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MOCA Living Well:

Clinical Trials: Current Clinical Trials at Mayo Clinic

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Objectives

- Reinforce the importance of clinical trials
- Discuss timing of clinical trials
- Brief overview of a few of the clinical trials available at Mayo Clinic Rochester
- Time for questions

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When do I think about clinical trials?

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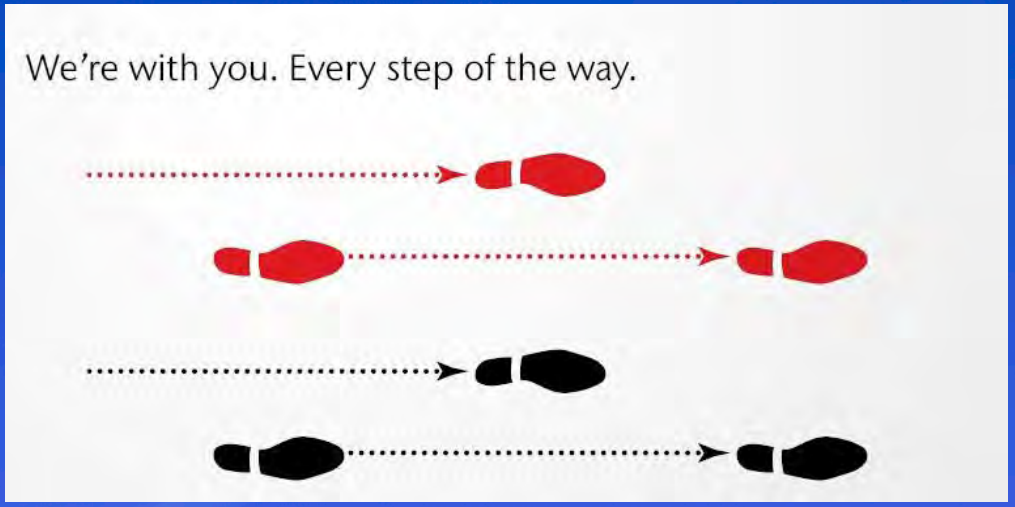
MOCA Living Well:
Timing of clinical trials

Clinical trials should be considered every step of the way!



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MOCA Living Well:
Clinical Trials at Mayo Clinic

- At time of Diagnosis
  - Addition of metformin
- Platinum Sensitive recurrence
  - Addition of a targeted therapy
- Platinum resistant recurrence
  - Using the immune system to fight the cancer
- Symptom management
  - Ureteral stent discomfort

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MOCA Living Well:
At time of diagnosis

- Can be overwhelming
  - Lots of information regarding surgery, chemotherapy, database studies, epidemiology studies and treatment studies
- It's OK to ask for a second appointment
- Ask for material to take home and review

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Clinical trial evaluating the role of metformin in ovarian cancer

- Epidemiologic studies in diabetic patients have suggested that those women with ovarian cancer on metformin did better than those who did not
- Laboratory studies have suggested that metformin may impact tumor metabolism and change the gut microenviroment

