstract](#)
- [Meeting presentation information](#)
- [More news from the meeting](#)
- Download high-res photo of the study author (*coming soon*)
- [Request an interview](#)

For Your Readers

- [Guide to Esophageal Cancer](#)
- [Chemoprevention](#)

Esophageal cancer accounts for only 1% of cancers diagnosed in the United States, but it is more common in other parts of the world. Esophageal adenocarcinoma is the most common type of esophageal cancer in the West, accounting for two-thirds of all esophageal cancers. Esophageal cancer is the seventh leading cause of death from cancer in the world. Barrett's esophagus can develop in some people who have chronic gastroesophageal reflux disease (GERD) or inflammation of the esophagus called esophagitis, even when a person does not have symptoms of chronic heartburn. Damage to the lining of the esophagus causes the squamous cells in the lining of the esophagus to turn into glandular tissue. People with Barrett's esophagus are more likely to develop adenocarcinoma of the esophagus, but the risk of developing esophageal cancer is still fairly low.

It is estimated that Barrett's esophagus occurs in only 2% of adults in Western countries, but experts believe that it may be underdiagnosed. Although people with this condition have a much higher risk for esophageal cancer compared to the general population, their absolute risk is still very small – the lifetime chance of developing the disease is only 2%.

It is estimated that 80-90% of esophageal cancers are preceded by Barrett's esophagus, but most of the time cancer is diagnosed before Barrett's esophagus, because prior endoscopy has not been undertaken properly or at all. Prior research has suggested that acid reduction with standard-dose proton pump inhibitors might prevent progression of Barrett's esophagus to cancer. There is also evidence from observational studies that aspirin is effective in preventing gastrointestinal cancers, including esophageal cancer.

About the Study

The ASPECT trial randomly assigned 2,563 people with Barrett's esophagus to four treatment groups:

- High dose proton pump inhibitor esomeprazole
- High dose esomeprazole with low dose aspirin
- Standard dose (e.g., low dose) esomeprazole
- Standard dose (e.g., low dose) esomeprazole with low dose aspirin

The primary endpoint was time to death from any cause, diagnosis of esophageal cancer or diagnosis of high-grade dysplasia (precancer) (three combined events). The analysis adjusted for patient's age and duration of Barrett's esophagus.

Key Findings

Patients were followed for a median of 8.9 years, and high dose esomeprazole had a statistically significant benefit on the combined endpoint compared to standard dose esomeprazole ($p=0.0459$). The most effective treatment was high dose esomeprazole with low dose aspirin.

Aspirin showed no benefit compared to no aspirin in the primary analysis. However, there was a weak effect when researchers censored for prior NSAID use.

Safety Precautions

The treatments were safe overall, with serious side effects reported in only 1% of patients. Although both medicines are generally very safe, precautions should be taken before starting this regimen, noted Dr. Jankowski.

The most common side effect of proton pump inhibitors is diarrhea. People with heart disease should be aware that these drugs can interact with various heart medications. Other, much more rare risks include *Clostridium difficile* infection and osteoporosis. The most serious side effects of aspirin include allergic reactions, bleeding in the stomach, and bleeding in the brain (particularly for people with high blood pressure). In addition, people who are already taking another non-steroidal anti-inflammatory drug (NSAID), should not be taking aspirin.

Next Steps

Although this was the largest chemoprevention randomized controlled trial in Barrett's esophagus and it had the longest follow-up, more research is needed, noted Dr. Jankowski. The research was conducted in only five countries with mostly White populations, so it is not known if this chemoprevention strategy would be as effective in Black and Asian people, as genetic ancestry can affect treatment efficacy. In addition, the researchers would like to follow patients on this study to see if 9-10 years of chemoprevention is even more effective and whether there is an increased risk for side effects with longer treatment.

This study received funding from Cancer Research UK.

Study at a Glance

Disease	Barrett's Esophagus/Esophageal Cancer
Trial Phase, Type	Phase III, Randomized, Chemoprevention
Patients on Trial	2,563
Intervention Tested	Proton pump inhibitor and aspirin
Primary Finding	Taking a high dose of esomeprazole with low dose aspirin for at least seven years can moderately reduce the risk of developing high grade dysplasia or esophageal cancer, or delay death from any cause in people with Barrett's esophagus.
Secondary Finding(s)	N/A

[View the disclosures](#) for the 2018 ASCO Annual Meeting News Planning Team.

ATTRIBUTION TO THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING IS REQUESTED IN ALL COVERAGE.

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About ASCO:

Founded in 1964, the American Society of Clinical Oncology, Inc. (ASCO®) is committed to making a world of difference in cancer care. As the world's leading organization of its kind, ASCO represents nearly 45,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at www.ASCO.org, explore patient education resources at www.Cancer.Net, and follow us on [Facebook](#), [Twitter](#), [LinkedIn](#), and [YouTube](#).

2018 ASCO Annual Meeting: Presentation Information

Gastrointestinal (Noncolorectal) Cancer Oral Abstract Session
Monday, June 4, 2018: 5:12-5:22 p.m. CT
McCormick Place, Arie Crown Theater

Janusz Jankowski, MD, MBBS
University of Central Lancashire
Preston, United Kingdom

Abstract LBA4008: Chemoprevention of esophageal cancer with esomeprazole and aspirin therapy: Efficacy and safety in the phase III randomized factorial ASPECT trial.

