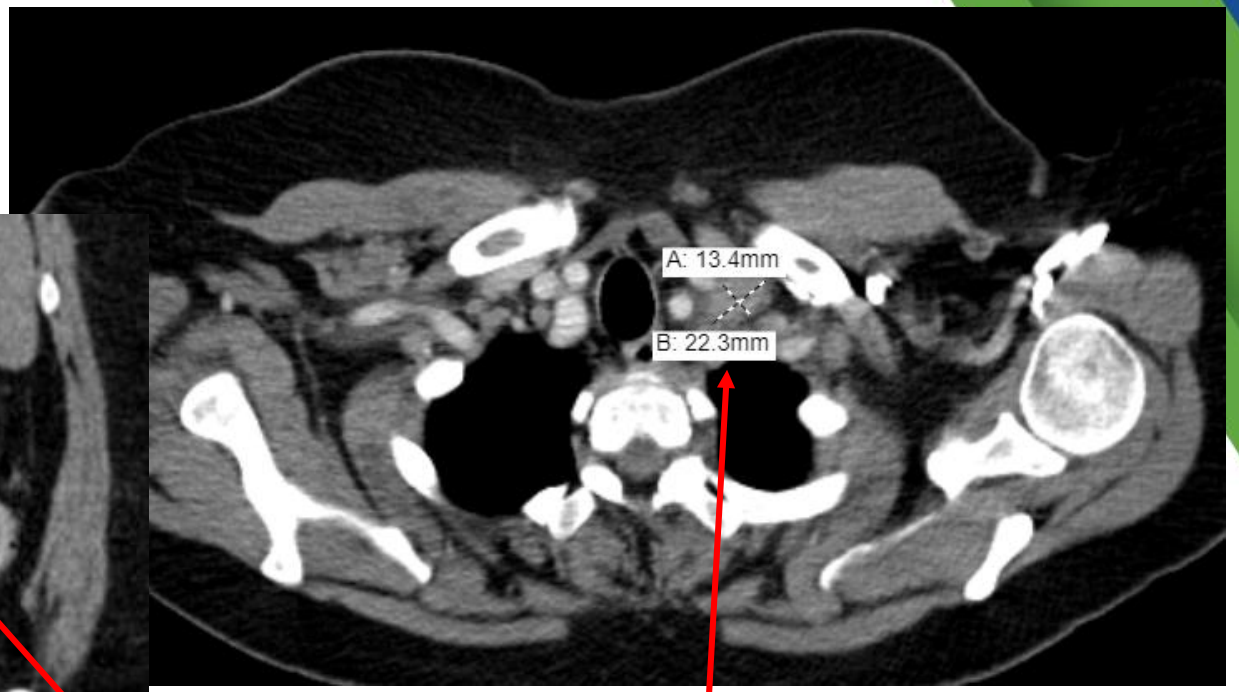
Case 1: Stage IV endometrial cancer Initial presentation

