

The Medical Management of Colon and Rectal Cancer

Bruce J Giantonio, MD

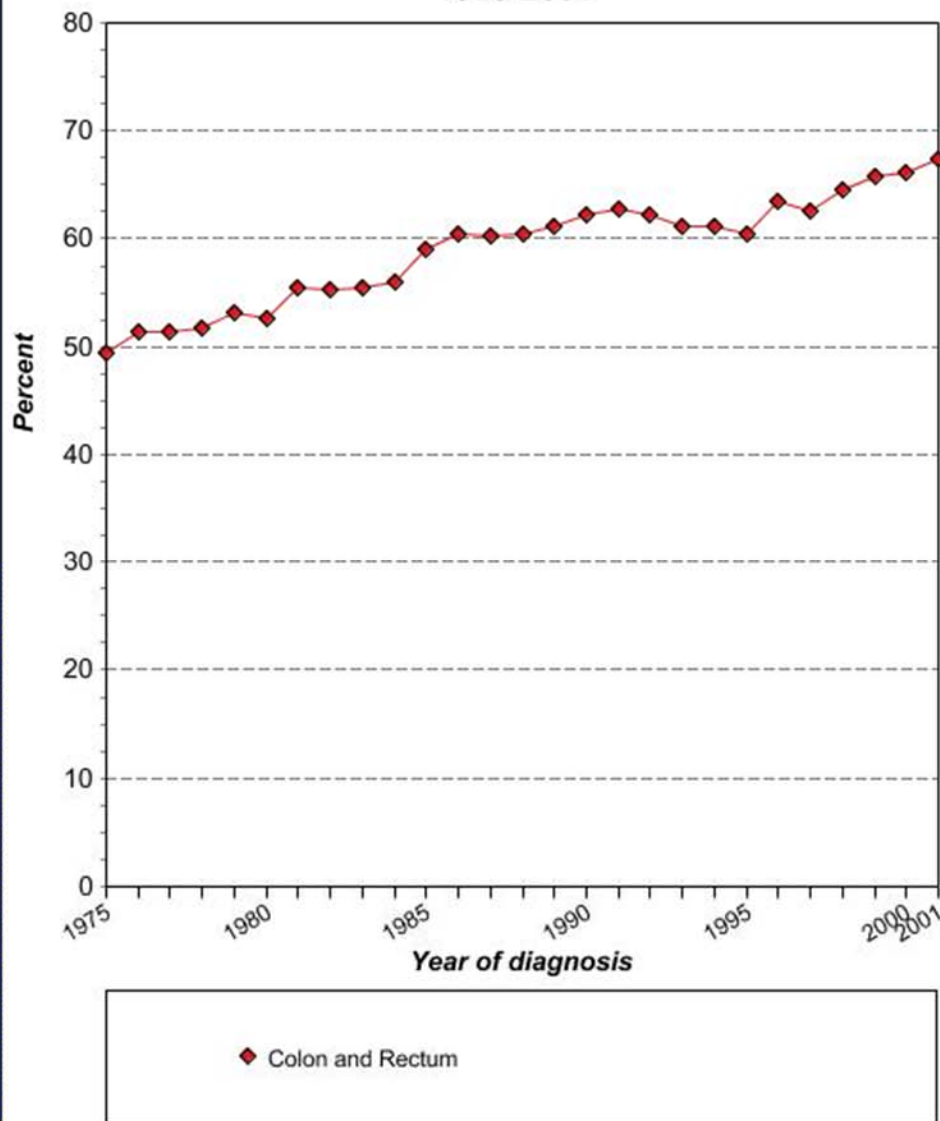
Understanding CRC

- Colorectal Cancer in the US:
 - 3rd most common cancer diagnosis in men & women respectively
 - 2nd leading cause of cancer death

The GOOD NEWS

- SCREENING can prevent colon cancer deaths
- More people with EARLY DISEASE can be cured:
 - Improved adjuvant therapy
- People with ADVANCED DISEASE live longer with treatment:
 - 4-5 times longer than NO treatment
 - YEARS instead of MONTHS
- Therapy can be TOLERABLE thru aggressive side effect management
- Many new therapies currently in CLINICAL TRIALS

**5-Year Relative Survival Rates By Year Dx
By Cancer Site
All Ages, All Races, Both Sexes
1975-2001**



Cancer sites include invasive cases only unless otherwise noted.

Survival source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta).

Survival rates are relative rates expressed as percents. The 5-year survival estimates are calculated using monthly intervals.

