International GI Training Grants

GRANT AWARDS: $10,000 | DEADLINE MARCH 31, 2022

Whether you live in the U.S. or another country, you may be eligible!

Acquire or develop new cognitive knowledge or technical skill to improve patient care in your geographic area. The grant is to be used for travel to and from the training center and to the ACG Annual Meeting as well as for incidental expenses related to the training.

Visit gi.org/trainees/gi-training-grants for more information.
ACG AWARDS

Nominate a Colleague by April 15th!

2022 Award Categories:

- New! NP/PA Award for Clinical Excellence
- Berk/Fise Clinical Achievement Award
- Community Service Award
- Distinguished Mentorship & Teaching Award
- Diversity, Equity & Inclusion Award
- International Leadership Award
- Master of the American College of Gastroenterology
- Samuel S. Weiss Award

Nominations for these awards will be presented at the College’s Annual Scientific Meeting in Charlotte, NC on October 22, 2022.

gi.org/about/awards

TUNE IT UP: A CONCERT TO RAISE COLON CANCER AWARENESS

ACG Virtual Community Event in honor of March Colorectal Cancer Awareness Month

Thursday, March 31, 2022 at 8 pm EDT

Hosted by Dr. Benjamin Levy and ACG Public Relations Committee

American College of Gastroenterology | gi.org/Concert
Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.
How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR
ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2023 for this activity.

MOC QUESTION
If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.
A link for Genetic Counselor continuing education credits will also be sent to all attendees following tonight’s webinar.

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

**Week 13**
*Chromoendoscopy in IBD Surveillance: Always, Sometimes or Never?*
Gursimran Singh Kochar, MD, FACP, CNSC
March 31, 2022 at Noon Eastern - No 8pm Broadcast

Join ACG at 8pm on Thursday March 31st for the Tune it Up Concert to Raise Colon Cancer Awareness!

**Week 14**
*CAM and Psychological Therapies for Functional and Inflammatory Bowel Disease*
Jill K. Deutsch, MD and Laurie A. Keefer, PhD
April 7, 2022 at Noon Eastern and [ACG]

Visit [gi.org/ACGVGR](http://gi.org/ACGVGR) to Register
ACG SPECIAL Grand Rounds
Join us for upcoming Virtual Grand Rounds!

March 29, 2022 at 8:00pm Eastern!
Private Equity in Gastroenterology - "I Went the Private Equity Model: Reflections and Guidance"
**Featured Speaker: Scott Frasier, MBA**

Special Edition ACG VRG April 11, 2022 8pm - 9pm EDT
THE POTENTIAL FOR EARLIER HEREDITARY GI CANCER DETECTION WITH INSIGHT FROM A GI PRACTICE

Register Now for April 11th Webinar
Visit gi.org/ACGVGR to Register
Disclosures:

Speaker:
Swati G. Patel MD, MS
Freenome Inc: Research Support
Olympus America: Research Support
ERBE USA: Speakers Bureau

Moderators:
Carol A. Burke, MD, FACG
Dr. Burke, moderator for this activity, has no relevant financial relationship(s) with ineligible companies to disclose.

Anu Chittenden MS, LGC
Dr. Chittenden, moderator for this activity, has no relevant financial relationship(s) with ineligible companies to disclose.

*All of the relevant financial relationships listed for these individuals have been mitigated

Colorectal Cancer Prevention & Early Detection in Lynch Syndrome

Swati G. Patel, MD MS
Associate Professor of Medicine
Division of Gastroenterology & Hepatology
Director, Gastrointestinal Cancer Risk and Prevention Center
University of Colorado Anschutz Medical Center
Rocky Mountain Regional Veterans Affairs Medical Center
Swati.Patel@cuanschutz.edu
Colorectal Cancer Prevention & Early Detection in Lynch Syndrome

Swati G. Patel, MD MS
Associate Professor of Medicine
Division of Gastroenterology & Hepatology
Director, Gastrointestinal Cancer Risk and Prevention Center
University of Colorado Anschutz Medical Center
Rocky Mountain Regional Veterans Affairs Medical Center
Swati.Patel@cuanschutz.edu

Objectives

• Review colorectal cancer pathogenesis & risk in Lynch Syndrome

• Review efficacy of colonoscopy

• Review non-colonoscopy approaches to risk reduction
I wish we had more time...