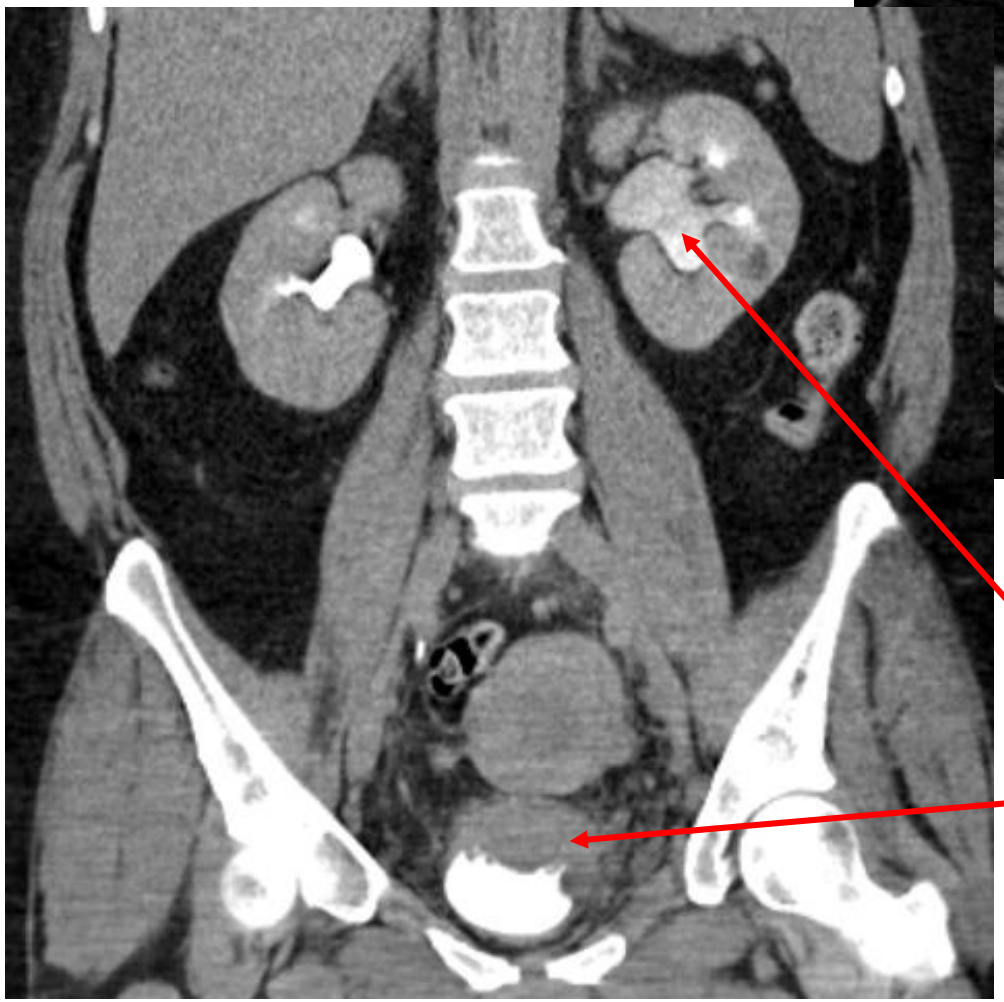
- 49 yo G2P2 referred from urology after TURBT procedure with pathology results demonstrating Mullerian tumor
- Presenting symptom was hematuria for 6 months, initially attributed to suspected kidney stones.
- Associated 20 lb weight loss, some suprapubic pain, leg swelling, constipation, early satiety, poor appetite, heavy menses
- Medical history: HTN on HCTZ, DM not requiring medication
- Surgical history: cholecystectomy, cesarean section, TURBT
- Family history: mother with uterine cancer, age 50; aunt unknown cancer
- 30 pack-year history of smoking, quit at diagnosis

Case 1: Stage IV endometrial cancer Imaging

- When symptoms worsened and she had difficulty voiding, a CT was done:
  - Large bladder mass with concern for vaginal involvement
  - Hydronephrosis
  - Retroperitoneal lymphadenopathy – iliac, periaortic
  - Hypoattenuation of the endometrium noted
- CT chest:
  - Supraclavicular and mediastinal lymphadenopathy
  - Multiple small pulmonary nodules

CT at presentation





Enlarged supraclavicular lymph node

Hydronephrosis

Tumor in the bladder

Case 1: Stage IV endometrial cancer Resection and pathology results

- Referred to urology, underwent TURBT with resection of 80% of tumor mass within the bladder.
- Noted to have a large sessile 5cm tumor encompassing the floor of the bladder; additional 3cm tumor in the left lateral wall of the bladder
- Pathology: carcinoma, likely extension from a Mullerian tumor
  - Glandular endometrioid adenocarcinoma component
  - Additional high grade, solid component
  - Other areas with papillary architecture
  - Positive staining: CK7, ER, PAX-8
  - Negative staining: WT1, CK20, GATA3, Napsin
  - P53wt
- High grade endometrial carcinoma with a serous component
- MSI-H: positive for a high degree of MSI
- Negative for MLH1 promoter methylation

Case 1: Stage IV endometrial cancer
Exam and initial treatment plan

- Exam upon presentation to gyn oncology clinic:
  - Percutaneous nephrostomy tube
  - No tumor visible in the vagina on speculum exam
  - Uterus was fixed with an enlarged lower uterine segment and parametrial involvement
  - No rectal invasion palpable
- Labs: Hgb 7.7, Cr 0.74
- Assessment: Stage IV high grade endometrial cancer
- Genetic testing: Lynch syndrome confirmed, MSH6 pos
- Plan: systemic chemotherapy with carboplatin/paclitaxel