Colon Cancer Treatment

21% Stage IV

**Chemotherapy +/-
surgery**

Surgery/chemotherapy

14% Stage I

Surgery

**Surgery +/-
chemo**

37% Stage III

28% Stage II

Cancer Statistics: Jemal et al; CA Cancer J Clin 2005;55:10-30

Rectal Cancer Treatment

21% Stage IV

**Chemotherapy +/-
surgery**

**Surgery/chemotherapy
+ Radiation**

37% Stage III

14% Stage I

Surgery

**Surgery +/-
chemo +
Radiation**

28% Stage II

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Multidisciplinary Team

- Successful treatment requires a team of health care specialists
 - Surgeon/Surgical Oncologist
 - Medical Oncologist
 - Radiation Oncologist
 - Oncology Nurse Specialist
 - Social Worker
 - Nutritionist

Medical Management of Colorectal Cancer

- **Chemotherapy:**

- 5-FU/leucovorin: intravenous
- capecitabine (Xeloda): oral form of 5-FU
- Oxaliplatin (Eloxatin): intravenous
- Irinotecan (Camptosar) – intravenous, metastatic only

- **Targeted therapies for metastatic colorectal cancer**

- Anti-EGFR: cetuximab (Erbix)
- Anti-EGFR: panitumumab (Vectibix)
- Anti-VEGF: bevacizumab (Avastin)

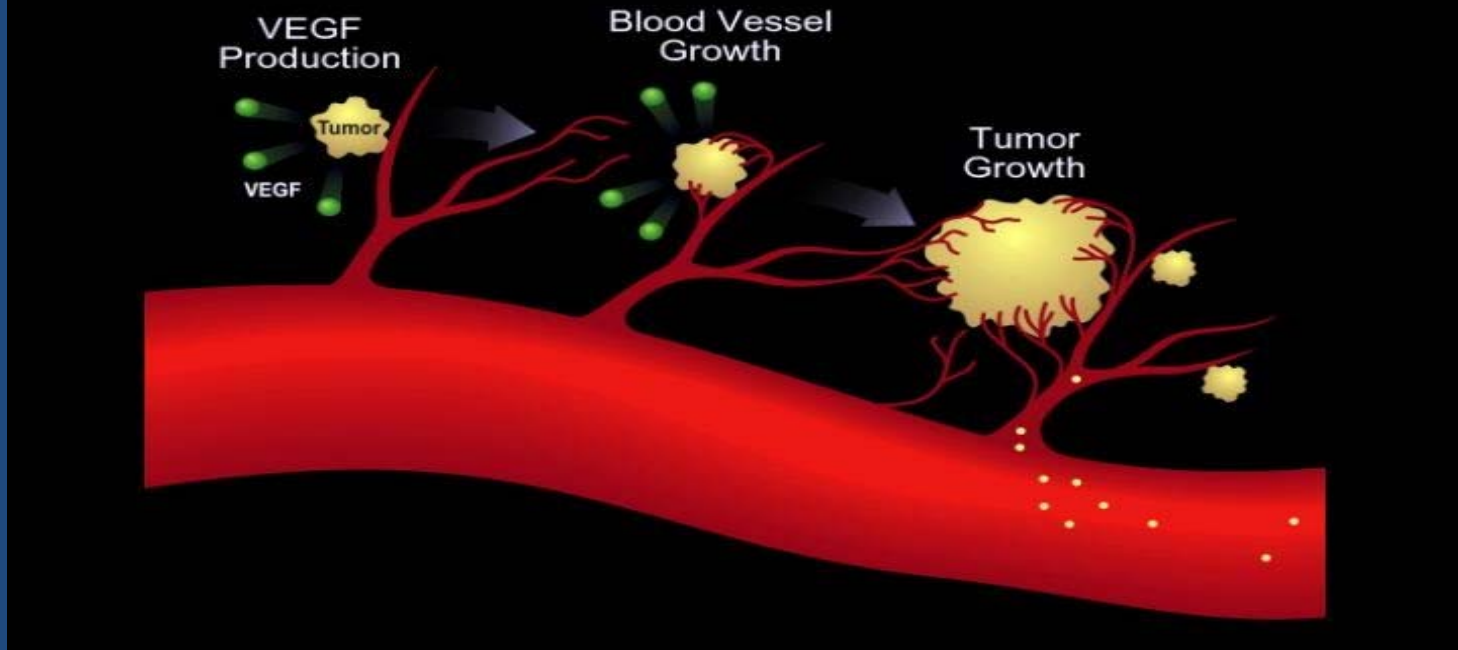
Medical Management of Colorectal Cancer

- Chemotherapy is used:
 - following surgery to reduce the chances of cancer recurrence (**adjuvant therapy**), or
 - Before surgery to shrink existing tumors and make the surgery possible (**neo-adjuvant therapy**), or
 - For the treatment of advanced disease, with the goal of helping one live longer *with the disease*.
- Targeted Therapy use is limited to the treatment of advanced disease

Targeting the tumor's blood supply: anti-angiogenesis therapy

- Angiogenesis = new blood vessel growth
 - Tumors cannot grow and spread without developing a blood supply.
- Anti-angiogenesis therapy:
 - 'starve' the tumor of nutrients and oxygen by ***stopping*** its ability to get its own blood supply.

