Early-Age Onset Colorectal Cancer

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Thursday, November 17, 3:30 PM
Young-Onset
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November 17, 2022
Conflict of Interest Disclosure (2021-2022)

- Institutional Research Funding:
  - Pharmavite, LLC
  - Evergrande Group
  - Janssen
  - Revolution Medicines

- Advisory Board / Consulting:
  - Bicara Therapeutics
  - GlaxoSmithKline
  - Redesign Health
  - Bayer
  - Pfizer
Young-Onset Colorectal Cancer Center: Mission statement

• Clinical care
  • Provide expert, compassionate, and multidisciplinary care to patients with young-onset colorectal cancer

• Education and awareness
  • Increase public education and awareness around the rising burden of colorectal cancer in young adults to improve prevention and early detection

• Research
  • Promote scientific discovery and innovation to elucidate underlying biological mechanisms, identify risk factors, and facilitate development of novel therapies
Clinical care: Unique clinical features and services

- **Multidisciplinary evaluation**
  - Upfront genetics appointment
  - Fertility, nutrition, sexual health, integrative oncology

- **Comprehensive psychosocial support**
  - Dedicated social worker with expertise in young patients
  - Customized programs tailored for young patients

- **Dedicated program coordinator**
  - Patient navigation
  - Liaison to clinical and research team

- **Personalized treatment**
  - GITARGET program
Clinical care: Comprehensive care model for young-onset CRC

• Pioneered a new model of care for young patients
• Implemented psychosocial distress screen
  • ↑ social work referrals
• Robust psychosocial programming
  • First to use Zoom for support groups and events
  • Created new peer-to-peer mentor program
Education and awareness: Creating community and educating healthcare professionals

Young-Onset Colorectal Cancer Center

Patient Spotlight
JAIME COWELL
Mayo Clinic Research & Program Coordinator

The first time I was diagnosed with colorectal cancer, I was 34 years old. I was devastated, and my mind was in a whirlwind of emotions. I was scared, but I quickly learned that I was not alone. Self-care is essential for anyone facing a cancer diagnosis, and after my treatment, I founded a support group for women with cervical cancer and young mothers. I often found myself thinking about how to help others who might be going through a similar experience. I joined the Young-Onset Colorectal Cancer Center to help others who are facing the same challenges. I want to provide a platform where people can share their experiences and learn from each other's stories. I believe that a strong support system is crucial for anyone facing cancer, and I hope that my story can inspire others to seek help and support when they need it. I am passionate about spreading awareness about young-onset colorectal cancer and empowering people to take control of their health. I encourage anyone who is feeling overwhelmed by their diagnosis to seek out support groups and other resources available to them.

Young-Onset Colorectal Cancer Center Patient and Family Forum

Beyond CRC: Better Understanding of Young-Onset Colorectal Cancer

Join the Young-Onset Colorectal Cancer Center for our second annual conference. This is a series of free educational events for individuals with young-onset colorectal cancer (diagnosed under 50 years old) and their caregivers. Attendees will hear from experts, attend breakout sessions, and meet others within the community.

Registration required:

rapecacbkg/bagordc

Follow us on Twitter: @DanaFarberCRC

You can find us on Facebook: @DanaFarberCRC

March 1st
6 - 7pm

Dr. Karen K. Komai: Hearing and Dialogue for an Inclusive Society: Living with Young-Onset Colorectal Cancer

March 6th
6 - 7pm

Gut Instincts: Best Practices for Screening Young People

March 8th
6 - 7pm

Best Practices for Screening Young People

March 14th
12 - 1pm

Lunch Break Social

March 15th
6 - 7pm

Lunchtime Social

March 22nd
6 - 7pm

Let's Talk Diet and Exercise - What Should I Eat? Young Onset

March 29th
6 - 3pm

Expert Panel: Latest Updates in Young-Onset Colorectal Cancer Research

Hosted by the Young-Onset Colorectal Cancer Center

Dana-Farber/Brigham and Women's Cancer Center

Gut Instincts: A Series on Young-Onset Colorectal Cancer

Best Practices for Screening Young People

March 4, 2021 at 6 PM

Please register here: bit.ly/bestpracticesyoung

We're on Twitter: Follow us @DanaFarberCRC

Young-Onset Colorectal Cancer Center
Education and awareness:
National platform to raise general public awareness

THE WALL STREET JOURNAL.
Adults as Young as 45 Should Be Screened for Colorectal Cancer, U.S. Panel Recommends
The final recommendation by the U.S. Preventive Services Task Force would lower the age for screening by five years and require many insurers to cover the testing

US task force proposes starting colorectal cancer screening at age 45
Education and awareness:
Government advocacy and partnership
Research:
Identification of Risk Factors in Nurses’ Health Study 2

n = 116,430 female nurses aged 25-42

Follow-up rates >90% in each 2-year cycle
Obesity is one leading hypothesis underlying young-onset CRC

Association of Obesity With Risk of Early-Onset Colorectal Cancer Among Women

Po-Hong Liu, MD, MPH; Kana Wu, MD, MPH, PhD; Kimmie Ng, MD, MPH; Ann G. Zauber, PhD; Long H. Nguyen, MD, MS; Mingyang Song, MD, ScD; Xiaosheng He, MD; Charles S. Fuchs, MD, MPH; Shuji Ogino, MD, PhD, MS; Walter C. Willett, MD, DrPH; Andrew T. Chan, MD, MPH; Edward L. Giovannucci, MD, ScD; Yin Cao, MPH, ScD

