## Follow-up Care in Colorectal Cancer

Howard Lim, MD, PhD, FRCPC Division of Medical Oncology, BC Cancer, Vancouver Centre Clinical Associate Professor, University of British Columbia Program Director, Medical Oncology Residency Training Program



### Disclosures

- Received honorariums from Eisai, Taiho, Roche, Lilly, Amgen, and Leo for consultant work
- Investigator on trials with Bayer, BMS, Lilly, Roche, Astra-Zenca and Amgen

### **Objectives**

1) Describe the follow-up care required for these patients;

2) Identify key factors in the seamless transition of care between oncology and primary care; and

3) Cite patient resources to improve the adherence to recommended guidelines.



### **Colorectal Cancer**

- Third most common cancer and 2<sup>nd</sup>/3rd leading cause of cancer death

   accounts for 25% of all cancer deaths
- Lifetime probability of 6% or 1 in 17
- Males=Females
- Risk increases with age
  - Median age 67-70y



## **CRC Epidemiology**

- 5 year survival (all comers) 62%
- Incidence highest in industrialized nations: Canada, US, N/W Europe
- 'Western' diet
  - high in red meat, fat
  - low in fiber, fruits & vegetables



### **CRC Screening Guidelines**

Average risk, age > 50 years ?45?	 	<ul><li>FIT q 2 years</li><li>If positive colonscopy</li></ul>
Previous adenomatous polyps	l	• @ 3 years then colonoscopy every 5 years
Previous CRC (curative intent)	Ш	•@ 1 year then every 3-5 years
IBD	ll	• @ 8 years after pancolitis or 15 years after L sided colitis then colonoscopy every 1-2 years. Consider colectomy.
FHx of FAP	Ш	•Colonoscopy @ puberty then annually – if polyposis or APC gene testing + then colectomy
FHx of HNPCC C Cancer Agency	Ш	•Colonoscopy age 21 then every 2 years, annually after age 40

3

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### Adenoma-Carcinoma Sequence

Adenomatous polyps ->Cancer

- ✓ Cancers rarely arise in the absence of polyps
- ✓ Polyps precede cancer
- Polyps > 1cm and multiple polyps (FAP) greatly increase cancer risk
- ✓ Removal of polyps reduces risk
- Rate of malignant transformation
  - 2.5 polyps / 1,000 / year
- Polyp dwell time
  - 10 years for a <1cm polyp to transform into invasive cancer



## **FIT testing**

- Detection of occult bleeding via poylps
- Detection of invasive cancer is
- Poylp removal to decrease risk of CRC
- Earlier dectection



## Colonoscopy





### Normal

Obstructing adenocarcinoma of the sigmoid colon



## Staging

- P/E, CXR, CT scan abdo/pelvis (can also do Chest/Abdo/pelvis) negative for metastases, CEA
- Referred to surgery
- Depending on pathology sent to Oncology for assessment



### Adjuvant Therapy for Colon Cancer

### Goal

- to eradicate micrometastatic disease

### • In whom?

- High risk stage II (no lymph nodes)– T4, obstruction, high grade, < 8 nodes examined</li>
  - Risk of Recurrence ~ 20%
- Stage III (lymph node positive)
  - Risk of Recurrence ~ 40 to 80%



Regimen	Administration	Decrease in Risk of Recurrence vs Surg alone	Toxicities
Capecitabine	Oral 1000mg/m2 BID q14/21d X 24 weeks (8 cycles)	30-40%	HFS, stomatitis, diarrhea, bili, neutropenia Rare: DPD def TRM: 0.7%
FOLFOX	IVAD Q2weekly infusional 5FU+LV+ oxaliplatin X 24 weeks (12 cycles)	50-60%	Neuropathy (early & late), N/V, alopecia, stomatitis, diarrhea, neutropenia, thrombocytopenia Rare: ILD TRM: 1%





#### Duration of Adjuvant Chemotherapy for Stage III Colon Cancer

A. Grothey, A.F. Sobrero, A.F. Shields, T. Yoshino, J. Paul, J. Taieb, J. Souglakos, Q. Shi, R. Kerr, R. Labianca, J.A. Meyerhardt, D. Vernerey, T. Yamanaka, I. Boukovinas, J.P. Meyers, L.A. Renfro, D. Niedzwiecki, T. Watanabe,\* V. Torri, M. Saunders, D.J. Sargent,\* T. Andre, and T. Iveson