Angiogenesis



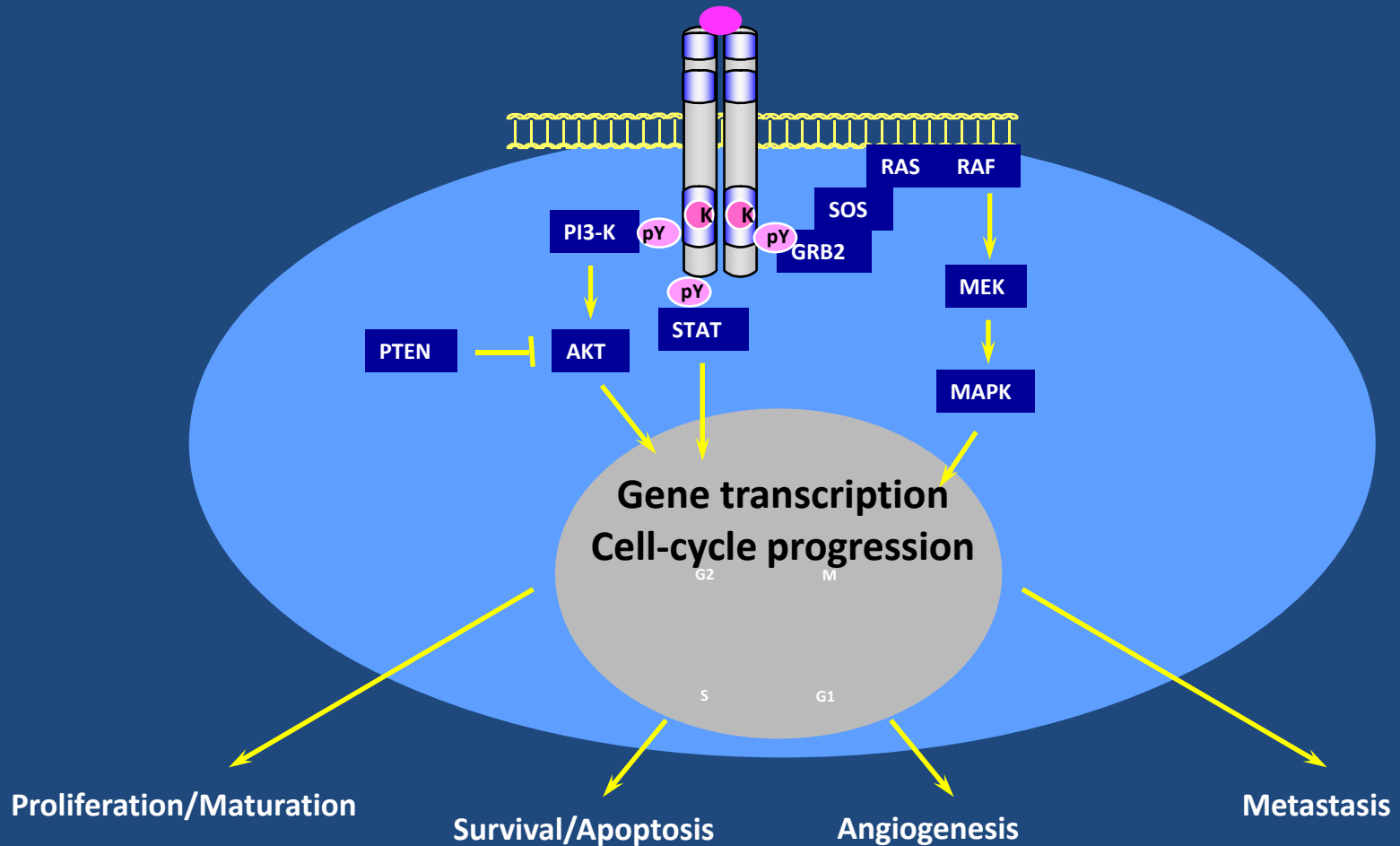
Bevacizumab (Avastin) is a monoclonal antibody that works to block angiogenesis

When given with chemotherapy, bevacizumab has been found to improve survival in people with advanced colorectal cancer.

Targeting the tumors growth factors: Anti-EGFR therapy

- Epidermal Growth Factor Receptor
 - a receptor that is found on the surface of a tumor cell
 - tells the cell to reproduce itself
 - Inhibited by:
 - Cetuximab (ERBITUX)
 - Panitumumab (VECTIBIX)

EGFR Signal Transduction



Managing Side Effects

- You may or may not experience common side effects
 - Ask about preventing side effects before treatment
- Many are reluctant to report side effects
 - Fear if chemo dose is reduced, the treatment might not work
 - Failure to adjust doses may lead to life-threatening toxicities, treatment delays and reduced quality of life
 - It is important to report them to your doctor!

Side Effects Management

Nausea and Vomiting:

- Antiemetics
- Diet (avoid fried, fatty foods)
- Smaller meals

Diarrhea:

- Loperamide (Immodium[®])
- Diphenoxylate with atropine (Lomotil[®])
- Octreotide (Sandostatin[®])

Side Effects Management

Peripheral Neuropathy:

- Common side effect of oxaliplatin
- Sense of touch is distorted or diminished-
 - ordinary touch can be unpleasant or painful.
- Burning or prickling feeling without stimulus
- Dose modifications, Calcium + Magnesium

Side Effects Management

Stomatitis and Mucositis:

- Baking Soda and salt mouthwash
- 'Magic Mouthwash'

Hand-Foot Syndrome:

- Keep hands & feet clean and moist, use mild soaps and no rubbing
- Use alcohol free emollients and creams (Aveeno[®], Lubriderm[®], Udder Cream[®], Bag Balm[®])
- Avoid topical anesthetics or creams containing diphenhydramine. (can worsen toxicity)
- Immerse hands and feet in cool water several times a day

