F!GHT COLORECTAL CANCER™ Early-Age Onset Colorectal Cancer Think Tank: Summary Report

Meeting Date:

December 1, 2023

Collaborators:

Fight Colorectal Cancer (Fight CRC), Vanderbilt University, and The National Cancer Institute

PENDING PUBLICATION

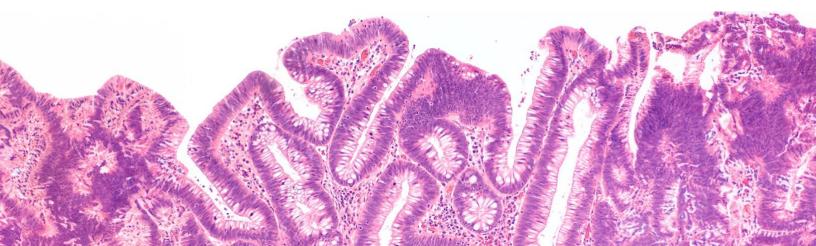


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Introduction

On December 1, 2023, Fight Colorectal Cancer (Fight CRC) orchestrated the pivotal Early-Age Onset (EAO) Think Tank in Nashville, Tennessee. This assembly united 60 esteemed, relentless advocates from across the U.S. and Europe. Our mission: to leverage collective wisdom and catalyze a paradigm shift in the battle against early-age onset colorectal cancer (EAO CRC).

Impact and Collaboration

The EAO Think Tank is more than a meeting; it's a movement. In partnership with Vanderbilt University and the National Cancer Institute, we've laid the groundwork for a global crusade against EAO CRC. Our discussions were not mere talks but a symphony of ideas, blending the expertise of oncologists, geneticists, and advocates to illuminate the path forward.

Meeting Achievements:

Our meeting achievements span cross-disciplinary dialogue, research innovation, community engagement, strategic partnerships with the NCI, and resource mobilization, shaping a dynamic landscape for transformative progress in EAO CRC research and treatment.

- **Cross-disciplinary Dialogue:** We broke down silos, fostering a rich tapestry of collaboration that promises to redefine EAO CRC research and treatment.
- **Research Innovation:** Our collective brainstorming has stimulated ideas that we hope will lead to groundbreaking research proposals, setting the stage for transformative discoveries.
- **Community Engagement:** We've empowered patients and caregivers, integrating their voices into the heart of our research agenda, ensuring that our pursuits are deeply rooted in real-world experiences.
- **Strategic Partnerships:** The partnership with the NCI is important. It underscores that we must work toward aligning our research efforts with national and global research priorities to make progress.
- **Resource Mobilization:** Our collaborative ethos has ignited interest among academia and industry partners, promising an infusion of resources to fuel our innovative projects.

Looking Ahead

Convening a Think Tank was just the beginning. Led by Fight CRC and our partners, our scientific champions will continue to expand the work with a series of virtual EAO Think Tank sessions in summer 2024, culminating in a seminal international meeting in Barcelona in summer 2025. These forums will not only continue the dialogue but will also set the stage for implementing our visionary research agenda on a global scale.

Thank you for supporting Fight CRC in addressing the rise in EAO CRC. The support of our sponsors and donors not only fuels groundbreaking research, it weaves you into the fabric of a community united in hope and action.

Attendees

Aasma Shaukat, MD, MPH New York University Abee Boyles, PhD National Institute of Environmental Health Sciences Al B. Benson III, MD

Northwestern University

Andrea Cercek, MD Memorial Sloan Kettering Cancer Center

Andrea (Andi) Dwyer, BS University of Colorado and Fight Colorectal Cancer

Andreana Holowatyj, PhD, MSCI Vanderbilt-Ingram Cancer Center

Andrew Kurtz, PhD National Cancer Institute

Aniruddha Rathod, PhD, MPH, MBBS University of Texas Southwestern Medical Center

Angela Nicholas, MD Caregiver, Fight Colorectal Cancer

Anjee Davis, MPPA President, Fight Colorectal Cancer

Ann Zauber, PhD Memorial Sloan Kettering Cancer Center

Arun Pandiri, BVSc & AH, PhD National Institute of Environmental Health Sciences

Caitlin Murphy, PhD, MPH University of Texas Houston Carli King, PhD Fight Colorectal Cancer

