Advances in Cancer Treatment and Screening

A Life Insurance Perspective

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Overview of the presentation

- Cancer Immunotherapy
- Cancer Screening

Cancer Immunotherapy

The History of Cancer Immunotherapy

- Fields of Immunology and Oncology have been linked since the late 19th century
  - William Coley reports the injection of killed bacteria into sites of sarcoma tumors can lead to tumor shrinkage.

Source: Prof Ben Willcox. Cancer Immunology and Immunotherapy Centre. University of Birmingham

The History of Cancer Immunotherapy

- **First generation** immunotherapeutics prior to **1980's**

- **Nonspecific immunostimulants**
  - Mechanism of action unknown
  - Rarely limited tumor growth
  - Provided impetus for creation of the Biologic Response Modifiers Program of the NCI

The History of Cancer Immunotherapy

- **Second generation** immunotherapeutics prior to **1990's**

- **Well-characterized Recombinant Cytokines**
  - FDA approved
  - Such as interferons and interleukin-2
  - These induce activation and proliferation of T cells and Natural Killer (NK) cells
  - Significant associated toxicities
  - Limited success (< 10% patients) but served as "Proof of Principle" that immune system if properly activated could produce durable cancer control

The History of Cancer Immunotherapy

- **Third generation** immunotherapeutics integrated into cancer care prior to **2000's**
- Utilized humanized and human **monoclonal antibodies** to cell surface receptor proteins present on tumor cells
  - Human epidermal growth factor receptor 2 (HER2)/Neu
  - Epidermal growth factor receptor (EGFR)
- **Vaccination** strategies
  - Using available peptides, whole tumor, recombinant proteins, dendritic cells
  - Only modestly successful
  - Vaccine of long peptides for HPV E6, E7 in precancerous lesions

The Established Cancer Treatment Landscape

- Chemotherapy
  - Disadvantages
    - Non-specific
    - Risk of infection
    - Frequent resistance means effects are short-lived
- Radiotherapy
  - Disadvantages
    - Non-specific
    - Not so effective for metastases
- Surgery
  - Disadvantages
    - Ineffective for metastases
    - May not be curative in advanced settings

Cancer Immunotherapy – The Current View

- **Modern** era (since 2005 – current) of immunotherapy launched by
  - Novel efficacy of **monoclonal antibodies to immune checkpoint inhibitors**
  - **Cellular engineering** with resultant **Chimeric Antigen Receptor (CAR) T cells** and expanded Tumor-Infiltrating Lymphocytes (TILs) that engage with the highly evolved communication network of immunity within the host

Modern Cancer Treatment

- **Immunotherapy integrated** with conventional surgical, chemotherapeutic and radiation oncologic strategies

- Chemotherapy and pathway-inhibitor drugs target intracellular mechanisms whereas immunotherapy targets primarily extracellular interactions

Two Modern Immunotherapy Approaches

- Immune **Checkpoint Inhibition**
  - “Removing the brakes from the immune system”

- Immunotherapy through **Cellular Engineering**
  - Engineering ‘smarter’ immune cells

Current Approvals

- **Melanoma**
  - Ipilumumab approved for the treatment of previously-treated metastatic (advanced) melanoma
  - Ipi and Nivo combo approved for advanced melanoma

- **Lung cancer**
  - Strong Nivolumab efficacy data

- **2014 – 2016 FDA Approval for anti-PD1 and anti-PD-L1 agents for treatment of:**
  - Kidney cancer
  - Urothelial cancer
  - Head and Neck cancers
  - Hodgkin disease

Checkpoint Blockade: Challenges

Arguably the most exciting area for pharma-oncology research currently but:

- Huge expense
  - ~ $100,000 per year per patient –
- Only some patients respond well (durable, complete response)
  - How to identify these patients?
- Side effects:
  - Can be severe

CAR Immunotherapy: Challenges

- Can you expand the success of CAR therapy beyond haematological malignancies?
- What molecular targets will allow safe and specific targeting of tumours?
- Can the cost of a cellular therapy be absorbed in current healthcare insurance cost structures?