Diagnosis of Lynch Syndrome

Extra-colonic risk reduction
I wish we had more time...

Diagnosis of Lynch Syndrome

Extra-colonic risk reduction

Objectives

- Review colorectal cancer pathogenesis & risk in Lynch Syndrome
- Review efficacy of colonoscopy
- Review non-colonoscopy approaches to risk reduction
Lynch Syndrome

- Accounts for 3-5% of all colorectal cancers
- Prevalence of 1/226-1/279
- Autosomal dominant inheritance of a pathogenic variant in a mismatch repair gene (MLH1, MSH2, MSH6, PMS2, EPCAM)

Lynch syndrome is a hereditary condition that increases the risk of colorectal cancer, among other cancers. It is caused by mutations in Lynch syndrome genes, which are responsible for repairing damaged DNA. If an individual has one normal gene and one damaged gene, they are considered to have Lynch syndrome. If they have two damaged genes, the risk of developing colorectal cancer is significantly higher.
Lynch Syndrome

Base pair mismatch

Normal DNA repair

Defective DNA repair (MMR+)

American College of Gastroenterology
Lynch Syndrome

Normal

Microsatellite instability
Colorectal Cancer Pathogenesis in LS


American College of Gastroenterology
Virtual Grand Rounds


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American College of Gastroenterology

17
Genotype-Specific Risk in LS

Bondadona et al. JAMA 2011;305:2304-10.

Mismatch Repair Consortium. Lancet Oncology 2021 22(7):1014-22
Objectives

- Review colorectal cancer pathogenesis & risk in Lynch Syndrome

- **Review efficacy of colonoscopy**

- Review non-colonoscopy approaches to risk reduction
Figure 1. Cumulative proportion of subjects free of CRC. 62% reduction in CRC (p=0.02) between the screening and control groups, including all subjects. 4P = 0.034 between mutation-positive subjects of the screening and control groups.


Table 2. Causes of Death Within the 15-Year Study Period

<table>
<thead>
<tr>
<th>Cause</th>
<th>Study group (n=133)</th>
<th>Control group (n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Brain cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Non-melanoma skin cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other malignant tumors</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other causes</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>26</td>
</tr>
</tbody>
</table>

AIDS, acquired immunodeficiency syndrome.
*Cause related to the HNPCC syndrome.

CRC Incidence

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds ratio M-H, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arriogoni et al. 2004</td>
<td>2</td>
<td>199</td>
<td>5</td>
<td>132</td>
<td>15.9%</td>
<td>0.26 [0.05, 1.35]</td>
</tr>
<tr>
<td>Jablonska et al. 1995</td>
<td>9</td>
<td>364</td>
<td>146</td>
<td>239</td>
<td>21.3%</td>
<td>0.02 [0.01, 0.03]</td>
</tr>
<tr>
<td>Jarvinen et al. 2000</td>
<td>6</td>
<td>133</td>
<td>17</td>
<td>119</td>
<td>20.0%</td>
<td>0.28 [0.11, 0.75]</td>
</tr>
<tr>
<td>Stuckless et al. 2012</td>
<td>28</td>
<td>152</td>
<td>116</td>
<td>170</td>
<td>22.1%</td>
<td>0.11 [0.06, 0.18]</td>
</tr>
<tr>
<td>Stupart et al. 2009</td>
<td>14</td>
<td>129</td>
<td>13</td>
<td>49</td>
<td>20.7%</td>
<td>0.34 [0.15, 0.78]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>977</td>
<td>709</td>
<td>100.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>59</td>
<td>297</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau²=1.55; Chi²=40.15; df=4 (P<.00001); I²=90%
Test for overall effect: Z=3.45 (P<.0006)

