Colorectal Cancer: What Patients Need to Know

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Paul Celano, MD FACP FASCO

Herman & Walter Samuelson Medical Director

Sandra & Malcolm Berman Cancer Institute

Greater Baltimore Medical Center

Eden Stotsky-Himelfarb, BS, BSN,RN,ONN-CG

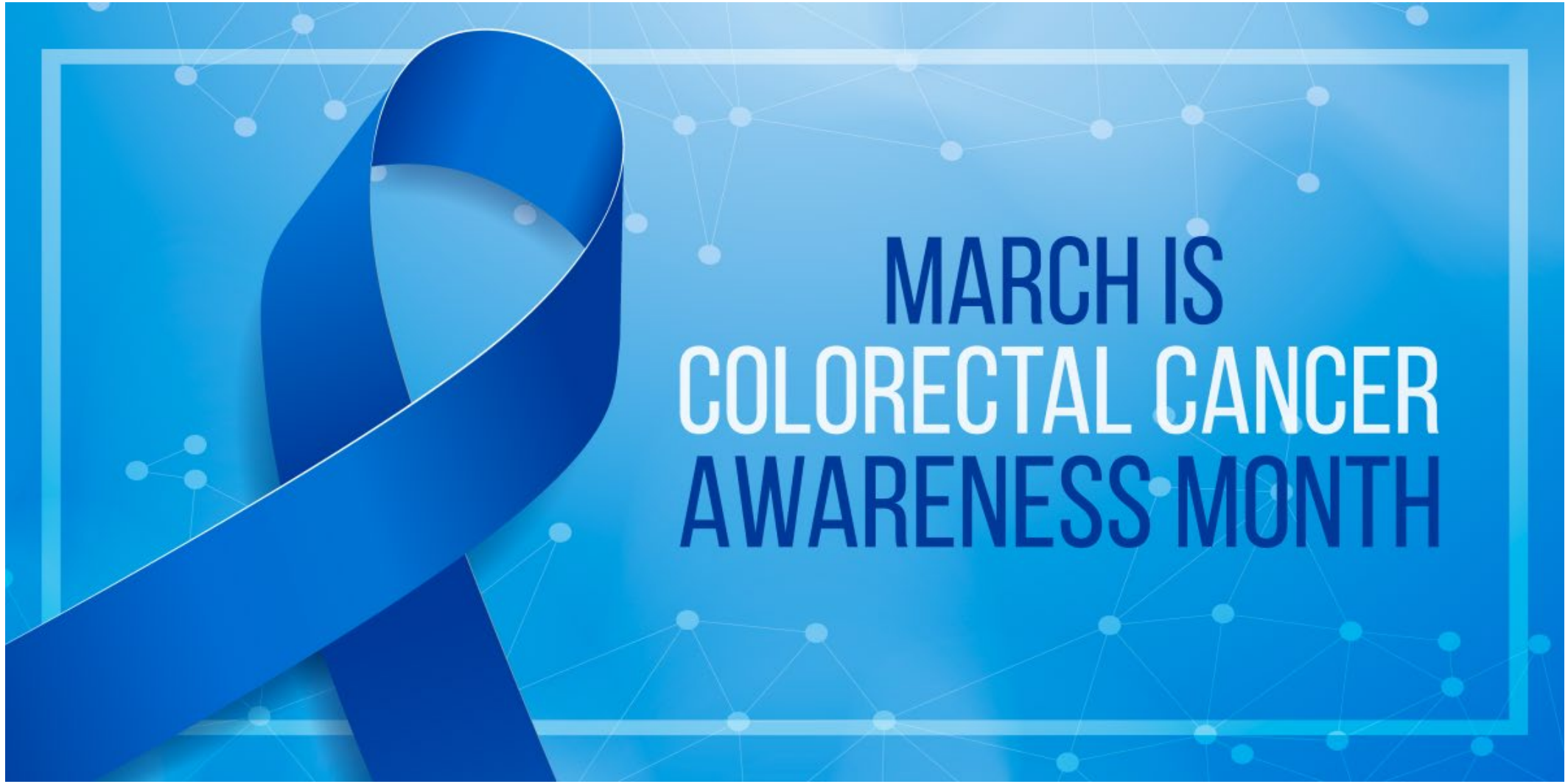
Breast Cancer Program

New Patient and Multidisciplinary Care Nurse Coordinator

Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

Critical Conversations

ONCOLOGY FOUNDATION OF MARYLAND AND THE DISTRICT OF COLUMBIA



Critical Conversations

ONCOLOGY FOUNDATION
OF MARYLAND AND THE DISTRICT OF COLUMBIA

Critical Discussion in Colorectal Cancer

1. Statistics
2. Risk Factors and Prevention
3. What Colorectal Cancer?
4. Colorectal Cancer Screening
5. Symptoms and Signs
6. Diagnosis
7. Genetics
8. Colorectal Cancer Stages
9. Treatments-
    - Surgery
    - Chemotherapy
    - Targeted Therapy
    - Immunotherapy
10. Personal Story and Survivorship

Colorectal Cancer Basics

1. **Colorectal cancer is a growth of cells that forms in the lower end of the digestive tract.**

   -Removing polyps can prevent cancer, screenings for those at high risk or over the age of 45.

2. **Symptoms might include blood in the stool, abdominal discomfort, change in bowel habits.**
3. **Colorectal cancer treatment depends on the size, location, genetic analysis and stage of cancer.**
4. **Treatments may include surgery, chemotherapy, immunotherapy, targeted therapy and radiation therapy.**
5. **Genetics and Immunology are playing an increasing role.**

COLORECTAL CANCER

SIGNS & SYMPTOMS

(many people experience no symptoms)

- Change in bowel habits, including diarrhoea/ constipation
- Rectal bleeding or blood in stools
- Persistent abdominal discomfort (cramps, gas or pain)
- A feeling that the bowel doesn't empty completely
- Weakness or fatigue
- Unexplained weight loss

EARLY DETECTION IS KEY

The risk for 30% of cancers can be reduced by changing your diet and lifestyle

- Go for regular colon screening tests such as a colonoscopy as from age 50 - every 10 years
- Some CANSA Care Centres & Mobile Health Clinics countrywide offer faecal occult blood tests (sample of stool collected on end of an applicator to help detect small quantities of blood). Although not always an indication of cancer, positive results require a referral to a doctor

RISK FOR COLON CANCER INCREASES WITH AGE (50+)

Most colerectal cancers begin as a **POLYP**, a small growth of tissue that starts in the lining & grows into the centre of the colon or rectum. Doctors can remove polyps during the colonoscopy procedure

Male lifetime risk
1:114

Female lifetime risk
1:182

Lifestyle factors that contribute to increase the risk of colorectal cancer:

Lack of regular exercise

Low fruit/ vegetable intake

Low-fibre & high-fat diet

Being overweight (obesity)

Alcohol consumption

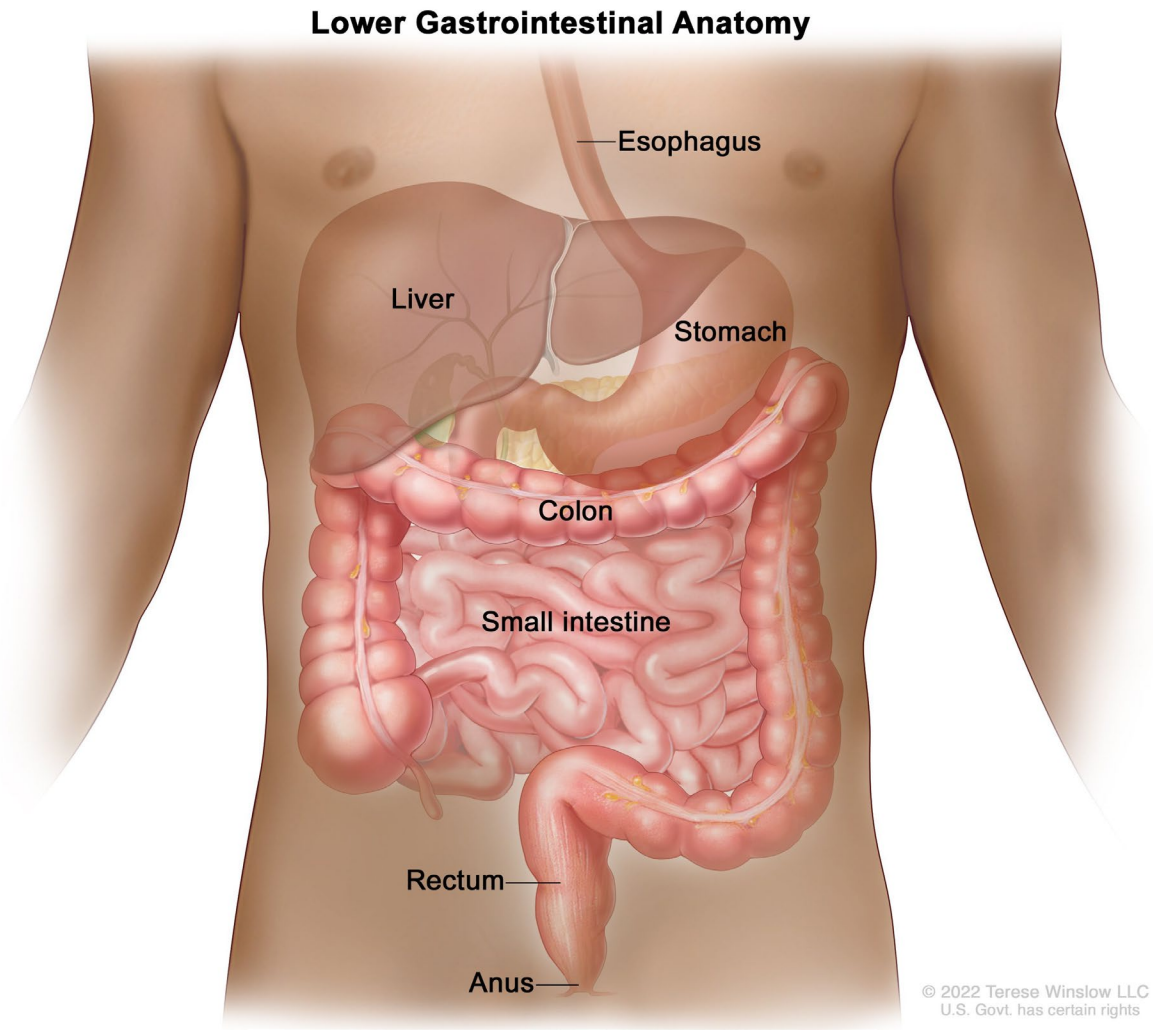
Insufficient intake of clean safe water

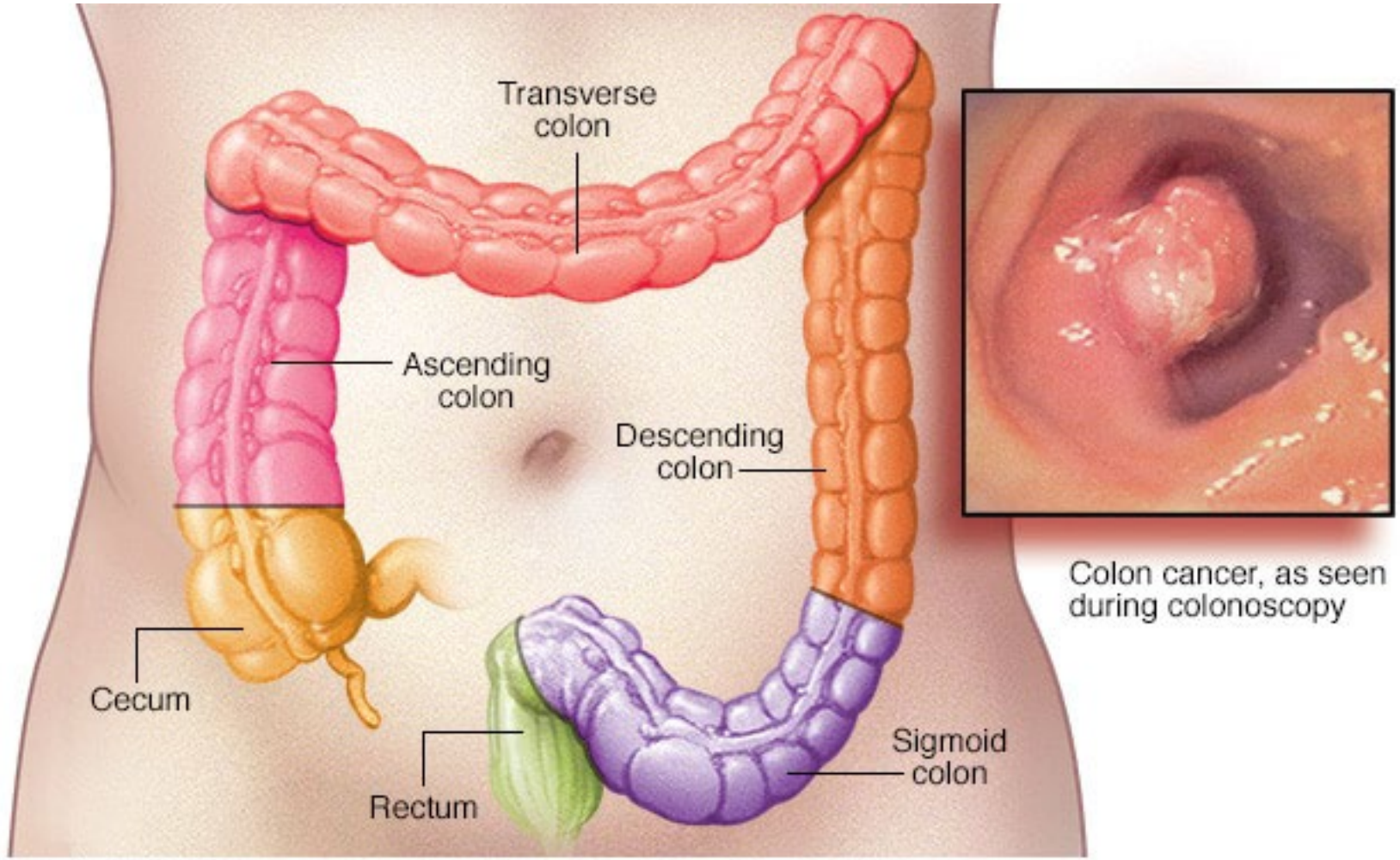
Tobacco use

Other risk factors:

- Inflammatory bowel disease
- Personal or family history of:
  - Colorectal polyps
  - Colorectal cancer

Colon cancer is a disease in which malignant (cancer) cells form in the tissues of the colon





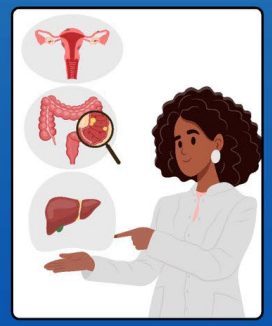
Colon cancer, as seen during colonoscopy

Cancer Statistics 2024

In 2024 there will be a milestone

2 million (2,001,140) new cancers diagnosed in the United States

Cancer mortality has declined continuously from 1991, when the rate peaked, through 2021, **averting 4.1 million deaths** due largely to reductions in smoking, improvements in treatment, and early detection for some cancers.



However, this progress is jeopardized by increasing incidence for many common cancers, including:

breast, prostate, pancreas, uterine corpus, melanoma, liver (female)**, kidney, HPV-associated oral cancers, colorectal** (0-54 years)**, and cervical** (ages 30-44 years)

Colorectal cancer has moved up from the 4th leading cause of cancer death **in people younger than 50 in the late 1990s to first in men and second in women (after breast).**

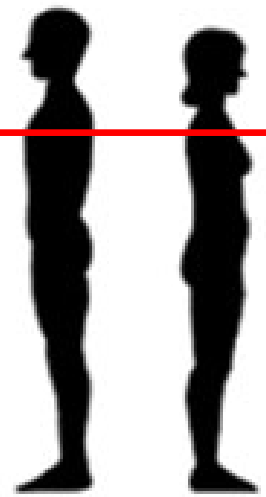
American Cancer Society

CA: A Cancer Journal for Clinicians
The flagship journal of the American Cancer Society

Cancer Statistics, 2024
DOI: 10.3322/caac.21820

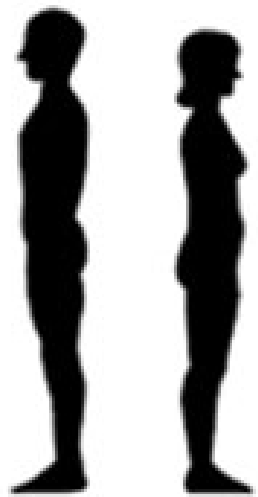
Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	



Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Are you at risk for Colorectal Cancer?

