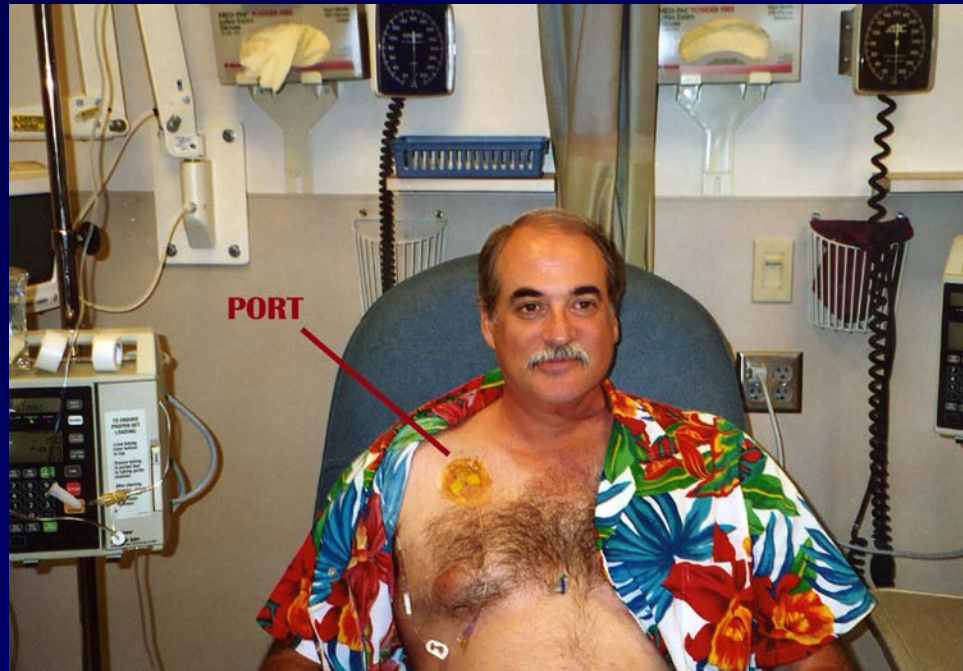


Systemic Therapy 101



What is chemotherapy?



Why do I need Chemotherapy?

- Goal is to prevent recurrence of the cancer after it has been surgically removed ('preventive')
- Chemotherapy treats microscopic cancer cells that may be left behind after surgery has completely removed all the tumor that we can see