Targeted Therapy Side Effects

Bevacizumab (Avastin)

- Hypertension
- Bleeding
- Delayed wound healing
- Arterial blood clots
- Gastrointestinal perforation (rare)
- Dumping protein into urine (Proteinuria)

Targeted Therapy Side Effects

Cetuximab (Erbix)

- Infusion reactions (occurs in 3% of patients)
- Acne-like rash
- Low magnesium and calcium levels (must be monitored)
- Interstitial lung disease: scarring of the lungs (rare)

Acneiform Rash

- Avoid sun, heat & humidity
- Use mild soaps
- Water based makeup is generally well tolerated
- Topical and/or antibiotics
- Topical and/or oral antihistamines
- Cool compresses
- Petroleum jelly, silver sulfadiazine ointment for ulcerative lesions

'Cancer Side Effects'

- Depression
 - A normal reaction to the cancer diagnosis
 - Signs:
 - Do you cry often or uncontrollably?
 - Have you lost interest in things that used to give you pleasure?
 - Have you stopped looking forward to “fun” events and occasions?
 - Are you eating and/or sleeping more or less than usual?
 - Management
 - Counseling
 - Medications
 - Celebrex, Zoloft, Prozac, Remeron

'Cancer Side Effects'

- Sexual
 - Emotional & physical stress can decrease libido
 - Body image may be altered
 - Pouch covers for ostomies
 - Erectile Dysfunction:
 - Viagra, Cialis, Levitra
 - Vaginal dryness:
 - Replens, AstroGlide
 - Early menopause/egg preservation & sperm banking

'Cancer Side Effects'

- Fear of Recurrence
 - Be informed
 - Talk about it with your medical team
 - Allow yourself to feel up and down—it is healthy to express negative emotions
 - Do not to let anxiety and fear prevent you from seeking medical care

Follow-up Care

Follow-Up Care Recommendation	Year 1	Year 2	Year 3	Years 4 & 5
Doctor's Visit	Every 3-6 mo.	Every 3-6 mo.	Every 3-6 mo.	Every 6 months
CEA test	Every 3 months	Every 3 months	Every 3 months	As determined by your doctor
CT scan (chest and abdomen)	Once per yr., if recommended	Once per yr., if recommended	Once per yr., if recommended	As determined by your doctor
CT scan (pelvis) (rectal cancer only)	Once per yr., if recommended	Once per yr., if recommended	Once per yr., if recommended	As determined by your doctor
Colonoscopy	Once		At 3 years	
Proctosigmoidoscopy (rectal cancer only)	Every 6 months (for patients who did not have pelvic radiation treatment) for 5 years			

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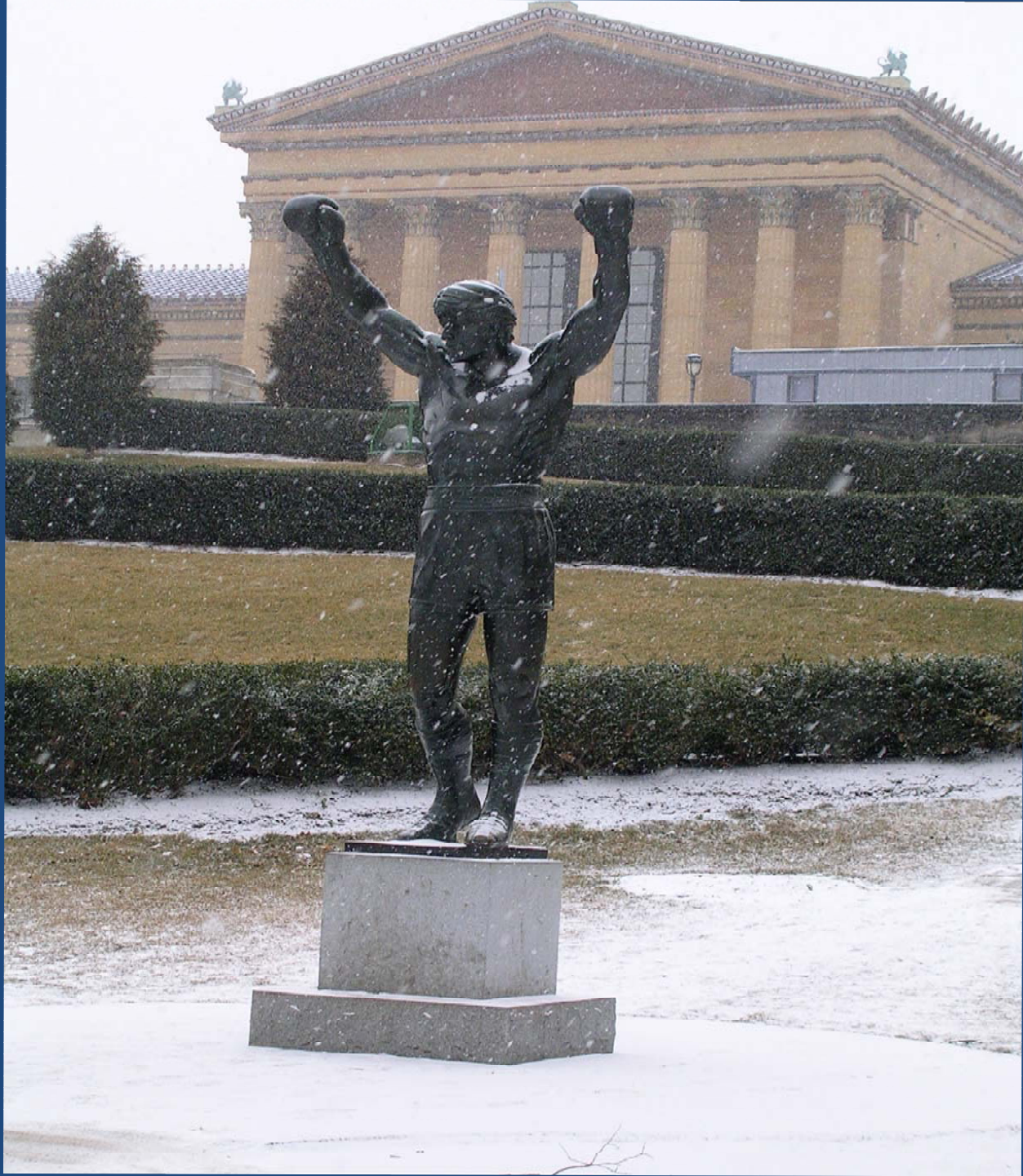
A Look to The Future...