CRC Mortality


NCCN Guidelines Version 1.2021
Lynch Syndrome

### NCCN Guidelines Version 1.2021
#### Lynch Syndrome

<table>
<thead>
<tr>
<th>Gene</th>
<th>Average Age of Presentation</th>
<th>Cumulative Lifetime Risk (age 80)</th>
<th>Age to Start Colonoscopy</th>
<th>Colonoscopy Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLH1</td>
<td>44</td>
<td>46-61%</td>
<td>20-25*</td>
<td>1-2 years</td>
</tr>
<tr>
<td>MSH2 &amp; EPCAM</td>
<td>44</td>
<td>33-52%</td>
<td>20-25*</td>
<td>1-2 years</td>
</tr>
<tr>
<td>MSH6</td>
<td>42-69</td>
<td>10-44%</td>
<td>30-35*</td>
<td>1-2 years</td>
</tr>
<tr>
<td>PMS2</td>
<td>61-66</td>
<td>8.7-20%</td>
<td>30-35*</td>
<td>1-2 years</td>
</tr>
</tbody>
</table>

*Or 2-5 years prior to earliest CRC diagnosis

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43

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44

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American College of Gastroenterology
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Average Age of Presentation</th>
<th>Cumulative Lifetime Risk (age 80)</th>
<th>Age to Start Colonoscopy</th>
<th>Colonoscopy Interval</th>
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### NCCN Guidelines Version 1.2021

#### Lynch Syndrome

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</tr>
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</table>

*Or 2-5 years prior to earliest CRC diagnosis

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**American College of Gastroenterology**

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[Virtual Grand Rounds](universe.gi.org)
Chromoendoscopy

• Chemical substance sprayed onto mucosal surface to highlight contrast of raised and deepened areas

• Absorptive (methylene blue) vs non-absorptive (indigo carmine) staining

• Requires clean bowel preparation

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n)</th>
<th>Modality</th>
<th>Withdrawal time (min)</th>
<th>Patients with ≥ 1 adenoma</th>
<th>Number of Adenomas Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>WLE</td>
<td>Chromo</td>
<td>WLE</td>
<td>Chromo</td>
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<tr>
<td>Hurlstone et al 2005</td>
<td>25</td>
<td>SD-WLE vs IC</td>
<td>14.8</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>UK</td>
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<td></td>
<td></td>
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<td></td>
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<td>Lecomte et al 2005</td>
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<td>17</td>
<td>3</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stoffel et al 2008</td>
<td>52</td>
<td>SD-WLE vs IC</td>
<td>25.3</td>
<td>29.8</td>
<td>8/34</td>
</tr>
<tr>
<td>US</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>East et al 2008</td>
<td>62</td>
<td>SD-WLE vs NBI</td>
<td>6.33</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Huneberg et al 2009</td>
<td>109</td>
<td>SD-WLE vs IC</td>
<td>7.6</td>
<td>18</td>
<td>7/109</td>
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<tr>
<td>Germany</td>
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<td></td>
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<tr>
<td>Ramosooh et al 2010</td>
<td>75</td>
<td>SD-WLE vs AFE</td>
<td>Not reported</td>
<td>Not reported</td>
<td>28</td>
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<td>Netherlands</td>
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<tr>
<td>Bisschops et al 2017</td>
<td>61</td>
<td>HD-WLE vs I-scan</td>
<td>8.1</td>
<td>8.9</td>
<td>8</td>
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<tr>
<td>Patients (n)</td>
<td>Modality</td>
<td>Withdrawal time (min)</td>
<td>Patients with ≥ 1 adenoma</td>
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<td></td>
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<td>-------------</td>
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<tr>
<td>Stoffel et al 2008 US</td>
<td>52</td>
<td>SD-WLE vs IC vs 2nd look</td>
<td>25.3</td>
<td>29.8</td>
<td>8/54</td>
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</tr>
</tbody>
</table>
Effect of chromoendoscopy in patients with Lynch syndrome: An individual patient data meta-analysis of randomized trials

INTRODUCTION:
The additional diagnostic value of dye-based chromoendoscopy (CE) for surveillance of patients with Lynch syndrome is subject of debate.