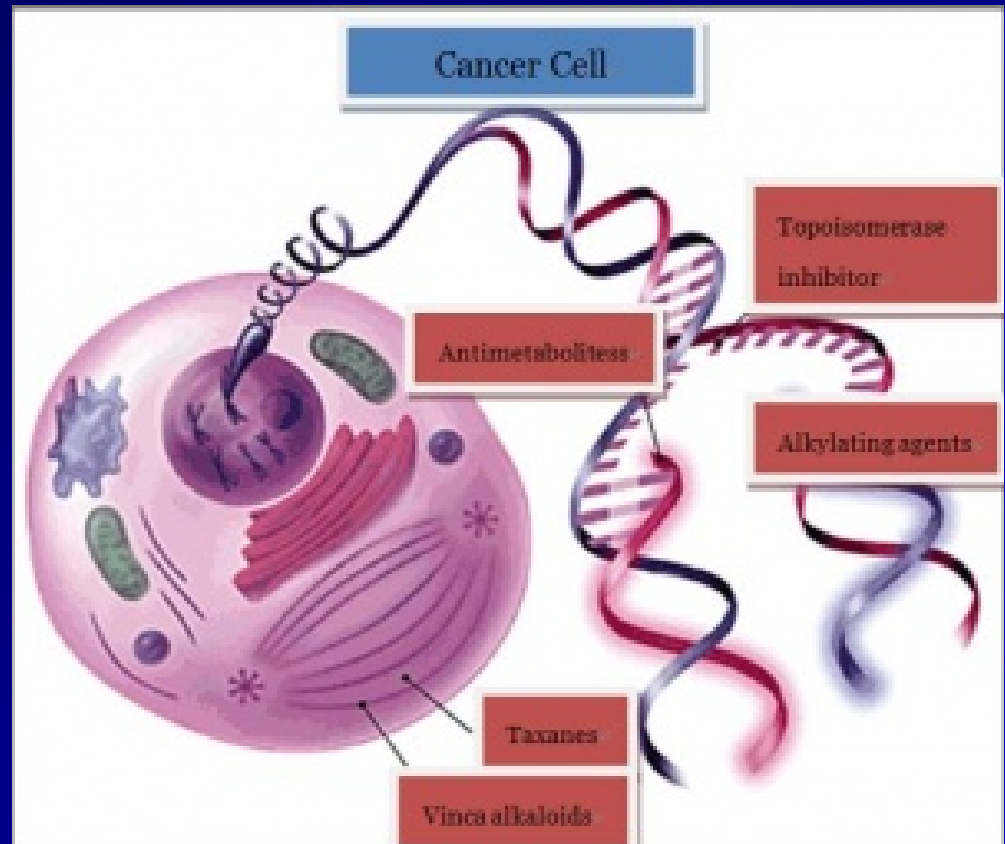
Why do I need Chemotherapy

- In patients where the disease has spread (metastatic):
- Control the growth of cancer
- Help with symptoms (improve quality of life)
- Chronic disease
- Extends life but not a cure

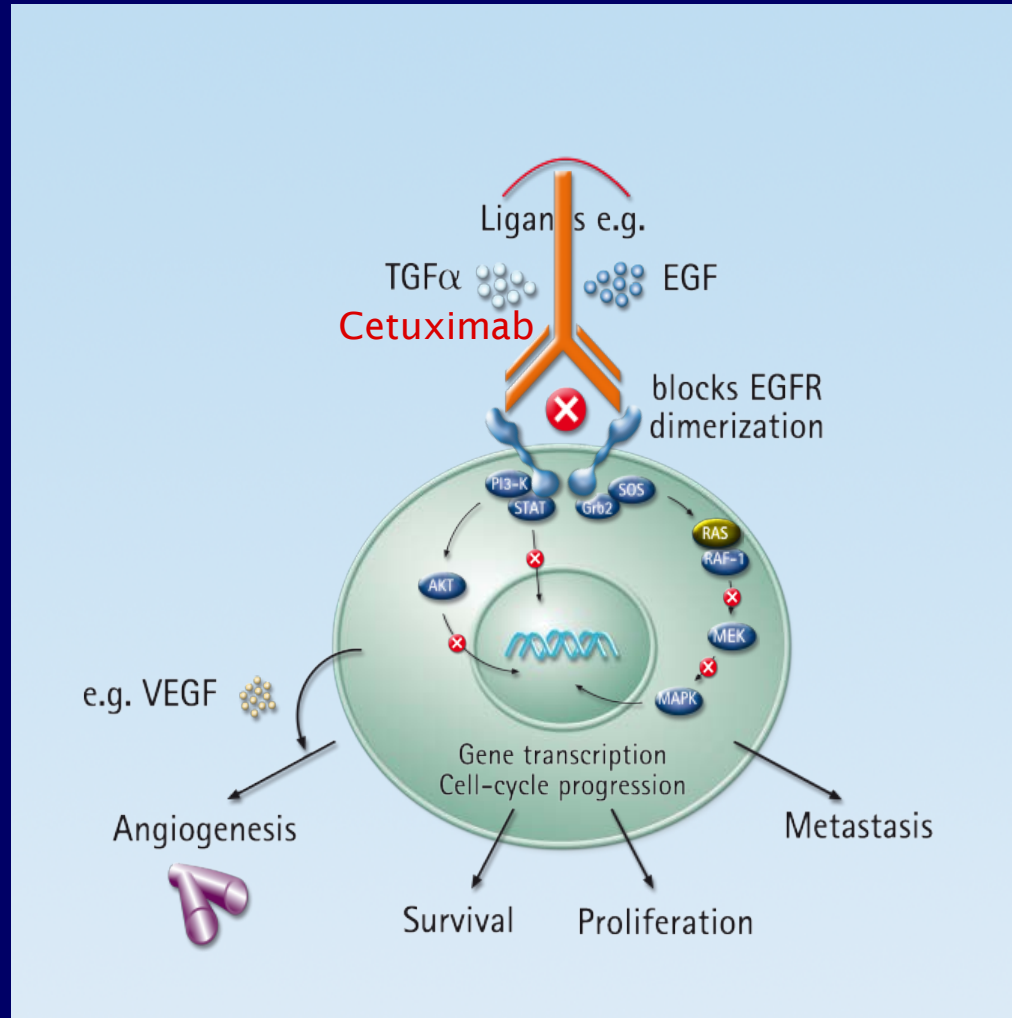


What are the different types of chemotherapy?