- Randomized noninferiority trial of 3 months versus 6 months of oxaliplatin based chemotherapy
- In low risk colon cancer (T3N1) – 3 months of chemotherapy is sufficient
- Resulted in significant decrease in side effects

   especially neuropathy



### What's different for rectal cancer?



### Goals of Neoadjuvant Pelvic Radiotherapy in Rectal Cancer

- Local Control
  - ~35-45% reduction in risk of local recurrence
- Survival
  - No significant difference
- Sphincter Preservation
  - Maybe



### Radiation therapy for rectal cancer Making the tumour smaller before surgery



### Before treatment

### 6 weeks after treatment



### Why pre-operative treatment?

- Lower toxicity/Better tolerated
- Target the tumour (if tumour is resected treating normal tissue small bowel falls into the treatment field)
- Greater chance of the patient completing treatment for curative intent
- Aid in surgical management (possibility in downstaging disease)







## Does everyone need surgery? – Ongoing clinical trials

- If a patient has a complete response to treatment – can we do surveillance?
- Can we enhance our neoadjuvant treatments to downstage cancers to surgery or improve the response rate so that patients can avoid surgery



### Surveillance

- Previously imaging CT Chest/Abdo/Pelvis every year for the first 3 years
- Now 2 within the the first 3 years (so can consider 1 at year 1 and 1 at year 3)
- Remaining surveillance is the same



### **Advanced Colorectal Cancer**



# Paradigm FOLFIRI/FOLFOX +/- Bev FOLFOX/FOLFIRI (maybe Bev beyond progression)

### Third line KRAS wt – EGFR therapy -/+ irinotecan





### **Overall Survival**

	Left Side		Right	Side	
	EGFR	Bev	EGFR	Bev	
CALGB 80405	<b>39.3mos</b> n=173	<b>32.6mos</b> n=152	<b>13.9mos</b> n=71	<b>29.2mos</b> n=78	
FOLFOX/FOLFIRI + Cmab vs FOLFOX/FOLFIRI + BEV	HR=0.77 HR= <sup>-</sup>		HR=0.77 HR=1.36		1.36
FIRE 3	<b>38.3mos</b> n=157	<b>28.0mos</b> n=149	<b>18.3mos</b> n=38	<b>23.0mos</b> n=50	
FOLFIRI + Cmab vs FOLFIRI + BEV	HR=	0.63	HR= <sup>-</sup>	1.31	
PEAK	<b>43.4mos</b> n=53	<b>32.0mos</b> n=54	<b>17.5mos</b> n=22	<b>21.0mos</b> n=14	
FOLFOX + Pmab vs FOLFOX + BEV	HR=	0.84	HR=(	0.45	

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## Regorafenib

- Multi-targeted oral tyrosine kinase inhibitor against VEGF, FGFR, PDGFR
- 6 weeks survival benefit
- Fatigue, hand foot syndrome, cytopenias
- Not funded user pay \$6000-7000 a month



## TAS 102

- Compassionate Access Program
- 8 week survival benefit
- Main side effect is neutropenia
- Not funded
- Oral medication 2 weeks on 2 weeks off



### **Mechanism of Action of Checkpoint Protein Inhibition: CTLA-4 and PD-1**

 Anti-PD-1 therapies are designed to bind to PD-1 on activated T cells in the tumor microenvironment, whereas anti-CTLA-4 agents are designed to act by binding to CTLA-4 on activated T cells in the lymph nodes.



## Mismatch Repair Testing MMR

- MMR proof reading of DNA
- IHC stain
- If altered: high mutation rate in cancer
- Germline mutation linked to Lynch syndrome
- Predictive Lack of response to 5FU therapy (alone) - Stage II colon cancers – may not give treatment
- May predict response to immunotherapy 5% of metastatic colorectal patients

NCCN National Comprehensive Cancer Network<sup>®</sup>

### UNDERSTANDING IMMUNOTHERAPY SIDE EFFECTS

Immune checkpoint inhibitors (a type of immunotherapy) offer a promising new way to treat cancer for some patients. But these medicines can occasionally cause your immune system to attack normal organs and tissues in your body, affecting the way they work. Serious side effects typically occur in less than **5%** of patients, but certain mild side effects can occur in up to **30% – 50%** of patients.