METHODS:
To clarify this debate, we performed an individual patient data meta-analysis of randomized studies that compared CE with WLE for the detection of adenomas in patients with Lynch syndrome.

RESULTS:
Three randomized studies comprising 533 patients were included. The adenoma detection rate was 74/265 (28%) in patients randomized to WLE compared with 83/266 (31%) in patients randomized to CE (odds ratio: 1.17; 95% confidence interval 0.81–1.70).

DISCUSSION:
Based on low-quality evidence, CE showed no apparent increase in adenoma detection compared to WLE during surveillance of patients with Lynch syndrome.
Post-Colonoscopy Colorectal Cancer (PC-CRC)

*Interval Cancer*

= CRC occurring after colonoscopy, before next due colonoscopy
Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the Prospective Lynch Syndrome Database

Pathogenic MLH1

1-2-Year Surveillance
N=505
4,525 observation years

3-Year Surveillance
N=439
3,299 observation years


American College of Gastroenterology

PLSD Calls into Question Colonoscopy Efficacy

1. Lifetime CRC incidence is similar to retrospective estimates from populations not exposed to colonoscopy
2. Colonoscopy surveillance interval is not associated with CRC incidence
3. Colonoscopy surveillance interval is not associated with stage of CRC diagnosis
4. Colonoscopy surveillance interval is not associated with CRC mortality

Post-Colonoscopy Colorectal Cancer (PC-CRC)

Interval Cancer

CRC occurring after colonoscopy, before next due colonoscopy
Post Colonoscopy CRC

American College of Gastroenterology
<table>
<thead>
<tr>
<th>N</th>
<th>Design</th>
<th>Modality</th>
<th>Number of Adenomas Detected</th>
<th>Adenoma Miss Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>First Pass</td>
<td>Second Pass</td>
</tr>
<tr>
<td>25</td>
<td>Tandem, same endoscopist</td>
<td>SD-WLE vs IC</td>
<td>11</td>
<td>32*</td>
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<tr>
<td>33</td>
<td>Tandem, same endoscopist</td>
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<td>11*</td>
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<td>RCT parallel</td>
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<td>109</td>
<td>Tandem, same endoscopist</td>
<td>SD-WLE vs IC</td>
<td>18</td>
<td>52**</td>
</tr>
<tr>
<td>75</td>
<td>Tandem, RCT</td>
<td>SD-WLE vs APE</td>
<td>57</td>
<td>95**</td>
</tr>
<tr>
<td>78</td>
<td>Tandem, different endoscopist</td>
<td>SD-WLE vs IC</td>
<td>26</td>
<td>29*</td>
</tr>
<tr>
<td>61</td>
<td>Tandem parallel</td>
<td>HD-WLE vs I-scan</td>
<td>20</td>
<td>30*</td>
</tr>
<tr>
<td>246</td>
<td>RCT Parallel</td>
<td>HD/SD-WLE vs IC</td>
<td>31</td>
<td>35</td>
</tr>
<tr>
<td>272</td>
<td>RCT Parallel</td>
<td>HD-WLE vs IC</td>
<td>36</td>
<td>44</td>
</tr>
<tr>
<td>138</td>
<td>Tandem</td>
<td>HD-NBI vs IC</td>
<td>39</td>
<td>36*</td>
</tr>
</tbody>
</table>