- Traditional chemotherapy – Drugs that act on the parts that help the cells grow
- Side effects – hair loss, bowel issues, skin changes, decrease immune system



Monoclonal Antibodies



Targeted Agents

Unaffected Growth of blood vessels and Tumors

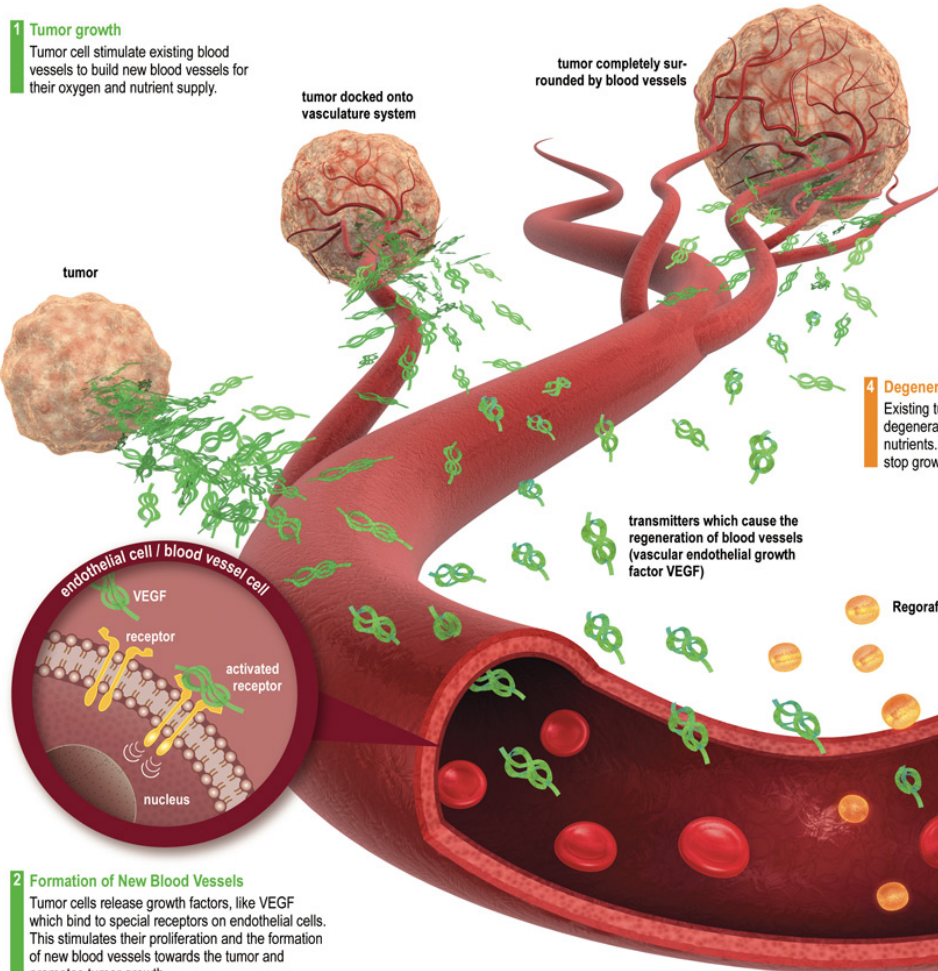
1 Tumor growth

Tumor cells stimulate existing blood vessels to build new blood vessels for their oxygen and nutrient supply.

tumor docked onto vasculature system

tumor completely surrounded by blood vessels

tumor



2 Formation of New Blood Vessels

Tumor cells release growth factors, like VEGF which bind to special receptors on endothelial cells. This stimulates their proliferation and the formation of new blood vessels towards the tumor and promotes tumor growth.