Future Trends in Immunotherapy

- Some obvious trends
  - Checkpoint Blockade Inhibition
  - CAR Immunotherapy
- But also a number of other approaches

Trends in Checkpoint Blockade

- Combination approaches to increase the proportion of patients who will respond:
  - Ipilumumab + Nivolumab (melanoma) – major improvement in response rate
  - Numerous combinations to test:
    - CB + CB;
    - CB + chemo
    - CB + targeted therapy
    - CB + other immunotherapy

Trends in Checkpoint Blockade

- Improved stratification of likely responders:

1. Colorectal cancer – MSI-hi subgroup (15% show high response rate)

2. Improved prediction of where durable responses will be observed – conversion of some conditions from critical to curable

TREND: Increasing number of patients/tumours/tumour subgroups where durable responses are observed

Trends in CAR Immunotherapy

- More sophisticated CAR targeting approaches
  - A trend away from single targets (e.g. CD19) towards multiple CAR targets to define tumour and tissue type
  - Different strategies (e.g. targeting the tumour's 'support structure')

- Extended success of CAR immunotherapy across haematological tumours
  - Adoption in some CD19-positive B cell tumours
  - Application in other tumours e.g. Myeloma

Ongoing CAR trials in multiple solid tumours

TREND: Increasing number of patients/tumours/tumour subgroups where CAR therapy can induce durable responses

somewhat different

Cancer Screening

- Colorectal Cancer
- Breast Cancer
- Lung Cancer

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Colorectal Cancer (CRC)

- Why screen?
  - CRC is common and lethal
  - Removal of premalignant adenomas can prevent CRC
  - Removal of localized cancer can prevent CRC-related deaths

- Recommended screening tests include stool-based tests or tests that visualize the colon
  - Fecal Occult Blood Test (FOBT)
  - Fecal Immunochemical Test (FIT)
  - FIT-DNA
    - Multitargeted stool DNA (Cologuard)