Being Older

Your risk goes up as you age

Personal + Family History

Having a parent, sibling, or child with colorectal cancer increases your risk

Race

African American men and women are at higher risk

Inflammatory Bowel Disease (IBD)

IBD, including ulcerative colitis and Crohn's disease put you at higher risk

Not Being Physically Active

Diets high in Red Meats and Processed Meats

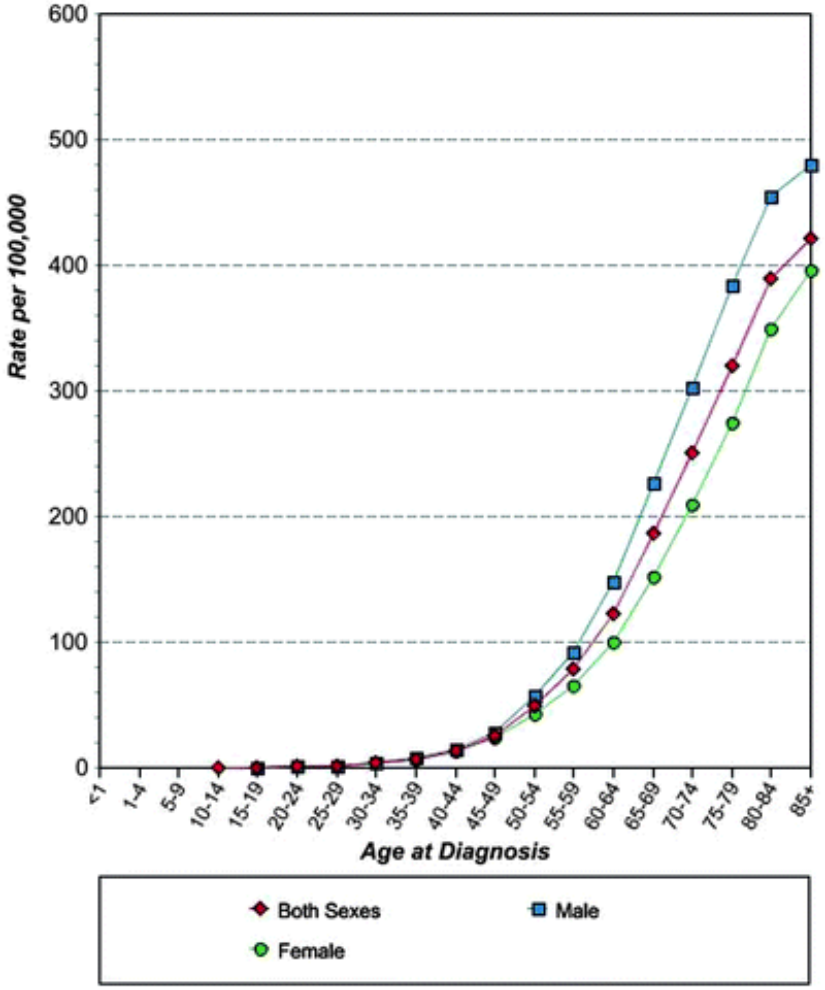
Being Overweight or Obese

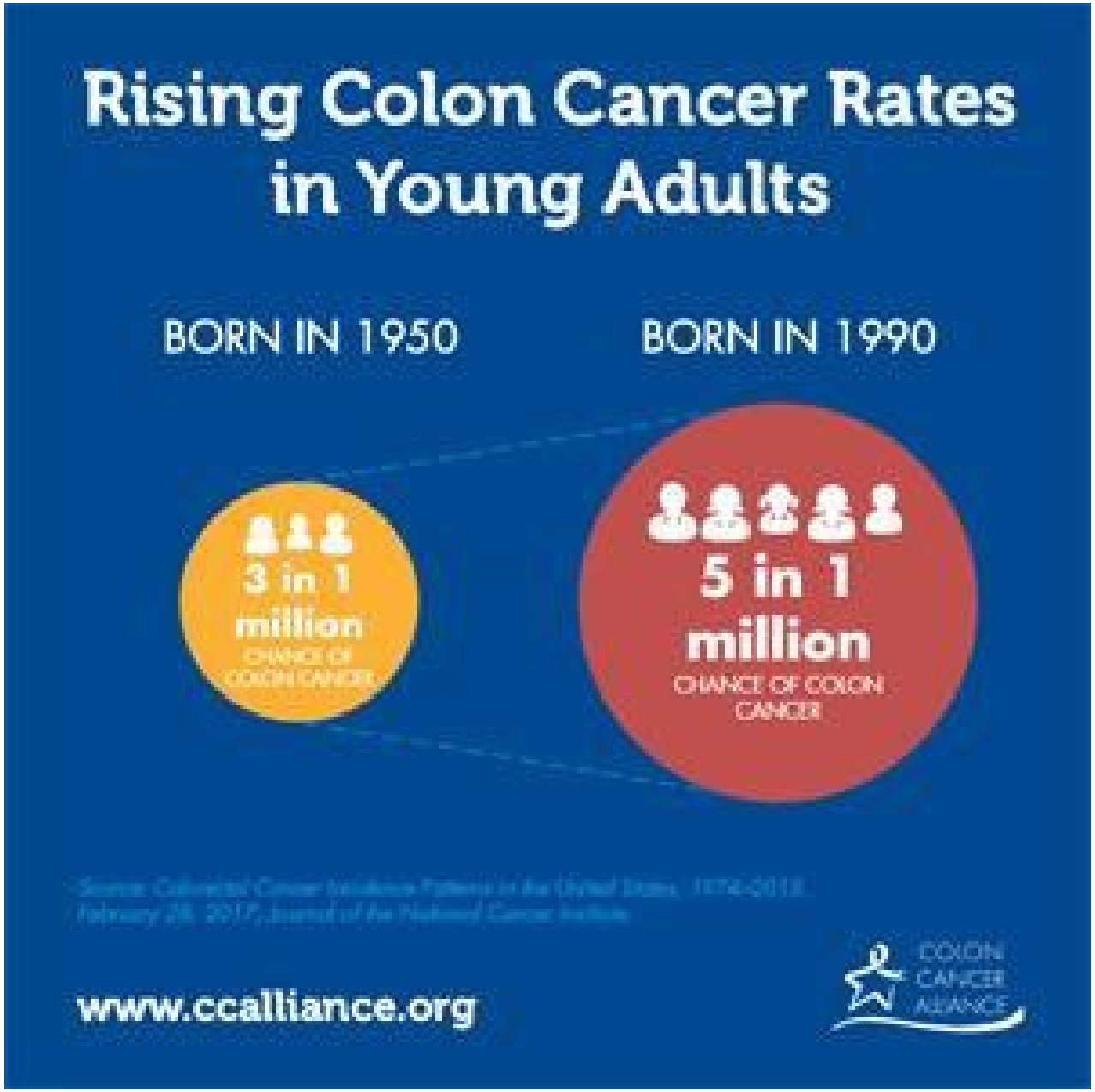
Alcohol Use

Smoking

HALIFAX HEALTH
CENTER FOR ONCOLOGY

Colon Cancer Incidence Rates in US by Age




Rising Colon Cancer Rates in Young Adults
BORN IN 1950
BORN IN 1990
3 in 1 million
CHANCE OF COLON CANCER
5 in 1 million
CHANCE OF COLON CANCER
www.ccalliance.org
COLON CANCER ALLIANCE

Colorectal Cancer Risk Factors

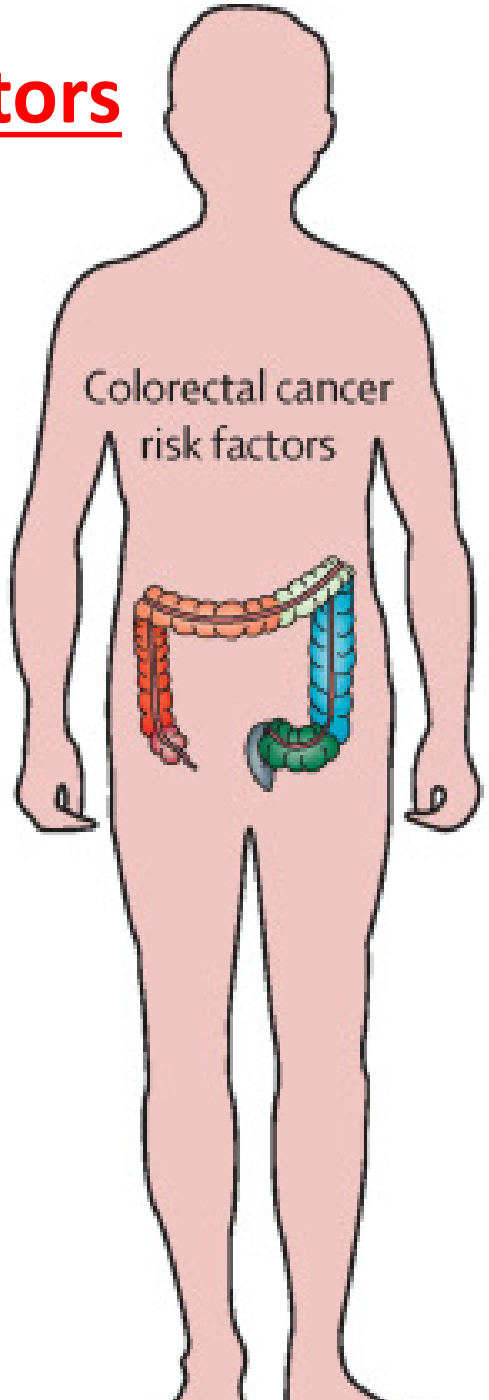
Hereditary factors

- Hereditary colorectal cancer syndromes
- Positive family history

Other factors

- Aspirin or NSAID use
- Menopausal hormone therapy
- Statin use

- Ethnicity
- Male gender
- Type 2 diabetes
- Inflammatory bowel disease



Modifiable risk factors ↑ risk

- Smoking
- Processed meat
- Alcohol intake
- Red meat
- Low intake of vegetables and fruits
- Body fat and obesity

Modifiable risk factors ↓ risk

- Physical activity
- Whole grains
- Dietary fibre
- Dairy products
- Fish intake
- Tree nuts
- Vitamins (D, C, and others)
- Calcium supplements

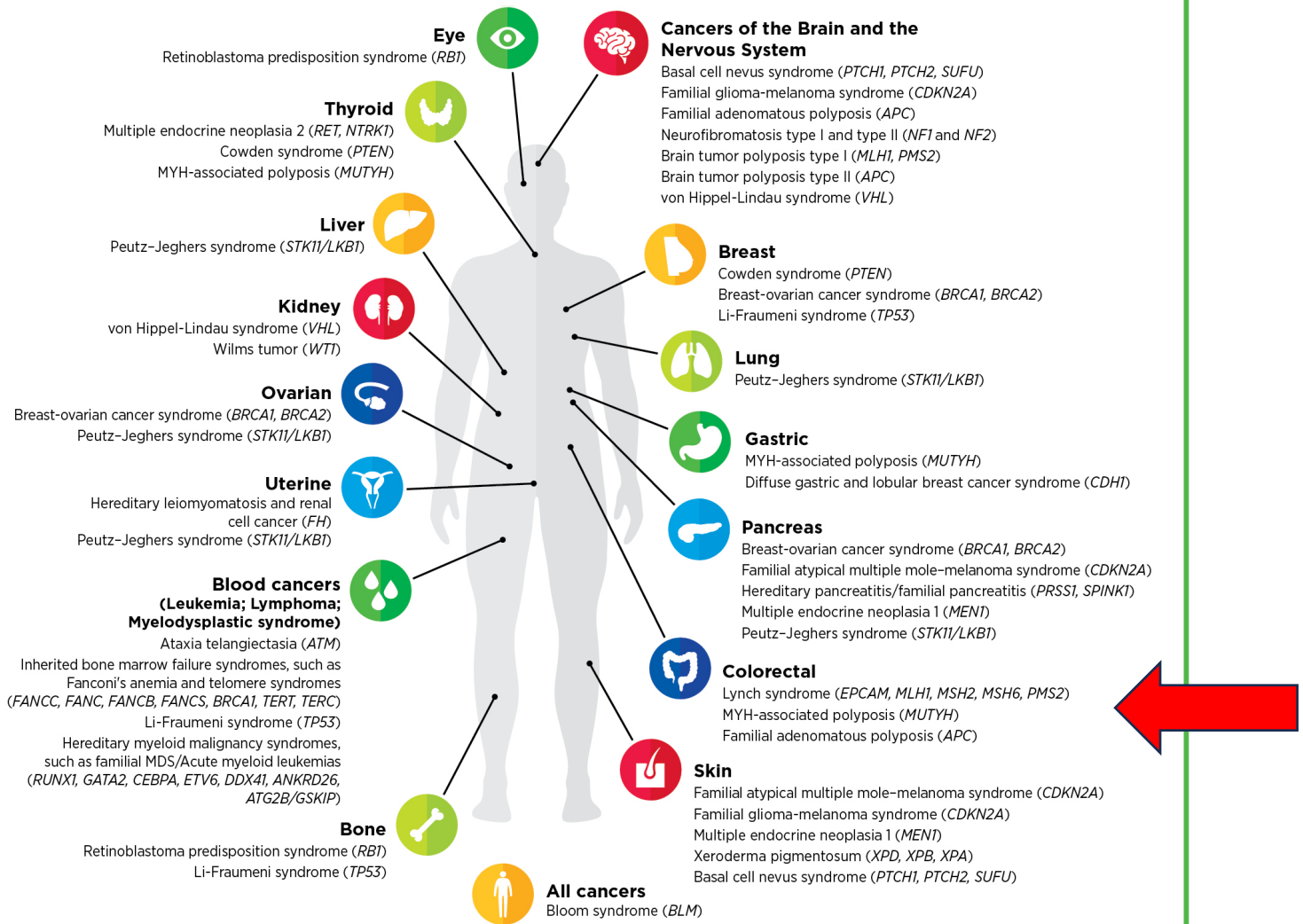
Types of Genetic Tests for Cancer

Germline:
Normal cells are tested for genetic mutations that may be inherited and increase your risk of cancer

Somatic tumor:
Cells from a known cancer are tested for mutations that could impact your prognosis or determine treatment

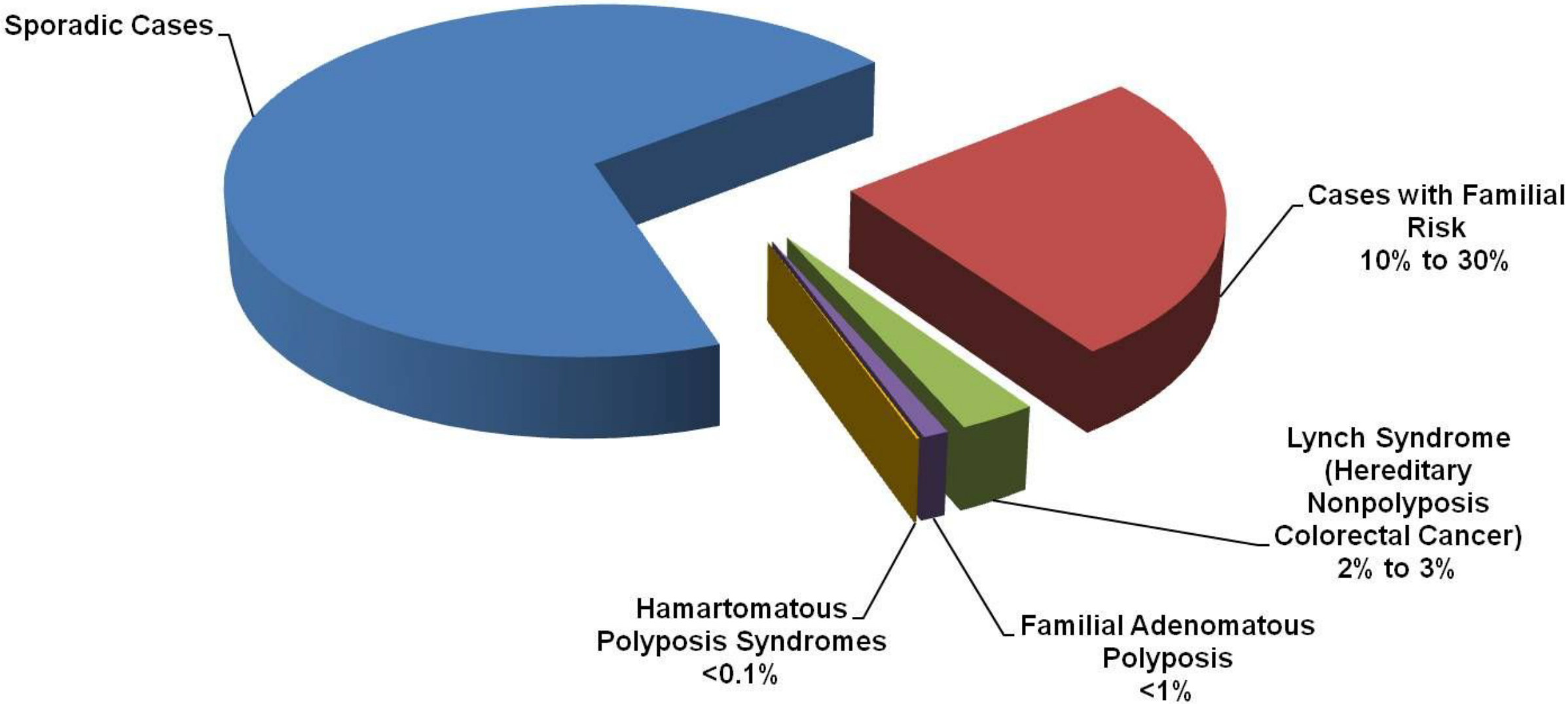
FIGURE 5

Inherited Cancer Risk

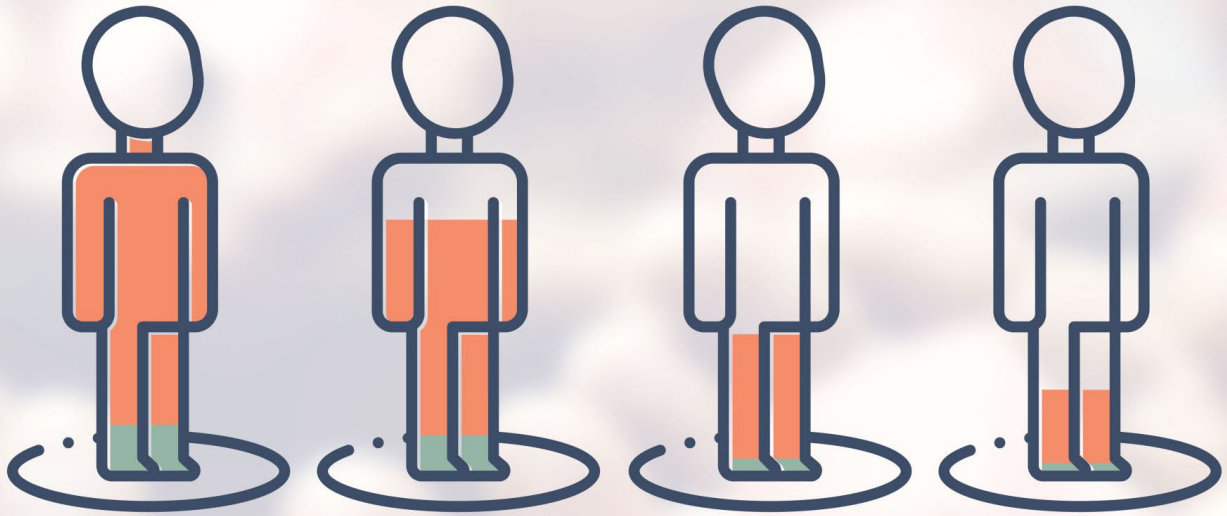


Depicted here are selected cancer types that are associated with inherited cancer syndromes. Also shown in parentheses are the genes, mutations in which are linked with various inherited cancer syndromes that predispose individuals to the shown cancer types.

Colon Cancer Cases Arising in Various Family Risk Settings



Lifetime Cancer Risk Comparison



<80%	<60%	<38%	<13%
5%	2.8%	1.2%	1%
COLORECTAL CANCER	ENDOMETRIAL CANCER	OVARIAN CANCER	STOMACH CANCER

PEOPLE WITH LYNCH SYNDROME

GENERAL POPULATION

Lynch syndrome versus FAP

NAME	Lynch syndrome	Familial adenomatous polyposis (FAP)
% OF ALL CRCs	3% to 10%	1%
PATHOGENESIS	Microsatellite instability	Chromosomal instability
INHERITANCE & PENETRANCE	Autosomal dominant 80% penetrance	Autosomal dominant Close to 100% penetrance
AGE OF ONSET	Mean at age 44 15% develop cancer by 40	Symptoms at age 16 (8 – 34) 90% develop cancer by 45
POLYPS	Not seen, few	Many
TYPICAL TUMOR CHARACTERISTICS	Rapid conversion of polyp to cancer; **right-sided**, large, non-fibrous tumors	Slower-converting polyps which degenerate to fibrous and bowel constricting tumors

Sources: Dr. David A. Owen, Department of Pathology, VGH, UBC. Buchanan *et al*. **Lessons from Lynch syndrome: a tumor biology-based approach to familial colorectal cancer**. *Future Oncology* 6(4):539-549. Bonis *et al*. **Lynch syndrome (hereditary nonpolyposis colorectal cancer): Screening and management of patients and families**. UpToDate (November 28th, 2011 revision). Ahnen *et al*. **Clinical features and diagnosis of familial adenomatous polyposis**. UpToDate (August 28th, 2010 revision). OncoLink.org.