Inhibition of blood vessels formation and Tumor growth

5 Inhibition of tumor cell growth

Regorafenib inhibits other growth factor receptors which are essential for tumor cell growth. This eventually results in tumor cell death and tumor regression.

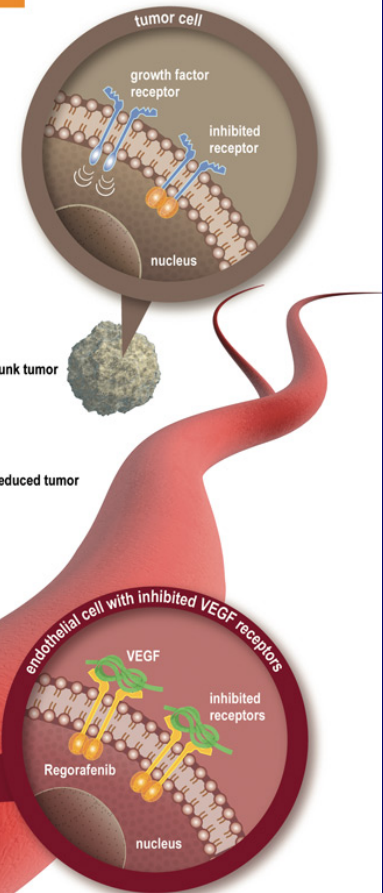
4 Degeneration of blood vessels

Existing tumor blood vessels degenerate, which leads to a lack of nutrients. As consequence tumors stop growing or even regress.

Regorafenib

shrunken tumor

reduced tumor



3 Inhibition of Vascularization

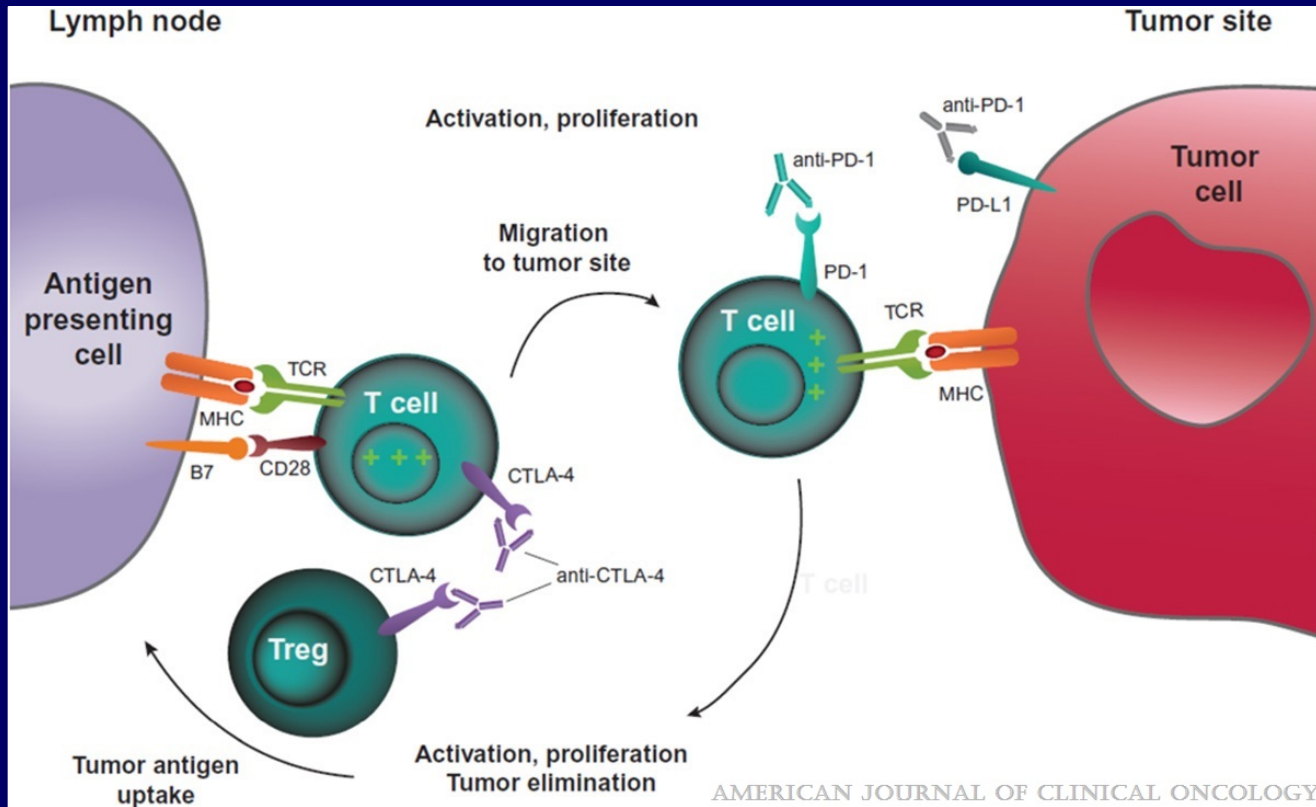
Regorafenib binds to VEGF receptors and inhibits their activity. This prevents the formation of new blood vessels by VEGF.