Table 2. Current BMI and Risk of Early-Onset Colorectal Cancer

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Cases</th>
<th>No. of Person-Years</th>
<th>Age-Adjusted RR (95% CI)</th>
<th>Multivariable-Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.5-22.9</td>
<td>29</td>
<td>455,250</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>23.0-24.9</td>
<td>20</td>
<td>217,271</td>
<td>1.27 (0.71-2.24)</td>
<td>1.33 (0.75-2.36)</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>30</td>
<td>296,763</td>
<td>1.32 (0.79-2.22)</td>
<td>1.37 (0.81-2.30)</td>
</tr>
<tr>
<td>≥30</td>
<td>35</td>
<td>230,169</td>
<td>1.86 (1.13-3.06)</td>
<td>1.93 (1.15-3.25)</td>
</tr>
<tr>
<td>Each 5-unit increase</td>
<td>NA</td>
<td>NA</td>
<td>1.18 (1.04-1.35)</td>
<td>1.20 (1.05-1.38)</td>
</tr>
<tr>
<td>P for trend</td>
<td>NA</td>
<td>NA</td>
<td>.01</td>
<td>.01</td>
</tr>
</tbody>
</table>

Weight Change Since 18 Years of Age

| Loss or gain <5.0 kg | 27 | 373,061 | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| Gain of 5.0-19.9 kg | 42 | 561,417 | 0.86 (0.53-1.41) | 0.86 (0.52-1.42) | 0.86 (0.52-1.43) |
| Gain of 20.0-39.9 kg | 34 | 214,633 | 1.66 (0.99-2.77) | 1.64 (0.96-2.81) | 1.65 (0.96-2.81) |
| Gain ≥40.0 kg | 11 | 47,342 | 2.25 (1.11-4.59) | 2.15 (1.02-4.54) | 2.15 (1.01-4.55) |
| Each 5-kg increase | NA | NA | 1.09 (1.03-1.16) | 1.09 (1.03-1.16) | 1.09 (1.02-1.16) |
| P for trend | NA | NA | .002 | .006 | .007 |

Beyond CRC

Young-Onset Colorectal Cancer Center
Sedentary Behaviors, TV Viewing Time, and Risk of Young-Onset Colorectal Cancer

Long H. Nguyen, Po-Hong Liu, Xiaobin Zheng, NaNa Keum, Xiaoyu Zong, Xiao Li, Kana Wu, Charles S. Fuchs, Shuji Ogino, Kimmie Ng, Walter C. Willett, Andrew T. Chan*, Edward L. Giovannucci*, Yin Cao*

Table 2. Sedentary TV viewing time and risk of young-onset CRC diagnosed prior to age 50 years

<table>
<thead>
<tr>
<th>Young-onset CRC</th>
<th>Sedentary TV viewing time, hours per week</th>
<th>( \leq 7 )</th>
<th>7.1-14</th>
<th>( &gt; 14 )</th>
<th>( P_{\text{trend}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td></td>
<td>52</td>
<td>33</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td></td>
<td>629,656</td>
<td>367,300</td>
<td>265,516</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1 (referent)</td>
<td>1.12 (0.72 to 1.74)</td>
<td>1.69 (1.09 to 2.63)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1 RR (95% CI)†</td>
<td>1 (referent)</td>
<td>1.15 (0.74 to 1.78)</td>
<td>1.75 (1.12 to 2.76)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 2 RR (95% CI)†</td>
<td>1 (referent)</td>
<td>1.15 (0.74 to 1.79)</td>
<td>1.77 (1.12 to 2.78)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 3 RR (95% CI)†</td>
<td>1 (referent)</td>
<td>1.12 (0.72 to 1.75)</td>
<td>1.69 (1.07 to 2.67)</td>
<td>.03</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Sedentary TV viewing time and risk of young-onset CRC diagnosed prior to age 50 years by anatomic site

<table>
<thead>
<tr>
<th>Anatomic site</th>
<th>Sedentary TV viewing time (hours per week)</th>
<th>( \leq 7 )</th>
<th>7.1-14</th>
<th>( &gt; 14 )</th>
<th>( P_{\text{trend}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon cancer</td>
<td></td>
<td>49</td>
<td>20</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td></td>
<td>629,664</td>
<td>367,382</td>
<td>265,527</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td></td>
<td>629,664</td>
<td>367,382</td>
<td>265,527</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1 (referent)</td>
<td>0.88 (0.51 to 1.51)</td>
<td>1.42 (0.84 to 2.46)</td>
<td>.25</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1 RR (95% CI)†</td>
<td>1 (referent)</td>
<td>0.89 (0.50 to 1.55)</td>
<td>1.47 (0.95 to 2.64)</td>
<td>.20</td>
<td></td>
</tr>
<tr>
<td>Rectal cancer</td>
<td></td>
<td>12</td>
<td>13</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td></td>
<td>629,696</td>
<td>367,385</td>
<td>265,534</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td></td>
<td>629,696</td>
<td>367,385</td>
<td>265,534</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1 (referent)</td>
<td>1.92 (0.87 to 4.22)</td>
<td>2.62 (1.15 to 6.00)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1 RR (95% CI)†</td>
<td>1 (referent)</td>
<td>1.91 (0.86 to 4.25)</td>
<td>2.44 (1.03 to 5.78)</td>
<td>.04</td>
<td></td>
</tr>
</tbody>
</table>
Sugar-sweetened beverage intake in adulthood and adolescence and risk of early-onset colorectal cancer among women

Jinhee Hur, Ebunoluwa Otegbeye, Hee-Kyung Joh, Katharina Nimptsch, Kimmie Ng, Shuji Ogino, Jeffrey A Meyerhardt, Andrew T Chan, Walter C Willett, Kana Wu, Edward Giovannucci, Yin Cao

Table 2: Sweetened beverage intake in adulthood and risk of early-onset colorectal cancer