Carmen Fong, MD, FACS Hemorrhoid Centers of America

Cathy Eng, MD, FACP, FASCO Vanderbilt-Ingram Cancer Center

Christopher Lieu, MD University of Colorado

Cynthia Sears, MD Johns Hopkins University

Dean Jones, PhD Emory University

Djenaba A Joseph, MD, MPH CDC's Division of Cancer Prevention and Control (DCPC)

Dustin Deming, MD University of Wisconsin

Eric Lander, MD Vanderbilt University Medical Center

Erin Verscheure Survivor, Fight Colorectal Cancer

Fanny Vuik, MD, PhD Erasmus University Medical Center

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Heather Hampel, MS, CGC City of Hope National Cancer Center Iris Lansdorp-Vogelaar, PhD Erasmus University Medical Center

Jennifer Weiss, MD, MS University of Wisconsin School of Medicine and Public Health

Jill MacDonald Survivor, Fight Colorectal Cancer

Jay Popp, MD Amsurg

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Mariana Byndloss, DVM, PhD Howard Hughes Medical Institute

Matt Young, PhD National Cancer Institute

Michael Frierson Caregiver, Fight Colorectal Cancer Phil Daschner, M.Sc. National Cancer Institute

Phuong Gallagher Survivor, Fight Colorectal Cancer

Qian Shi, PhD Mayo Clinic

Rebecca Siegel, MPH American Cancer Society

Rich Goldberg, MD West Virginia University

Richard Kuntz, MD Medtronic

Scott Kopetz, MD, PhD University of Texas MD Anderson Cancer Center

Sharlene Gill, MD University of British Columbia

Sonia Kupfer, MD University of Chicago

Steve Greene Survivor, Fight Colorectal Cancer

Suneel Kamath, MD Cleveland Clinic Taussig Cancer Institute

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Tabassum Khan, MD, MPH Komodo Health

Tony Dickherber, PhD National Cancer Institute

Van Morris, MD University of Texas MD Anderson Cancer Center

Y. Nancy You, MD, MHSC University of Texas MD Anderson Cancer Center

Ymke van der Pol, PhD Fight Colorectal Cancer Fellow at Tempus Health

Thank you to these experts who volunteered their time!

Summary

On December 1, 2023, the EAO Think Tank was convened by Fight CRC in Nashville, Tennessee, in partnership with Vanderbilt University and the National Cancer Institute. This assembly brought together a select cohort of 60 U.S. and European advocates, building on the initiatives and symposiums led by Fight CRC since 2019 aimed at addressing EAO colorectal cancer.

The report encapsulates the dynamic and unified efforts of this gathering, setting the stage for an expansive, international Think Tank to be conducted virtually on June 25, 2024, followed by a global inperson discourse in Barcelona, Spain, in 2025. These efforts underscore the commitment to leveraging collective expertise for advancing the fight against EAO CRC.



Background and Context:

The Think Tank Model represents a strategic forum led by Fight CRC to continue to advance the research agenda and activate the initiatives outlined in the Path to a Cure (PTAC) report. Through the convening of Think Tank sessions, Fight CRC aims to translate the PTAC report's vision into actionable strategies, rallying the community toward impactful action.

The session held on December 1 was a comprehensive, day-long workshop that concentrated on the initial chapters of the PTAC report, emphasizing the critical need to advance research efforts in the realm of EAO CRC.

Why host a Think Tank?

In our pursuit of progress against EAO-CRC, hosting a Think Tank has proven instrumental in fostering collaboration and innovation. The key motivations behind this initiative include:

- Interdisciplinary Collaboration: We successfully created a platform for dynamic interactions among oncology, epidemiology, genetics, and industry professionals to foster the exchange of groundbreaking ideas and strategies aimed at combating EAO CRC.
- Gap Analysis in Research: The agenda was designed to address essential research voids in EAO CRC, covering areas like causation, genetic factors, exposure risks, and intervention strategies, to guide future research endeavors.
- Innovation in Research: Attendees were invited because of their bodies of work and commitment to innovative research concepts with the potential to revolutionize our understanding, prevention, diagnosis, and treatment of EAO CRC.
- Involvement of Advocacy Groups: Fight CRC successfully bridged meaningful participation of patients, caregivers, and advocacy groups in setting research priorities, thus incorporating the experiences and insights of the EAO CRC community.
- Engaging Cancer Research Organizations: Harnessing the knowledge and resources of the NCI to ensure that Think Tank's efforts are in harmony with wider national research goals.
- **Resource Mobilization:** Stimulating partnerships between academic institutions, industry, and funding bodies to gather the essential resources for pioneering research in EAO CRC.
- Advancing Toward a Cure: Fostering an environment conducive to innovative thinking and scientific breakthroughs aimed at the prevention of EAO CRC.