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Phase 2

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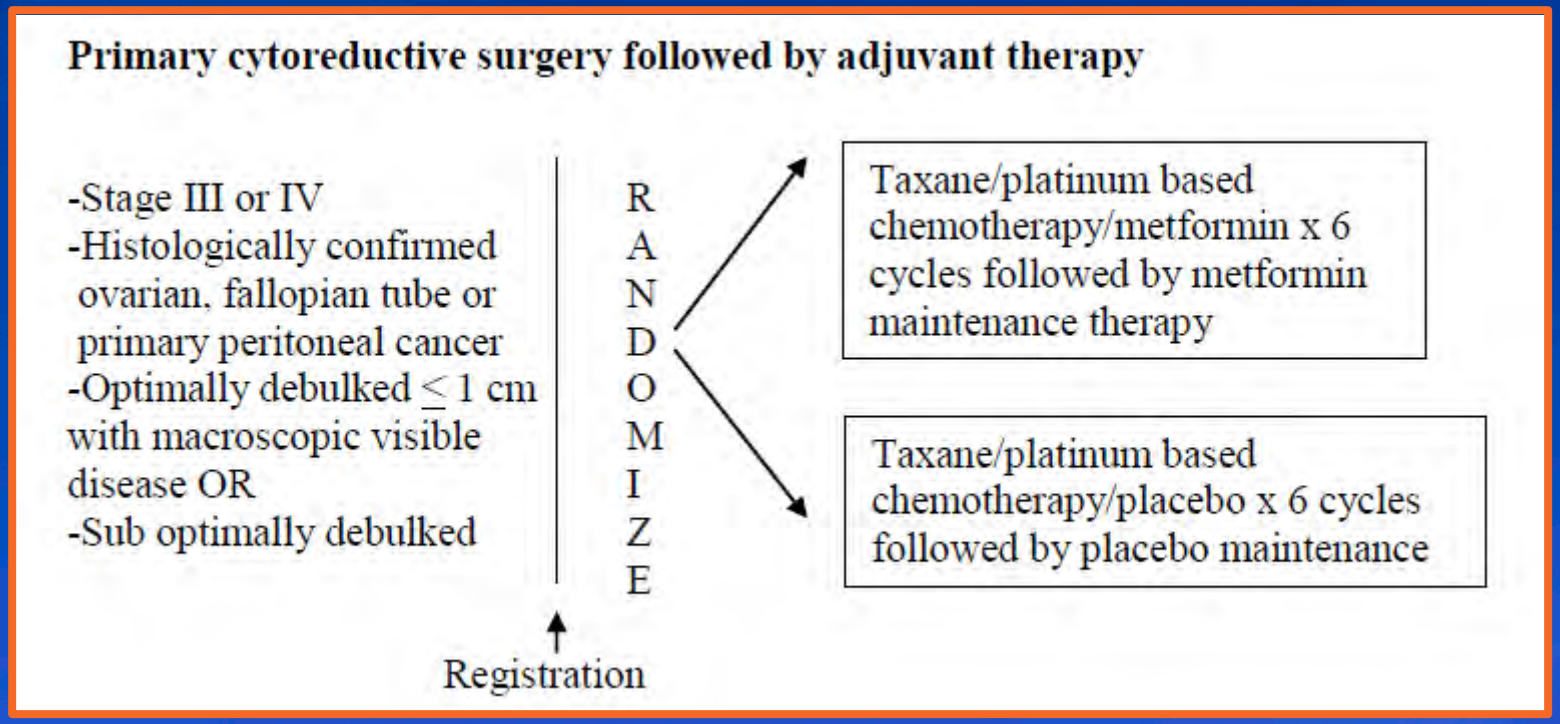
Standard treatment +/- metformin



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Platinum sensitive recurrence

Clinical Trial Options

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Platinum sensitive recurrence

- Cancer has returned MORE than 6 months after treatment with platinum
  - Carboplatin or cisplatin

- General recommendation is to retreat with carboplatin and a second drug
  - Carboplatin and paclitaxel
  - Carboplatin and gemcitabine
  - Carboplatin and Doxil

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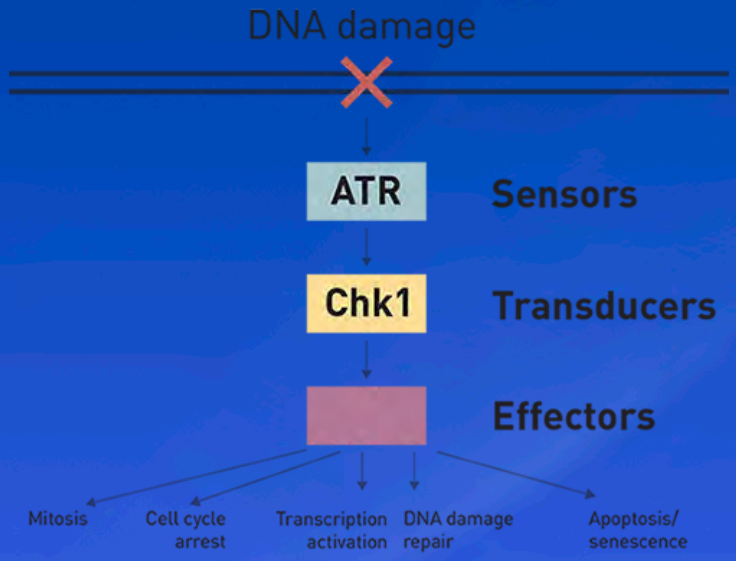
Clinical trial evaluating MM6620