Case 1: Stage IV endometrial cancer
Assessment of response to chemotherapy

- CT after cycle 3:
  - Marked reduction in tumor burden
    - Bladder wall tumor 1.4cm, previously 4.7cm
    - Uterine mass 1.5 cm, previously 7.3cm
  - Resolution of hydronephrosis
  - One paraaortic LN increased in size
- Plan to continue chemotherapy and optimize fitness for possible surgery
- PCN removed

Case 1: Stage IV endometrial cancer
Assessment of response to chemotherapy

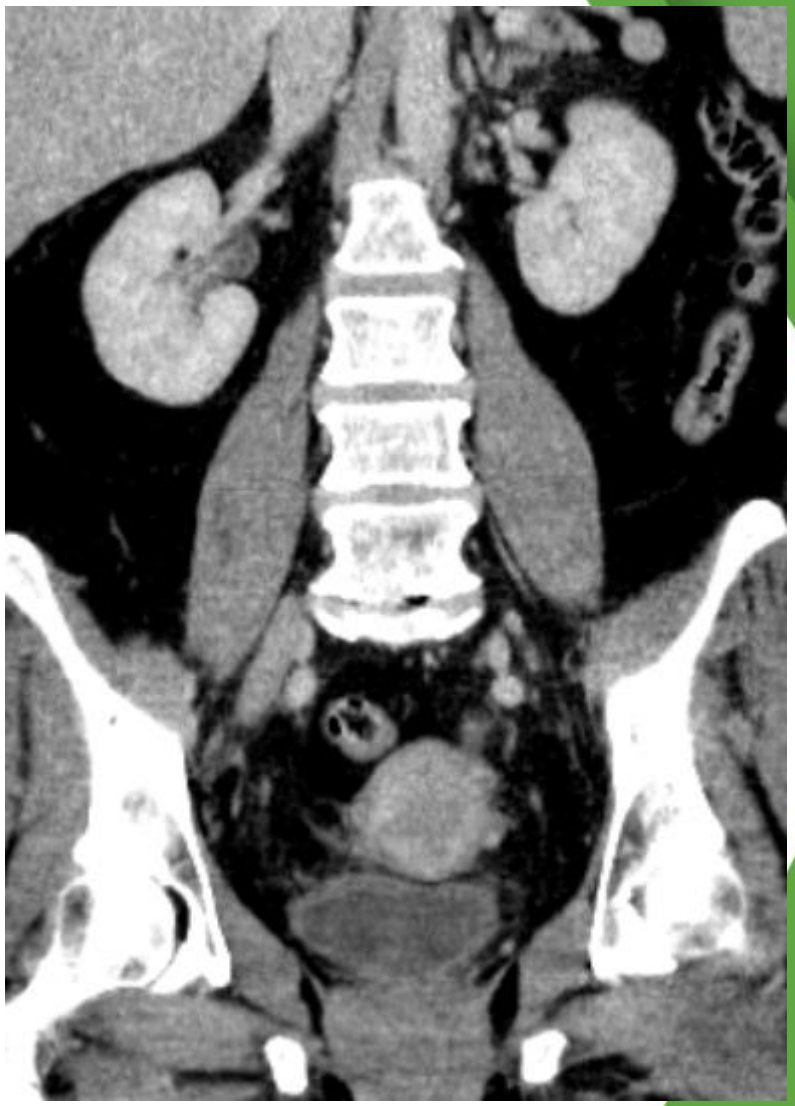
- CT after cycle 6:
  - Worsening pelvic disease
    - Enlarging adnexal mass
    - Enlarging pelvic adenopathy
    - New left vaginal wall lesion
- Progression during platinum-based chemotherapy
- Clinical trials offered but declined
- Initiated pembrolizumab based on MSI-H status