WHO SHOULD CONSIDER TESTING FOR LYNCH SYNDROME

(Consult your Physician)

FAMILY HISTORY

- If you have a family member that has been diagnosed with Lynch Syndrome
- If at least 3 relatives had cancer linked to Lynch Syndrome
- If at least 1 first degree relative and 2 successive generations are affected
- If at least 1 relative was diagnosed before the age of 50

PERSONAL HISTORY

- If you have had more than 1 cancer linked to Lynch Syndrome at any age
- If you had colorectal or endometrial cancer before age 50
- If you have had a cancer linked to Lynch Syndrome and 1 or more relatives also had a cancer linked to Lynch Syndrome
- If at least 1 relative was diagnosed with a Lynch Syndrome related cancer before the age of 50

SCREENINGS
Make a Difference

Lifetime risk of cancer diagnosis (based on 2016 – 2018 data):

Breast cancer
About **12.9 percent** of women

Colorectal cancer
About **4.1 percent** of adults

Cervical cancer
About **0.6 percent** of women

Cancer death rates dropped by 31 percent between 1991 and 2018.

This amounts to **3.1 million lives saved** through reduced smoking and improved detection and treatment.

About **39 percent** of adults will be diagnosed with cancer in their lifetimes.

As of 2019, there were an estimated

16 million cancer survivors in the United States.

SIDEBAR 18

USPSTF-recommended Tests to Screen for Cancer

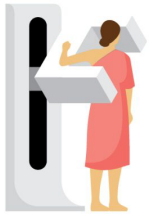
The U.S. Preventive Services Task Force (USPSTF) is an independent Congressionally mandated panel of experts in preventive care convened by the Agency for Healthcare Research and Quality. USPSTF rigorously reviews the evidence on the benefits and harms of behavioral counseling, preventive medications, and screening strategies related to cancer.

Described below are screening tests that are included as part of evidence-based recommendations by USPSTF to screen for four cancer types in individuals who are at an average risk of being diagnosed with cancer, and to screen for lung cancer in individuals who are at a higher-than-average risk of being diagnosed with cancer.

BREAST CANCER

Digital mammography

Uses X-rays to generate two dimensional images of the breast that can be stored electronically and analyzed for signs of breast cancer.



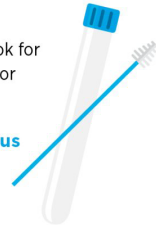
Digital breast tomosynthesis

Also called three-dimensional mammography, this screening method generates 3D images of the breast that are analyzed for signs of breast cancer. Must be accompanied by digital mammography.

CERVICAL CANCER

Cytology

Samples cervical cells, which are analyzed under a microscope to look for abnormalities. Also called Pap test or Pap smear.



High-risk Human Papillomavirus (HPV) test

Detects the presence of certain cervical cancer-causing types of HPV and identifies people for whom further testing is recommended. Does not directly detect precancerous or cancerous cervical lesions.

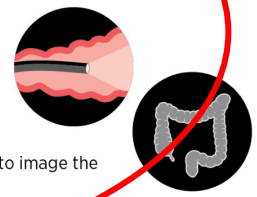
COLORECTAL CANCER

Stool-based tests

Some test for the presence of a product of red blood cells. Others test for both the presence of a product of red blood cell and certain genetic mutations linked to colorectal cancer. Do not directly detect precancerous lesions or cancers but identify people for whom further testing is recommended.

Direct visualization tests

Flexible sigmoidoscopy and colonoscopy Use a thin, flexible, lighted tube with a small video camera on the end to examine the lining of the entire colon and rectum (as is the case with colonoscopy), or only certain parts (as is the case with flexible sigmoidoscopy).



Computed tomography (CT) colonography (virtual colonoscopy) Uses X-rays to image the colon and rectum.

LUNG CANCER

Low-dose spiral CT scan

Uses low doses of X-rays to rapidly image the lungs and detect any structural abnormalities suggestive of lung cancer. Suspicious lesions are then biopsied to examine for the presence of abnormal or cancer cells.

PROSTATE CANCER

PSA test

Measures the level of a protein called prostate-specific antigen (PSA) in blood, which is often elevated in men with prostate cancer. Does not directly detect prostate cancer but identifies men for whom further testing is recommended.

Learn About Your SCREENING OPTIONS for COLORECTAL CANCER

What

COLORECTAL CANCER IS THE THIRD MOST COMMON CANCER yet it is one of the **most preventable**. It is **highly treatable** and is often **curable** when caught early.

Who

AGE 45 to 75
Adults at **average risk** for Colorectal Cancer should **get screened**

AGE 75+
The decision to continue **screening should be personalized** in adults over age 75

When

10 VS. 1

In general, **colonoscopy every 10 years** starting at age 45 for average risk adults is recommended as a screening test as compared to the alternate **stool FIT test** which you have to undergo **every 1 year**.

Why

POLYPS

Removing polyps with Colonoscopy **reduces the risk of Colorectal Cancer** and **saves lives**.

How

1-Step Test

COLONOSCOPY
Your doctor can see and remove pre-cancers called polyps and preventor detect or confirm colorectal cancer **ALL IN 1 STEP**.

2-Step Test

1ST STEP
Stool-Based Test
FIT Test (Fecal Immunochemical Test)
Multitarget Stool DNA

OR

Flexible Sigmoidoscopy

OR

Imaging Test
CT Colonography
Colon Capsule

↓

POSITIVE TEST?

↓

2ND STEP
Colonoscopy

1-STEP TEST
Colonoscopy is a one-step test that looks for growths called polyps in your entire colon (large intestine) and rectum. Your doctor can remove polyps and prevent colorectal cancer.

2-STEP TESTS
If they are positive, tests such as Fecal Immunochemical Tests (FIT) or Multitarget Stool DNA tests need a follow-up colonoscopy to diagnose any problems. Two steps are needed to screen.

Learn About Your Screening Options for Colorectal Cancer: **gi.org/coloncancer**

Find a gastroenterologist near you: **gi.org/find-a-gastroenterologist**

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45 IS THE NEW 50!
YOU CAN PREVENT
COLORECTAL CANCER
NEW SCREENING RECOMMENDATIONS FROM
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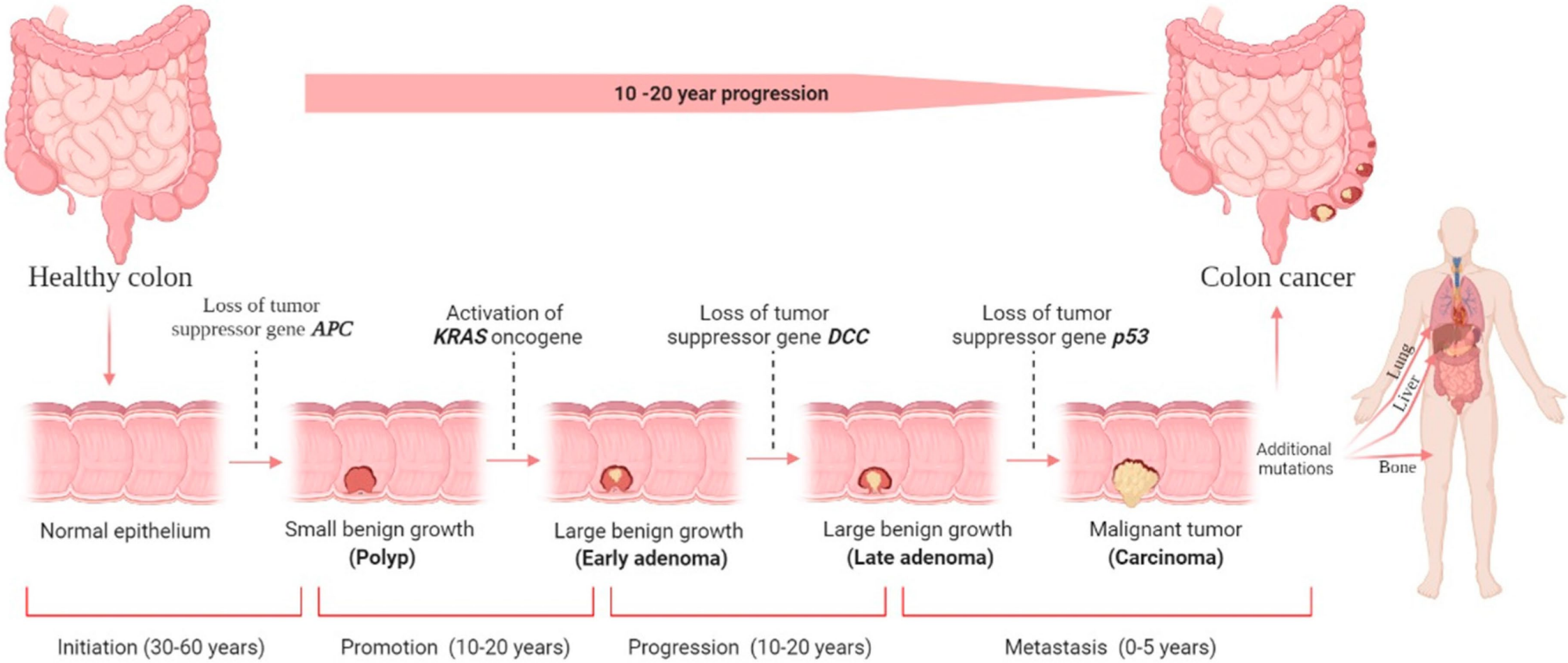
Digestive Disease Specialists
Committed to Quality
in Patient Care


10 -20 year progression
Healthy colon
Colon cancer
Loss of tumor suppressor gene APC
Activation of KRAS oncogene
Loss of tumor suppressor gene DCC
Loss of tumor suppressor gene p53
Additional mutations
Lung
Liver
Bone
Normal epithelium
Small benign growth (Polyp)
Large benign growth (Early adenoma)
Large benign growth (Late adenoma)
Malignant tumor (Carcinoma)
Initiation (30-60 years)
Promotion (10-20 years)
Progression (10-20 years)
Metastasis (0-5 years)

COLORECTAL CANCER SCREENING GUIDELINES

for people at average risk

AGES **45 to 75**

Get screened.

Several types of tests can be used. Talk to your doctor about which option is best for you.

No matter which test you choose, the most important thing is to get screened regularly.

AGES **76 to 85**

Talk to your doctor

about whether you should continue screening. When deciding, take into account your own preferences, overall health, and past screening history.

OVER AGE **85**

No longer screen.

People over age 85 should no longer get colorectal cancer screening.

YOUR AGE IN YEARS

TESTING OPTIONS

- Visual exams such as colonoscopy or CT colonography look at the inside of the colon and rectum for polyps (growths) or cancer.
- Stool-based tests look for signs of cancer in stool and can be done at home. These tests include the fecal immunochemical test (FIT), fecal occult blood test (FOBT), and multi-target stool DNA test.
- All abnormal results on non-colonoscopy screening tests should be followed up with a timely colonoscopy.
- People with a family history of polyps or colorectal cancer, or who have other risk factors, might need to start screening before age 45, be screened more often, and/or get specific tests.

American Cancer Society®

CANCER SCREENING SAVES LIVES. GET SCREENED.

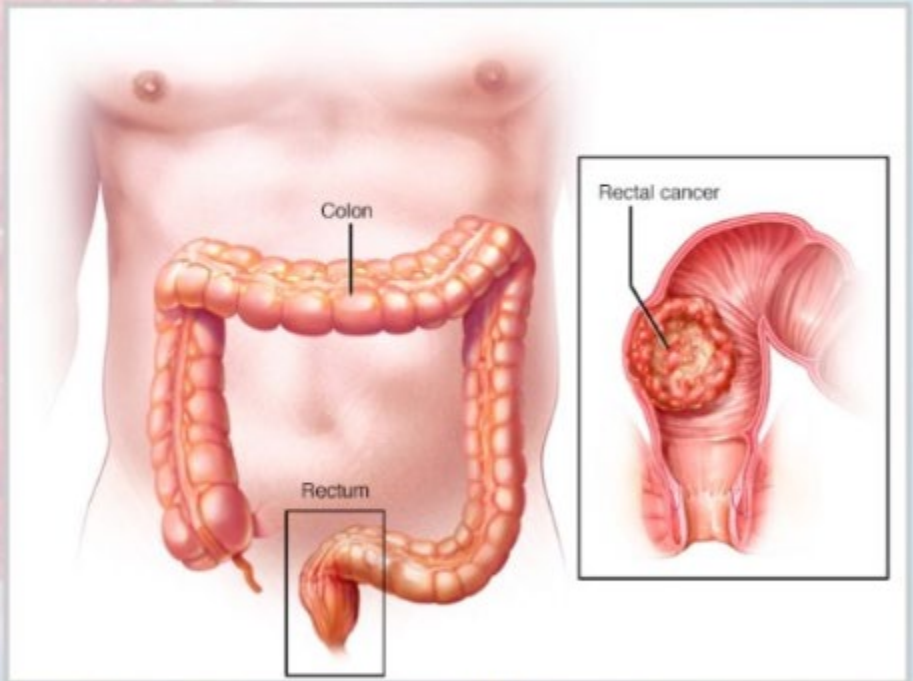
Talk to your doctor about screening, and contact your insurance provider about insurance coverage for screening.
To learn more, **visit cancer.org/get-screened** or call **1-800-227-2345**.

COLON CANCER

Colorectal cancer is a growth of cells that forms in the lower end of the digestive tract. Most of these cancers start as non-cancerous growths called polyps. Removing polyps can prevent cancer, so health care providers recommend screenings for those at high risk or over the age of 45.

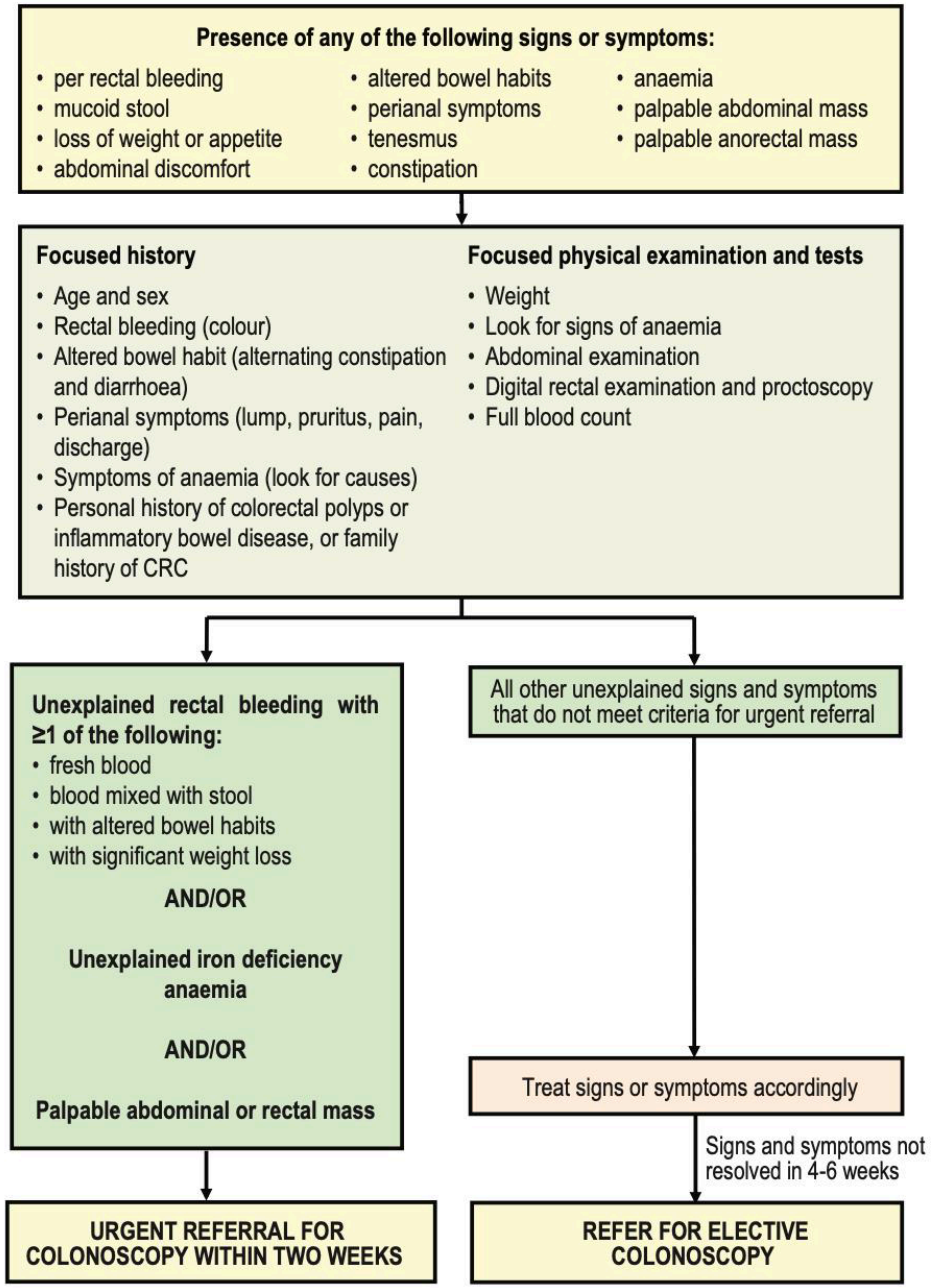
Early Stage Symptoms

- Changes in bowel habits
- Bloody Stools
- Pain or cramping in the abdomen
- Unintended weight loss
- Cancer spreading to lymph nodes
- Bowel obstructions
- Cancer spreading to liver and other organs




Signs & Symptoms
Symptoms of colorectal cancer may appear only in the advanced stages of the disease:
- Change in bowel habits
- Continual feeling of need for a bowel movement
- Bleeding from the rectum or bloody stools
- Abdominal cramping or pain
- Frequent gas or indigestion
- Weakness or fatigue
- Unexplained weight loss
THE BLOOD VESSELS THAT FEED A TUMOR TEND TO BE MORE FRAGILE THAN NORMAL BLOOD VESSELS AND BLEED EASILY. THIS LEADS TO INTERNAL BLEEDING IN THE COLON, ONE OF THE SYMPTOMS OF COLORECTAL CANCER.