Contact your health care professional right away if you think you may be experiencing ...

#### Brain inflammation (encephalitis)

Fever; confusion; changes in mood or behavior; neck stiffness; seizures; extreme sensitivity to light.

#### Hormone gland problems (especially the thyroid, pituitary, adrenal glands, pancreas)

Persistent or unusual headaches; extreme tiredness; weight loss or gain; rapid heartbeat; increased sweating; hair loss; constipation; dizziness or fainting.

#### Kidney problems

Decrease in the amount of urine; blood in the urine.

#### Skin problems

Rashes; itching; blistering; painful sores or ulcers.

#### Joint or muscle problems

Severe or persistent muscle or joint pain; severe muscle weakness Eye problems Blurry or double vision or other vision problems; eye

#### Lung problems (pneumonitis)

New or worsening cough; shortness of breath.

#### Liver problems (hepatitis)

Yellowing of the skin or the whites of the eyes; severe nausea or vomiting; pain on the right side of the stomach area; dark urine; bleeding or bruising more easily than normal.

#### Intestinal problems (colitis)

Diarrhea or more bowel movements than usual; stools that have blood or are dark, tarry, or sticky; severe stomach-area pain.

#### Nerve problems

Numbness or tingling in hands or feet; unusual weakness in legs, arms, or face.



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### Mismatch-repair Status Predicted Benefit of Pembrolizumab





The NEW ENGLAND JOURNAL of MEDICINE

Le DT et al. N Engl J Med 2015;372:2509-2520

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Presented by: Lukas Wartman, MD

Presented By Lukas Wartman at 2016 ASCO Annual Meeting

### **Overall Survival: All Patients**



oxaliplatin and irinotecan).

PRESENTED AT: 2018 Gastrointestinal Cancers Symposium #GI18 Presented by: Dr. Michael J. Overman Slides are the property of the author. Permission required for reuse.

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Supportive Care	×	SCIMMUNE_Protocol	× +	(Marchineg II)	eartheast base field a	Country and the	-		
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#### SCHYPCAL

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Guidelines for the diagnosis and management of malignancy related hypercalcemia

#### /PCAL Protocol

to PharmaCare:

onate

#### SCIMMUNE

Management of Immune-Mediated Adverse Reactions to Checkpoint Inhibitors Immunotherapy

- <u>SCIMMUNE Protocol</u>
- SCIMMUNE Patient Handout

#### SCMESNA

MESNA dosage modification for hematuria secondary to oxazaphosphorines (eg. Ifosfamide and Cyclophosphamide)

<u>SCMESNA Protocol</u>

#### SCNAUSEA

Antiemetic guidelines

- <u>SCNAUSEA Protocol</u>
- <u>SCNAUSEA Appendix Antiemetic Guidelines</u>

Hyperlinks to PharmaCare:

- <u>Ondansetron</u>
- <u>Granisetron</u>

P

<u>Aprepitant</u>

📔 Understanding\_Im....jpg \land

Miscellaneous Origin
Neuro-Oncology
Ocular
Primary Unknown
Sarcoma
Skin & Melanoma
Supportive Care
Interim Protocols
Immunotherapy

Lymphoma & Myeloma



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MMR-def/MSI-H – post 2 lines chemo: Consider immunotherapy – PDL1 +/- CTLA4 if KRAS WT – sequence unknown – IO/EGFR or EGFR/IO



### Estimated Costs of Therapy for Metastatic Colon Cancer/cycle

- Infusional 5FU
- Capecitabine
- FOLFOX
- FOLFIRI
- plus bevacizumab
- plus cetuximab
- plus panitumumab
- Regorafenib
- Immunotherapy