Authors: Janusz Jankowski, John de Caestecker, Sharon Love, Gavin Reilly, Yeng Ang, Krish Rangunath, Arthur Tucker, Ian Penman, Colin Rodgers, Emma Roffe, Claire E Brooks, Stephen Attwood, Danielle Morris, Rebecca Harrison, Pradeep Bhandari, Peter Watson, Scott Sanders, Hugh Barr, Paul Moayyedi, James Neale, AspECT Trial Team; University of Central Lancashire, Preston, United Kingdom; University Hospitals Leicester NHS Trust, Leicester, United Kingdom; Centre for Statistics in Medicine and Oxford Clinical Trials Research Unit (OCTRU), Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom; University of Oxford, Oxford, United Kingdom; Wrightington, Wigan and Leigh NHS Trust, Wigan, United Kingdom; Nottingham University Hospitals NHS Trust, Nottingham, GB; Queen Mary University London, London, United Kingdom; NHS Lothian, Edinburgh, United Kingdom; Northern Health and Social Care Trust, Antrim, United Kingdom; Takeda UK, London, United Kingdom; Oxford Clinical Trials Research Unit (OCTRU), University of Oxford, Oxford, United Kingdom; Durham University, Durham, United Kingdom; East and North Hertfordshire NHS Trust, Lister, United Kingdom; Portsmouth Hospital NHS Trust, Portsmouth, United Kingdom; Queens University Belfast, Belfast, United Kingdom; Ninewells Hospital Dundee, Dundee, United Kingdom; Gloucestershire Hospitals NHS Trust, Gloucester, United Kingdom; McMaster University, Hamilton, ON; Torbay and South Devon NHS Foundation Trust, Devon, United Kingdom

Background: Esophageal adenocarcinoma (EA) is the sixth most common cause of global cancer death. We rely on endoscopy screening to identify and monitor patients with Barrett's esophagus (BE) and find neoplastic lesions early enough to manage their EA. . This approach has a modest effect on EA supported by low quality evidence. We evaluated the efficacy of aspirin and high dose acid suppression in preventing EA in patients with BE. **Methods:** We recruited patients with ≥ 1 cm of BE and no high grade dysplasia (HGD) or EA at baseline in UK and Canadian hospitals. To conceal allocation, a central trials unit randomized patients using a computer-generated schedule. Patients were randomized unblinded 1:1:1:1 in a 2X2 factorial design to high dose (40mg twice daily) or low dose (20mg once daily)esomeprazole proton pump inhibitor acid suppression (PPI) , alone or combined with low dose aspirin 300mg/day (330mg in Canada). The primary composite endpoint was time to all-cause mortality or EA or HGD analyzed using accelerated failure time modelling adjusting for minimization factors (age, length of Barrett's esophagus and presence of intestinal metaplasia). **Results:** We recruited 2563 Barrett's patients followed-up for a median of 8.9 years (interquartile range 8.2-9.8) with 20,095 years of follow up. There were 313 events of the composite primary endpoint. High dose PPI was statistically significantly superior to low dose PPI ($p = 0.037$, $N = 2535$, Time Ratio (TR) 1.27, 95% CI = 1.01-1.58). Aspirin therapy showed a trend to benefit but was not statistically significant ($p = 0.068$, $N = 2280$, TR = 1.24, 95% CI = 0.98 – 1.57). The combination of aspirin with high dose PPI had the strongest effect compared to low dose PPI with no aspirin (TR = 1.59, 95% CI = 1.14 to 2.23, $p = 0.007$). There were few serious adverse events reported (1.0% of patients), with 99.9% data collected. **Conclusions:** This is the largest randomized controlled chemoprevention trial in patients with Barrett's esophagus. We have shown that PPI high dose and aspirin chemoprevention therapy, especially in combination significantly reduces rates of death, EA or HGD occurrence and is safe.

Disclosures: Janusz Jankowski, MD, MBBS, Honoraria from Teueda, Speakers' Bureau for Teueda, Research Funding (Institutional) from AstraZeneca; John de Caestecker, Consulting or Advisory Role with Falk Pharma; Sharon Love, Travel, Accommodations, Expenses from Amgen; Yeng Ang, Research Funding (Institutional) from Medtronic, Travel, Accommodations, Expenses from Medtronic; Arthur Tucker, Leadership with Seal Biosciences, Stock and Other Ownership Interests with EdixoMed, First Choice Health, Seal Biosciences, Consulting or Advisory Role with EndoStim, Patents, Royalties, Other Intellectual Property with Seahose Laboratories Ltd, Edixomed Ltd, Firstkind Ltd; Ian Penman, Travel, Accommodations, Expenses from Olympus Medical Systems, Boston Scientific; Emma Roffe, Employment with Takeda; Stephen Attwood, Consulting or Advisory Role with EndoStim, Danielle Morris, Consulting or Advisory Role with Dr Falk Pharma UK Ltd, Travel, Accommodations, Expenses from Dr Falk Pharma UK Ltd; Pradeep Bhandari, Honoraria from Fujifilm, Pentax Medical Devices, Boston Scientific, Consulting or Advisory Role with 3D Matrix,

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