- Research is underway for better cancer treatment
 - New chemotherapies and targeted therapies
 - The US government, and most major pharmaceutical companies are investing billions of dollars in cancer research
 - Screening tools and tests to predict benefit from treatment
 - Human Genome Project
 - Pharmaco-genomics
 - Identifying cell targets
 - Linking drug response to genetic mutations
 - Increased role of tissue sampling
- IMPORTANCE OF CLINICAL RESEARCH

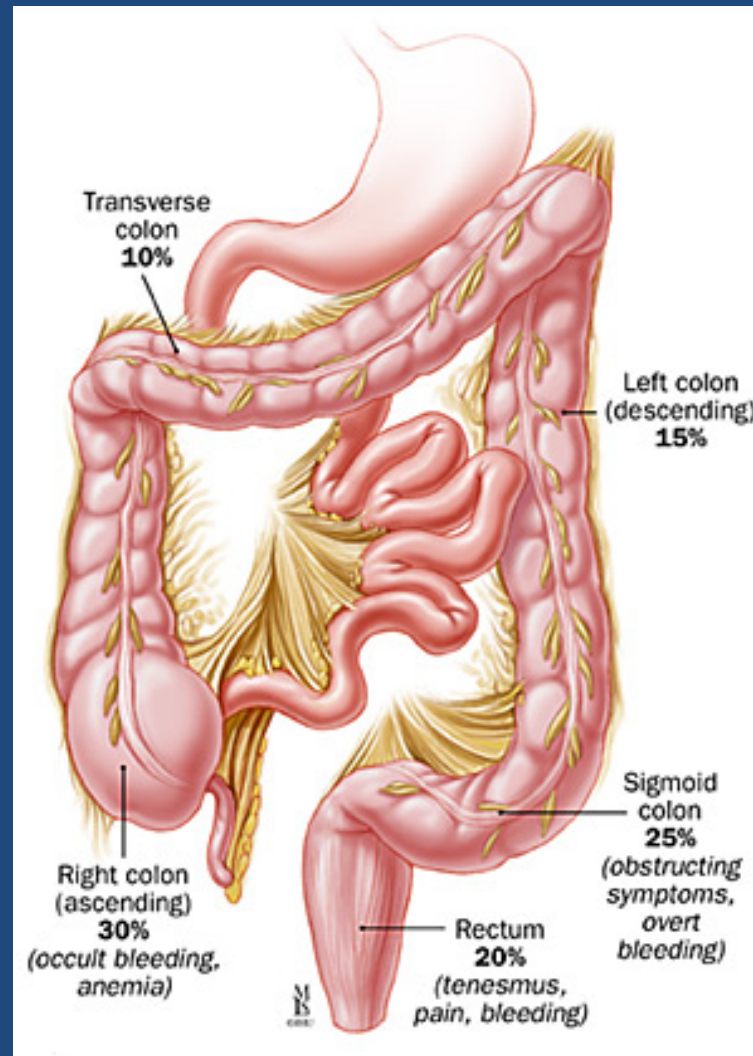
The BAD NEWS

- Few people undergo screening
- Not all people with advanced disease benefit from treatment
 - Need to further refine our ability to ‘tailor’ treatment based on risk
- Side effects remain a problem
- Only 2-3% of adults with cancer in the US participate in clinical trials