ALGORITHM B: PRIMARY CARE REFERRAL FOR SYMPTOMS OF COLORECTAL CARCINOMA

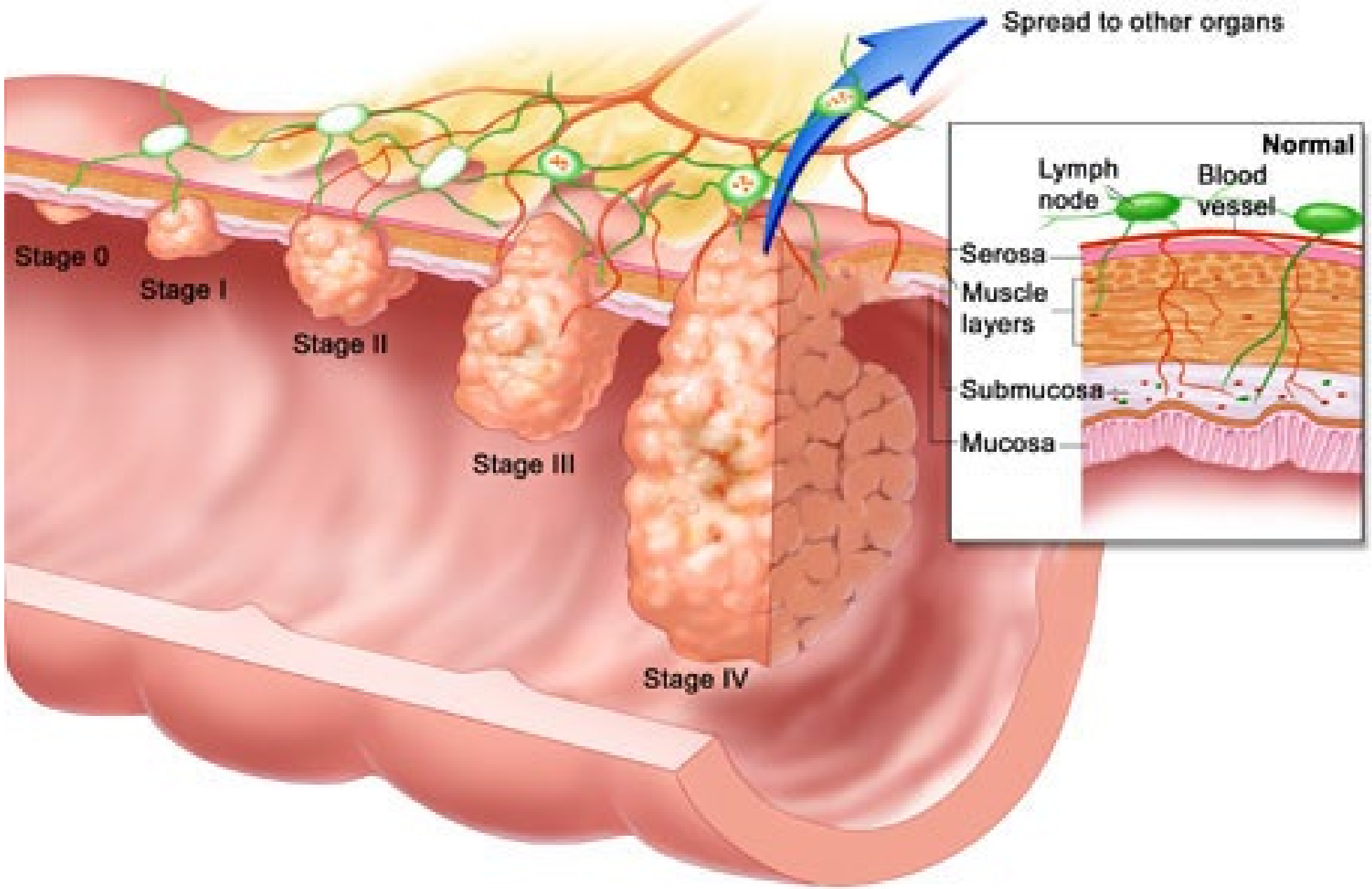


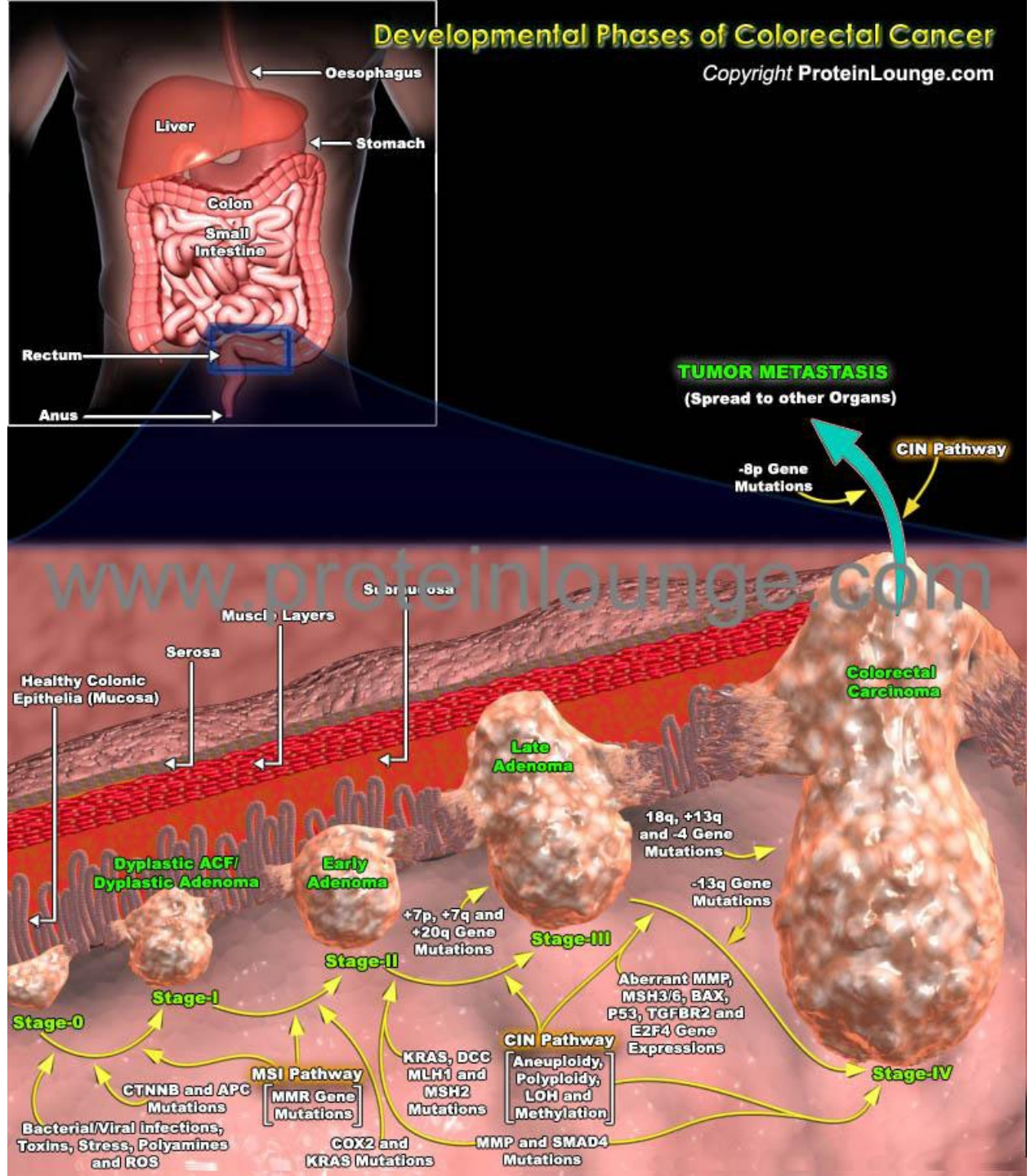
ACTC
Advanced Cancer
Treatment Centers

UNDERSTANDING THE

STAGES OF COLON CANCER

AND THEIR TREATMENT


Spread to other organs
Stage 0
Stage I
Stage II
Stage III
Stage IV
Normal
Lymph node
Blood vessel
Serosa
Muscle layers
Submucosa
Mucosa


Developmental Phases of Colorectal Cancer
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Rectum
Anus
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Late Adenoma
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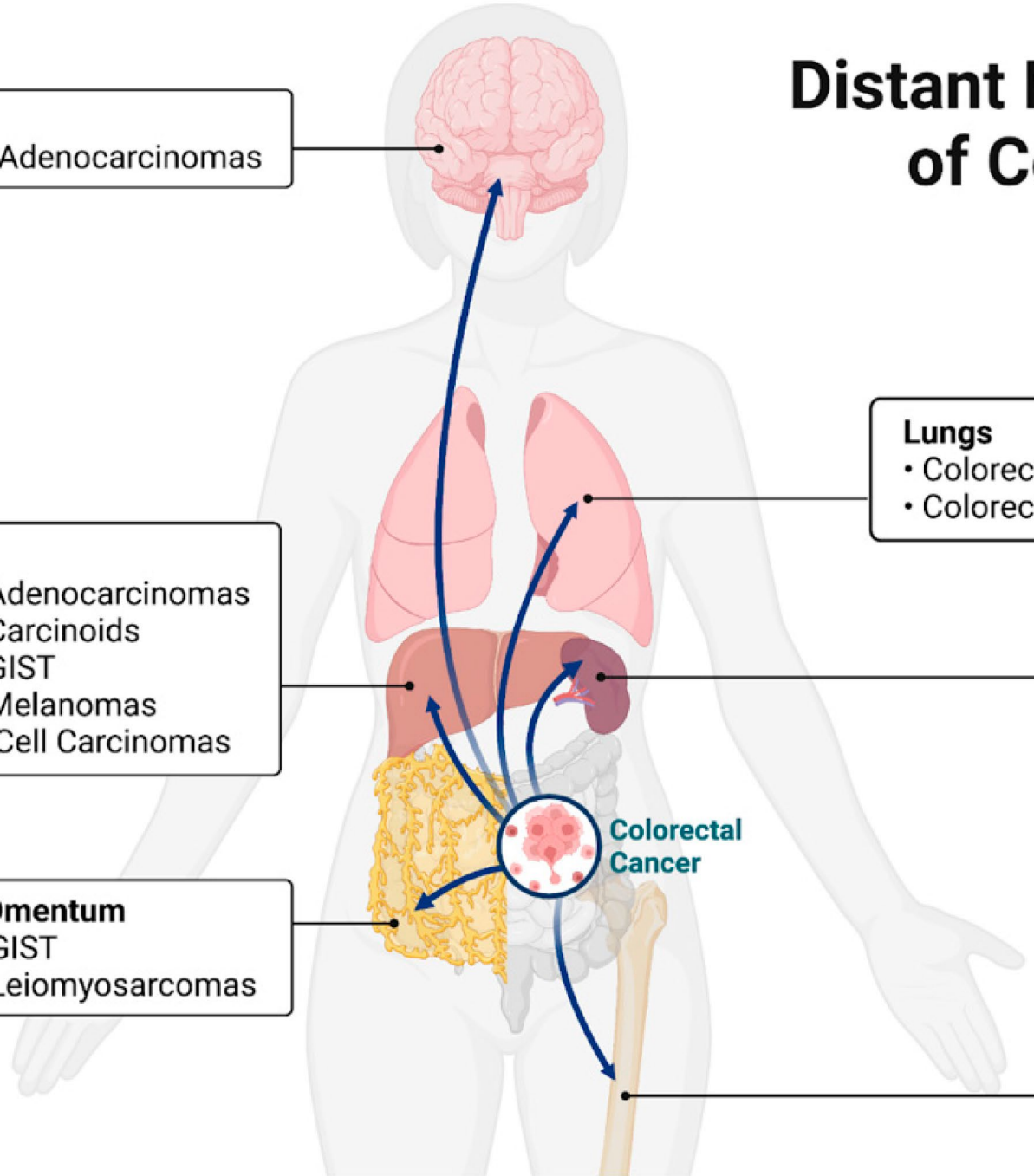
Dyplastic ACF/ Dyplastic Adenoma
Early Adenoma
-13q Gene Mutations
+7p, +7q and +20q Gene Mutations
Stage-III
Stage-II
Aberrant MMP, MSH3/6, BAX, P53, TGFBR2 and E2F4 Gene Expressions
Stage-I
Stage-0
CIN Pathway
Aneuploidy, Polyploidy, LOH and Methylation
KRAS, DCC MLH1 and MSH2 Mutations
Stage-IV
MSI Pathway
MMR Gene Mutations
CTNNB and APC Mutations
Bacterial/Viral infections, Toxins, Stress, Polyamines and ROS
COX2 and KRAS Mutations
MMP and SMAD4 Mutations

Distant Metastasis Sites of Colorectal Cancer



Brain
- Colorectal Adenocarcinomas

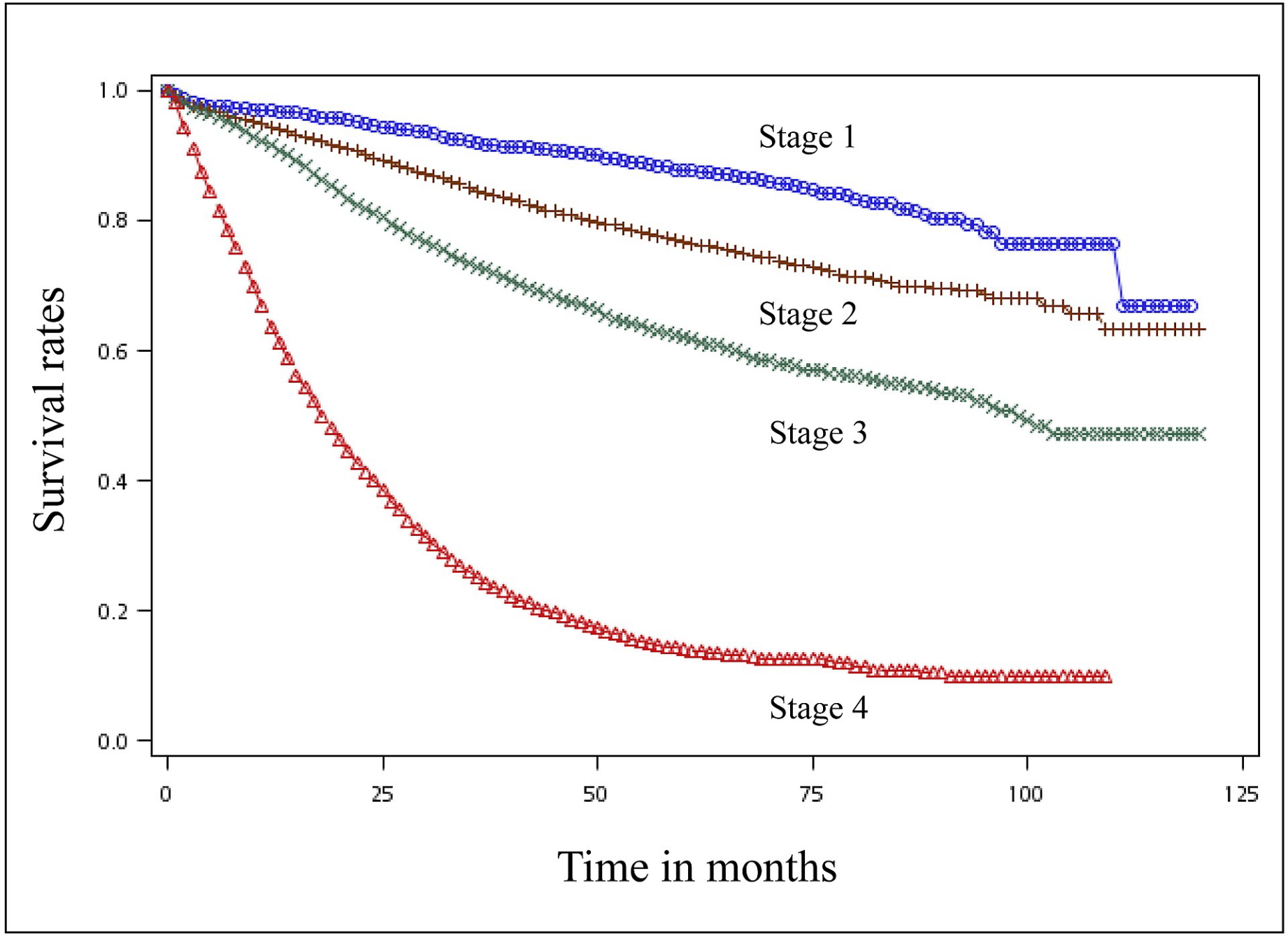
Lungs
- Colorectal Melanoma
- Colorectal Leiomyosarcomas

Liver
- Colorectal Adenocarcinomas
- Colorectal Carcinoids
- Colorectal GIST
- Colorectal Melanomas
- Squamous Cell Carcinomas

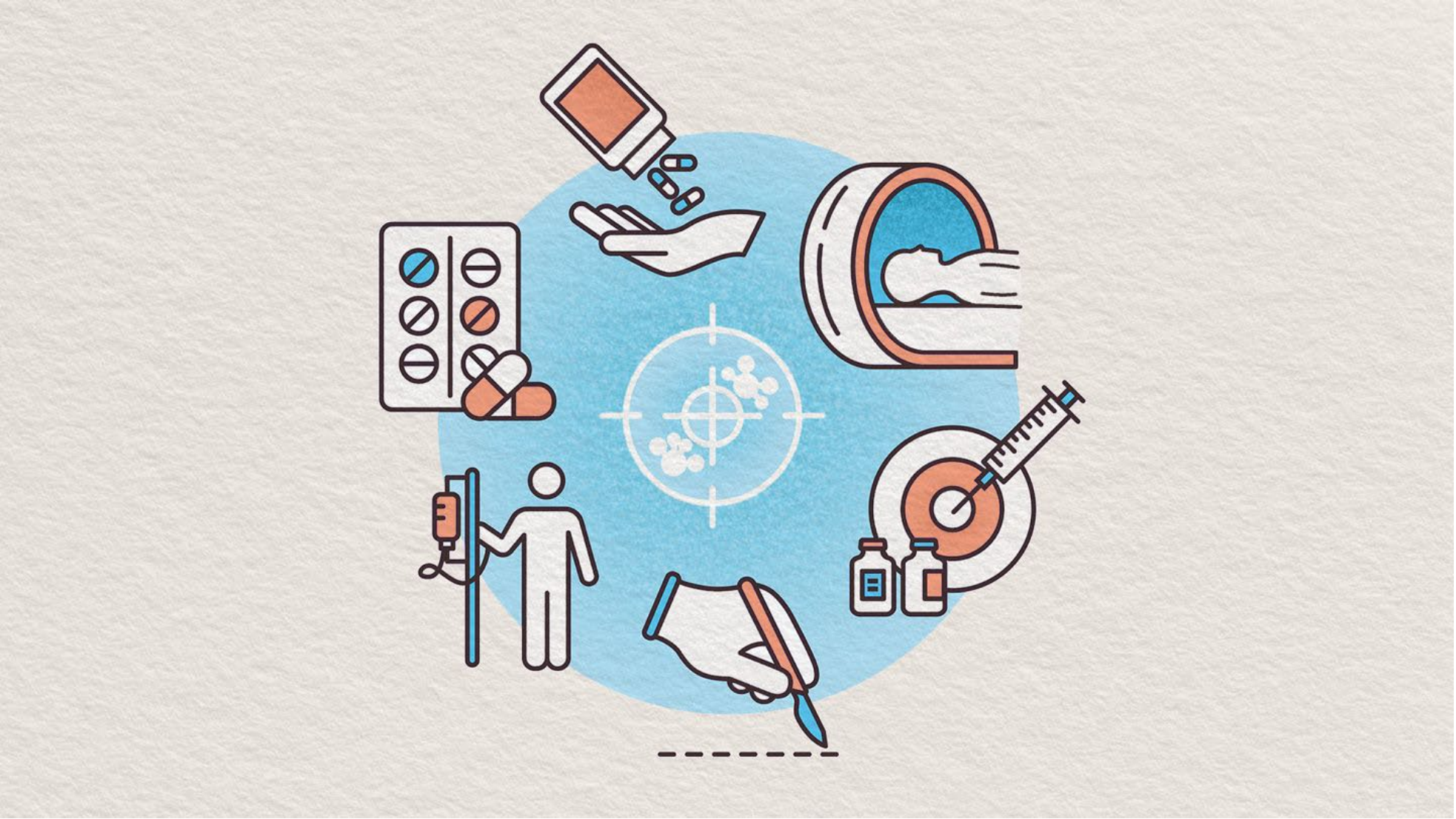
Spleen
- Colorectal Lymphomas

Mesentery/Omentum
- Colorectal GIST
- Colorectal Leiomyosarcomas

Bone
- Colorectal Lymphomas


Survival rates
1.0
0.8
0.6
0.4
0.2
0.0
Stage 1
Stage 2
Stage 3
Stage 4
0
25
50
75
100
125
Time in months