Case 1: Stage IV endometrial cancer
Palliative radiation

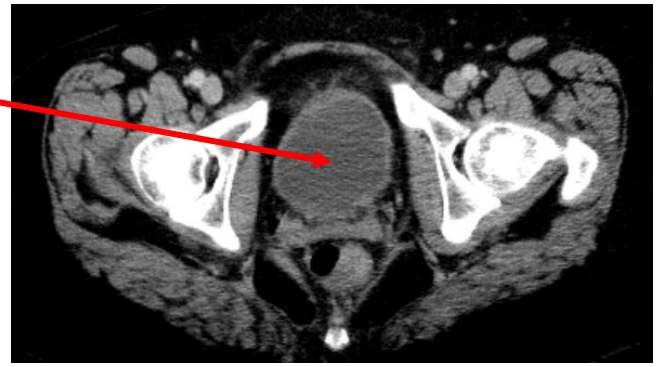
- Reported heavy vaginal bleeding when she presented for cycle 2 of pembrolizumab
- Hgb 5
- Received 4u PRBC total
- Referred to radiation oncology for palliative RT
- Resolution of vaginal bleeding after 30 Gy/10 fractions

Assessment of response

- CT after cycle 3 of pembrolizumab
  - Decrease in size of retroperitoneal lymph nodes (none >1.5cm)
  - Marked decrease in pelvic disease
    - Reduction in the size of bilateral adnexal masses
    - Decrease in vaginal mass
    - No bladder mass visible
  - No new sites of disease



Bladder



Case 1: Stage IV endometrial cancer *Response to immunotherapy*

- Continued pembrolizumab treatment with evidence of ongoing treatment effect
  - Cycle 6: 4cm L ovary but no other sites of measurable disease
  - Cycle 18: 1.8 cm subtly enhancing lesion on the medial limb of the right adrenal gland
    - Random cortisol normal
  - Cycle 33: increase in size of the right adrenal gland lesion to 4.9 cm, referred to radiation oncology
    - Received 40 Gy to the R adrenal gland
  - Cycle 47: Right adrenal gland with 1.9 cm lesion; no other measurable lesions

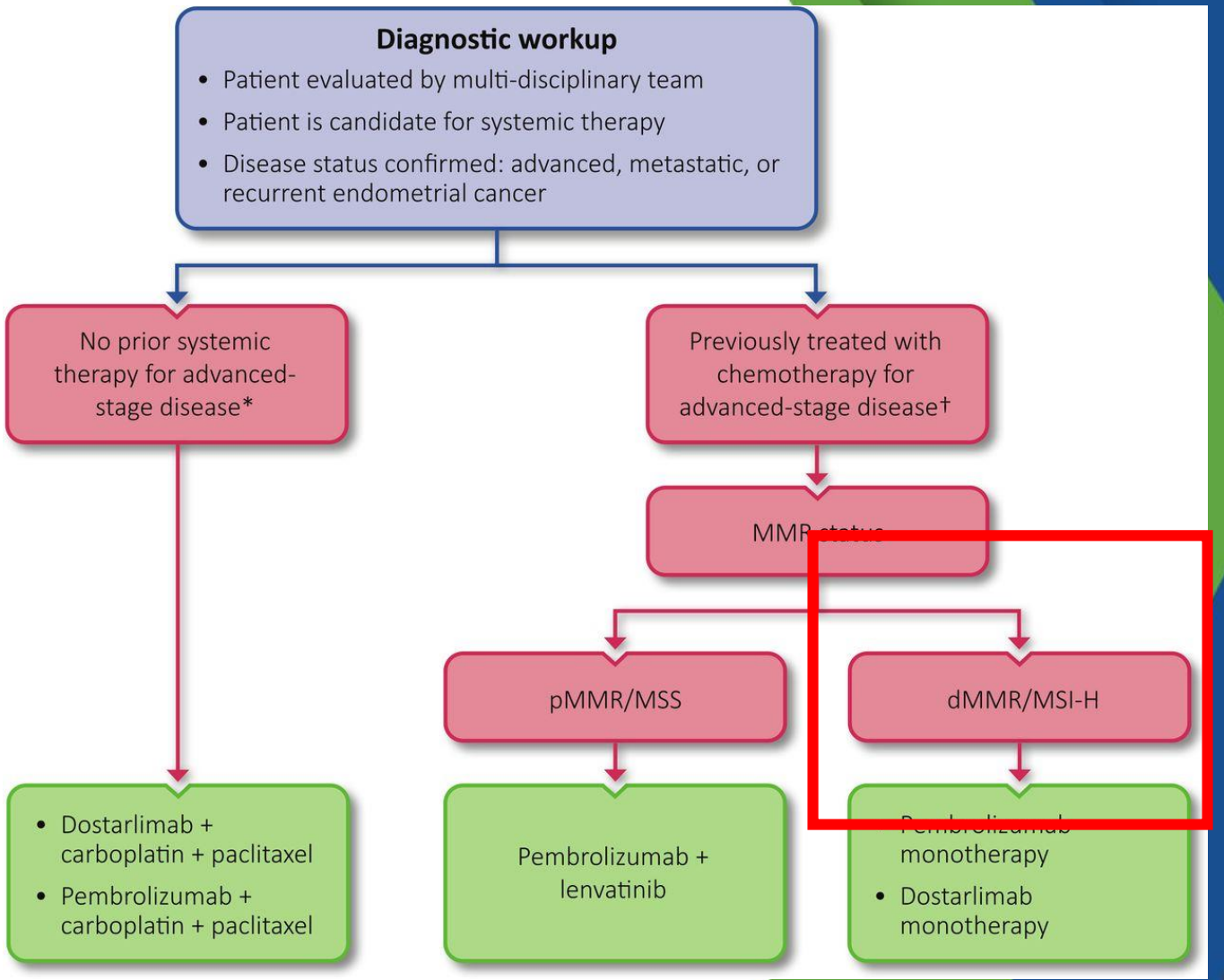
Case 1: Stage IV endometrial cancer
Immune related toxicity during treatment