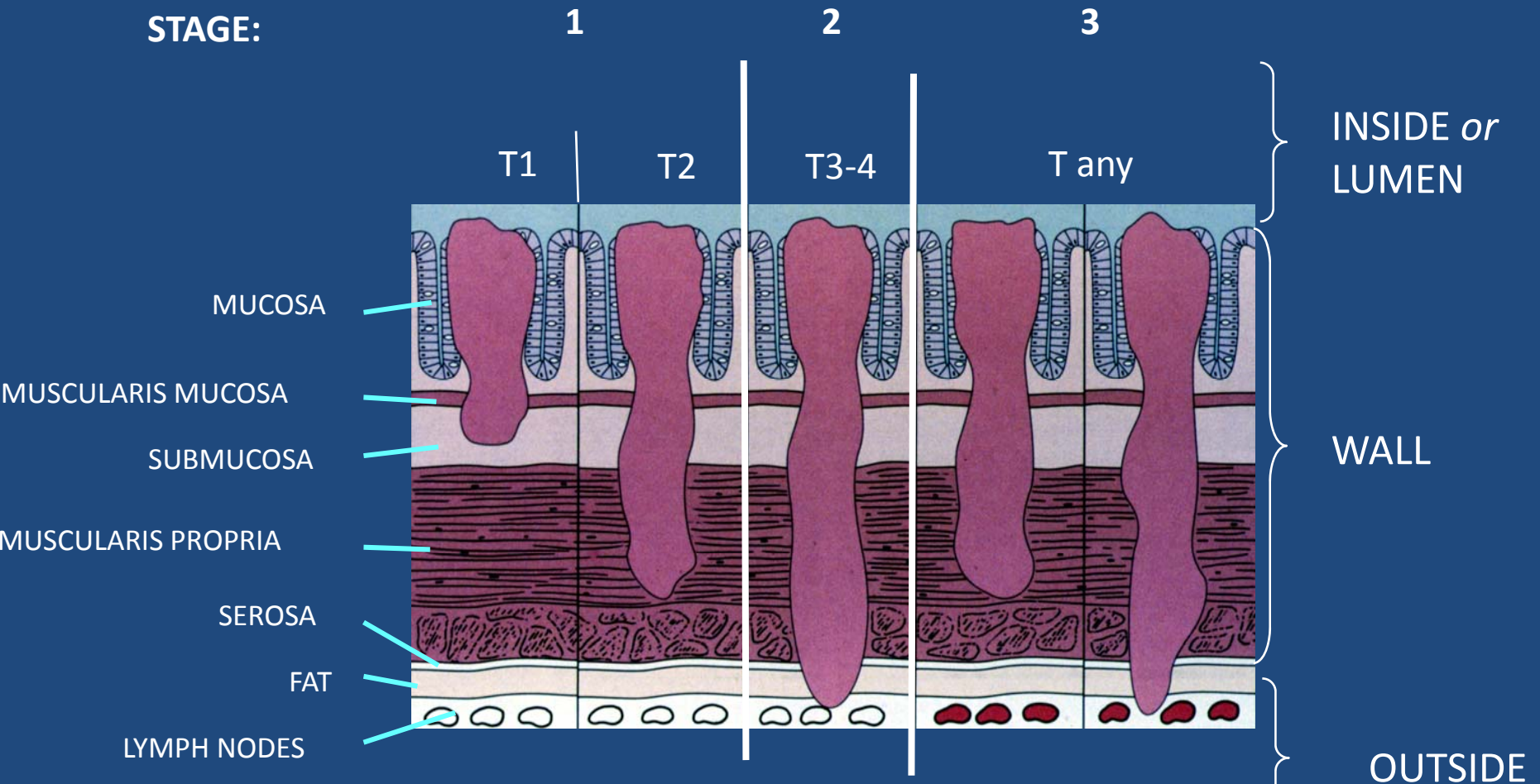
YO!



Distribution of cancers in the colon&rectum



Staging of Colorectal Cancer



Adapted from Skarin. *Slide Atlas of Diagnostic Oncology*. Gower Medical Publishing; 1997:Fig 5.98.