~\$50 ~\$700 ~\$1,750 ~\$250 +\$1,750+\$3,350 ~\$2,500 \$6000 \$10,000

## Survivorship – Financial Toxicity

- Job/disability Recommend 1 month recovery per month of treatment
- Recovery from side effects some may be permanent – especially neuropathy
- Anxiety surveillance/fear of recurrence
- Loss of income during the time of treatment of recovery





#### Digital Oncology

Patients' crowdfunding campaigns for alternative cancer treatments

We found three categories of rationales for seeking CAM cancer treatments: individuals who want to try every available treatment; and who are using it to complement traditional treatment; individuals who chose to forgo traditional treatment because of fear of its effects or skepticism about its activity; and individuals who cannot pursue traditional treatment for financial or medical reasons but do not wish to forgo treatment.

are not available. Campaigns driven by any of these rationales have the potential to exacerbate problems associated with the use of alternative cancer treatments, including wasting resources and raising false hopes for better health. Importantly, through crowdfunding and the power of social networks, these problems are spread to larger communities. This funding source also gives patients who have been told that continued care with traditional methods is futile the opportunity to preserve the hopes of themselves and their social networks that some unproven method of treatment will reverse their cancer. As such, crowdfunding might make it more difficult to acknowledge a terminal diagnosis and accept pallative care options insofar as pallative care is viewed by many patients as giving up on treatment.



### **Alternative Treatments**

- Patient discuss with pharmacists
- Typically will say no:
  - 1) Uncertain on what is in the product
  - 2) Interactions with treatment
- Try to have a dialogue what is hope of using alternative treatments – what is the cost?



### Cannabis

- There are clinically trials looking at symptom benefit of cannabis in cancer patients
- There is no known anti-neoplastic effects of cannabis
- If refractory to medications for nausea or pain – reasonably to consider (reality – most of my patients have likely already tired it)



### Diets

- Sugar does NOT feed cancer
  - Increase in obesity increase in obesity related cancers
  - Handout on BC Cancer site
- Fad diets eg Gerson diet
- No magic diet Canada Food guide
  - Eat the foods that make you feel well
  - Can call 811 Oncology dietician



### Exercise

- Can exercise on chemotherapy
  - Decrease toxicity
  - Maintain lifestyle
  - Otherwise hard to "delump" inactive for 6-8 months – takes time to be active again
  - Call 811 oncology physiotherapist
- Decrease risk of recurrence as long as increase activity from baseline
- Currently have a clinical trial at BC Cancer for colon patients post adjuvant chemotherapy



## Fertility

- Chemotherapy/Cancer can impact fertility
- Rectal Cancer Radiate the uterus therefore can not become pregnant
- Refer patients for fertility consults
  - Sperm banking
  - Egg harvest
  - Embryos



### **Colorectal Cancer (CRC)**





## Hereditary Issues

- Hereditary Issues in 20% of patients
- Most common Lynch Syndrome
- Working with the Ministry of Health for screening for Lynch Syndrome in patients diagnosed with colorectal cancer – test done on tumor tissue
- Up to the affected individual to tell family
- Can self refer to Hereditary Cancer Program









RE & RESEARCH

Ancestry Composition tells you what percent of your DNA comes from each of 31 populations worldwide. The analysis includes DNA you received from all of your ancestors, on both sides of your family. The results reflect where your ancestors lived 500 years ago, before ocean-crossing ships and airplanes came on the scene.

37.4%	European
	Southern European
11.1%	📕 Iberian
13.8%	Nonspecific Southern European
	Northern European
3.2%	British & Irish
0.8%	Scandinavian
2.2%	Nonspecific Northern European
0.3%	Ashkenazi
6.0%	Nonspecific European
36.2%	Sub-Saharan African
36.0%	West African
0.3%	Nonspecific Sub-Saharan African
22.9%	East Asian & Native American
22.9% 17.5%	East Asian & Native American Native American
22.9% 17.5%	East Asian & Native American <ul> <li>Native American</li> <li>East Asian</li> </ul>
22.9% 17.5% 0.3%	East Asian & Native American <ul> <li>Native American</li> <li>East Asian</li> <li>Nonspecific East Asian</li> </ul>
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22.9% 17.5% 0.3% 0.1% 5.0%	<ul> <li>East Asian &amp; Native American</li> <li>Native American</li> <li>East Asian         <ul> <li>Nonspecific East Asian</li> <li>Southeast Asian</li> <li>Nonspecific East Asian &amp; Native Am</li> </ul> </li> </ul>
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100% Yvette Porter Moore



#### HEALTH OVERVIEW

X 23andMe Research Discoveries were made possible by 23andMe members who took surveys.