<table>
<thead>
<tr>
<th>Exposure</th>
<th>&lt;1 serving/week</th>
<th>1 serving/week to &lt;1 serving/day</th>
<th>1 serving/day to &lt;2 servings/day</th>
<th>≥2 servings/day</th>
<th>F_test*</th>
<th>Each serving/day increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugar-sweetened beverages</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>536/466</td>
<td>504/341</td>
<td>178/866</td>
<td>138/469</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>45</td>
<td>34</td>
<td>14</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age- and energy-adjusted RR (95% CI)</td>
<td>1 (reference)</td>
<td>0.80 (0.54 to 1.14)</td>
<td>1.63 (0.55 to 4.72)</td>
<td>1.32 (0.93 to 1.86)</td>
<td>0.04</td>
<td>1.11 (0.96 to 1.29)</td>
</tr>
<tr>
<td>Multivariable RR (95% CI)</td>
<td>1 (reference)</td>
<td>0.59 (0.31 to 1.05)</td>
<td>1.24 (0.65 to 2.39)</td>
<td>2.18 (0.40 to 12.73)</td>
<td>0.02</td>
<td>1.10 (0.60 to 1.93)</td>
</tr>
<tr>
<td>Artifically-sweetened beverages</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>424/263</td>
<td>321/864</td>
<td>258/215</td>
<td>353/782</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>32</td>
<td>33</td>
<td>19</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age- and energy-adjusted RR (95% CI)</td>
<td>1 (reference)</td>
<td>1.25 (0.76 to 2.04)</td>
<td>0.95 (0.54 to 1.70)</td>
<td>0.86 (0.50 to 1.50)</td>
<td>0.32</td>
<td>0.95 (0.86 to 1.07)</td>
</tr>
<tr>
<td>Multivariable RR (95% CI)</td>
<td>1 (reference)</td>
<td>1.20 (0.73 to 1.94)</td>
<td>0.86 (0.48 to 1.54)</td>
<td>0.72 (0.42 to 1.27)</td>
<td>0.11</td>
<td>0.95 (0.63 to 1.45)</td>
</tr>
<tr>
<td>Hull juice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>450/950</td>
<td>750/662</td>
<td>92/635</td>
<td>14/25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>44</td>
<td>59</td>
<td>5</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age- and energy-adjusted RR (95% CI)</td>
<td>1 (reference)</td>
<td>0.81 (0.53 to 1.22)</td>
<td>0.66 (0.22 to 1.71)</td>
<td>0.70 (0.22 to 2.35)</td>
<td>0.41</td>
<td>1.04 (0.64 to 1.67)</td>
</tr>
<tr>
<td>Multivariable RR (95% CI)</td>
<td>1 (reference)</td>
<td>0.86 (0.56 to 1.31)</td>
<td>0.77 (0.29 to 2.35)</td>
<td>1.20 (0.56 to 2.16)</td>
<td>0.69</td>
<td>1.20 (0.74 to 1.94)</td>
</tr>
</tbody>
</table>

One serving serving: 8 fl oz

* Calculated using the mean of each category of beverage intake as a continuous variable.

Table 3: Sugar-sweetened beverage intake at age 13–18 years and risk of early-onset colorectal cancer

<table>
<thead>
<tr>
<th>Person-years</th>
<th>1 serving/week</th>
<th>1 serving/week to &lt;2 serving/day</th>
<th>≥2 serving/day</th>
<th>F_test*</th>
<th>Each serving/day increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>112,675</td>
<td>218,172</td>
<td>25,780</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>12</td>
<td>17</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age- and energy-adjusted RR (95% CI)</td>
<td>1 (reference)</td>
<td>0.87 (0.54 to 1.50)</td>
<td>1.74 (1.01 to 2.95)</td>
<td>0.05</td>
<td>1.10 (0.58 to 2.16)</td>
</tr>
<tr>
<td>Multivariable RR (95% CI)</td>
<td>1 (reference)</td>
<td>0.76 (0.46 to 1.27)</td>
<td>3.61 (0.80 to 16.62)</td>
<td>0.01</td>
<td>3.22 (1.00 to 10.20)</td>
</tr>
</tbody>
</table>

One serving serving: 8 fl oz

*Calculated using the mean of each category of beverage intake as a continuous variable.

**Additionally adjusted for race (white, non-white, height [continuous]), body mass index at age 18 years [continuous], pack-years of smoking before age 20 years [continuous], intake of alcohol at age 15–17 years, total intake of fruits and vegetables at age 15–17 years [continuous], multivitamin use at age 13–18 years [yes, no] and physical activity at age 9–12 (continuous), BMI, relative risk.
Total Vitamin D Intake and Risks of Early-Onset Colorectal Cancer and Precursors

Hanseul Kim, Marla Lipsyc-Sharf, Xiaoyu Zong, Xiaoyan Wang, Jinhee Hur, Mingyang Song, Molin Wang, Stephanie A. Smith-Warner, Charles Fuchs, Shuji Ogino, Kana Wu, Andrew T. Chan, Yin Cao, Kimmie Ng, and Edward L. Giovannucci

Table 2. Total Vitamin D Intake and Risk of Early-Onset CRC in the NHS II, 1991–2015

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>Cases/person-years</th>
<th>Age-adjusted model</th>
<th>MV-adjusted model 1</th>
<th>MV-adjusted model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;300</td>
<td>29,028.107</td>
<td>1.19</td>
<td>1.19</td>
<td>1.19</td>
</tr>
<tr>
<td>300 to &lt;450</td>
<td>20,316.284</td>
<td>0.52 (0.31–0.86)</td>
<td>0.51 (0.31–0.86)</td>
<td>0.51 (0.30–0.86)</td>
</tr>
<tr>
<td>≥450</td>
<td>27,408.189</td>
<td>0.57 (0.36–0.91)</td>
<td>0.56 (0.35–0.86)</td>
<td>0.49 (0.26–0.83)</td>
</tr>
</tbody>
</table>

P for trend: 0.01 0.01 0.01

Per 400 IU/day increase: 0.61 (0.41–0.91) 0.59 (0.39–0.89) 0.46 (0.26–0.83)

CI, confidence interval; HR, hazard ratio; MV, multivariable; other abbreviations as in Table 1.

