NRG ONCOLOGY

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Gynecologic Cancer Basics

Laura Sorci
Rachel Lacy

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Poll 1

Do you restage gynecologic cancers?
Yes or No

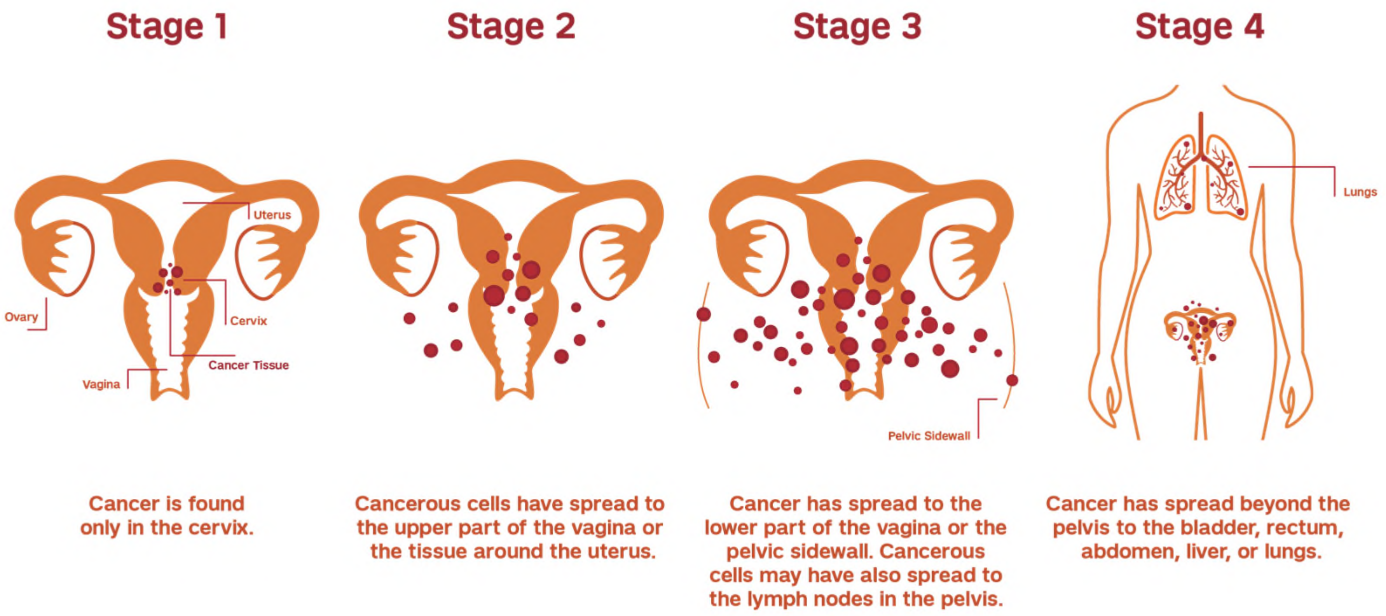
Staging

Staging uses a combination of histology, disease distribution, clinical presentation, and imaging.

We do not restage in GYN Cancers.

(which is a big difference from other solid tumors)