*Additional adenomas
**Total adenomas
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Modality</th>
<th>Number of Adenomas Detected</th>
<th>Adenoma Miss Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Pass</td>
<td>Second Pass</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hurlstone et al. 2005</td>
<td>Tandem, same endoscopist</td>
<td>SD-WLE vs IC</td>
<td>11</td>
<td>32*</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td>32*</td>
<td>74.4%</td>
</tr>
<tr>
<td>Leconte et al. 2005</td>
<td>Tandem, same endoscopist</td>
<td>SD-WLE vs IC</td>
<td>7</td>
<td>11*</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td>11*</td>
<td>61.1%</td>
</tr>
<tr>
<td>Stoffel et al. 2008</td>
<td>RCT parallel</td>
<td>SD-WLE vs IC</td>
<td>17</td>
<td>16*</td>
</tr>
<tr>
<td>US</td>
<td></td>
<td></td>
<td>16*</td>
<td>48.4%</td>
</tr>
<tr>
<td>East et al. 2008</td>
<td>Tandem, same endoscopist</td>
<td>SD-WLE vs NBI</td>
<td>25</td>
<td>46*</td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td></td>
<td>46*</td>
<td>64.9%</td>
</tr>
<tr>
<td>Huneberg et al. 2009</td>
<td>Tandem, same endoscopist</td>
<td>SD-WLE vs IC</td>
<td>18</td>
<td>52**</td>
</tr>
<tr>
<td>Germany</td>
<td></td>
<td></td>
<td>52**</td>
<td>65.4%</td>
</tr>
<tr>
<td>Ramsoekh et al. 2010</td>
<td>Tandem, RCT</td>
<td>SD-WLE vs AFE</td>
<td>57</td>
<td>95**</td>
</tr>
<tr>
<td>Netherlands</td>
<td></td>
<td></td>
<td>95**</td>
<td>40.0%</td>
</tr>
<tr>
<td>Rahmi et al. 2015</td>
<td>Tandem, different endoscopist</td>
<td>SD-WLE vs IC</td>
<td>26</td>
<td>29*</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td>29*</td>
<td>52.7%</td>
</tr>
<tr>
<td>Bisschops et al. 2017</td>
<td>Tandem parallel</td>
<td>HD-WLE vs i-scan</td>
<td>20</td>
<td>30*</td>
</tr>
<tr>
<td>Belgium</td>
<td></td>
<td></td>
<td>30*</td>
<td>33.3%</td>
</tr>
<tr>
<td>Haanstra et al. 2019</td>
<td>RCT Parallel</td>
<td>HD/SD-WLE vs IC</td>
<td>31</td>
<td>35</td>
</tr>
<tr>
<td>Netherlands</td>
<td></td>
<td></td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Rivero-Sanchez et al.</td>
<td>RCT Parallel</td>
<td>HD-WLE vs IC</td>
<td>36</td>
<td>44</td>
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<tr>
<td>2020 Spain</td>
<td></td>
<td></td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Cellier et al. 2019</td>
<td>Tandem</td>
<td>HD-NBI vs IC</td>
<td>39</td>
<td>36*</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td>36*</td>
<td></td>
</tr>
</tbody>
</table>

*Additional adenomas
**total adenomas
Rate of “optimal” colonoscopy
41% (87/211) → 86% (304/353)

ADR and PDR the same
Flat adenoma 6.2% → 15.6%

PC-CRC
2.8% (6/211) vs. 0.3% (1/353)
893 Healthy LS carriers
- 4,177 colonoscopies
- Median interval 16.6 months
- Median follow up 5.34 years
<table>
<thead>
<tr>
<th>Quality Indicator</th>
<th>N (%) of 893</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete to cecum</td>
<td>797 (89.2%)</td>
</tr>
<tr>
<td>Adequate bowel preparation</td>
<td>447 (50.1%)</td>
</tr>
<tr>
<td>High-definition equipment</td>
<td>110 (12.3%)</td>
</tr>
<tr>
<td>Chromoendoscopy</td>
<td>41 (4.6%)</td>
</tr>
<tr>
<td>Surveillance within 2 years</td>
<td>453 (50.7%)</td>
</tr>
<tr>
<td>Surveillance within 3 years</td>
<td>701 (78.5%)</td>
</tr>
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<td>Quality Indicator</td>
<td>N (%) of 893</td>
</tr>
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<td>--------------------------------</td>
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<td>Surveillance within 3 years</td>
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</tr>
</tbody>
</table>