Table 4. Total Vitamin D Intake and Risk of Early-Onset Conventional Adenoma and Serrated Polyp in the NHS II, 1991–2011

<table>
<thead>
<tr>
<th>CR (95% CI)</th>
<th>No. of cases</th>
<th>Age-adjusted model</th>
<th>MV-adjusted model 1</th>
<th>MV-adjusted model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any conventional adenoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total vitamin D intake, IU/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;300</td>
<td>559</td>
<td>1.19</td>
<td>1.19</td>
<td>1.19</td>
</tr>
<tr>
<td>300 to &lt;450</td>
<td>350</td>
<td>0.85 (0.75–0.97)</td>
<td>0.87 (0.76–0.99)</td>
<td>0.83 (0.71–0.98)</td>
</tr>
<tr>
<td>≥450</td>
<td>202</td>
<td>0.77 (0.65–0.91)</td>
<td>0.80 (0.68–0.94)</td>
<td>0.71 (0.56–0.99)</td>
</tr>
</tbody>
</table>

P for trend: 0.001 0.01 0.02

Per 400 IU/day increase: 0.82 (0.74–0.90) 0.85 (0.76–0.94) 0.76 (0.65–0.88)

Any serrated poly |              |                     |                     |                     |
| Total vitamin D intake, IU/day |              |                     |                     |                     |
| <300        | 719          | 1.19                  | 1.19                  | 1.19                  |
| 300 to <450 | 510          | 0.94 (0.84–1.06)     | 0.96 (0.86–1.08)     | 0.91 (0.80–1.04)     |
| 450 to <600 | 360          | 0.98 (0.86–1.01)     | 1.02 (0.89–1.21)     | 0.93 (0.79–1.09)     |
| ≥600        | 281          | 0.88 (0.77–1.00)     | 0.94 (0.81–1.08)     | 0.85 (0.70–1.03)     |

P for trend: 0.14 0.54 0.11

Per 400 IU/day increase: 0.91 (0.84–1.00) 0.95 (0.87–1.03) 0.85 (0.75–0.97)

CR, odds ratio; other abbreviations as in Table 1 and 2.

1Adjusted for age, sex, smoking status, alcohol consumption, body mass index, physical activity, family history of colorectal cancer, and history of lower endoscopy within the previous 10 years.
2Adjusted for age, sex, smoking status, alcohol consumption, body mass index, physical activity, family history of colorectal cancer, and history of lower endoscopy within the previous 10 years.
Prospective evaluation of dietary and lifestyle pattern indices with risk of colorectal cancer in a cohort of younger women

Y. Yue¹, J. Hur¹, Y. Cao²,³,⁴, F. K. Tabung¹,⁵,⁶, M. Wang⁷,⁸,¹⁰, K. Wu¹, M. Song¹,⁷,⁹,¹⁰, X. Zhang⁹, Y. Liu⁹,¹¹, J. A. Meyerhardt¹², K. Ng¹², S. A. Smith-Warner¹,⁷, W. C. Willett¹,⁷,⁹¹ & E. Giovannucci¹,⁷,⁹¹

<p>| Table 3. Associations of cumulative average dietary and lifestyle indices with risk of colorectal cancer diagnosed before and after age 50 years in the Nurses’ Health Study II, 1991-2015 |</p>
<table>
<thead>
<tr>
<th>Age at colorectal cancer diagnosis</th>
<th>P-heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 years</td>
<td>≥50 years</td>
</tr>
<tr>
<td>Number of events</td>
<td></td>
</tr>
<tr>
<td>Prime diet quality score</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Overall plant-based diet index</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Empirical dietary index for hyperinsulinemia</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Empirical lifestyle index for hyperinsulinemia</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>&lt;50 years</th>
<th>≥50 years</th>
<th>p-heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prime diet quality score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td>0.90 (0.55-1.48)</td>
<td>0.84 (0.59-1.20)</td>
<td>0.82</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td>0.90 (0.55-1.50)</td>
<td>0.91 (0.62-1.31)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Overall plant-based diet index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td>1.13 (0.68-1.88)</td>
<td>1.03 (0.70-1.50)</td>
<td>0.75</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td>1.24 (0.74-2.08)</td>
<td>1.10 (0.75-1.62)</td>
<td>0.70</td>
</tr>
<tr>
<td>Empirical dietary index for hyperinsulinemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td>1.34 (0.80-2.27)</td>
<td>1.50 (1.02-2.19)</td>
<td>0.72</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td>1.24 (0.72-2.16)</td>
<td>1.51 (1.00-2.29)</td>
<td>0.54</td>
</tr>
<tr>
<td>Empirical lifestyle index for hyperinsulinemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td>1.71 (1.04-2.81)</td>
<td>1.17 (0.82-1.66)</td>
<td>0.21</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)</td>
<td>1.86 (1.12-3.07)</td>
<td>1.20 (0.83-1.73)</td>
<td>0.16</td>
</tr>
</tbody>
</table>
Complex interplay of diet, host immunity, and microbiome

Putative early life and environmental exposures

Fig. 1 | Examples of life-course exposures with potential effects on CRC tumorigenesis. The exposome describes the totality of exposures and interactions thereof. The exposome can influence disease processes at any time from early life (the prenatal to adolescent periods) to adulthood. Gene-by-environment (GxE) interactions during the life-course might have important roles in the aetiology of early-onset colorectal cancer (CRC). Early-life biospecimens, such as blood, stool, saliva, urine, cord blood and placental tissue collected from either mothers or their offspring (at various timepoints during childhood), or both, might provide information on the early-life exposome when analysed in future studies of the aetiological factors underlying early-onset CRC. Of note, the composition of the gut microbiota can be influenced by various life-course exposures and might, in turn, influence GxE interactions that affect the development of CRC.