- Tolerated treatment well
  - Cycle 15: Grade 1 rash, treated with triamcinolone after Dermatology consultation
  - Cycle 17: Grade 2 fatigue, TSH 77; T3 37 – started replacement therapy

    Grade 2 dyspnea requiring home O2, referred to pulmonology, workup for pneumonitis negative, albuterol inhaler started, sleep study recommended
  - Transitioned to q6 week treatment
  - Cycle 31: held for increased O2 requirement; PFTs with mild restrictive disease attributed to hypoventilation, OSA, sleep study recommended
  - Cycle 33: held for Grade 2 colitis, steroid taper initiated; treatment resumed after completion of steroid course

Case 1: Stage IV endometrial cancer
Current status

- Now 5 yrs out from initial diagnosis with NED on scan
  - Historically, 5yr OS for stage IV endometrial cancer of 20%
  - This patient's tumor was platinum refractory with progression during frontline treatment
- Resolution of immune toxicities



Case 1: Stage IV endometrial cancer
Possible discussion points

- Efficacy of immunotherapy after progression on frontline platinum based chemotherapy
- Role of surgery
- Possible impact of radiation
- Emergence of irAEs
- Duration of treatment

Case 2: Recurrent ovarian cancer – Phase I/II immunotherapy clinical trial

- 54 yr old with a germline BRCA1m and a personal history of breast cancer enrolled in an immunotherapy trial for treatment of recurrent high grade serous ovarian cancer.
- Oncology history:
  - Breast cancer treated with chemotherapy, surgery, radiation
  - Ovarian cancer treated with debulking surgery and adjuvant chemotherapy
  - Tamoxifen
  - Doxil
  - Clinical trial with a PARP inhibitor and CTLA4 immune checkpoint antibody

Case 2: Recurrent ovarian cancer Immunotherapy trial – *tumor burden*

- CT at enrollment
  - Enlarged aortocaval nodes, pelvic adenopathy, largest 3.4x2.1cm

- CA125 17

Case 2: Recurrent ovarian cancer Immunotherapy trial – *treatment response*

- CT after cycle 3:
  - Aortocaval lymph node 1.8 x 1.3 cm → 0.9 x 0.4 cm
  - Left external iliac lymph node 1.5 x 1.5 → 0.7 x 0.7 cm
  - Right common iliac lymph node 2.1 x 2.0 cm → 1.7 x 0.9 cm
  - Right external iliac lymph node 3.4 x 2.1cm → 2.0 x 1.0cm

- CT after cycle 6
  - Aortocaval lymph node 0.9 x 0.4 cm, unchanged
  - Left external iliac lymph node 0.7 x 0.7 cm, unchanged
  - Right common iliac lymph node 1.7 x 0.9 cm →1.5 x 0.8 cm
  - Right external iliac lymph node 2.0 x 1.0cm → 1.7 x 0.8 cm