The assembly featured two distinct tracks of expert-led presentations that introduced cutting-edge concepts and stimulated dialogue on key issues, facilitating the identification of common themes and further expanding the research landscape based on established knowledge of risk factors and etiology.

Each track was enriched with expert insights, introducing novel scientific approaches and technologies, some of which have been applied in other cancers but are now being considered for CRC, particularly in understanding its etiology and developing interventions for EAO cases.

Discussions also emphasized inclusivity, with a focus on ensuring equity and access in research and interventions, addressing disparities, and enhancing engagement across diverse populations.

Survivor and Research Advocate Perspective

Within each discussion group, a research advocate who has personally experienced EAO CRC contributed insights and perspectives following each presentation. This inclusion aimed to ground the scientific

discussions in real-world experiences, addressing prevalent concerns and themes that emerged during the sessions.

Jill McDonald, a stage IV patient and survivor, shared her reflections:



"Being invited to speak at the Fight CRC EAO Think Tank was an immense honor. To share my journey in such a distinguished gathering, filled with top experts from around the globe, was incredibly uplifting. The collective drive toward not just finding a cure but also emphasizing prevention and early detection was palpable. Witnessing the commitment and potential for change firsthand was both overwhelming and hope-inspiring. It was a powerful reminder that in this fight against colorectal cancer, we are never alone."

Scan or click here to hear Jill's story



Following the Nashville EAO Think Tank, a virtual meeting tailored for patients was held the subsequent week to recap the December 1, 2023, event. This virtual meeting actively engaged 49 participants, including survivors, caregivers, research advocates, and health care professionals. Ensuring we continue to engage our community of EAO patients, Fight CRC summarized the day's key themes and shared insights from the research advocates who participated, further bridging the gap between the patient community and ongoing research efforts.

Scan or click here to watch the recording.



Meeting Agenda

TIME	ΤΟΡΙΟ			
7–8am	Breakfast			
7:45–8am	Welcome & Opening Session Speakers: - Anjee Davis, MPPA, President, Fight Colorectal Cancer - Cathy Eng, MD, FACP, FASCO, Medical Oncologist; Professor of Medicine, Division on Hematology/Oncology; Co-Leader, VICC Gastrointestinal Cancer Research Program; Co-Director, GI Oncology, Director, VICC Young Adults Program; Vanderbilt University - Phil Daschner, Program Director; Division of Cancer Biology, Cancer Immunology, Hematology, and Etiology Branch; National Cancer Institute			
8–8:30am	 Early-age Onset (Under 50): Path to a Cure Speakers: Andrea (Andi) Dwyer, BS, University of Colorado Cancer Center–Advisor to Fight CRC Jill MacDonald, Early-age Onset Colon Cancer Survivor, Fight CRC Ambassador Cathy Eng, MD, FACP, FASCO Brittany O'Brian, GI Onc Research, CTRC III,Young Adult Cancer Initiative, Program Manager;Vanderbilt- Ingram Cancer Center 			
8:30–9am	Year in Review: Current/Latest Data from American Cancer Society Report Speaker: - - Andrea Cercek, MD, Gastrointestinal Oncologist; Co-Director of the Center for Young Onset Colorectal and Gastrointestinal Cancers; Section Head, Colorectal Cancers; Memorial Sloan Kettering Cancer Center			
9–10:15am	 State of the State EAO Post Pandemic (US vs. Global Funding) Moderators: Chris Lieu, MD, Associate Director for Clinical Research, Director of GI Medical Oncology at the University of Colorado Cancer Center, Associate Professor in the Division of Medical Oncology, and Associate Director for Clinical Research at the University of Colorado School of Medicine; Vice-Chair of the National Cancer Institute Colon Cancer Task Force Panelists: International Investment José Perea García, MD, PhD, Consultant Surgeon; Adjunct Professor of Surgery; Institute of Biomedical Research of Salamanca, Madrid NCI Activities and Initiatives on EOCRC Research Phil Daschner, Program Director; Division of Cancer Biology, Cancer Immunology, Hematology, and Etiology Branch; National Cancer Institute Matt Young, PhD, Program Director for Gastrointestinal Cancers at the Cancer Biomarkers Research Group, Division of Cancer Prevention, National Cancer Institute Cancer Grand Challenge on EAO (International Component) Richard Kuntz, MD, Senior Vice President, Chief Medical and Scientific Officer Metronic Anthony Dickherber, PhD, Program Director in the National Cancer Institute's-Office of the Director, Center for Strategic Scientific Initiatives, and Director of the NCI Innovative Molecular Analysis Technologies Department of Defense Funding Julia Huiberts, MS, Program Manager, Congressionally Directed Medical Research Programs NIEHS Presenting Abee Boyles, PhD, Health Scientist Administrator, National Institute of Enviornmental Health Sciences Arun Pandiri, PhD, DACBP, DABT, Leader, Molecular Pathology Group, Cellular and Molecular Pathology Branch, National Institute of Environmental Health Sciences (virtual) 			
10:15–10:30am	BREAK and Move into Tracks			
CONCURRENT SESSIONS – PICK ONE				