Beyond CRC
Better understanding of Young Onset colorectal cancer
Limitations of current cohorts

• Limited number of cases in existing contemporary cohorts
• Minimal racial, ethnic, and geographic diversity
• Lack of stool specimens for microbiome analyses
• Non-uniform, non-validated collection of dietary and lifestyle data
• No genomic correlates
• Single time point of collection of biospecimens and data
• Suboptimal clinical annotation
Study objectives

1) Improve our understanding of risk factors and biology of young-onset colorectal cancer

2) Discover novel means of prevention, early detection, and treatment for young-onset colorectal cancer
Prospective longitudinal cohort study

Patients diagnosed with CRC <50 years old

Healthy control patients <50 years old
Data and biospecimen collection

Patient Enrollment

Treatment 1

Treatment 2

Treatment 3

selective fresh tumor biopsies

once a year
Number of New Patients Seen at the Young-Onset Colorectal Cancer Center

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>176</td>
</tr>
<tr>
<td>2017</td>
<td>170</td>
</tr>
<tr>
<td>2018</td>
<td>188</td>
</tr>
<tr>
<td>2019</td>
<td>224</td>
</tr>
<tr>
<td>2020</td>
<td>243</td>
</tr>
<tr>
<td>2021</td>
<td>267</td>
</tr>
</tbody>
</table>
Beyond CRC: National and international expansion
Count Me In: Patient-partnered research is the future

- Digital social media platform to directly engage and partner with patients to accelerate colorectal cancer research
- Allows for much more rapid accrual and collection of biospecimens and data
- Enhances diversity and inclusion in research
  - Racial/ethnic
  - Socioeconomic
  - Geographic
- Enables research to continue during pandemic times

https://colorectalcancerproject.org/
Count Me In: Current enrollment

Co-Scientific Leads:
Kimmie Ng, MD, MPH
Andrea Cercek, MD
Acknowledgments

DANA-FARBER CANCER INSTITUTE
- Jeffrey Meyerhardt, MD, MPH
- Marios Giannakis, MD, PhD
- Brian Wolpin, MD, MPH
- Matthew Yurgelun, MD
- Nadine Jackson McCleary, MD, MPH
- Andrew Aguirre, MD, PhD
- Matthew Meyerson, MD, PhD
- Wendy Garrett, MD, PhD
- Ronald Bleday, MD
- Ann Partridge, MD, MPH
- Kalen Fletcher, MSW, LICSW, MPH
- Lauren Brais, MPH
- William Tan, MSW, LCSW
- Mary-Brent Brown
- Brigette Arsenault
- GCC research data specialists

BROAD INSTITUTE / COUNT ME IN TEAM
- Neus Bayo, PhD
- Mireia Sanchis

HARVARD T. H. CHAN SCHOOL OF PUBLIC HEALTH
- Curtis Huttenhower, PhD
- Edward Giovannucci, MD, ScD
- Mingyang Song, ScD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
- Alan Venook, MD
- Chloe Atreya, MD, PhD
- Erin Van Blarigan, ScD
- Sorbarikor Piawah, MD, MPH

ST. LUKE’S CANCER INSTITUTE
- Dan Zuckerman, MD

PATIENT ADVOCATES
- Patrick Beauregard
- David Thau
- Laura Porter
- Candace Henley
Thank You!
Young-Onset Colorectal Cancer Program

Thursday, November 17, 3:30 PM
Young-Onset Colorectal Cancer Program

We are the place for you. We are with you every step of the way.

Y. Nancy You, MD, MHSc
Devon Harrison
Benny Johnson, DO
Grace Li Smith, MD PhD MPH
Opportunity for Interception

Factors thought to contribute to the decline in death rate:

1. **Opportunity for Interception**
   - Young-onset Colorectal Cancer (CRC)

2. **Impact of Screening**

---

Figures and images include:

- **Figure 2. Stages of Colorectal Cancer Growth**
- **Figure 6. Trends in Colorectal Cancer Incidence (1975-2016) and Mortality (1930-2017) Rates by Sex, US**

---


Colorectal Cancer Facts & Figures 2020-2022
Among 47 states reporting data, increased incidence is reported in 42 (89.4%).

- Highest rates in Southern/Western states

**Figure 1. Median Age at Colorectal Cancer Diagnosis in the United States, 1990–2016**

Siegel et al, ASCO Ed Bk 2020

Siegel et al, JNCI 2019
Young-onset Colorectal Cancer
Risk Factors Unknown; Diagnosis Difficult

"When young colorectal cancer patients come to see us, they are completely lost and feel out of control."

NEVER TOO YOUNG SURVEY REPORT 2020 — Colorectal Cancer Alliance

Table 1: Exposomal elements driving EO CRC

<table>
<thead>
<tr>
<th>Exposomal element</th>
<th>Temporal trend</th>
<th>Global trend</th>
<th>Effect on inflammation/microbiome or known effect on distal colon or rectum</th>
<th>Exposure during development (conception to adulthood)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Westernized diets</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Red and processed meat</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Obesity</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Stress</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Synthetic dyes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Monosodium glutamate</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>High-fructose corn syrup</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

Key exposomal suspects driving early-onset colorectal cancer (EOCRC) emerge when four metrics are fulfilled: first, a temporal relationship exists, similar to EO CRC; second, exposure is global, as is EOCRC; third, molecular evidence exists of inflammatory or microbiome-modifying properties or evidence of an effect on the distal colon or rectum; and four, exposure occurs at any time during development from conception until adulthood.

Hofseth et al. Nat Rev Clin Onc 2020; Mauri et al, Molecular Oncology 2019
**Young-onset CRC**

**Scope & Urgency**

**The Increasing Incidence of Young-Onset Colorectal Cancer: A Call to Action**

Young-Onset Colorectal Cancer Program

Y. Nancy You, MD, MHSc
Devon Harrison
Benny Johnson, DO
Grace Li Smith, MD PhD MPH

We are the place for you. We are with you every step of the way.
MDACC: YOCRC significantly over-represented (35% vs. ~12% nationally)
Please join us on Tuesday, March 1st at 7:30 am

Young-Onset Colorectal Cancer Program Launch Party

- Guest speaker
- Patient and provider education materials
- FAQ

ZOOM LINK

Meeting ID: 
Password:

**Mission**

To offer the best integrated care for young-onset colorectal cancer patients across the cancer spectrum, including diagnosis, treatment, survivorship and prevention.

**Vision**

To be a worldwide leader dedicated to ending the burden of young-onset colorectal cancer.

**Values**

**PATIENT CENTRICITY**
We focus on coordinated and whole-person care to provide a personalized, holistic and caring experience.