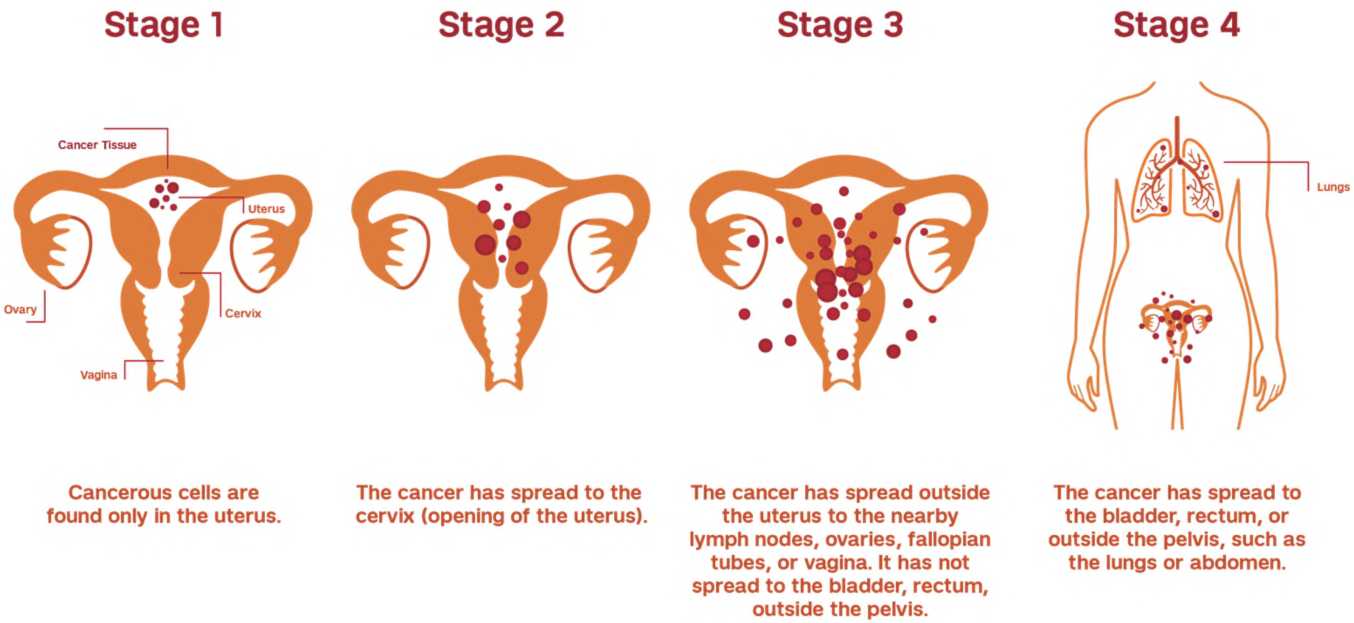
Cervical Staging



Full Cervical Cancer Staging

https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/staged.html

Endometrial Staging

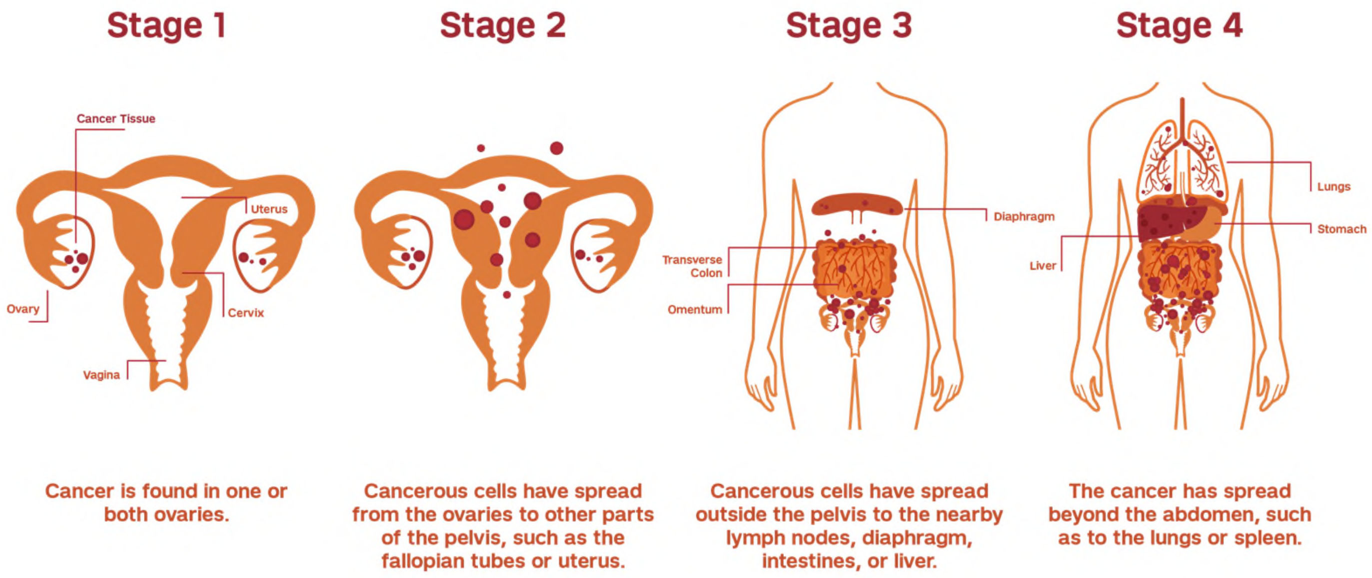


Full Endometrial Cancer Staging:

https://www.cancer.org/cancer/types/endometrial-cancer/detection-diagnosis-staging/staging.html

https://weillcornell.org/services/obstetrics-and-gynecology/gynecologic-oncology/conditions-we-treat/endometrial-and-uterine-cancer

Ovarian Staging



Full Ovarian Cancer Staging:

https://www.cancer.org/cancer/types/ovarian-cancer/detection-diagnosis-staging/staging.html

https://weillcornell.org/services/obstetrics-and-gynecology/gynecologic-oncology/conditions-we-treat/ovarian-cancer

Poll 2

Stage versus grade in gynecologic cancers-are they the same?