Side Effects

- **Vary – hair loss, mouth sores, nausea, bowel irritation, and skin changes**
- **Side effects and treatment response are not the same**
- **Can have side effects with oral or iv medications**

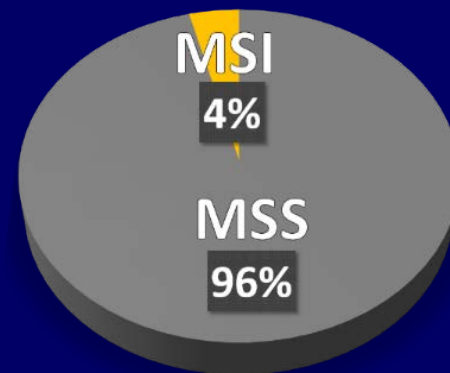
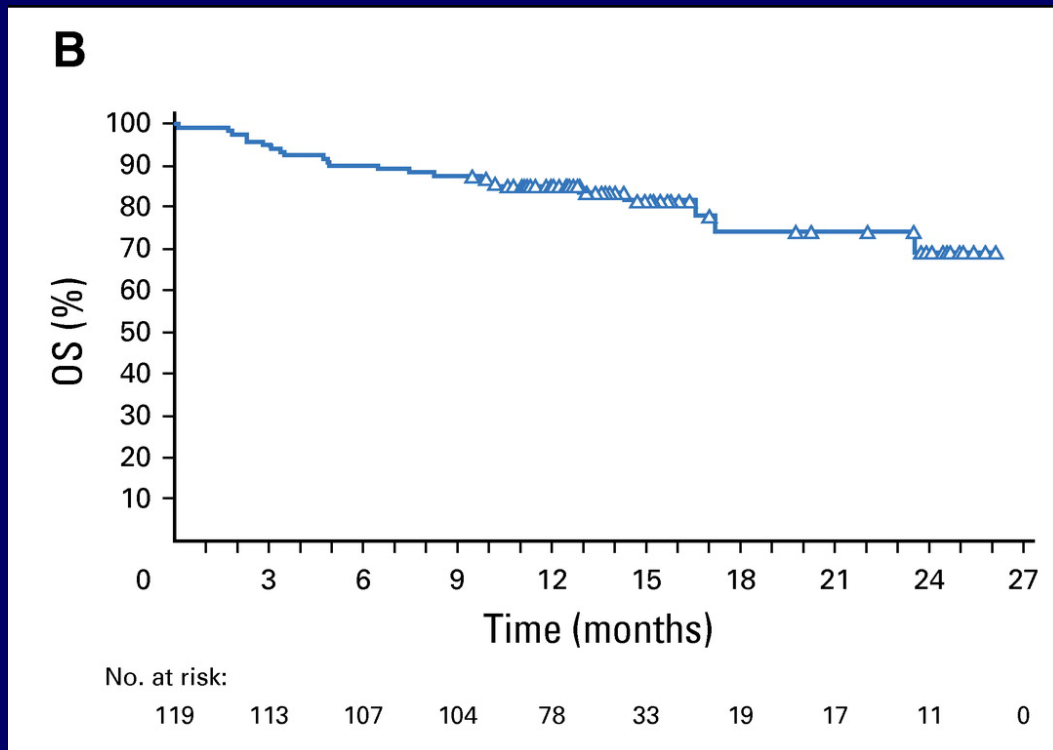
Immunotherapy