**INNOVATION**
We strive for modern, innovative approaches and utilize technology to advance the mission.

**EXCELLENCE**
We deliver state-of-the-art, expert clinical care integrated with research.
Goals

- Expedite and coordinate access to cancer and multidimensional consults
- Create a technology platform for patient care navigation and communication
- Offer universal genetic testing with novel care delivery (telegenetics)
- Provide research-driven care with molecular profiling (solid and liquid)

- Build a multidisciplinary clinical trials pipeline (neoadjuvant, adjuvant, metastatic)
- Launch a longitudinal research repository
- Standardize care pathways throughout MD Anderson and MD Anderson Cancer Network®
Young-onset CRC
Universal germline testing

• 2009 Universal tumor screening for DNA mismatch repair deficiency (dMMR)
  • 11% dMMR
  
  Dineen et al, JNCCN 2015

• 2019 Universal germline multiplex testing
  • 25 (19.2%): Pathogenic mutations
  • 23 (17.7%): Variant of uncertain significance

You et al, DCR in press
GOAL 3. Offer Universal Genetic Testing With Novel Care Delivery (Tele-genetics)

Among 130 patients with test results:

- 25 (19.2%): Pathogenic mutations
- 23 (17.7%): Variant of uncertain significance

Pathogenic germline mutation was found in:
- 71% dMMR vs. 13% pMMR tumors [p<0.001]
- 32% positive family history vs. 12% no family history [p=0.015]

You et al, DCR in press
GOAL 3. Offer Universal Genetic Testing With Novel Care Delivery (Tele-genetics)

Pre-test Genetic counseling:

- Self-view a pre-taped session (7 min),
- or Attend a live session (in person or virtual).

Test: 47-gene Common Hereditary Cancer Panel

Post-test: Counseling & High-risk clinic

* Will not replicate testing if pre-referral testing available; extremely low insurance denial rate; video-consent successful in pilot
Young-onset CRC
Patient-centric Care Experience

CRC Operative Cases

<table>
<thead>
<tr>
<th>Year</th>
<th>Conversion (%)</th>
<th>MIS (%)</th>
<th>Open (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021</td>
<td>27%</td>
<td>44%</td>
<td>33%</td>
</tr>
<tr>
<td>2020</td>
<td>33%</td>
<td>44%</td>
<td>24%</td>
</tr>
<tr>
<td>2019</td>
<td>44%</td>
<td>33%</td>
<td>23%</td>
</tr>
<tr>
<td>2018</td>
<td>27%</td>
<td>44%</td>
<td>29%</td>
</tr>
<tr>
<td>2017</td>
<td>28%</td>
<td>44%</td>
<td>28%</td>
</tr>
</tbody>
</table>

Enhance Patient Surgical Experience

Patient-centric Treatments

Intense multi-modality therapy

Neoadjuvant Regimen: Response adaptive & individualized

Precision Adjuvant Therapy

Benchmarking Outcomes for Definitive Treatment of Young-Onset, Locally Advanced Rectal Cancer

- Median: 6cm from anal verge; 75% locally advanced 90% tri-modality therapy

NRG GI005 (COBRA): ctDNA as a predictive marker for response to adjuvant chemotherapy in stage II colon cancer

Individualized Treatment Sequencing Selection Contributes to Optimized Survival in Patients with Rectal Cancer and Synchronous Liver Metastases

- 1999-2014, rectal primary and synchronous resectable liver mets: N=268
Patient-centric Treatments

**Biomarker-directed: Metastatic, adjuvant, neoadjuvant, pre-emptive settings**

**PHASE III ATOMIC TRIAL**

N = 700

Eligibility Criteria
- Stage III colon adenocarcinoma with any tumor (T4a, N1-2M0, including N1G) originating or entirely located in colon
- Completely resected tumor
- dMMR
- No residual involved lymph node or metastatic disease at time of registration
- No prior chemotherapy, immunotherapy, biologic, targeted therapy, or radiation therapy; 1 previous cycle of mFOLFOX6 permitted.
- ECOG performance status ≤2
- No known active autoimmune disease or hepatitis B or C

**Endpoints:**
- Primary DFS
- Secondary OS, AEs

**Experimental arm:**
- mFOLFOX6 with atezolizumab (12 cycles) followed by atezolizumab (6 months)

**Control arm:**
- mFOLFOX6 (12 cycles)

AE indicates adverse event; DFS, disease-free survival; dMMR, DNA mismatch repair; mFOLFOX6, modified leucovorin calcium, fluorouracil, and oxaliplatin; OS, overall survival.

**Pathological Tumor Response Following Immune Checkpoint Blockade for Deficient Mismatch Repair Advanced Colorectal Cancer**

**PD-1 Blockade in Mismatch Repair–Deficient, Locally Advanced Rectal Cancer**

**Neoadjuvant Pembrolizumab for Patients with Mismatch Repair Deficient Localized and Locally Advanced Solid Cancers**

**ESMO 2021**

**EA2201:** An ECOG-ACRIN phase II study of neoadjuvant nivolumab plus ipilimumab and short course radiation in MSI-H/dMMR rectal tumors.

**ASCO 2022**
Supporting the Patient Journey

CANCER DIAGNOSIS
Access Navigation Community Genetics Financial Counseling

ACTIVE TREATMENT
Systemic Therapies Surgery Radiation Clinical Trials

ACTIVE SURVEILLANCE
Psychosocial Support Surveillance Clinical Trials

SURVIVORSHIP
Secondary Prevention Care Transition

We are the place for you. We are with you every step of the way.
Goal 1: Expedited & Coordinated Access to Multi-Dimensional Care

Survivorship: How does cancer impact life?