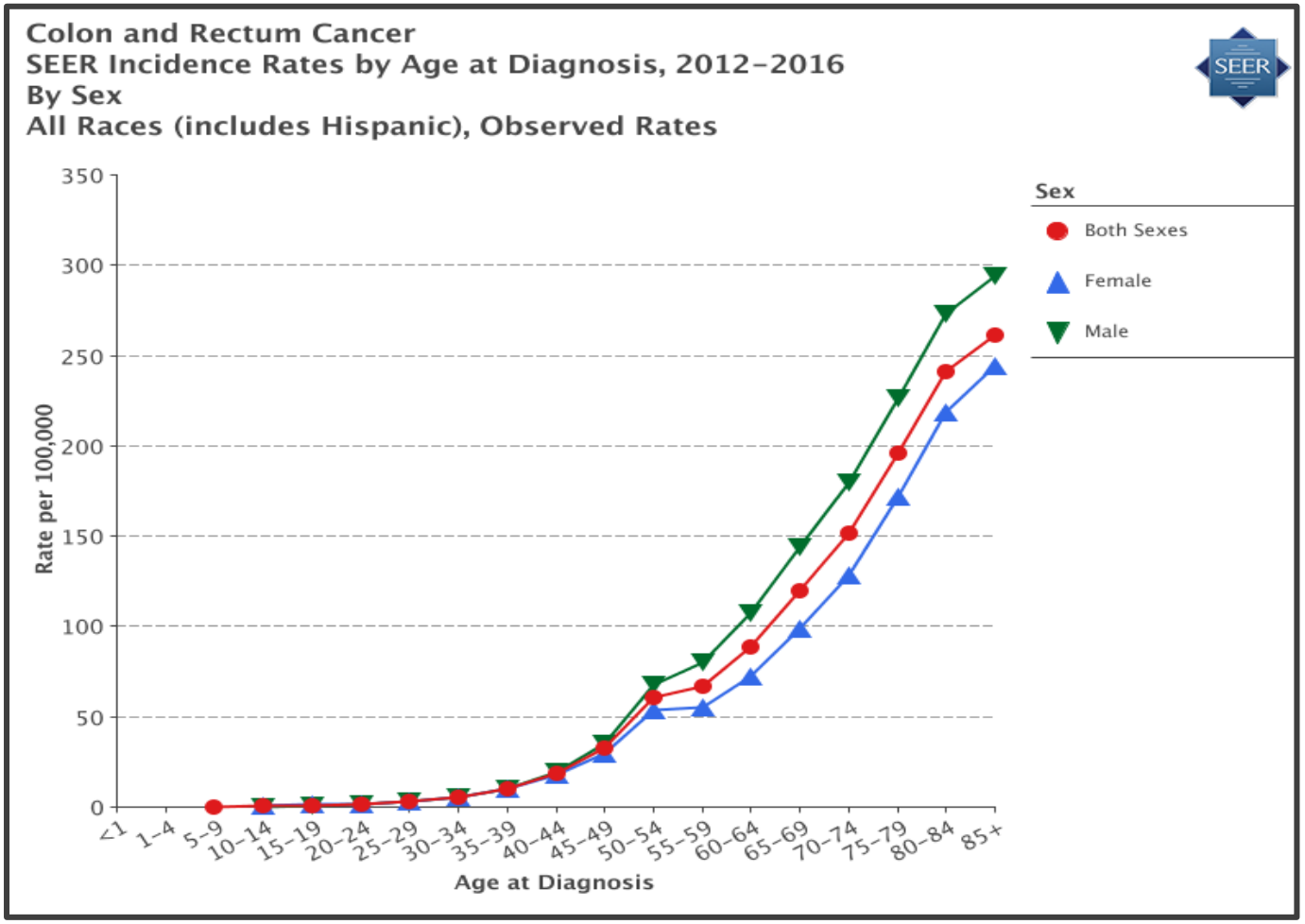
  Stool-based Tests

  - Colonoscopy
  - CT Colonography
  - Flexible sigmoidoscopy
  - Capsule Colonoscopy

  Endoscopic and Radiologic Examinations

Colorectal Cancer (CRC)

- 90% of CRC occurs after age 50



Colorectal Cancer (CRC) – Assessing CRC Risk

- Clinical Tools to assess degree of CRC risk - **NIH National Cancer Institute** https://ccrisktool.cancer.gov/calculator.html
  - Demographics (Race/Ethnicity; Age, Sex, Height and Weight)
  - Diet and Physical Activity (Vegetables/Salads; Moderate and Vigorous Physical Activity
  - Medical History (previous endoscopy of large bowel, medications containing aspirin and NSAIDs)
  - Family History of CRC (number of immediate relatives)

Colorectal Cancer (CRC) – Assessing CRC Risk

- Age

- Increased-Risk Medical Conditions
  - Inflammatory Bowel Disease (UC and Crohn's)
  - Abdominal radiation for childhood cancer

- Personal and family history of polyps and cancer
  - Previous adenomatous polyp or CRC
  - Any immediate family members (parent, sibling, child)
    - If Yes → how many and at what age(s)

If No to all of these → consider to be at Average Risk

Colorectal Cancer (CRC) Screening – Average Risk

- The 2016 Canadian Task Force on Preventive Health Care recommends:
  - Screening adults aged 50 to 74 years with FOBT every two years or
  - Flexible sigmoidoscopy every 10 years .
  - They do not recommend screening adults >75 years for CRC or using colonoscopy as a screening test.