Case 2: Recurrent ovarian cancer Immunotherapy trial – *treatment response*

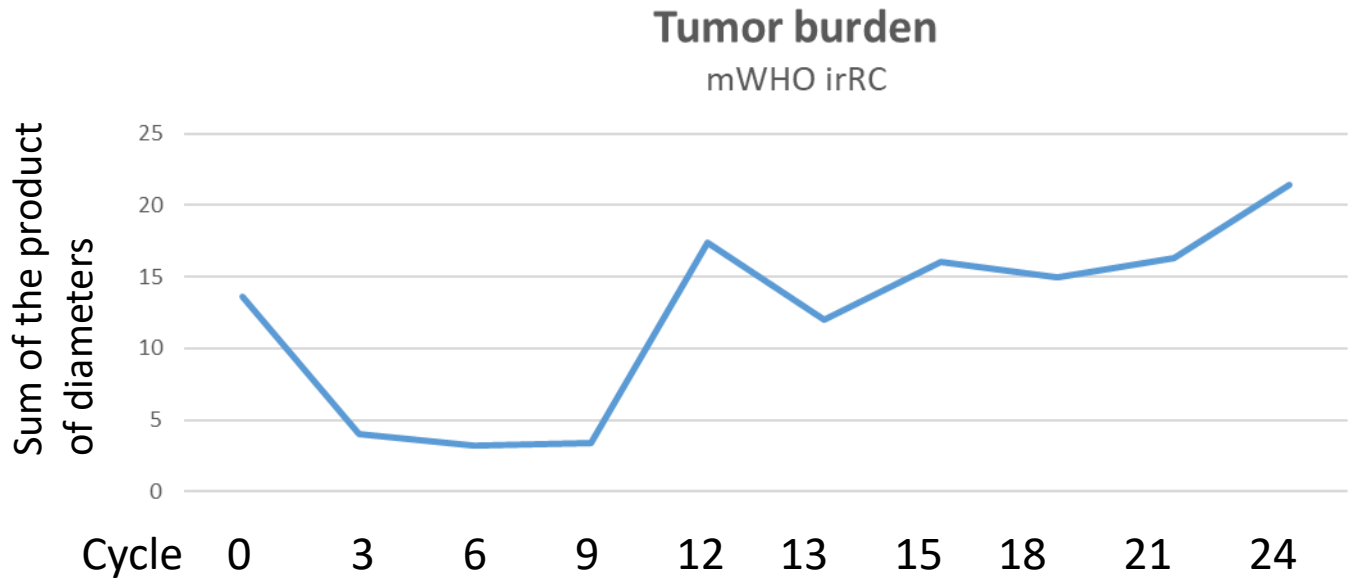
- CT after cycle 9
  - Aortocaval lymph node 0.9 x 0.4 cm unchanged
  - Left external iliac lymph node 0.7 x 0.7 cm unchanged
  - Right common iliac lymph node 1.5 x 0.8 cm → 1.4 x 0.8 cm
  - Right external iliac lymph node 1.7 x 0.8 cm → 1.8 x 0.9 cm

- CT after cycle 12 → 13
  - Aortocaval lymph node 0.9 x 0.4 cm → 1.8 x 1.8 cm → unchanged
  - Left external iliac lymph node 0.7 x 0.7 cm, unchanged → 1.0 x 0.9 cm
  - Right common iliac lymph node 1.4 x 0.8 cm, unchanged → 1.4 x 0.9 cm
  - Right external iliac lymph node 1.8 x 0.9 cm→ 2.2 x 1.2 → 1.4 x 2.0 cm
  - New vaginal cuff nodularity → stable