Functional Deficits and Symptoms of Long-Term Survivors of Colorectal Cancer Treated by Multimodality Therapy Differ by Age at Diagnosis

![Bar chart showing the percent of respondents reporting score ≥ 3 for anxiety, body image, male sexual function, and female sexual function among young-onset survivors (YS), late-onset survivors (LS), and all survivors.](chart.png)
EORTC Symptoms Scales

- Micturition problem
- Abdominal and pelvic pain
- Defecation problems
- Fecal incontinence
- Bloated feeling
- Dry mouth
- Hair loss
- Trouble with taste
- Sore skin
- Embarrassed by bowel movement
- Stoma-related problems
- Impotence
- Dyspareunia

Young-Onset Survivors vs Late-Onset Survivors

*P<0.05

Bailey/You et al.  J GI Surg 2015
Age 31-50 : SUPPORT Consult Bundle SmartSet

- Select any or all that are applicable for the patient

SUPPORT
GI High Risk & Genetics
Social work
Nutrition
Psychiatry
Supportive care
Oncofertility
Integrative medicine
Ostomy/wound
Physical Therapy
Age 18-30: AYA Oncology Consult Bundle

Panel: Ambulatory referral to AYA (Adolescent and Young Adult) (aka AYA)

- Status: Normal
- Expected Date: 5/16/2022
- Referral Priority: One Day
- Does the patient have an existing/previous cancer diagnosis? Yes
- Reason for referral: Fertility Counseling, Genetic Counseling, Psychosocial Services, Comprehensive Needs Assessment, Supportive and Survivorship Care

If a specialty service is available/selected from above, use its dept listed in parentheses when choosing the To dept.
Thank You!
Center for Young Onset Colorectal Cancer: A Clinical and Research Center

Thursday, November 17, 3:30 PM
Center for Young Onset Colorectal Cancer: A clinical and research center

Andrea Cercek, MD
Section Head, Colorectal Cancer
Co-Director, Center for Young Onset Colorectal & Gastrointestinal Cancers
Memorial Sloan Kettering Cancer Center
Early Onset Colorectal Cancer: The incidence is rising

Currently
- Incidence of CRC is declining among people over 50
- But the incidence is increasing among people under 50

By 2030:
- Incidence of CRC in young adults will nearly DOUBLE
- 1 in 10 colon and 1 in 4 rectal cancers will be diagnosed in those younger than 50
Early Onset Colorectal Cancer: The cause is unknown
Early Onset Colorectal Cancer: Top 20

<table>
<thead>
<tr>
<th>Country</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korea</td>
<td>12.9</td>
</tr>
<tr>
<td>USA</td>
<td>11.2</td>
</tr>
<tr>
<td>Japan</td>
<td>10.0</td>
</tr>
<tr>
<td>Netherlands</td>
<td>10.0</td>
</tr>
<tr>
<td>Norway</td>
<td>9.7</td>
</tr>
<tr>
<td>Slovenia</td>
<td>9.7</td>
</tr>
<tr>
<td>Brazil</td>
<td>8.8</td>
</tr>
<tr>
<td>Israel</td>
<td>8.4</td>
</tr>
<tr>
<td>Spain</td>
<td>8.1</td>
</tr>
<tr>
<td>Kuwait</td>
<td>7.9</td>
</tr>
<tr>
<td>South Korea</td>
<td>7.9</td>
</tr>
<tr>
<td>Colombia</td>
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<tr>
<td>Greece</td>
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<tr>
<td>Singapore</td>
<td>7.6</td>
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<tr>
<td>France</td>
<td>7.5</td>
</tr>
<tr>
<td>Australia</td>
<td>7.5</td>
</tr>
</tbody>
</table>

GLOBAL PHENOMENON
Main Objectives:
- Coordinated clinical program
- Clinical database, biospecimen repository, research

Patients Enrolled

2018

2022

201 → 2101
Center for Young Onset Colorectal Cancer

Established March 2018
First in the World


Mendelsohn, Palmaira, Cercek The Oncologist 2021
Center for Young Onset Colorectal Cancer
A Coordinated Clinical and Research Center

Age at Diagnosis

- <20: 9
- 20-29: 133
- 30-39: 597
- 40-49: 1362

- <20: 0.6%
- 20-29: 6%
- 30-39: 28%
- 40-49: 65%
Optimize introduction of ancillary services

Optimize patient communication/engagement

Research in tumor biology, microbiome and epigenetics

Outreach programs to raise awareness of young onset CRC

Clinical Trials designed to improve outcomes
<table>
<thead>
<tr>
<th>Ancillary Service</th>
<th>Patient Usage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Work</td>
<td>86%</td>
</tr>
<tr>
<td>Integrative Medicine</td>
<td>28%</td>
</tr>
<tr>
<td>Nutrition</td>
<td>69%</td>
</tr>
<tr>
<td>Psychology and Psychiatry</td>
<td>27%</td>
</tr>
<tr>
<td>Fertility</td>
<td>22%</td>
</tr>
<tr>
<td>Online Portal Use</td>
<td>97%</td>
</tr>
<tr>
<td>12-245 Part A (tumor genomics)</td>
<td>83%</td>
</tr>
<tr>
<td>12-245 Part C (germline)</td>
<td>79%</td>
</tr>
</tbody>
</table>


Mendelsohn, Palmaira, Cercek The Oncologist 2021
### Patient Satisfaction Survey Results

#### Patient Reported Service Utility and Timing (n=91)

<table>
<thead>
<tr>
<th>Support Service Used</th>
<th>Positive Service Utility¹</th>
<th>Appropriate Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Work (n=51)</td>
<td>70.59%</td>
<td>83.70%</td>
</tr>
<tr>
<td>Nutrition (n=54)</td>
<td>88.89%</td>
<td>88.50%</td>
</tr>
<tr>
<td>Fertility (n=18)</td>
<td>77.78%</td>
<td>100.00%</td>
</tr>
<tr>
<td>Sexual Health (n=16)</td>
<td>87.50%</td>
<td>68.80%</td>
</tr>
<tr>
<td>Integrative Medicine (n=31)</td>
<td>70.97%</td>
<td>80.00%</td>
</tr>
<tr>
<td>Psychology/Psychiatry (n=16)</td>
<td>87.50%</td>
<td>75.00%</td>
</tr>
</tbody>
</table>

¹: Patient rating 4 or 5 (somewhat helpful or very helpful)

n = patients who used and remembered using the service


Mendelsohn, Palmaira, Cercek The Oncologist 2021
Colorectal Cancer
Under Age 50

What we know about early onset colorectal cancer

70% have late disease - stage 3/4

67% saw at least 2 physicians before diagnosis

60% of cases under 50 years of age are random — not genetic
Is Early Onset Colorectal Cancer Biologically Different?