Yes or No

Histology

- Serous
  - Most common for ovary, less common for endometrial
  - Can be High Grade (fast cell turn over) or Low Grade (slower cell turn over)
- Endometroid
  - Most common histology for endometrial, rarer for ovary
- Clear Cell
  - Rarer histology
  - Can be found in ovary and endometrial, sometimes in cervix
- Sarcoma
  - Aggressive cell type
- Squamous
  - Most common in cervix in Gyn world

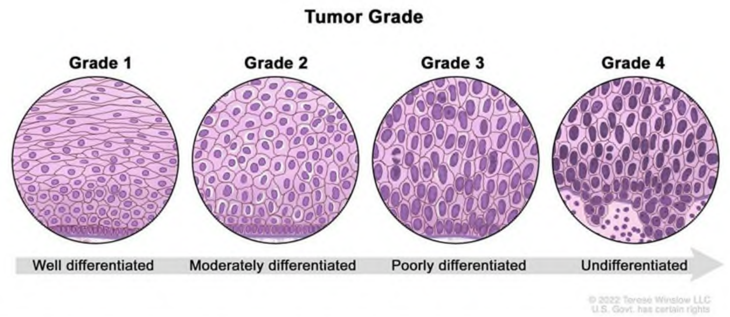
Poll 3

Endometroid versus endometrial cancer-are they the same?

Yes or No

Tumor Grading

- Grade, histology and stage and interconnected but not the same
- Grade is how the cells look under the microscope
  - the higher the grade the more abnormal the cells are
- For ovarian cancer, the grade is typically high v low rather than the numbers
- For endometrial cancer, the grades are typically sequential

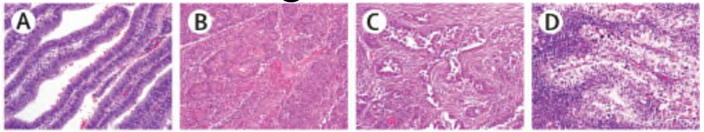


Tumor grade describes how normal or abnormal cancer cells look under a microscope. The higher the grade, the more abnormal the cells look and the faster it is likely to grow and spread.
Credit: © Terese Winslow

https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-grade

Clinicopathological and molecular characteristics of the common types of epithelial endometrial carcinoma

- Using endometrial cancer as an example, you can see the difference visually in the histologies and the grades.



Histological type	Endometrioid	Endometrioid	Serous	Clear cell
Histological grade	Low	High	High	High
Metastasis	Uncommon	Lymph nodes Distant organs	Lymph nodes Peritoneal Distant organs	Lymph nodes Peritoneal –/+
Prognosis	Favourable	Poor	Poor*	Poor*†
Molecular markers[18–21]				
ER/PR expression	+	+/–	–/+	–
PTEN expression	–/+	–/+	+	+
DNA MMR loss	–/+	–/+	–	–/+
Aberrant P53	–	–/+	+	–/+
Ki-67/MIB-1	Low	High	High	Low or high

Classification of endometrial carcinoma: more than two types. Murali, Rajmohan et al. The Lancet Oncology, Volume 15, Issue 7, e268 - e278

Common Ancillary Testing

- CA-125 (Cancer Antigen 125)
- BRCA and HRD (homologous recombination deficiency)
- MMR/MSI (mismatch-repair/microsatellite instability)
- HER2 (human epidermal growth factor receptor 2)

CA-125
(Cancer Antigen 125)

- Blood test that measures the amount of a protein that is found to be elevated in more than 80% of advanced ovarian cancers and 50% of early-stage cancers.
- Tested in those with signs/symptoms of ovarian malignancy– but can also be elevated in non-ovarian malignancies, (including GI tract, endometrial, and breast cancers) or other non-cancerous conditions.
- After cancer diagnosis, a CA-125 test is repeated during and after treatment to monitor chemotherapy response, or to confirm disease recurrence.