How Will My Colon Cancer Be Treated



Treatment Of Colon Cancer

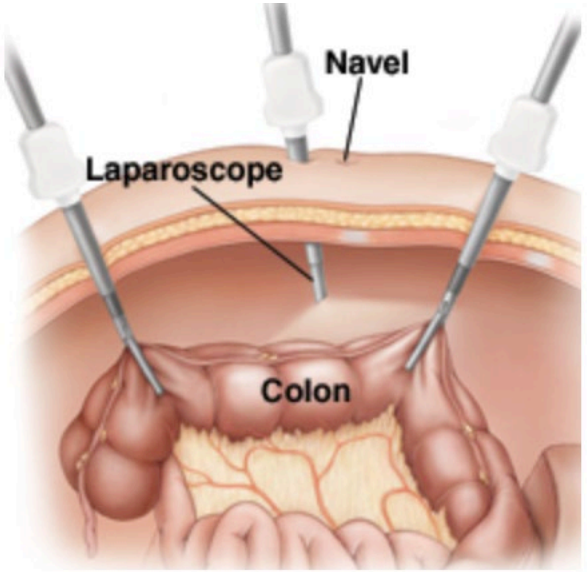
(AS PER STAGES)

STAGE 00	Surgery is often the only treatment needed for stage 0 colon cancer.
STAGE 01	Surgery alone is recommended for stage 1 colon cancer. The technique used may vary based on the location and size of the tumor.
STAGE 02	Surgery is recommended to remove the cancerous section of the colon and nearby lymph nodes. Chemotherapy may be recommended in certain circumstances, such as if the cancer is considered high-grade or if there are high-risk features.
STAGE 03	Treatment includes surgery to remove the tumor and lymph nodes followed by chemotherapy. In some instances, radiation therapy may also be recommended.
STAGE 04	Treatment may include surgery, chemotherapy, and possibly radiation therapy. In some instances, targeted therapy or immunotherapy may also be recommended.

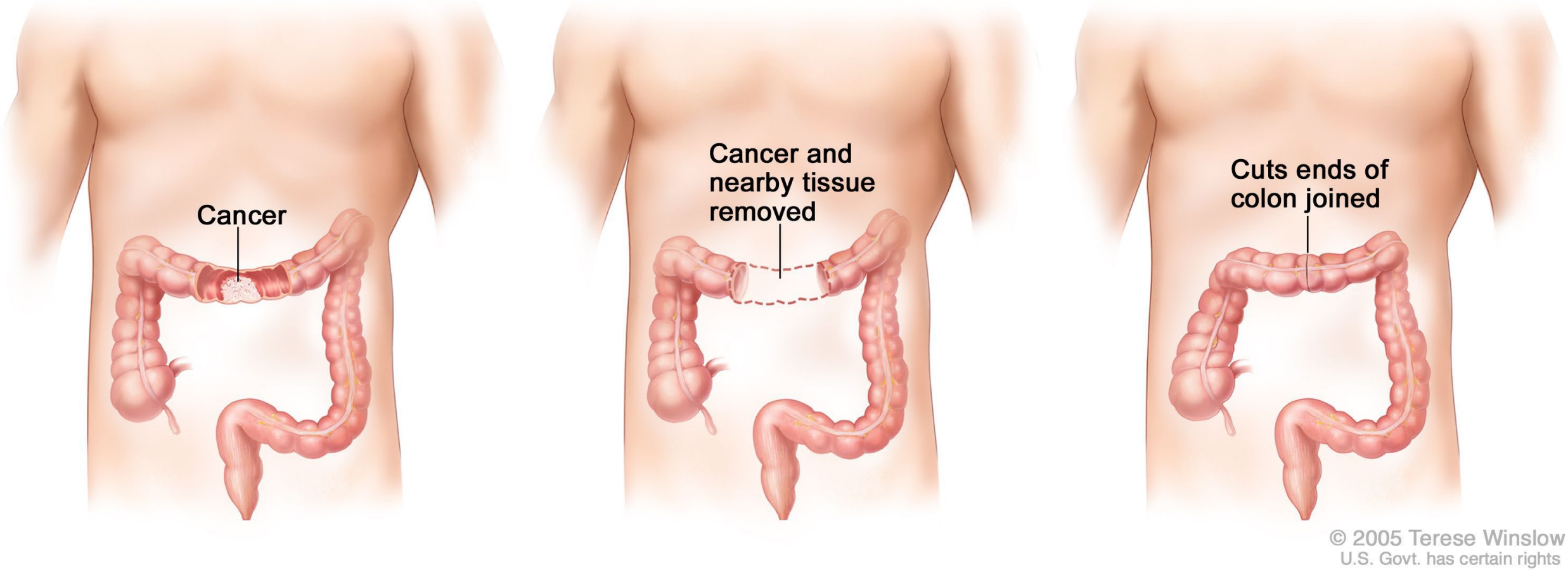
Robotic surgery often has improved outcomes for most colon cancer patients

Possible benefits of a laparoscopic approach

- Less scarring
- Less pain
- Faster recovery
- Shorter hospital stay
- Quicker return to normal activity



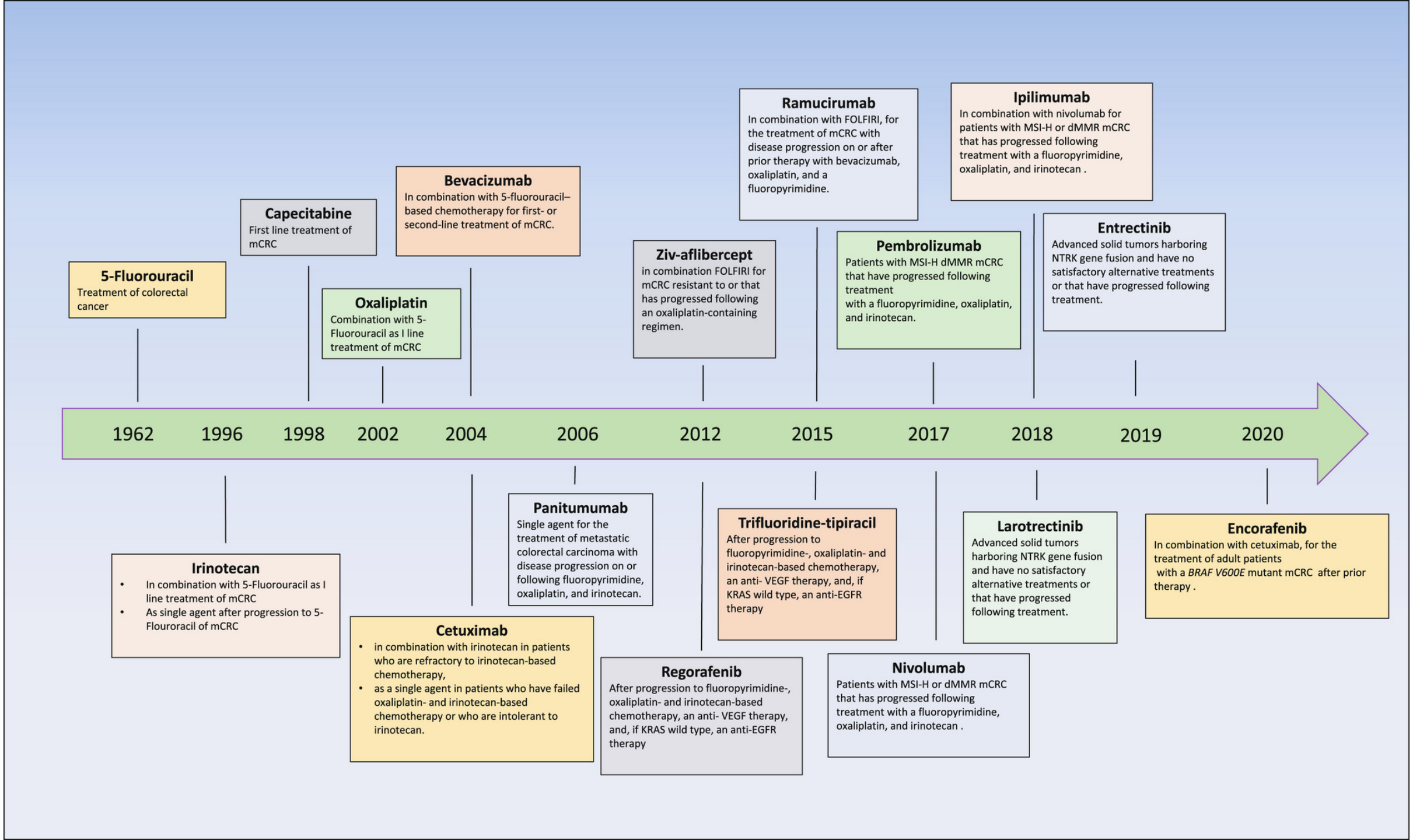
Resection of the Colon with Anastomosis



When is chemotherapy used?

Chemo may be used at different times during treatment for colorectal cancer:

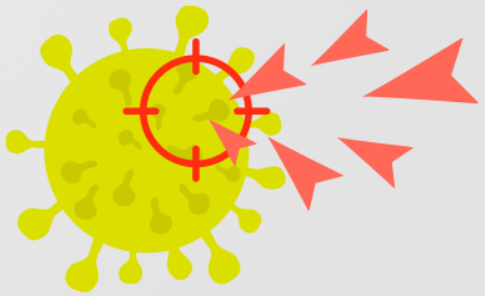
- **Neoadjuvant chemo** is given (sometimes with radiation) **before surgery** to try to shrink the cancer and make it easier to remove. This is often done for rectal cancer.
- **Adjuvant chemo** is given **after surgery.** The goal is to kill cancer cells that might have been left behind at surgery because they were too small to see, as well as cancer cells that might have escaped from the main colon or rectal cancer to settle in other parts of the body but are too small to see on imaging tests. This helps lower the chance that the cancer will come back.
- **For advanced cancers** that have spread to other organs like the liver, chemo can be used to help shrink tumors and ease problems they're causing. While it's not likely to cure the cancer, this often helps people feel better and live longer.


5-Fluorouracil
Treatment of colorectal cancer
Capecitabine
First line treatment of mCRC
Oxaliplatin
Combination with 5-Fluorouracil as I line treatment of mCRC
Bevacizumab
In combination with 5-fluorouracil–based chemotherapy for first- or second-line treatment of mCRC.
Ziv-aflibercept
in combination FOLFIRI for mCRC resistant to or that has progressed following an oxaliplatin-containing regimen.
Ramucirumab
In combination with FOLFIRI, for the treatment of mCRC with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
Pembrolizumab
Patients with MSI-H dMMR mCRC that have progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
Ipilimumab
In combination with nivolumab for patients with MSI-H or dMMR mCRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan .
Entrectinib
Advanced solid tumors harboring NTRK gene fusion and have no satisfactory alternative treatments or that have progressed following treatment.
1962
1996
1998
2002
2004
2006
2012
2015
2017
2018
2019
2020
Irinotecan
In combination with 5-Fluorouracil as I line treatment of mCRC
As single agent after progression to 5-Flouroracil of mCRC
Cetuximab
in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
as a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.
Panitumumab
Single agent for the treatment of metastatic colorectal carcinoma with disease progression on or following fluoropyrimidine, oxaliplatin, and irinotecan.
Regorafenib
After progression to fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti- VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy
Trifluoridine-tipiracil
After progression to fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti- VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy
Nivolumab
Patients with MSI-H or dMMR mCRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan .
Larotrectinib
Advanced solid tumors harboring NTRK gene fusion and have no satisfactory alternative treatments or that have progressed following treatment.
Encorafenib
In combination with cetuximab, for the treatment of adult patients with a BRAF V600E mutant mCRC after prior therapy .

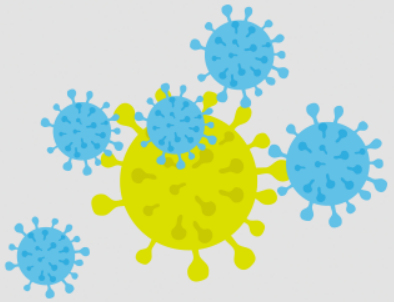
Difference between Chemotherapy, Targeted Therapy and Immunotherapy

Centre *for* Clinical Haematology

Chemotherapy



Targeted Therapy



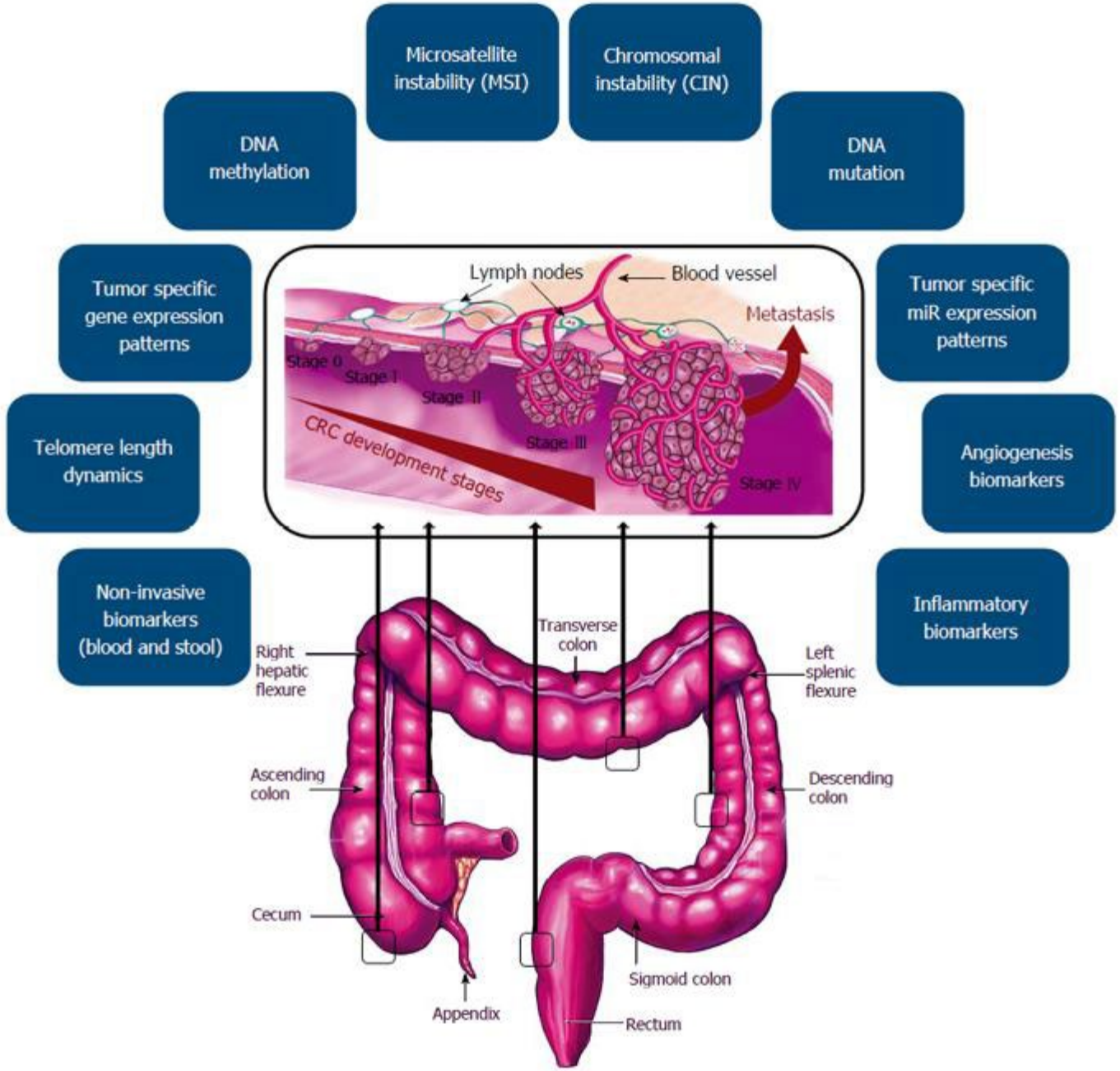
Immunotherapy

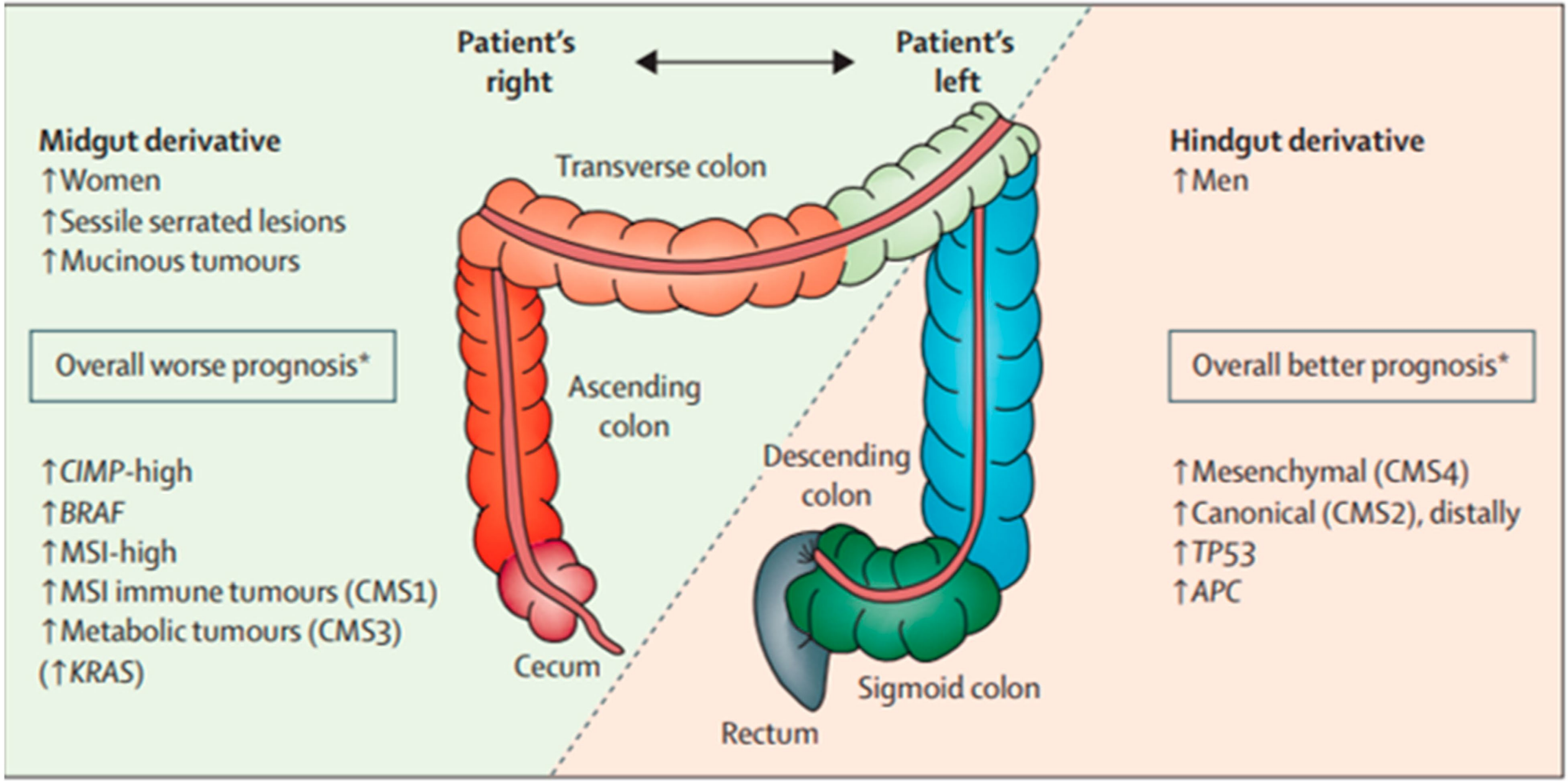
	Chemotherapy	Targeted Therapy	Immunotherapy
How does it work?	Targets rapidly dividing cells (mostly cancer cells)	Targets Proteins required for cancer growth	Uses our immune system against cancer
Side Effects	Hair loss, intestinal damage, nausea	Liver problems, diarrhea, skin rash	Autoimmune effects
Limitations	Cancer cells develop resistance to chemotherapy, not specific	Cancer cells develop resistance	Tailored and expensive