- The immune system helps eliminate abnormal cells in our body
- This is how our body fights infections but it can also attack cancers
- Many cancers develop mechanisms to “hide” from the immune system
- New medications that release the immune system to “attack” tumor cells have shown activity in select colorectal cancers



CTLA-4 and PD-1 pathway blockade. CTLA-4 blockade allows for activation and proliferation of more T-cell clones, and reduces Treg-mediated immunosuppression. PD-1 pathway blockade restores the activity of antitumor T cells that have become quiescent. A dual pathway blockade could have a synergistic effect, resulting in a larger and longer lasting antitumor immune response. CTLA-4 indicates cytotoxic T-lymphocyte-associated antigen 4; MHC, major histocompatibility complex; PD-1, programmed death 1; PD-L1, programmed death ligand 1; TCR, T-cell receptor; Treg, regulatory T cell.

Why we are excited



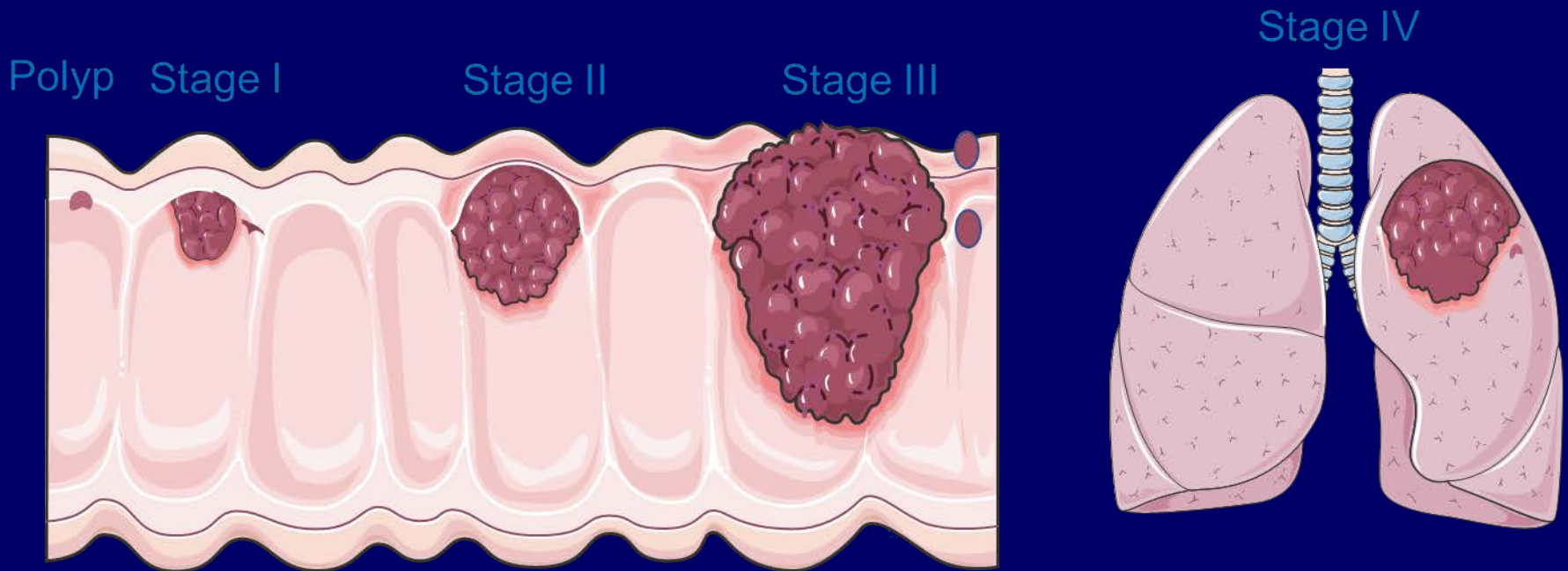
Overman et al., *JCO* (2018)