- ATR inhibitor
  - Makes cancer cells more susceptible to DNA damaging drugs
  - Cancer cells are less able to repair the damage caused by some chemotherapy drugs
  - Chemotherapy drugs that work by damaging cancer cell DNA
    - Carboplatin
    - Cisplatin
    - Gemcitabine
    - PARPi



DNA Damage Checkpoint Signaling

Figure 1. Sensing DNA damage or replication stress, ATR responds by phosphorylating downstream transducers such as Chk1 (checkpoint kinase 1). Activated Chk1 leads to several downstream effects, including cell cycle arrest, transcription repression or activation, DNA damage repair, and apoptosis or senescence (cell death).

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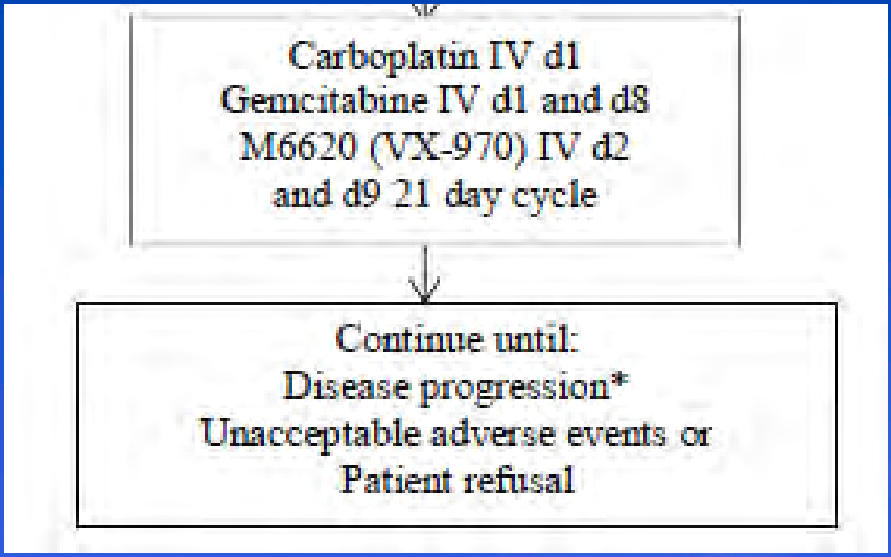
Phase I clinical trial with M6620

- Women with first or second recurrence of platinum sensitive ovarian cancer
- High grade serous or endometrioid histology

- All women will receive all three agents



Phase 1

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Platinum resistant recurrence

Clinical trial options

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Phase I trial with M6620

- Adds appointments
  - M6620 given 24 hours after chemotherapy

- Biopsies are required
  - Want to look in tumor tissue to see if the addition causes problems with DNA repair
  - Can we predict in the future who will respond?

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Phase I trial with M6620

- Adds appointments
  - M6620 given 24 hours after chemotherapy

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Platinum resistant recurrence

- Disease that comes back within 6 months from completion of last chemotherapy with a platinum

- Many treatment options available, including clinical trials
  - There is no one right answer!