10:30–10:40am	 Track 1: Research Opportunities for Biology and Etiology: Exposures/ Microbiome/Study- Design Cohorts Moderators: Caitlin Murphy, PhD, MPH, Associate Professor, Health Promotion & Behavioral Sciences, University of Texas Health Houston, School of Public Health Cathy Eng, MD, FACP, FASCO, Medical Oncologist; Professor of Medicine, Division on Hematology/Oncology; Co-Leader, VICC Gastrointestinal Cancer Research Program; Co- Director, GI Oncology, Director, VICC Young Adults Program; Vanderbilt University 	 Track 2: Research Opportunities for Under 50 Risk Stratification and Population-based Early Intervention Strategies Moderators: Josh Demb, MPH, PhD, Postdoctoral Fellow at UC San Diego Division of Gastroentorology, Department of Medicine, UC San Diego Fola May, MD, PhD, Associate Professor of Medicine at the University of California Los Angeles (UCLA), Director of Quality Improvement in the Vatche and Tamar Manoukian Division of Digestive Diseases, Director of the May Laboratory, Associate Director of the UCLA Kaiser Permanente Center for Health Equity 	
10:45 to 11:30am	 Environmental and Occupational Exposures: Key Considerations for Discussion Exposome Dean Jones, PhD, Professor, Department of Medicine, Pulmonary Division; Professor, Department of Biochemistry; Director of the Emory Clinical Biomarkers Laboratory; Co- Director of the Emory Center for Clinical and Molecular Nutrition; Emory University 	 Contrasting Colorectal Cancer Screening; Guidelines Worldwide Ann Zauber, PhD, Attending Biostatistician, Memorial Sloan Kettering Cancer Center Iris Lansdorp-Vogelaar, PhD, Professor, Department of Public Health of Erasmus MC, Erasmus MC, Rotterdam, Netherlands (virtual) 	
11:30am to 12:15pm	 Microbiome or Epigenome and CRC Cindy Sears, MD, Professor of Medicine and Oncology, Johns Hopkins University School of Medicine; Professor of Molecular Microbiology and Immunology, Bloomberg School of Public Health; Microbiome Program Leader, Bloomberg- Kimmel Institute for Cancer Immunotherapy; Johns Hopkins Mariana Byndloss, DVM, PhD, Assistant Professor of Pathology, Microbiology and Immunology; Vanderbilt University 	 Research in Implementation of Risk Assesment, Family History, and Risk Stratification José Perea García, MD, PhD, Consultant Surgeon; Adjunct Professor of Surgery; Institute of Biomedical Research of Salamanca, Madrid, Spain Heather Hampel, MS, CGC, Associate Director, Division of Genetics and Genetic Counseling; Clinical Professor, Department of Medical Oncology and Therapeutics Research; City of Hope National Cancer Center Ohio 	
12:15 to 12:45pm	LUNCH		
12:45 to 1:30pm	Aging Markers - Kit Curtius, PhD, Assistant Professor of Medicine, Division of Biomedical Informatics; Associate Member of the Cancer Control Program at UCSD Moores Cancer Center, UC San Diego	 Populating Identification Using Stool-based Screening and Emerging Technologies (Triage Symptoms and Beyond), and Research Opportunities for EAO and Beyond (FIT, rRNA, MCEDs) Aasma Shaukat, MD, MPH, Robert M. and Mary H. Glickman Professor of Medicine, Dept. of Medicine at NYU Grossman School of Medicine; Professor, Dept. of Population Health at NYU Grossman School of Medicine; Director, Outcomes Research, Division of Gastroenterology and Hepatology; Co-director, Translational Research Education and Careers; New York University Langone Health 	
2:30 to 2:45p	Next Steps		
	- December 6, 2023 – EAO Think Tank Summary and Discussion (virtual) - International EAO Think Tank – Barcelona, Spain 2024		