Loree et al., *JGO* (2016)

Side Effects

- **Vary – diarrhea, tiredness, rash, autoimmune conditions**
- **Side effects are not necessarily related to response to therapy**
- **Management of side effects includes stopping the medication and suppressing the immune system**

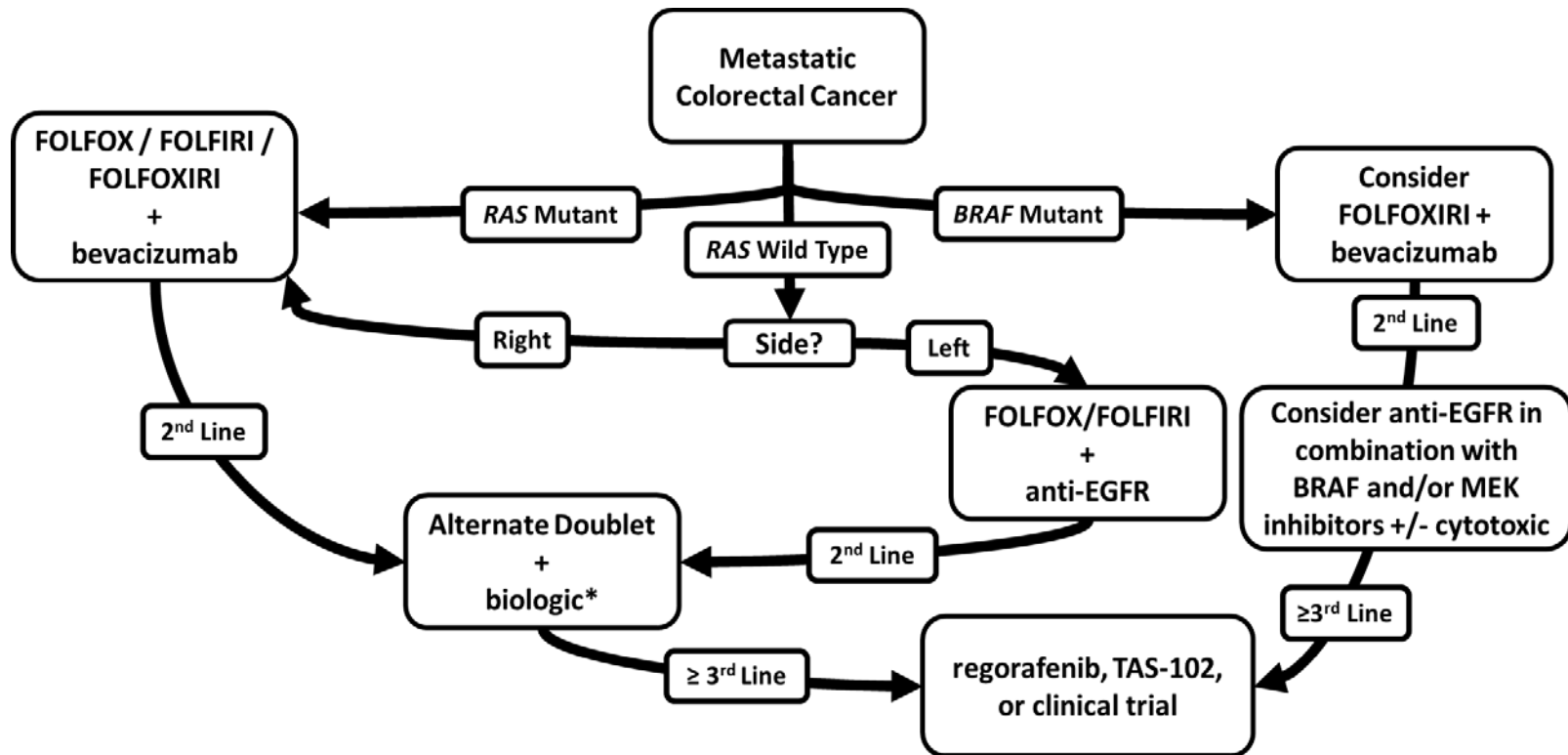
How do we decide what to use?



