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 cell stimulates existing blood vessels to build new blood vessels for their oxygen and nutrient supply.

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.

3. **Inhibition of Vascularization**
   - Regorafenib binds to VEGF receptors and inhibits their activity.
   - This prevents the formation of new blood vessels by VEGF.

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

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.

**Inhibition of blood vessels formation and Tumor growth**

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

Polyp  Stage I  Stage II  Stage III

Stage IV

Servier Medical Art
How do we decide what to use?

Stage I
• No adjuvant chemotherapy

Stage II
• Observation
• Capecitabine/5-FU
• CAPOX/FOLFOX

Stage III
• CAPOX/FOLFOX
• Duration?
How do we decide what to use?

Loree et al., *Ther Adv Oncology* (2017)
How do we decide what to use? Version 2.0

Trastuzumab + Lapatinib?
Trastuzumab + Pertuzumab?
Cetuximab / Panitumumab
FOLFOXIRI + Bev?
EGFRi, BRAFi, MEKi?

HER2
Amplified 4%
Normal 96%

BRAF
MT 9%
WT 91%

PIK3CA
MT 23%
WT 77%

MSI Status
MSI 4%
MSS 96%

RAS
MT 56%
WT 44%

Immunotherapy

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
- Regorafinib/Tas-102 ~$6,500
Questions