Presentations and Tracks

Funding Opportunities Track

In the realm of EAO CRC research, a wide array of funding sources is available, spanning both the global and domestic landscapes. These opportunities are designed to support scientists dedicated to unraveling the complexities of EAO CRC, offering a pathway to innovative discoveries and advancements.

- Global Funding: International funding opportunities welcome applications from researchers worldwide, fostering a global collaborative effort in the fight against EAO CRC. Some of these international funding streams, however, may necessitate partnerships with specific countries, encouraging cross-border collaborations that enrich the research landscape with diverse perspectives and expertise.
- Domestic Funding in the United States: Within the U.S., esteemed institutions such as the National Institutes of Health, the National Cancer Institute, the Department of Defense's Congressionally Directed Medical Research Program, and the National Institute of Environmental Health Sciences are at the forefront of providing financial support. These grants encompass the full spectrum of EAO CRC research, from the initial exploratory phases to the expansion of professional networks and the facilitation of critical meetings.
- A Call for Innovative Collaboration: The consistent theme across these funding opportunities is the emphasis on collaborative and innovative approaches to EAO CRC research. By uniting diverse disciplines and fostering novel methodologies, these funding sources aim to accelerate progress in understanding, preventing, and treating EAO CRC.

DATA HIGHLIGHT

Rebecca Siegel, MPH, from the American Cancer Society, provided essential data to contextualize our discussions at the meeting, highlighting a significant trend: the increasing incidence of CRC among younger individuals. This data sheds light on diagnostic trends, screening rates, and the notable disparities that exist.

- Younger Patients: A significant rise in CRC cases has been observed among younger individuals, with cases in those under 55 years increasing from 11% in 1995 to 20%, and cases under 65 years from 27% to 45% ^[1].
- Screening Rates: Screening uptake remains critically low, with only 2% of the population ages 45-49 undergoing stool testing in 2021, pointing to a vital area for improvement in early detection efforts^[2].
- Left-Sided Tumors: A notable observation is the increase in left-sided tumors, especially in individuals ages 45-49, where the majority of EAO cases are found, suggesting a potential area for targeted research and intervention ^[3, 4].
- Disparities: The data also highlight significant disparities in EAO CRC disease burden, with Native Americans experiencing the highest incidence and Black individuals having the lowest survival rates ^[1, 5]. Additionally, there are significant racial disparities in treatment, underscoring the need for equity in health care access and treatment strategies ^[6].

This data is instrumental in guiding our research priorities, focusing on early detection, understanding the rise in younger patient cases, and addressing the profound disparities that impact outcomes in CRC.

Biology and Etiology Track

The Etiology Track delved into the complex origins of EAO CRC, emphasizing the critical role of various factors including environmental exposures, metabolic processes, microbial influences, and genetic changes. The key points highlighted the necessity of understanding these diverse factors for both prevention and treatment strategies.