SHOW RESULTS FOR

#### Health Risks (122)

ELEVATED RISKS	YOUR RISK	AVERAGE RISK
Age-related Macular Degeneration	22.5%	7.0%
Restless Legs Syndrome	5.2%	4.2%
Chronic Kidney Disease	2.7%	2.2%
Crohn's Disease	1.3%	0.5%
Ulcerative Colitis	0.88%	0.51%
	See all 12	O viels very ente

See all 122 risk reports...

#### Inherited Conditions (53)

REPORT	RESULT
Hemochromatosis (HFE-related)	Variant Present
ARSACS	Variant Absent
Agenesis of the Corpus Callosum with Peripheral Neuropathy (ACCPN)	Variant Absent
Alpha-1 Antitrypsin Deficiency	Variant Absent
Autosomal Recessive Polycystic Kidney Disease	Variant Absent
See al	53 carrier status

SEE NEW AND RECENTLY UPDATED REPORTS »

#### Traits (63) 🕜

REPORT	RESULT
Alcohol Flush Reaction	Does Not Flush
Bitter Taste Perception	Unlikely to Taste
Blond Hair	28% Chance
Earwax Type	Wet
Eye Color	Likely Brown

#### Drug Response (25)

REPORT	
Proton Pump Inhibitor (PPI) Metabolism (CYP2C19-related)	Rapid
Phenytoin Sensitivity (Epilepsy Drug)	Increased
Sulfonylurea Metabolism	Reduced
Abacavir Hypersensitivity	Typical
Acetaldehyde Toxicity	Typical



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#### HEALTH

## Unhidden Traits: Genomic Data Privacy Debates Heat Up

We shield social security numbers, conceal credit cards and shred sensitive records. Now it's time to think about how closely we guard our genomes





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## **23andMe to Mine Genetic Database for Drug Discovery**

Personal genetics company names Richard Scheller chief science officer

The company sends customers their genetic data but says 80% of them agree that 23andMe owns the aggregated data with rights to use it for research. It says the database is the largest repository of human genetic data in the world.





# How genetic testing can be used against you – and how Bill S-201 could change that



Brynne Stainsby, who was at a high risk for Huntington's Disease but later learned she didn't carry the gene for the disease, says her insurance provider took longer than normal to process a life-insurance application because of her genetic-testing results.

KEVIN VAN PAASSEN/THE GLOBE AND MAIL



#### TRENDING

- 1 U.S. ambassador to Mexico to resign amid strained relations
- 2 Woman suffers burns after cellphone caught fire on Air Canada plane
- 3 Canada slams planned U.S. tariffs on steel and aluminum imports **•••**
- 4 The close: \$300-billion in U.S. market cap wiped out as stocks plunge on Trump steel tariffs
- 5 CIBC's new rules for foreign clients could squeeze Vancouver market

#### LATEST VIDEOS

Liberals ready to 'intervene' to avoid grain crisis 2:00

## Bill S-201

- Create a Genetic Non-Discrimination Act
  - Prohibit requirement that genetic test results be disclosed as a provision of good and services
  - Amend the labour code to prevent employee from being required to take a genetic test or disclose results
  - Amend the Human Rights act to prohibit genetic discrimination



### Vaccines

- Flu shots preferable to start before treatment – can do a shot but may not be as effective. Best for handwashing and avoid sick people. If family member sick – they should wear a mask
- Live vaccines technically not on chemo should wait 3 months
- Measles- depends on exposure should discuss with oncologist (can check titres)



## Summary

- Newer therapies helping with patient survival
- There are significant survivorship issues ongoing support for these patients enhance their survival
- Support to adapt to the diagnosis
- Greater social issues with genomic testing