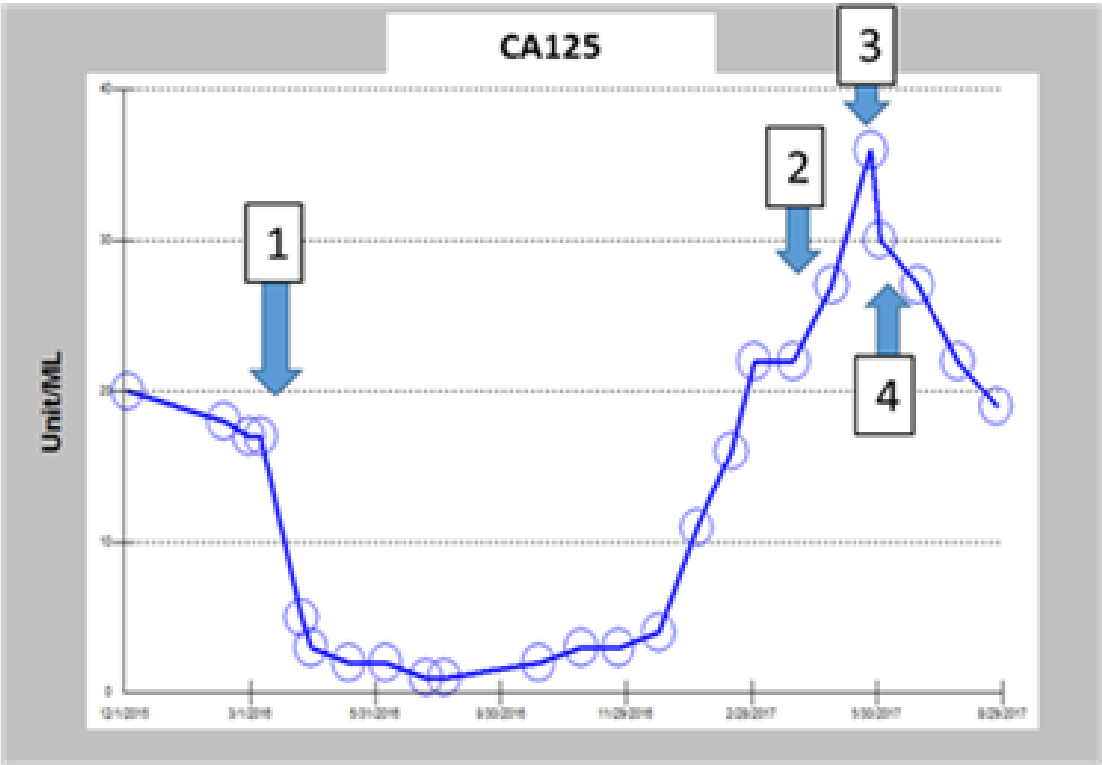
Case 2: Recurrent ovarian cancer Immunotherapy trial – *tumor burden*

CT after cycle 15

- Aortocaval conglomerate 2.6 x 2.5 → 3.3 x 2.6 cm
- Left external iliac lymph node 1.0 x 0.9 cm → 1.2 x 1.1 cm
- Right common iliac lymph node 1.4 x 0.9 cm → 0.9 x 0.6 cm
- Right external iliac lymph node 2.0 x 1.4 → 2.1 x 1.6 cm
- Vaginal cuff nodularity improved



Case 2: Recurrent ovarian cancer Phase I/II clinical trial – *tumor marker*



1. Study enrollment, initiation of olaparib/tremelimumab
2. New adenopathy, increase in target lesion size, cycle 12
3. Stable disease on repeat CT after 4 weeks
4. Decrease in size of new adenopathy, stable target lesions

Case 2: Recurrent ovarian cancer Immunotherapy trial – *toxicities*

- Cycle 2 - Gr 1 nausea
- Cycle 3 - Gr 1 rash → topical Benadryl
- Cycle 4 – Gr2 nausea, diarrhea → treatment held, stool cultures collected, IVF administered, steroids prescribed
- Cycle 6 – syncopal episode, evaluated in the ER; Gr 2 fatigue, treatment held for one week
- Cycle 9 – Gr1 diarrhea
- Cycle 12 – Gr2 diarrhea → treatment held, steroids prescribed
- Cycle 14 – Gr 1 rash

Case 2: Recurrent ovarian cancer Immunotherapy trial – *end of treatment*

- Waxing and waning adenopathy followed by progression
- Intermittent immune related toxicity, primarily colitis
- Completed 24 cycles of treatment

Case 2: Recurrent ovarian cancer Immunotherapy trial – *discussion points*

- Available immunotherapy trials for ovarian cancer
- Toxicities experienced by patients with ovarian cancer
- Continued treatment with overall clinical stability despite radiologic evidence of progression
- Role of tumor markers