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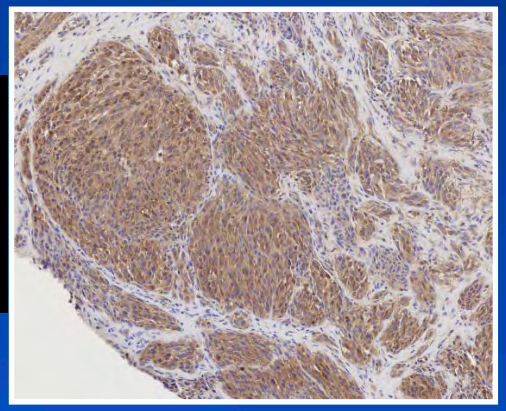
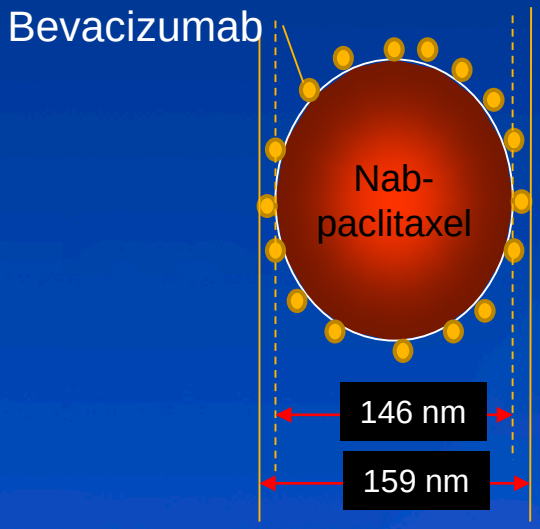
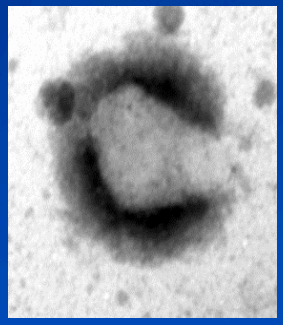
Abraxane/Bevacizumab Complex

VEGF IHC







- Multiple tumor types are rich in VEGF, including ovarian cancer
- Defined addition of bevacizumab, an anti-VEGF antibody to nab-paclitaxel can form a stable,160 nm particle
- Paclitaxel cytotoxicity and bevacizumab VEGF affinity/specificity remain intact in AB160

Abraxane/Bevacizumab Complex

- Platinum resistant, any number of prior lines of treatment
  - Weekly treatment

- Exclusion
  - Significant peripheral neuropathy
  - Treatment with paclitaxel within 30 days
  - Treatment with bevacizumab within 60 days

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Phase 1

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What about immunotherapy?

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Pembrolizumab in a subtype of ovarian cancer

- Different molecular subtypes of high grade serous ovarian cancer
  - Can be assessed by testing the tumor tissue
    - NanoString technology
      - Looks at the expression pattern of certain genes

- Hypothesis:
  - Immunoreactive subgroup will respond well to immunotherapy (Pembrolizumab)

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Pembrolizumab in immunoreactive ovarian cancer

- Screening portion:
  - Tumor sample needed to test
  - Initially platinum sensitive

- Avoid if:
  - Autoimmune disease
  - Prior immunotherapy

- Pembrolizumab given every three weeks

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Viral Therapy (measles virus)

- Natural measles infection can result in an antitumor effect
  - Strain used in the trials has been shown to slow tumor growth in mice
  - Ovarian cancer cells have overexpression of a measles virus receptor

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Measles virus versus Chemotherapy

- Randomized clinical trial
  - Comparing the FDA approved IV chemotherapy to monthly viral therapy

- Eligibility
  - Disease confined to the abdomen
  - Intraperitoneal administration

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Phase 2

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Measles virus

- Can we enhance the ability of the virus to evade the immune system by using cells infected with the virus?

- Cells collected from fat cells
  - Fat biopsies
  - Done after consent and when the port is placed

- All women enrolling receive the viral therapy

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Phase 2

Other options

- Larger multi-center clinical trials
  - Two for low grade serous ovarian cancer opening soon
  - Immunotherapy combination study in platinum resistant ovarian cancer
- Experimental Therapeutics Clinic
  - Phase 1 clinical trials
  - Not tumor specific

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Questions?

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Thank you!

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