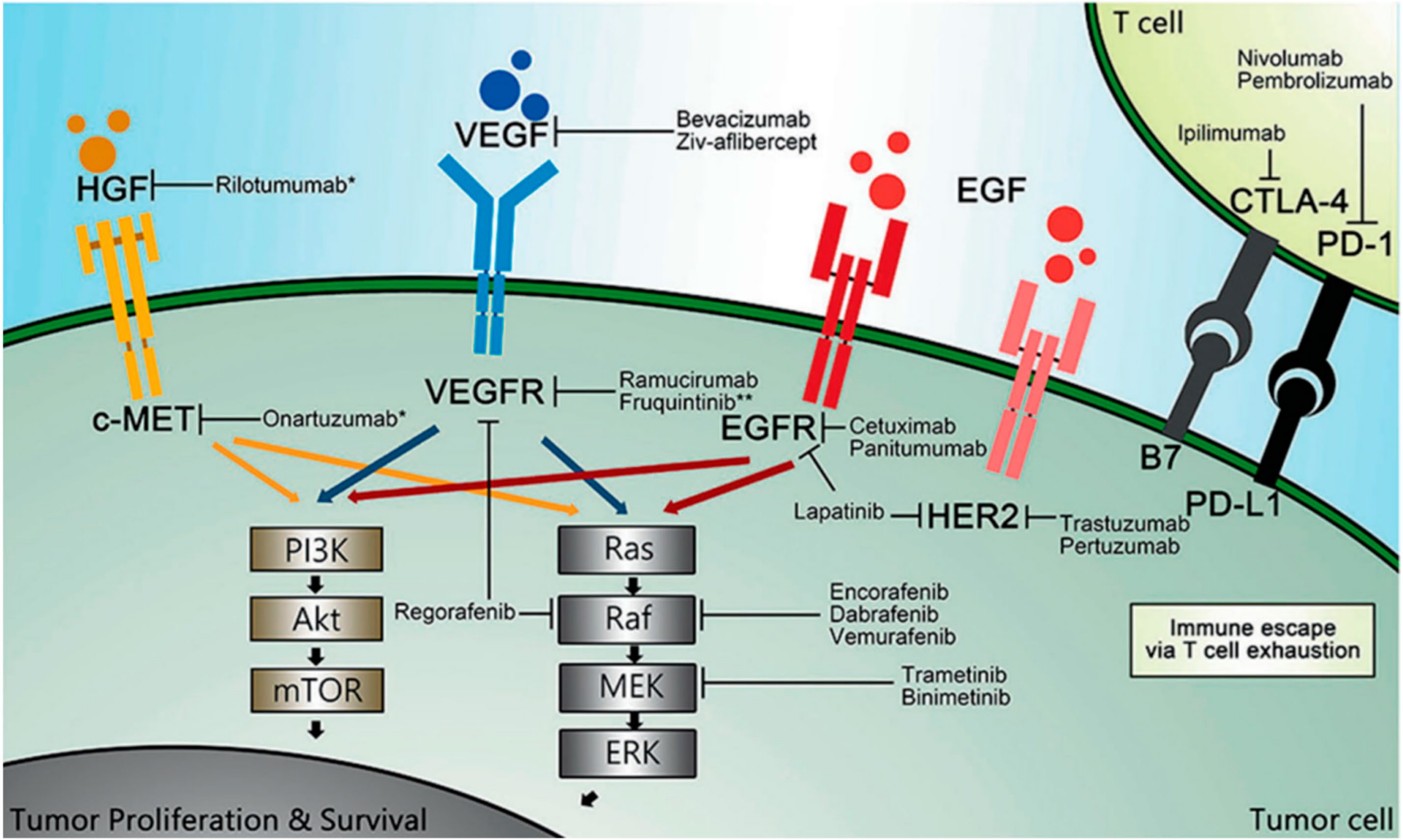
Types of Genetic Tests for Cancer

Germline:
Normal cells are tested for genetic mutations that may be inherited and increase your risk of cancer

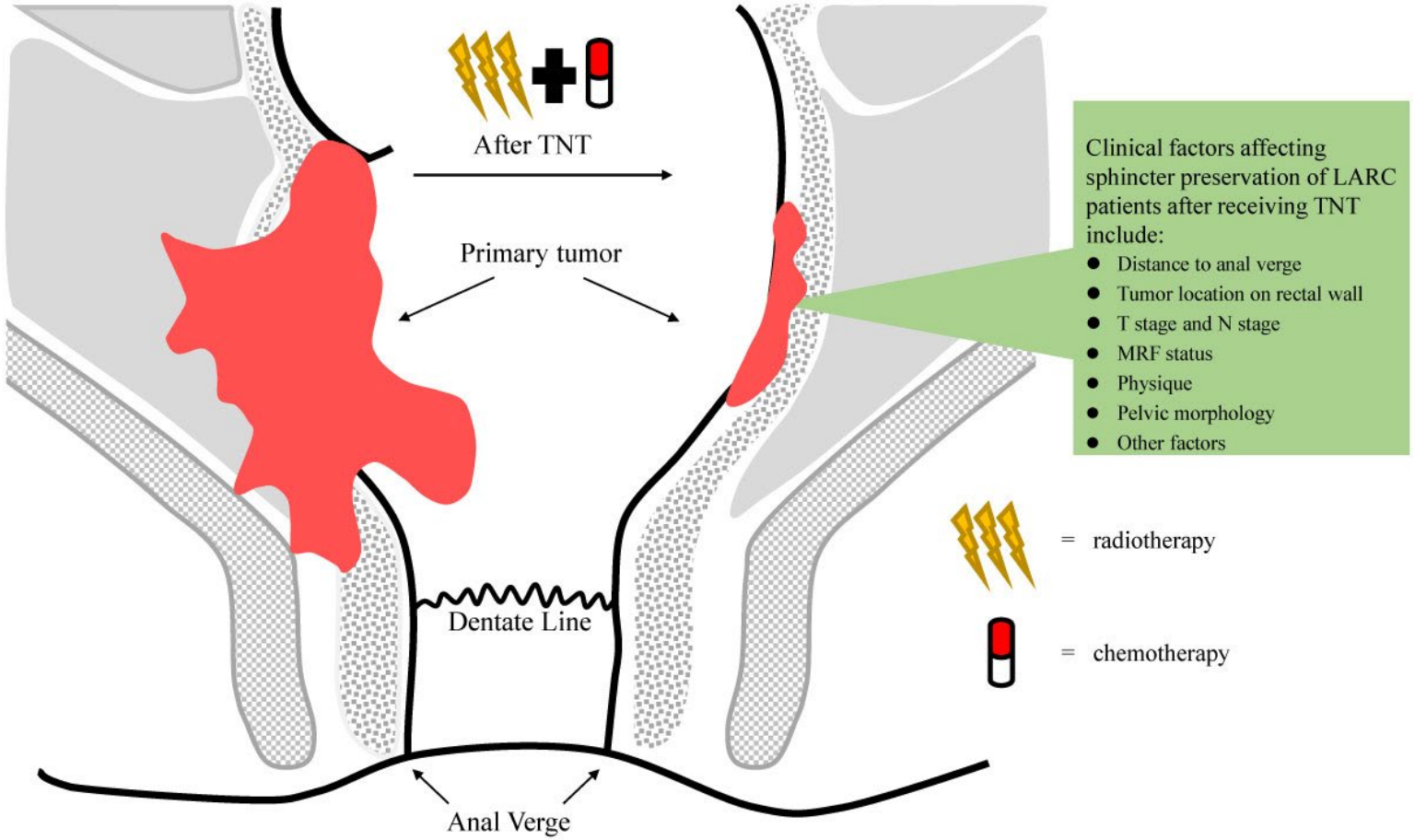
Somatic tumor:
Cells from a known cancer are tested for mutations that could impact your prognosis or determine treatment


Microsatellite instability (MSI)
Chromosomal instability (CIN)
DNA methylation
DNA mutation
Tumor specific gene expression patterns
Tumor specific miR expression patterns
Telomere length dynamics
Angiogenesis biomarkers
Non-invasive biomarkers (blood and stool)
Inflammatory biomarkers
Lymph nodes
Blood vessel
Metastasis
Stage 0
Stage I
Stage II
Stage III
Stage IV
CRC development stages
Transverse colon
Right hepatic flexure
Left splenic flexure
Ascending colon
Descending colon
Cecum
Appendix
Sigmoid colon
Rectum


Patient's right
Patient's left
Midgut derivative
↑Women
↑Sessile serrated lesions
↑Mucinous tumours
Overall worse prognosis*
↑CIMP-high
↑BRAF
↑MSI-high
↑MSI immune tumours (CMS1)
↑Metabolic tumours (CMS3)
(↑KRAS)
Transverse colon
Ascending colon
Cecum
Descending colon
Sigmoid colon
Rectum
Hindgut derivative
↑Men
Overall better prognosis*
↑Mesenchymal (CMS4)
↑Canonical (CMS2), distally
↑TP53
↑APC


T cell
Nivolumab
Pembrolizumab
Ipilimumab
CTLA-4
PD-1
VEGF
Bevacizumab
Ziv-aflibercept
HGF
Rilotumumab*
EGF
B7
PD-L1
VEGFR
Ramucirumab
Fruquintinib**
c-MET
Onartuzumab*
EGFR
Cetuximab
Panitumumab
Lapatinib
HER2
Trastuzumab
Pertuzumab
PI3K
Akt
mTOR
Ras
Raf
MEK
ERK
Regorafenib
Encorafenib
Dabrafenib
Vemurafenib
Trametinib
Binimetinib
Immune escape
via T cell exhaustion
Tumor Proliferation & Survival
Tumor cell

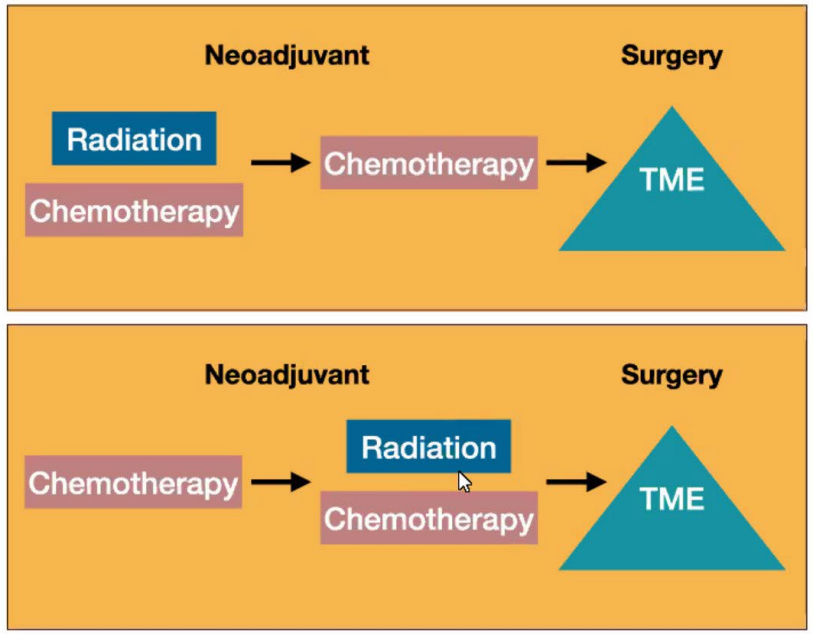
Rectal Cancer



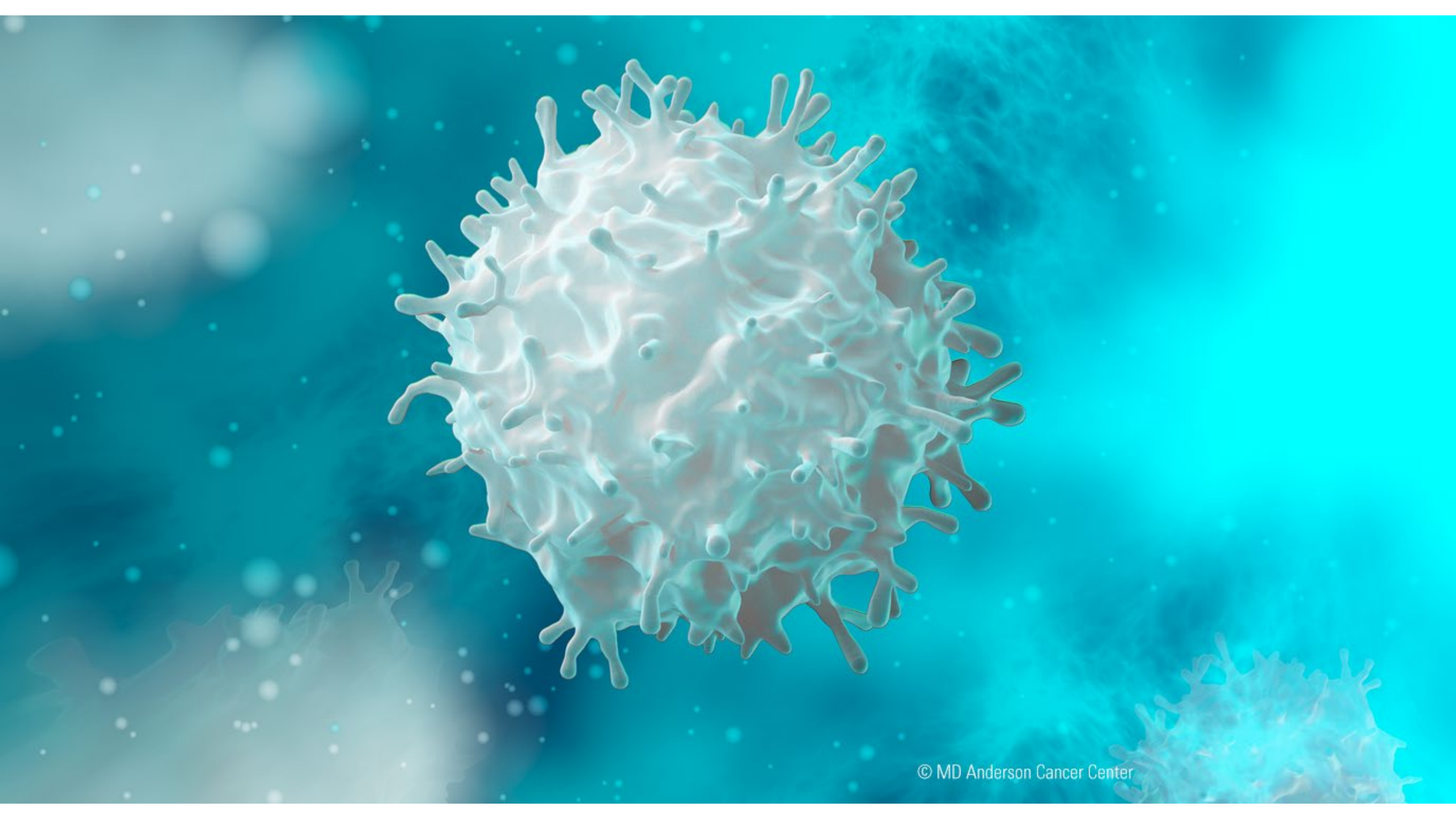
Rectal cancer

What's emerging:

The Total Neoadjuvant Therapy Paradigm



- Several trials have demonstrated the feasibility of TNT, with chemo either after chemoRT (consolidation) or before chemoRT (induction)
- **Rationale**:
  - Increase tumor regression and complete resectability
  - Maximize compliance
  - Improve delivery of planned systemic treatment
  - Address potential micrometastatic disease and reduce risk of DM
  - Improve overall survival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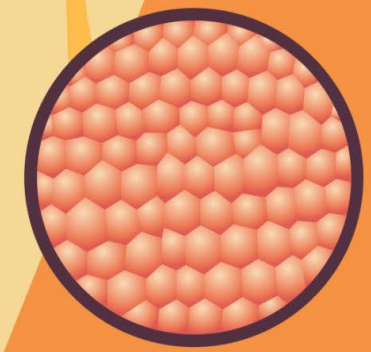
TRADITIONAL CANCER THERAPIES