Overall adenoma detection rate
- Complete to cecum: 20% vs 0%, p=0.01
- Bowel prep: 2.07 (1.06-4.30)
- Chromo: 2.14 (1.15-3.95)

< 10 mm adenoma detection rate (15% HGD)
- All quality indicators: 2.18 (1.13-4.20)
- High-def scopes: 1.99 (1.05-3.76)

Flat adenoma detection rate
- High-def scopes: 3.04 (1.34-6.85)
- Chromo: 6.44 (2.29-19.59)
Post-Colonoscopy Cancer Rate 2.6% (N=23)
- Surveillance < 3 years: 0.35 (0.14-0.97)

PC-CRC Etiology

- Incomplete resection rate (IRR) of up to 10 (6.5 – 22.7%)
- IRR 23.3% for polyps 15 – 20mm
- IRR 31% for sessile serrated polyps


Post Colonoscopy CRC

Colorectal Cancer Pathogenesis in LS

Colorectal Cancer Pathogenesis in LS


Post Colonoscopy CRC

Missed

Rapid Growth

Incomplete Resection
Objectives

• Review colorectal cancer pathogenesis & risk in Lynch Syndrome

• Review efficacy of colonoscopy

• Review non-colonoscopy approaches to risk reduction

• Biomarker surveillance
• Chemoprevention
• Immune modulation
Objectives

• Review colorectal cancer pathogenesis & risk in Lynch Syndrome

• Review efficacy of colonoscopy

• Review non-colonoscopy approaches to risk reduction
  • Biomarker surveillance
  • Chemoprevention
  • Immune modulation

Management strategies for the colonoscopic surveillance of people with Lynch syndrome during the COVID-19 pandemic

Objectives

- Review colorectal cancer pathogenesis & risk in Lynch Syndrome

- Review efficacy of colonoscopy

- Review non-colonoscopy approaches to risk reduction
  - Biomarker surveillance
  - Chemoprevention
  - Immune modulation
Epidemiologic Observations

A Incidence
All randomized patients

B Mortality

C Patients with scheduled duration of trial treatment ≥ 3.5 years


Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial

CAPP2

CAPP2—CRC


CAPP2—LAC

Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial


CAPP2 Follow Up

<table>
<thead>
<tr>
<th>537 participants commenced intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>861 randomised to aspirin or placebo</td>
</tr>
<tr>
<td>26 randomised only for resistant starch</td>
</tr>
<tr>
<td>427 allocated to 600 mg aspirin</td>
</tr>
<tr>
<td>436 allocated to placebo</td>
</tr>
<tr>
<td>66 followed during intervention period only</td>
</tr>
<tr>
<td>2 participants had CRCs</td>
</tr>
<tr>
<td>2 participants had other LCa</td>
</tr>
<tr>
<td>5 participants had non-LCa</td>
</tr>
<tr>
<td>66 followed during intervention period only</td>
</tr>
<tr>
<td>2 participants had CRCs</td>
</tr>
<tr>
<td>4 participants had other LCa</td>
</tr>
<tr>
<td>2 participants had non-LCa</td>
</tr>
<tr>
<td>37 participants had CRCs</td>
</tr>
<tr>
<td>5 participants had other LCa</td>
</tr>
<tr>
<td>6 participants had non-LCa</td>
</tr>
<tr>
<td>58 participants had CRCs</td>
</tr>
<tr>
<td>12 participants had other LCa</td>
</tr>
<tr>
<td>11 participants had non-LCa</td>
</tr>
</tbody>
</table>

CAPP2 Follow Up

Number Needed To Treat to Prevent 1 CRC = 24


CAPP2

Obesity is associated with significantly increased risk of CRC

CRC risk in obese patients is mitigated with Aspirin Use

Questions that Remain
Questions that Remain

How exactly does Aspirin work to reduce CRC risk in Lynch Syndrome?

Anti-Inflammatory: COX-1 Inhibition

Questions that Remain

How exactly does Aspirin work to reduce CRC risk in Lynch Syndrome?