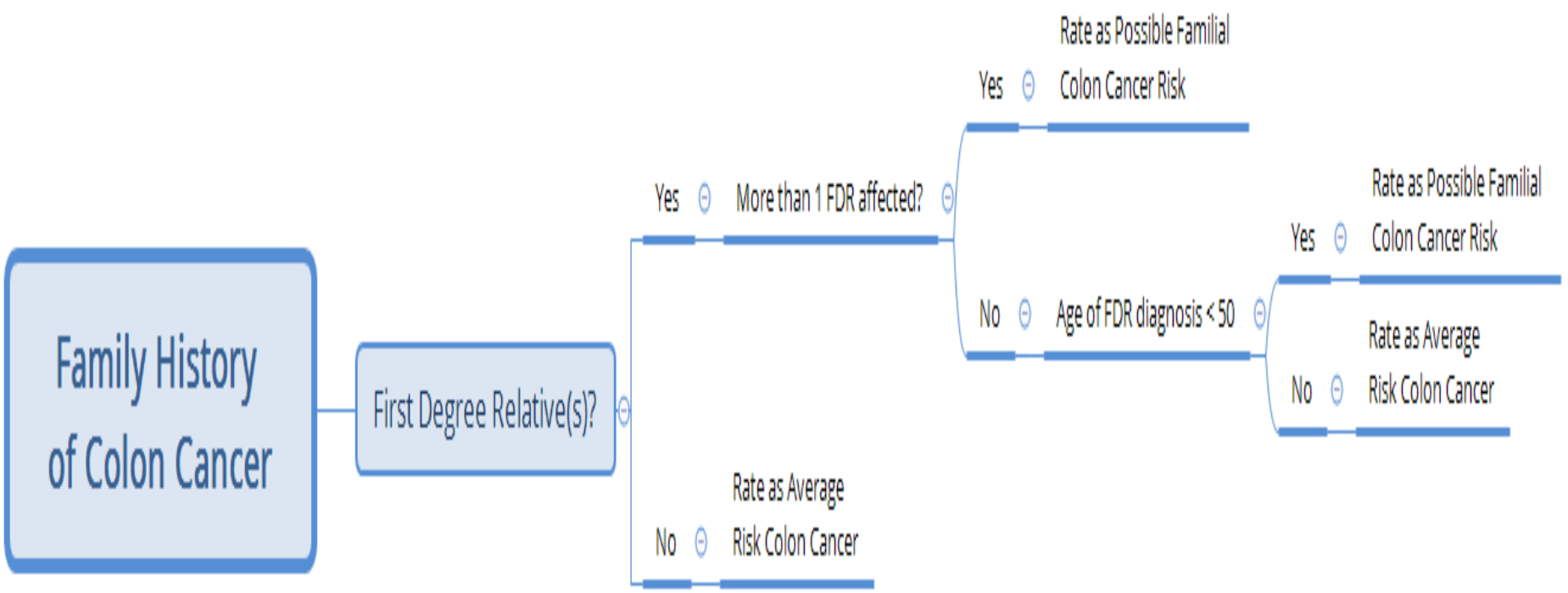
Colorectal Cancer (CRC) – Assessing Polyp Risk

- High-risk adenomas:
  - Three or more adenomas
- Advanced adenoma
  - Tubular adenoma ≥10 mm or
  - Adenoma with villous histology, or high grade dysplasia

Colorectal Cancer (CRC) Screening – History of polyp(s)

Baseline Colonoscopy Finding:	Recommended Surveillance
1 to 2 small (<10mm) tubular adenomas	5 to 10 years
3 to 10 tubular adenomas	3 years
> 10 tubular adenomas	< 3 years
Tubular adenoma > 10mm	3 years
Villous adenoma	3 years
Adenoma with high grade dysplasia	3 years
Sessile serrated adenoma (<10 mm) no dysplasia	5 years
Sessile serrated adenoma > 10mm	3 years
Sessile serrated adenoma with dysplasia	3 years

Colorectal Cancer (CRC) – Assessing Family History



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Female Breast Cancer Screening

- Average Risk – Negative for FDR with breast, ovarian or peritoneal cancer
  - Age 50 to 74
  - Mammogram every 2 years
- Intermediate Risk – FDR with breast cancer but NOT familial cancer syndrome
  - Age 50 to 74
  - Mammogram every 2 years
- High Risk – BRCA or other high risk genes; history of chest radiation therapy or >20% lifetime risk of developing breast cancer
  - Annual screening mammogram AND annual breast magnetic resonance imaging (MRI)
  - Beginning 10 years prior to the youngest affected family member but not prior to age 30 for mammography and not prior to age 25 for MRI

Lung Cancer Screening

- Low dose chest CT screening has been found to reduce lung cancer mortality in a well-defined population of patients at high risk for lung cancer defined by all of the following:
  - Age 55-74
  - At least a 30-pack year history of tobacco use,
  - Smoking within the last 15 years.

https://choosingwiselycanada.org/respiratory-medicine/

Questions?

somewhat different

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