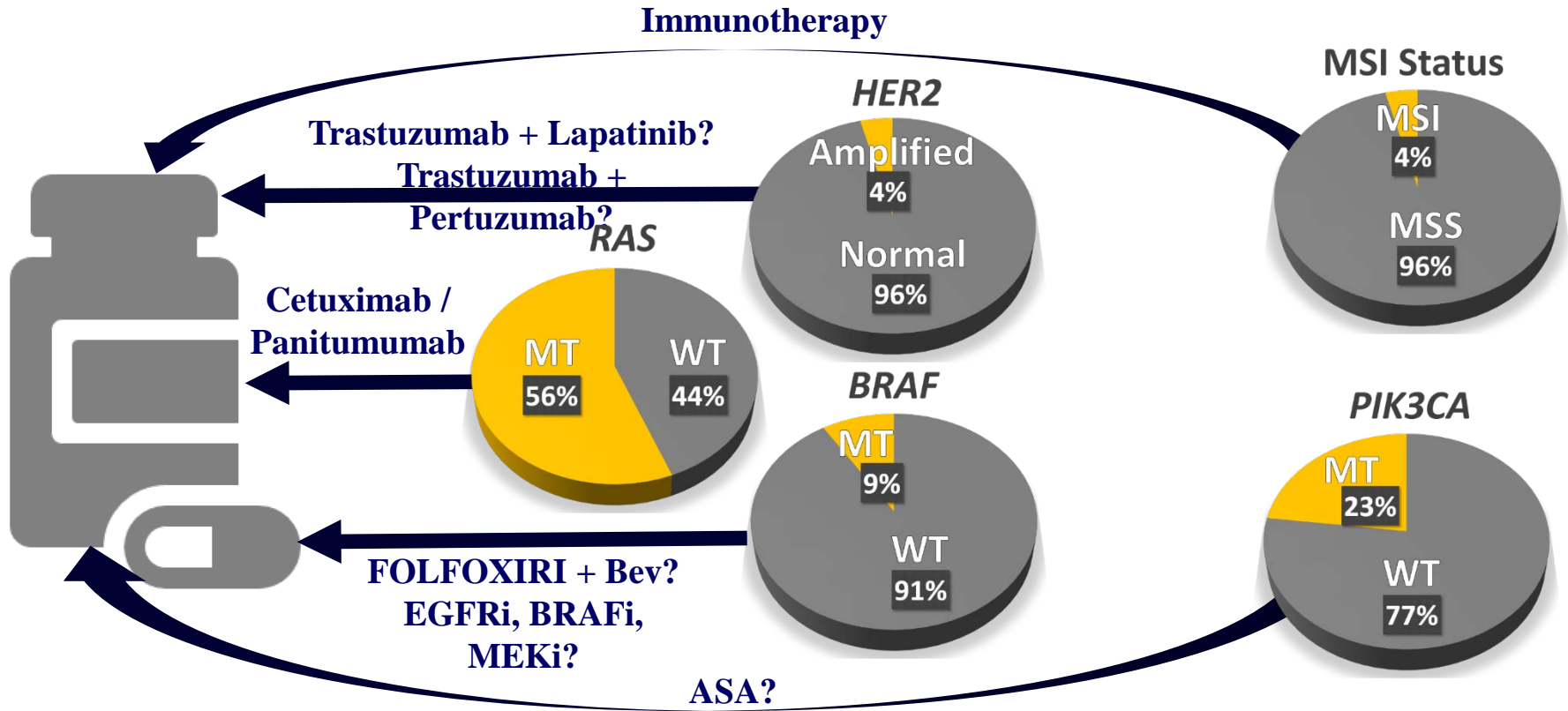
How do we decide what to use?



How do we decide what to use?



How do we decide what to use? Version 2.0



Estimated Costs of Therapy for Metastatic Colon Cancer/month

- 5FU/LV ~\$20
- 5FU/oxaliplatin ~\$2,000
- 5FU/irinotecan ~\$2,000
- plus bevacizumab +\$5,000
- plus cetuximab +\$6,000
- Regorafenib/Tas-102 ~\$6,500

Questions