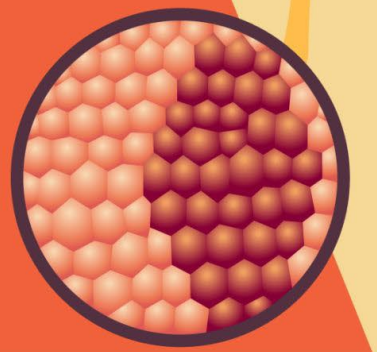
RADIATION OR DRUGS

KILLS

HEALTHY CELLS



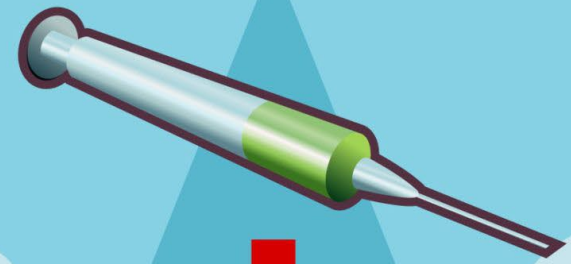
CANCEROUS CELLS



MANY SIDE EFFECTS

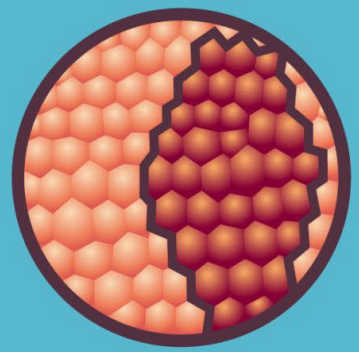
CANCER IMMUNOTHERAPIES

IMMUNOTHERAPY UNLEASHES THE PATIENT'S OWN IMMUNE SYSTEM

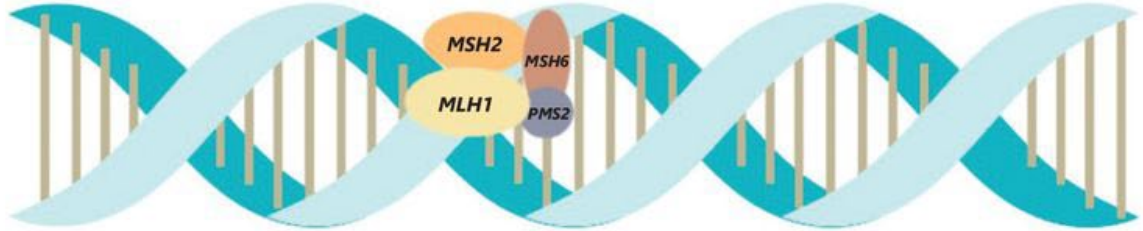


KILLS

SELECTIVELY CANCEROUS CELLS



FEW TO NO SIDE EFFECTS



Immunotherapy

Opportunities

Longer survival

Higher response rate

Lower AE rate

Better quality of life

Challenges

Patient selection

Regimen selection

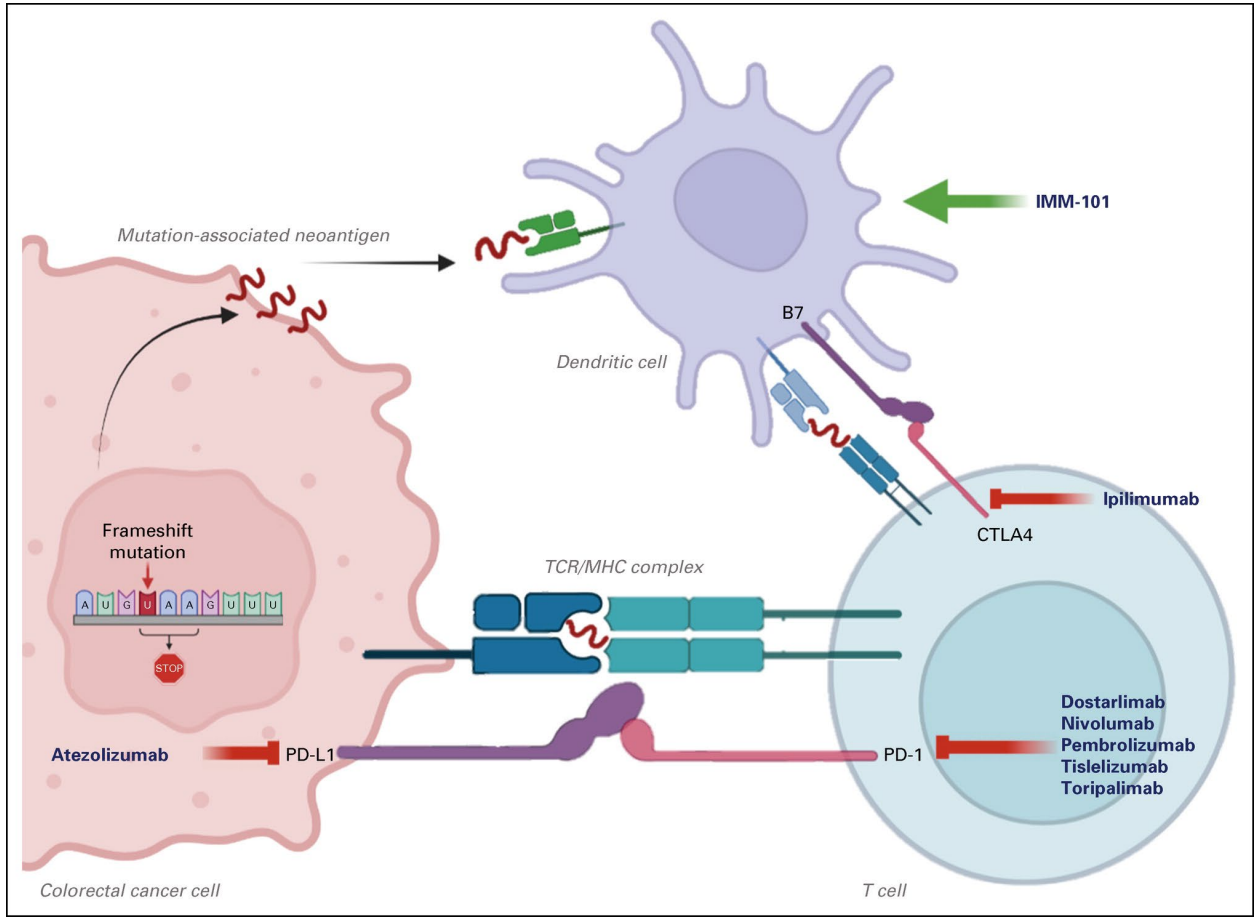
Treatment duration

Radiographic evaluation

Immune-related AE

Resistance

Immune checkpoint inhibitor therapy activates mutation-associated neoantigen-primed T cells and induces antitumor response.

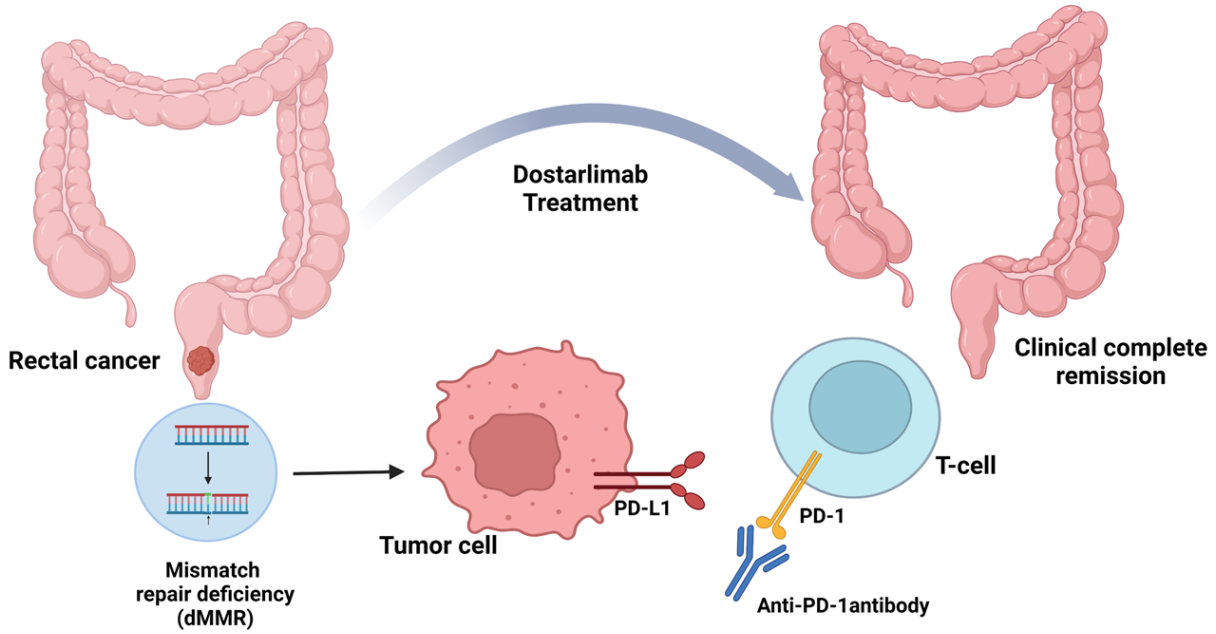


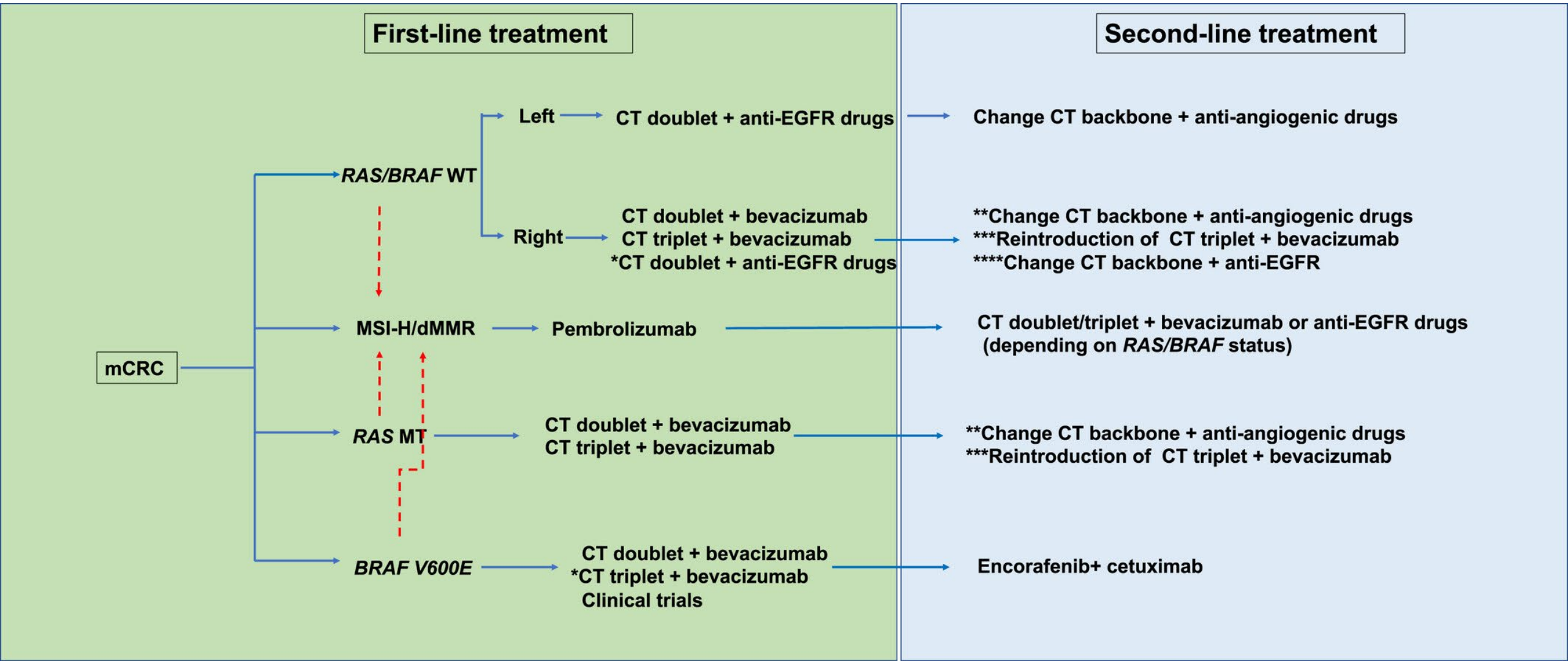
Neoadjuvant PD-1 blockade: mismatch repair–deficient, locally advanced rectal cancer

a

Summary of published clinical trials of neoadjuvant immunotherapy in dMMR, locally advanced CRCs					
Trials	**Setting**	**Phase**	**Patients (lynch syndrome,%)**	**Therapy**	**Outcome**
NICHE	Neoadjuvant	II	32 (13, 41%)	Nivolumab+ipilimumab	pCR (69%)
PICC	Neoadjuvant	II	17 vs 17 (4, 24% vs 1, 6%)	Toripalimab+celecoxib vs Toripalimab	pCR (88% vs 65%)
NCT04165772	Neoadjuvant	II	14 (8, 57%)	Dostarlimab	cCR (100%)

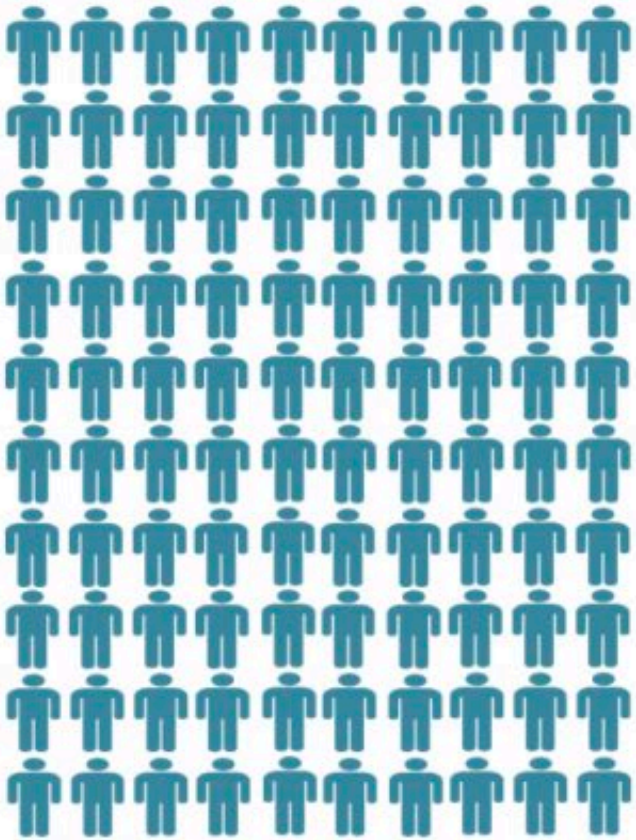
b




First-line treatment
Second-line treatment
mCRC
RAS/BRAF WT
Left
CT doublet + anti-EGFR drugs
Change CT backbone + anti-angiogenic drugs
Right
CT doublet + bevacizumab
CT triplet + bevacizumab
*CT doublet + anti-EGFR drugs
**Change CT backbone + anti-angiogenic drugs
***Reintroduction of CT triplet + bevacizumab
****Change CT backbone + anti-EGFR
MSI-H/dMMR
Pembrolizumab
CT doublet/triplet + bevacizumab or anti-EGFR drugs
(depending on RAS/BRAF status)
RAS MT
CT doublet + bevacizumab
CT triplet + bevacizumab
**Change CT backbone + anti-angiogenic drugs
***Reintroduction of CT triplet + bevacizumab
BRAF V600E
CT doublet + bevacizumab
*CT triplet + bevacizumab
Clinical trials
Encorafenib+ cetuximab

The Crux of Adjuvant Therapy in CRC: Treat Many to Save a Few

Stage II Colon Cancer

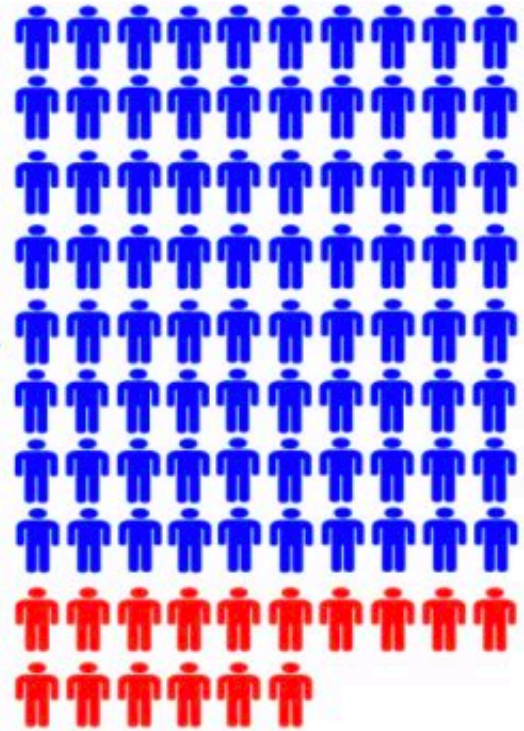


Adjuvant Chemo

Benefit

Up to 4% cured by chemo (chemo-sensitive)

No Benefit



80% cured by surgery alone

16% recur despite chemo (chemo-resistant)

Using cancer DNA in the blood (ctDNA) to determine management for patients who have had surgery for colon cancer

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Advancing Research. Improving Lives.™

ABOUT THE TRIAL

NRG-GI008: Colon Adjuvant Chemotherapy Based on Evaluation of Residual Disease (CIRCULATE-US)