- Environmental and Genetic Interplay: A significant portion of diseases, estimated between 85% to 95%, result from the interactions between genetics and environmental exposures over one's lifetime. This underscores the importance of the exposome in understanding and potentially preventing EAO CRC^[7].
- Microbiome's Influence: The intricate role of the microbiome in CRC development was highlighted, particularly the impact of microbial biofilms. The increased prevalence of biofilms in sporadic CRC cases, especially on the right side of the colon, suggests a potential pathway for CRC development, with specific bacteria like Fusobacterium, pks+ E. coli, and Bacteroides fragilis playing pivotal roles ^[8,9]. The focus is on understanding how these microbial communities, along with specific bacterial species known to influence CRC, contribute to the disease process ^[10,11].
- Microbial Biofilms and CRC: Studies have shown that biofilms, particularly on the right side of the colon, may play a critical role in CRC development by altering normal cell functions. Ongoing research aims to fill the knowledge gaps regarding the pathogenicity and persistence of these biofilms.
- Microbiome and Metabolism: Changes in the microbiome can disrupt the balance in the intestinal environment, favoring the growth of pathogenic and cancer-promoting bacteria. This imbalance, influenced by factors like antibiotic use and dietary habits, may contribute to CRC development and progression by altering microbial metabolites, especially short-chain fatty acids, thereby inducing host inflammation ^[10-14].
- Epigenetics as a Biomarker: The study of epigenetic changes, such as DNA methylation patterns, provides insights into the risk factors for young adults developing CRC. This area of research holds potential for identifying individuals at risk and understanding the disease's progression ^[15-21].
- Need for Comprehensive Research: The complexity of EAO CRC's etiology, influenced by a myriad of factors from genetic to environmental, underscores the necessity for extensive multiomic studies. These future investigations aim to decipher the interplay between different biological layers, from genes to proteins, to better predict, prevent, and treat EAO CRC.

This track emphasized the importance of a multidisciplinary approach to uncover the multifaceted causes of EAO CRC, highlighting the need for continued research and collaboration to advance our understanding and improve patient outcomes.

Recurring Themes



exposures, metabolomics, and microbial factors.

sharing data, samples, modeling, and research findings as well as deeper communication between researchers, clinicians, and investigative teams.

will likely be tailored to individuals based on their exposures, epigenetic age, and risk.

Interventions for Risk Stratification and Early Detection Track

The rise in CRC cases and mortality among those under 50 (EAO CRC) highlights a critical gap in riskbased screening. Family history of CRC and advanced adenomas are key risk factors, leading to recommendations for earlier screening in at-risk individuals, starting at age 40 or 10 years younger than the earliest family diagnosis ^[22]. Research indicates that adhering to these guidelines could have led to earlier detection in 50% of EAO CRC cases, with 15% potentially preventable ^[23].

During this Track's discussions, it was clear that the effectiveness of early screening is often hampered by insufficient family history assessments, contributing to delayed screenings for those at increased risk. It's reported that only 70% of primary care physicians consistently recommend CRC screening for at-risk young adults ages 40-to-49^[24]. There's a need for further research to understand how frequently primary care providers discuss family history and the obstacles they face, such as limited consultation time or a lack of guideline knowledge.

To address this, the creation and implementation of a standardized system, like a national CRC registry or enhancements in electronic health record systems, are essential for better tracking of family history and risk communication to those with a familial risk of CRC or advanced adenomas.

Moreover, strategies to improve screening adherence and address disparities are crucial to combat the increasing trend in EAO CRC cases and deaths. These measures include organized screening programs, patient navigation services, and educational initiatives to increase awareness and utilization of screening, particularly among young adults.

Recurring Themes



There are significant disparities across each nation in the adherence to CRC screening guidelines. Identifying factors that are associated with the lack of screening in communities will provide an avenue for intervention.



All stakeholders (industry, advocacy organizations, survivors, caregivers, researchers) must be involved in collaboration at an international level. Needs to include: (1) infrastructure development (2) multidisciplinary approaches (3) data sharing.

Future interventions will likely be tailored

on their exposures, microbiomes, epigenetic age, and risk.

Central Insight and Future Directions

A key insight from the discussions is the imperative to integrate scientific disciplines to enhance our understanding of interventions and risk-based stratification, necessitating a deeper knowledge of the exposome and biological factors. This interdisciplinary approach is crucial for advancing risk stratification methods.

Moving forward, Fight CRC and its collaborators plan to extend these efforts through a global EAO Think Tank series slated for spring, leading up to an intensive session in June 2024. This initiative aims to unite leading figures across the oncology spectrum to sustain dialogue and innovation. The series, building on the foundational discussions from the December 2023 assembly at Vanderbilt's EAO Cancer Center and with the NCI, is set to culminate in a significant international research meeting in Barcelona, Spain, in summer 2025. In partnership with the NCI and Dr. José Perea García of Spain, these gatherings are envisioned as a launchpad for pioneering ideas and collaborative ventures, drawing worldwide focus and propelling the quest to mitigate and ultimately eradicate CRC through shared knowledge and collaborative scientific efforts.

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