- Genetic analysis of tumors: 1,446 MSK patients
- More rectal tumors in younger onset
- Same cancer biology in both younger and older patients

Cercek et al, JNCI 2021
Is Early Onset Colorectal Cancer
What is the Etiology?

Ongoing research effort to identify etiology

• Risk factor questionnaire and stool collection for analysis of microbiome

• Further investigation of disease biology
Troubling New Trend:
Other young onset GI cancers are also rising

621 New Patients
Center expansion in 2021

Pancreas
Appendix
Gastric and others
Ongoing Research: What’s Causing the Rise in Cases and how to improve treatment?

- Optimizing clinical care
- Collaboration with other academic centers
- Research in etiology
- Clinical Trials
  - early treatment
  - changes in reproductive and sexual health in people with early onset colorectal cancer (NCT041812912)
Ongoing and Future Research:
What’s Causing the Rise in Cases and how to improve treatment?

- Optimizing clinical care
- Collaboration with other academic centers
- Research in etiology
- Clinical Trials
  --early treatment
  --changes in reproductive and sexual health in people with early onset colorectal cancer (NCT041812912)
Clinical Trials

Locally advanced rectal cancer

Goal is to move therapy into early stage to improve outcomes AND decrease treatment related toxicity

Phase II Study of Induction PD-1 Blockade in Patients with Locally Advanced Mismatch Repair Deficient Rectal Adenocarcinoma

NCT04165772
Standard Of Care

Cure is frequently achieved, but radiation and surgery can have life-altering consequences.
GOAL: OPTIONS TO STANDARD OF CARE

Reduce, Eliminate Radiation Side Effects

Short- and long-term toxicity, negatively impacting the function of:

- Bowels
- Bladder
- Sexual functioning
- Reproductive organs
Reduce, Eliminate Radical Surgery Side Effects

Significant Bowel Removal Surgery* Can Result in One or More Complications

- Hospital Mortality: 5%, 15%, 20%, 28%, 28%, 30%, 37%, 39%, 40%
- Re-admission 30 days: 5%, 15%, 20%, 28%, 28%, 30%, 37%, 39%, 40%
- Permanent stoma: 5%, 15%, 20%, 28%, 28%, 30%, 37%, 39%, 40%
- Urinary incontinence: 5%, 15%, 20%, 28%, 28%, 30%, 37%, 39%, 40%

*Total Mesorectal Excision
Biomarker: Mismatch Repair Deficient Rectal Cancer

Global annual incidence rectal cancer

750,000

5-10%
Mismatch Repair-Deficient rectal cancer cases
(40,000 to 75,000 patients annually)
EARLY STAGE RECTAL CANCER

Standard Of Care Prior To Study

RECTAL CANCER INITIAL TREATMENT
Cure is frequently achieved, but radiation and surgery can have life-altering consequences

TREATMENT OF METASTASES
Successful treatment of Mismatch Repair Deficient of MSI that has spread or metastasized

Chemo  Radiation  Surgery

Checkpoint Blockade
Treatment Uses a Highly Specific Drug to Target Cancer Cells

Treatment

Restarts the natural T-cell physiological process (that had been “turned off” by tumor) that plays a key role in the elimination of damaged, unwanted, and diseased cells.
MONOCLONAL ANTIBODIES

Treatment Uses a Highly Specific Drug to Target Cancer Cells

DOSTARLIMAB PD-1 Inhibitor

T-Cell

PD-1

Tumor Cell

PD-L1
STUDY PROPOSAL

Change Treatment for 'Mismatch Repair-Deficient' Rectal Cancer Patients

Checkpoint Blockade
Hypothesis based on success of treating advanced metastatic mismatch repair-deficient (complete response rate of about 10%)

Checkpoint Blockade

Chemo
Radiation
Surgery
Study Design

GOAL TO REPLACE ANY / ALL PREVIOUS TREATMENTS

Immunotherapy First

Dostarlimab
Treatment every three weeks for six months

Evaluation
Radiologic & Endoscopic

Dostarlimab Evaluation

Residual disease

Complete clinical response

Radiation

Residual disease

Complete clinical response

Non-operative follow up every four months

Surgery

81
Clinical Trial Approach

14 Patients
Ages 26 to 78
Stage II or III (Mismatch Repair Deficient Rectal cancer)

Consultations
Patients met with oncologists, surgeons, radiological oncologists

Dostarlimab
Single dose, every three weeks, for six months
Patient on study: planned treatment for 6 months

ENDOSCOPY IMAGES: PATIENT #2

Baseline
1.5
3.0
6.0
FU2 14
FU3 18
FU4 22

After 3 Treatments

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline
1.5
3.0
6.0
FU2 14
FU3 18
FU4 22
3 month assessment

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline
1.5
3.0
6.0
FU2  14
FU3  18
FU4  22
6 month assessment; end of treatment

ENDOSCOPY IMAGES: PATIENT #2

Months

Baseline
1.5
3.0
6.0
FU2 14
FU3 18
FU4 22
Non-operative Follow up 14 months

ENDOSCOPY IMAGES: PATIENT #2
Non-operative Follow up 18 months

ENDOSCOPY IMAGES: PATIENT #2
Non-operative Follow up 22 months; patient remains disease free

ENDOSCOPY IMAGES: PATIENT #2

Months
Baseline
1.5
3.0
6.0
FU2 14
FU3 18
FU4 22
Duration of Response

OUTCOMES (JUNE 2022)

Dostarlimab Treatment (6 months)

Patient 1

Patient 3

Patient 5

Patient 7

Patient 9

Patient 11

Patient 13

Complete Clinical Response

Duration (in months):

0 6 12 18 24 30 36
Future Research in Early Onset Colorectal Cancer:

- Genetics
- Dedicated Clinical Research Fellow
- Collaboration with basic science
- Evaluation of microbiome
- US and International Partnerships Colorectal Cancer
  - Project: DFCI and Broad Institute of MIT and Harvard
- Clinical Trials
QUESTIONS
Thank You!
Thank You!

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