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Average Stage at Diagnosis

2009 new cases colon cancer: 106,100

rectal cancer: 40,870

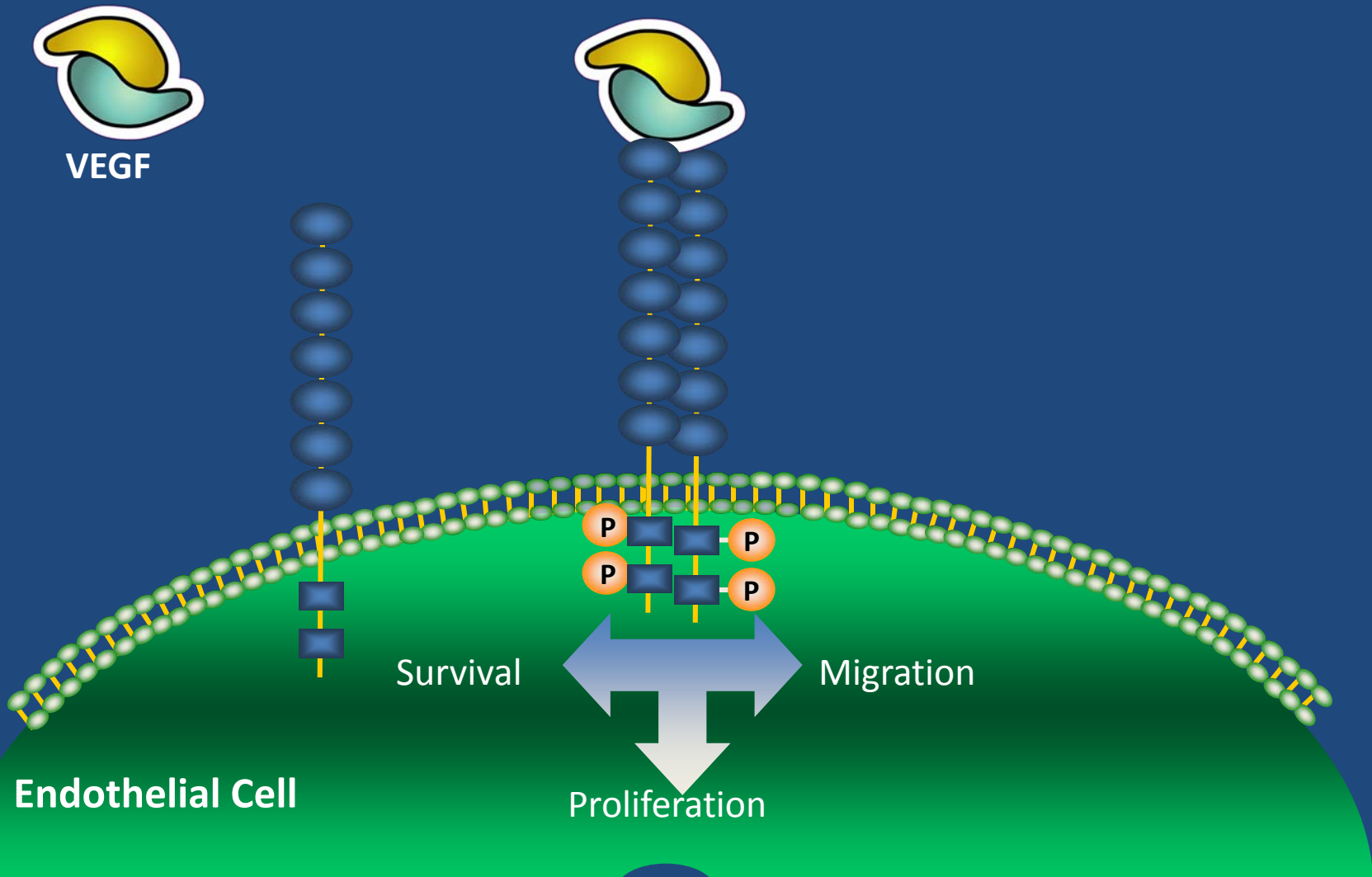
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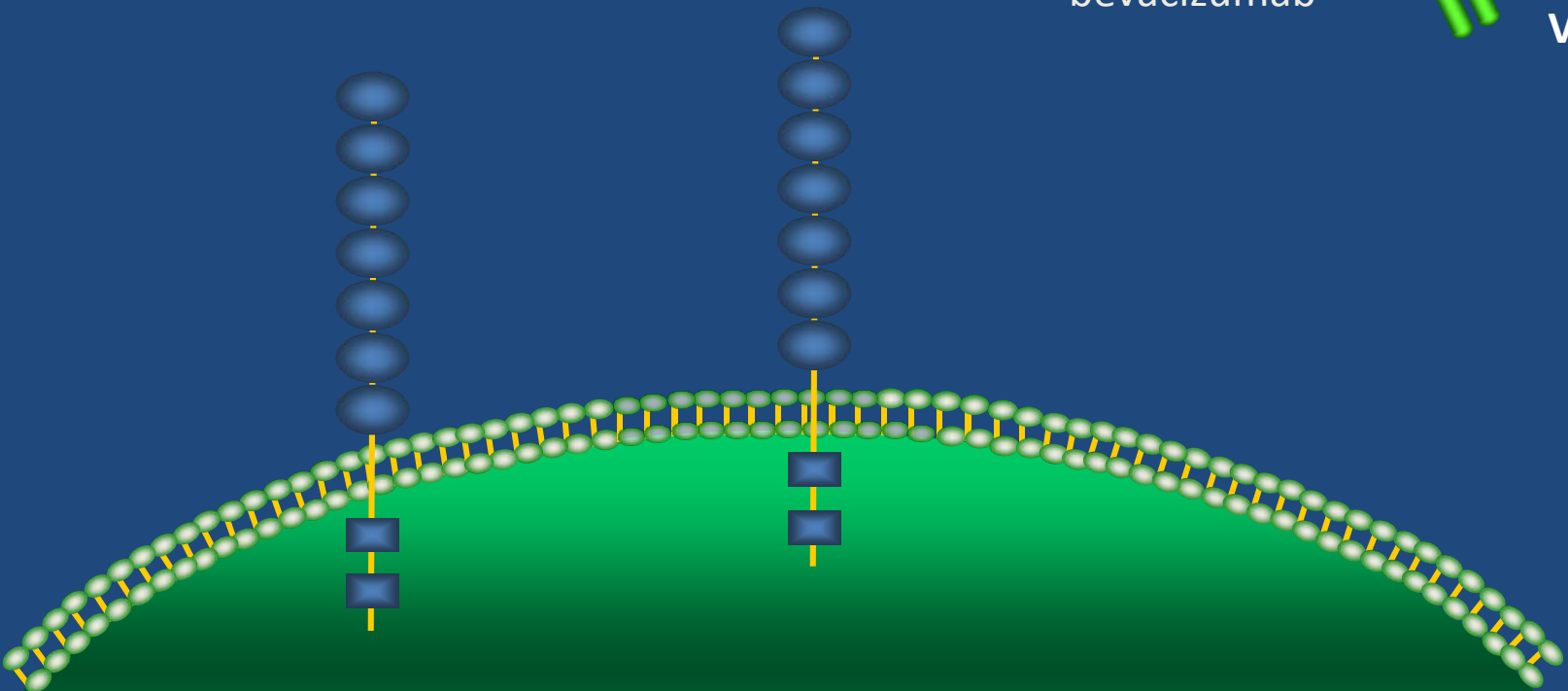
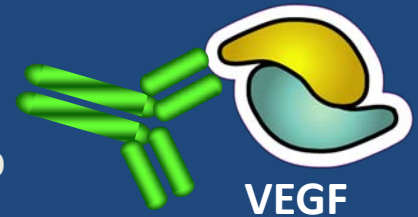
37% Stage III