ABOUT NRG ONCOLOGY

As one of the five research groups in

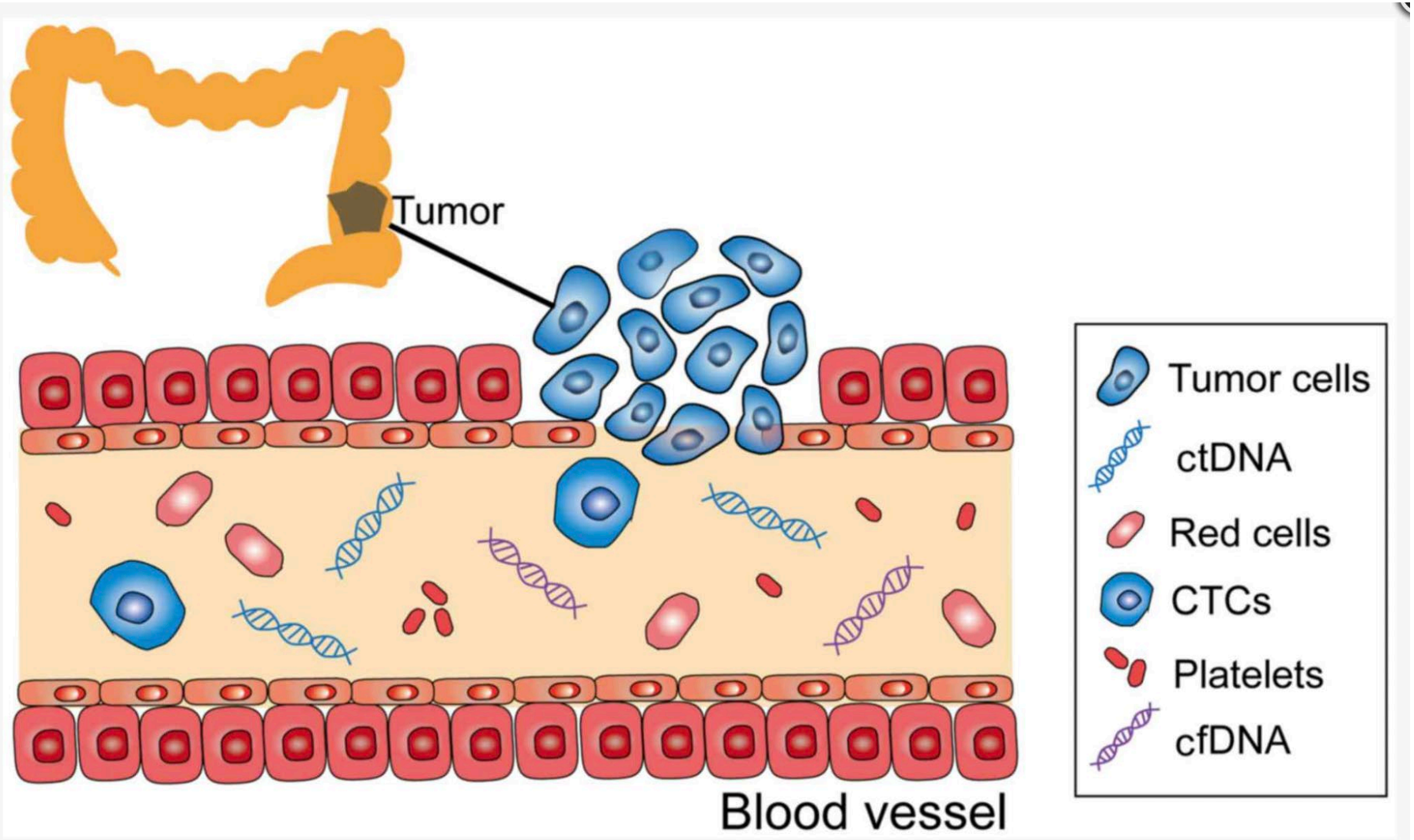
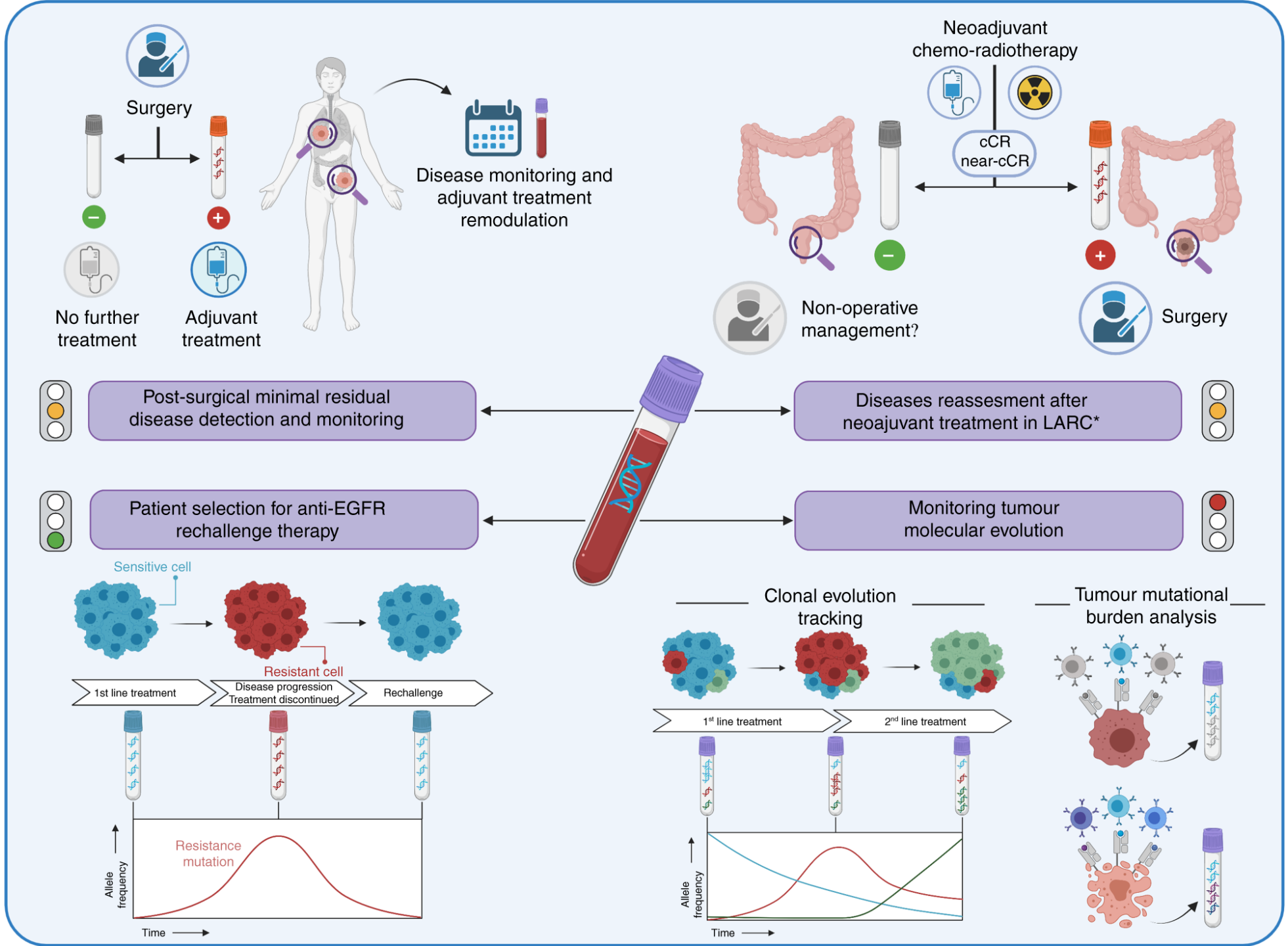
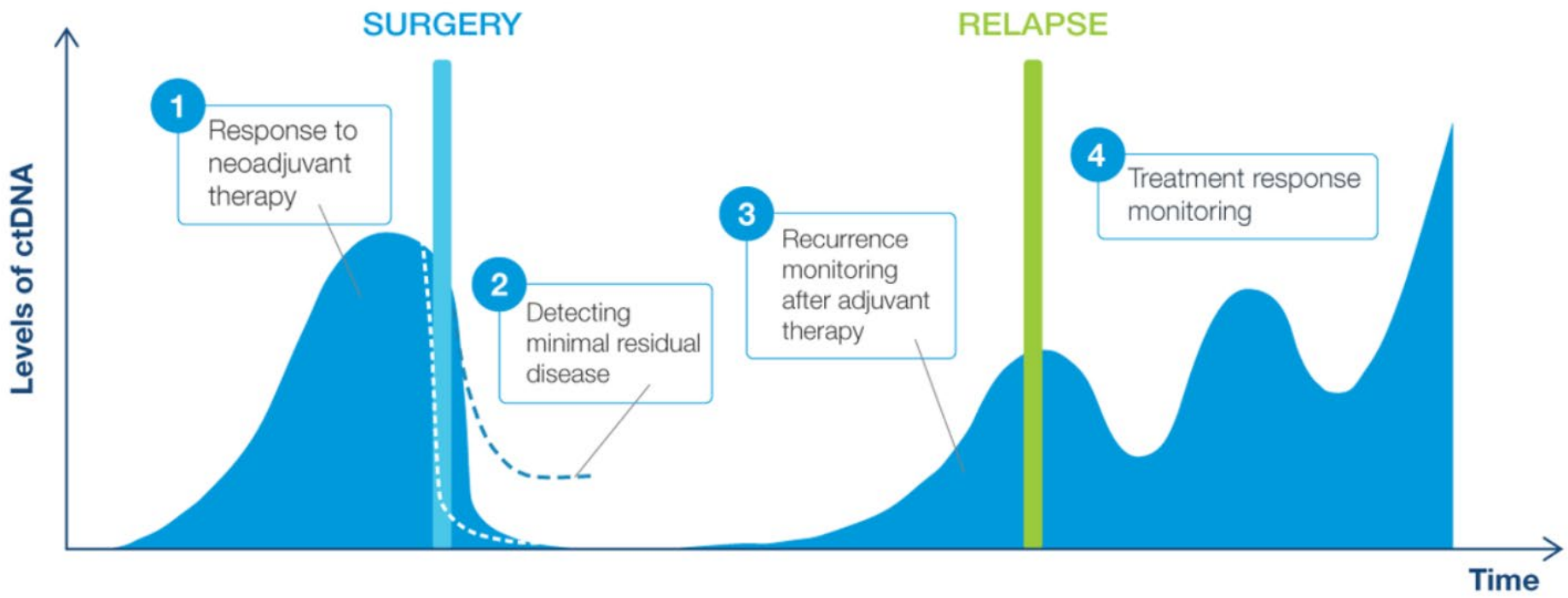
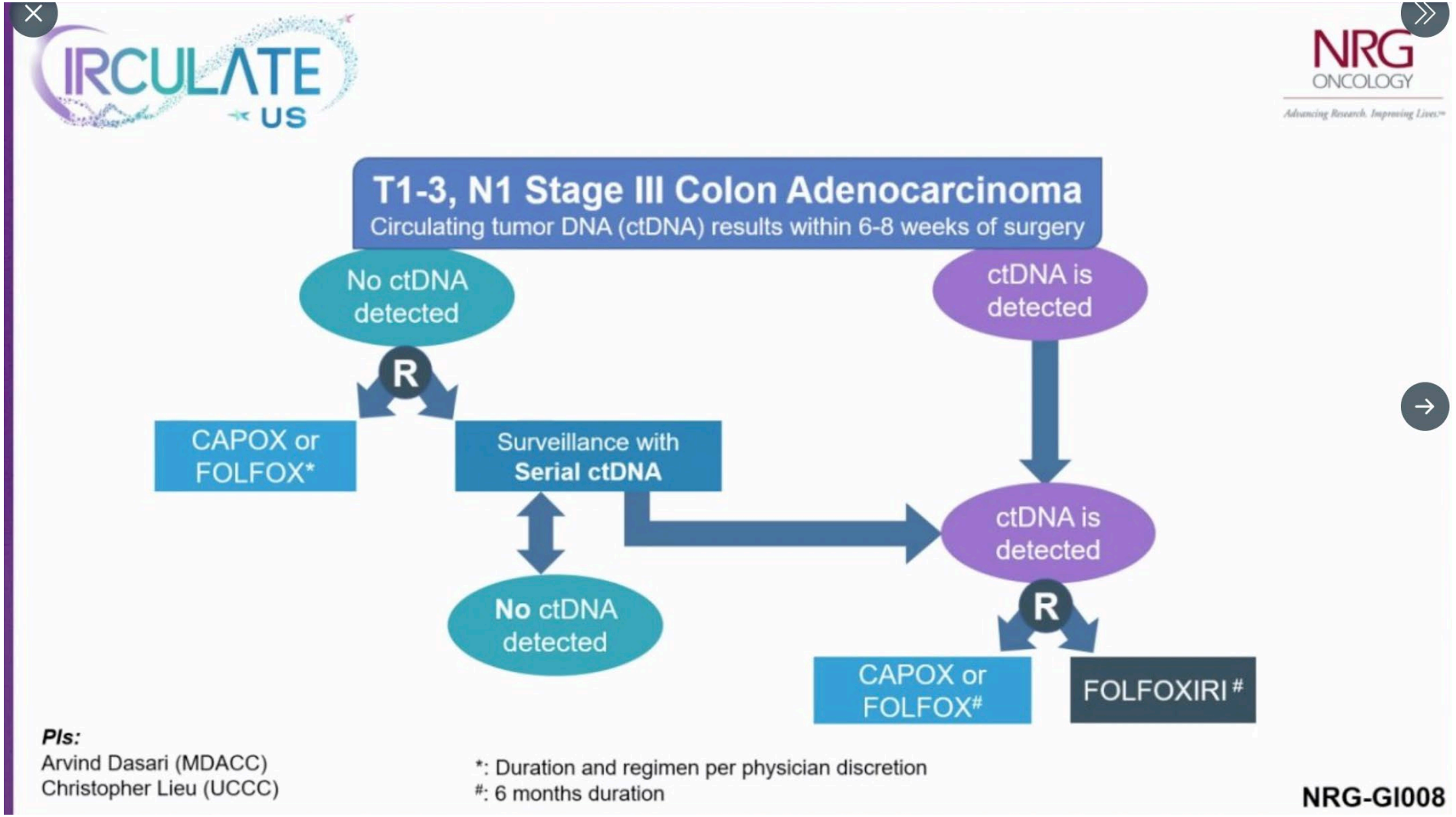


Figure 1. - CTCs, ctDNA and cfDNA in the peripheral blood stream. ctDNA, circulating tumor DNA; CTC, circulating tumor cell; cfDNA, cell-free DNA.


Surgery
No further treatment
Adjuvant treatment
Disease monitoring and adjuvant treatment remodulation
Neoadjuvant chemo-radiotherapy
cCR near-cCR
Non-operative management?
Surgery
Post-surgical minimal residual disease detection and monitoring
Diseases reassesment after neoajuvant treatment in LARC*
Patient selection for anti-EGFR rechallenge therapy
Monitoring tumour molecular evolution
Sensitive cell
Resistant cell
1st line treatment
Disease progression Treatment discontinued
Rechallenge
Resistance mutation
Allele frequency
Time
Clonal evolution tracking
1st line treatment
2nd line treatment
Allele frequency
Time
Tumour mutational burden analysis


SURGERY
RELAPSE
1
Response to neoadjuvant therapy
2
Detecting minimal residual disease
3
Recurrence monitoring after adjuvant therapy
4
Treatment response monitoring
Levels of ctDNA
Time


IRCULATE US
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T1-3, N1 Stage III Colon Adenocarcinoma
Circulating tumor DNA (ctDNA) results within 6-8 weeks of surgery
No ctDNA detected
R
CAPOX or FOLFOX*
Surveillance with Serial ctDNA
No ctDNA detected
ctDNA is detected
ctDNA is detected
R
CAPOX or FOLFOX#
FOLFOXIRI #
PIs:
Arvind Dasari (MDACC)
Christopher Lieu (UCCC)
*: Duration and regimen per physician discretion
#: 6 months duration
NRG-GI008

Colorectal Cancer Conclusions

1. **Colorectal cancer is a growth of cells that forms in the lower end of the digestive tract.**

   -Removing polyps can prevent cancer, screenings for those at high risk or over the age of 45.

2. **Symptoms might include blood in the stool, abdominal discomfort, change in bowel habits.**
3. **Colorectal cancer treatment depends on the size, location, genetic analysis and stage of cancer.**
4. **Treatments may include surgery, chemotherapy, immunotherapy, targeted therapy and radiation therapy.**
5. **Genetics and Immunology are playing an increasing role.**

Colorectal Cancer: What Patients Need To Know

Eden Stotsky-Himelfarb, BSN, RN, ONN-CG

Breast Cancer Clinical Triage Coordinator

Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

Baltimore, Maryland

March 20, 2024

Critical Conversations

ONCOLOGY FOUNDATION
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Personal Story - Statistics

1 diagnosis – 1997 – Stage 3b rectal cancer

2 surgeries – 1997 and 2018

30 radiation treatments - 1998

30 chemotherapy treatments - 1998

24 colonoscopies and counting – 1997 - 2021

Numerous blood draws

Countless CT scans

Multiple PET scans

Six unsuccessful cycles of invitro fertilization – 2010-2012

1 successful adoption - 2013

Critical Conversations

ONCOLOGY FOUNDATION
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Survivorship

- Surveillance – H&P, CEA, CT c/a/p, colonoscopy
- Impact on Quality of Life – physical and emotional impact

Critical Conversations

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Survivorship

- Long-term side effects – GI problems, uterine dysfunction, vaginal stenonis, menopause, fatigue, sleep difficulty, fear of recurrence/scanxiety, anxiety, depression, negative body images, peripheral neuropathy, urinary incontinence, sexual dysfunction, difficulties with sexual health or intimacy

- Late term effects – secondary cancers s/p radiation

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Survivorship

- Finding a PCP with knowledge of cancer surveillance
- Impact on relationships

Critical Conversations

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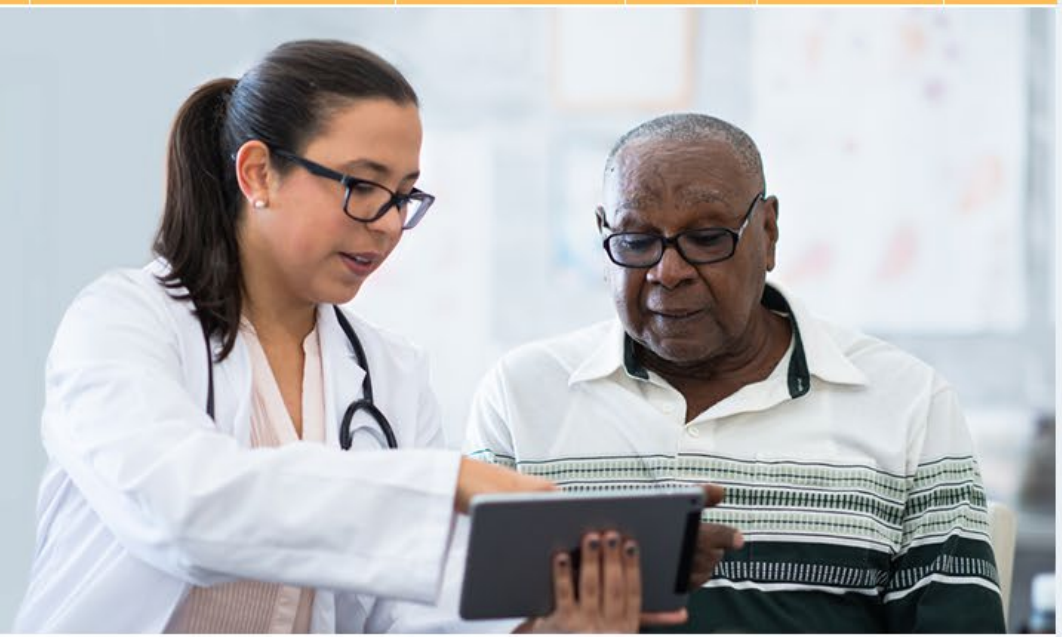

Critical Conversations

ONCOLOGY FOUNDATION OF MARYLAND AND THE DISTRICT OF COLUMBIA

Contact Information

Paul Celano, MD FACP FASCO

Herman & Walter Samuelson Medical Director

Sandra & Malcolm Berman Cancer Institute

Greater Baltimore Medical Center

pcelano@gbmc.org

Office: 443-849-3051

Eden Stotsky-Himelfarb, BS, BSN,RN,ONN-CG

Breast Cancer Program

New Patient and Multidisciplinary Care Nurse Coordinator

Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

eden@jhmi.edu

Office: 443-287-9045

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