Microbiome: COX-1 Inhibition


American College of Gastroenterology
Questions that Remain

How exactly does Aspirin work to reduce CRC risk in Lynch Syndrome?

Questions that Remain

What is the right dose of Aspirin in Lynch Syndrome?
Questions that Remain

What is the right dose of Aspirin in Lynch Syndrome?

CaPP3
Cancer Prevention Programme

closed to recruitment (21.03.19)

Study has closed to recruitment but CaPP3 participants are receiving treatment and are in follow-up

600mg of aspirin each day for 2 years
300mg of aspirin each day for 2 years
100mg of aspirin each day for 2 years
600 mg of aspirin each day for 3 years
300 mg of aspirin each day for 3 years
75 mg of aspirin each day for 3 years

Questions that Remain

When to start? When to stop?
Questions that Remain

When to start? When to stop?


Questions that Remain

Risk-specific approach?
Questions that Remain

Risk-specific approach?

Willingness to prescribe
Questions that Remain

Willingness to prescribe


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S.3 Ep. 5 Cancer prevention with aspirin in hereditary colorectal cancer (Lynch Syndrome), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial

The fifth episode, hosted by CGA-ICG Council Member Dr. Swati Patel, features Sir John Burn, who is a professor of clinical genetics at Newcastle University, and Dr. Toni Seppäkä, who is a GI surgeon from University of Helsinki currently conducting a research fellowship at Johns Hopkins University. They discuss recently updated data from the CAPP2 study of aspirin chemoprevention in individuals with Lynch syndrome that was published in Lancet this summer, found here: https://pubmed.ncbi.nlm.nih.gov/32534547/

This episode was recorded on September 22, 2020, and reflects expert opinion at the time of the recording.
Objectives

• Review colorectal cancer pathogenesis & risk in Lynch Syndrome

• Review efficacy of colonoscopy

• **Review non-colonoscopy approaches to risk reduction**
  • Biomarker surveillance
  • Chemoprevention
  • Immune modulation

Colorectal Cancer Pathogenesis in LS


Requirements for a Vaccine

1. Predictability of finding microsatellites

2. Identical, recurrent antigens
Optimizing success of vaccine

1. **Potentiating the immune response** with the use of agents such as cytokines
   - N803 is an IL-15 superagonist immunocytokine. Shown to enhance T cell and NK responses

2. **Reducing or eliminating immunosuppressive** entities systematically or in the tumor microenvironment

3. Alter the phenotype of the premalignant or tumor cells to make them more **susceptible to immune mediated lysis**
Cancer Preventive Vaccine Nous-209 for Lynch Syndrome Patients

• Trivalent multitargeted recombinant adenovirus 5 (Ad5) vaccine (Tri-Ad5)

• Targets 209 neoantigens

• To maximize immunogenicity with high numbers of circulating immune cells, add IL-15 (N-803) which can promote vaccine’s efficacy
  • Well-tolerated in 25 completed and ongoing studies (>600 participants)

Primary endpoints
  • Cumulative incidence of colorectal neoplasm on 2 colonoscopies

Secondary endpoints
  • Antigen-specific T cells
  • Antibody levels
  • Immune cell types
  • Effect of NSAIDs, smoking, etoh on immune response
  • Extracolonic cancer
TO COLONOSCOPY AND BEYOND
My Practice

**Colonoscopy**
- Genotype-specific approach
- High-quality colonoscopy
- Surveillance every 1-2 years

**Aspirin Chemoprevention**
- H. Pylori eradication
- Aspirin 325 mg daily for all LS patients ≥ 60 kg
- 81 mg daily if not tolerated
- Stop in patients ≥ 70

Stay tuned...
- Extended colonoscopy surveillance intervals
- Lynch-syndrome specific quality indicators
- Adjunctive biomarker-based surveillance
- Aspirin dosing
- Cancer prevention vaccine
Questions?

Speaker:
Swati G. Patel MD, MS

Moderators:
Carol A. Burke, MD, FACG

Anu Chittenden MS, LGC