Endothelial Cell Activation: VEGF Signal Transduction



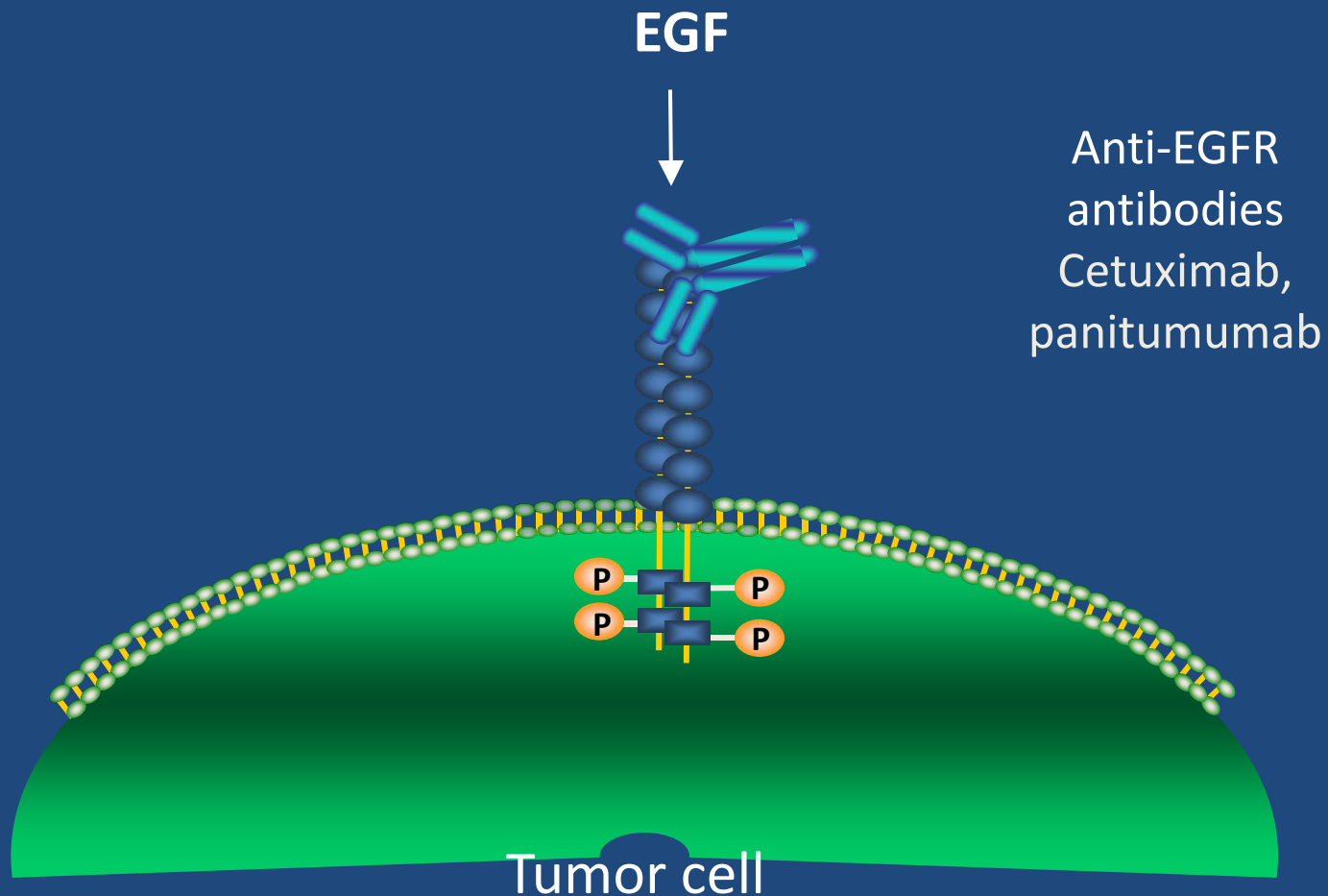
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Anti-VEGF
antibodies
bevacizumab



Endothelial Cell

Agents Targeting the Epidermal Growth Factor Pathway



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