BRCA and HRD (homologous recombination deficiency)

- Recommended blood and tumor testing for all patients with a new diagnosis of high-grade (advanced) ovarian cancer.
- BRCA1 and BRCA2 are genes that help cells repair DNA damage. HRD occurs when the cell's ability to repair DNA damage is disrupted.
- Tumors which are positive for BRCA 1/2 or HRD gene mutations are sensitive to treatment with PARP inhibitors which work by preventing cancer cells from repairing and dividing. They are used as maintenance therapy after response to platinum-based first-line chemotherapy has been shown to extend progression-free survival and overall survival, especially in this population of patients.
    - E.g. GY036

HER2
(human epidermal growth factor receptor 2)

- HER2 testing in gyn cancer is most commonly done on advanced or recurrent serous endometrial cancer tumor tissue.
- HER2 is a protein found in cells, and when higher than normal levels of HER2 are found it causes cancer cells to grow more quickly.
- HER2+ patients have a poorer prognosis with standard therapy than HER2 negative patients. Therefore, HER2+ patients could benefit from the addition of an anti-HER2 targeted therapy (e.g., trastuzumab) which could extend progression-free and overall survival.
    - E.g. GY026

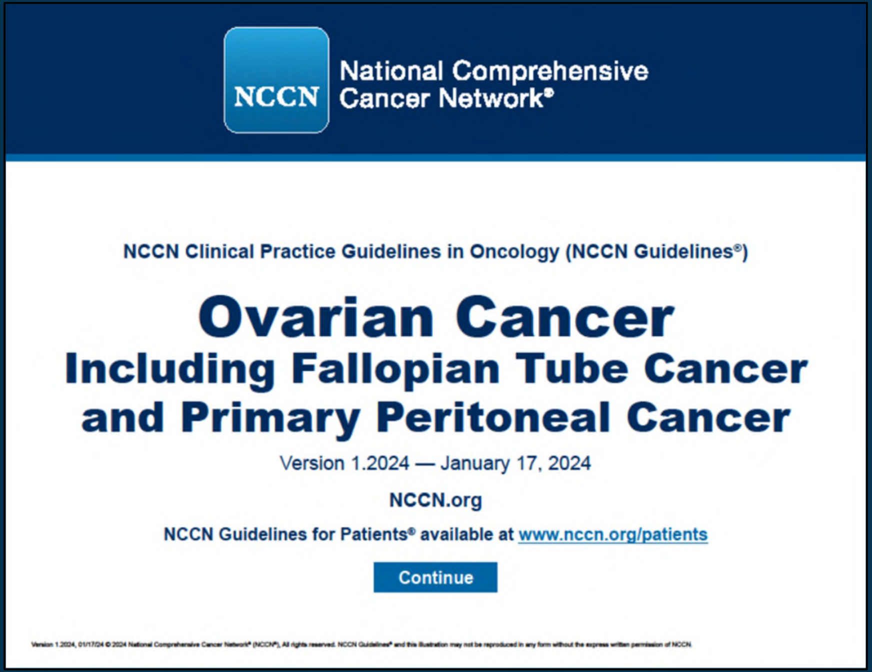
MMR/MSI
(mismatch-repair/microsatellite instability)

- MMR and/or MSI tumor testing is used to guide therapy options and is recommended for patients with endometrial cancer.
- Deficiencies in MMR/MSI occur when the DNA repair system isn't working properly and is found in 20-40% of endometrial cancers.
- MMR/MSI testing can identify patients with Lynch syndrome (a hereditary cancer syndrome) and identify patients who may have a more beneficial response to treatment with immunotherapy agents.
  - E.g. GY025

Treatment

Here is a basic overview of treatment lines but please always refer to NCCN guidelines for the most up-to-date treatment guidelines

https://www.nccn.org/home


NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer

Version 1.2024 — January 17, 2024

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

Continue

Ovarian Treatment

Upfront

- Treatment Naïve → Surgery → Adjuvant therapy
- Neoadjuvant Chemo (NACT) → Surgery → Adjuvant therapy

Adjuvant therapy can include +/- PARPi maintenance +/- bevacizumab (Avastin) maintenance

Recurrent

- Treatment Naïve → Adjuvant therapy
- If platinum sensitive, platinum+ other cytotoxic agent
- If platinum resistant/refractory, combination of cytotoxic agents or single agent

Platinum Therapy Responses

- Platinum Refractory
  - Progression while on platinum therapy or within 3 months of end of platinum therapy (depending on protocol definition)
  - Primary refractory is first line
- Platinum Sensitive
  - Recurrence > 6 months post end of platinum therapy
  - This can be in first line or subsequent therapies
- Platinum Resistant
  - Recurrence < 6 Months post end of platinum therapy
  - This can be in first line or subsequent therapies

Platinum Therapy Response

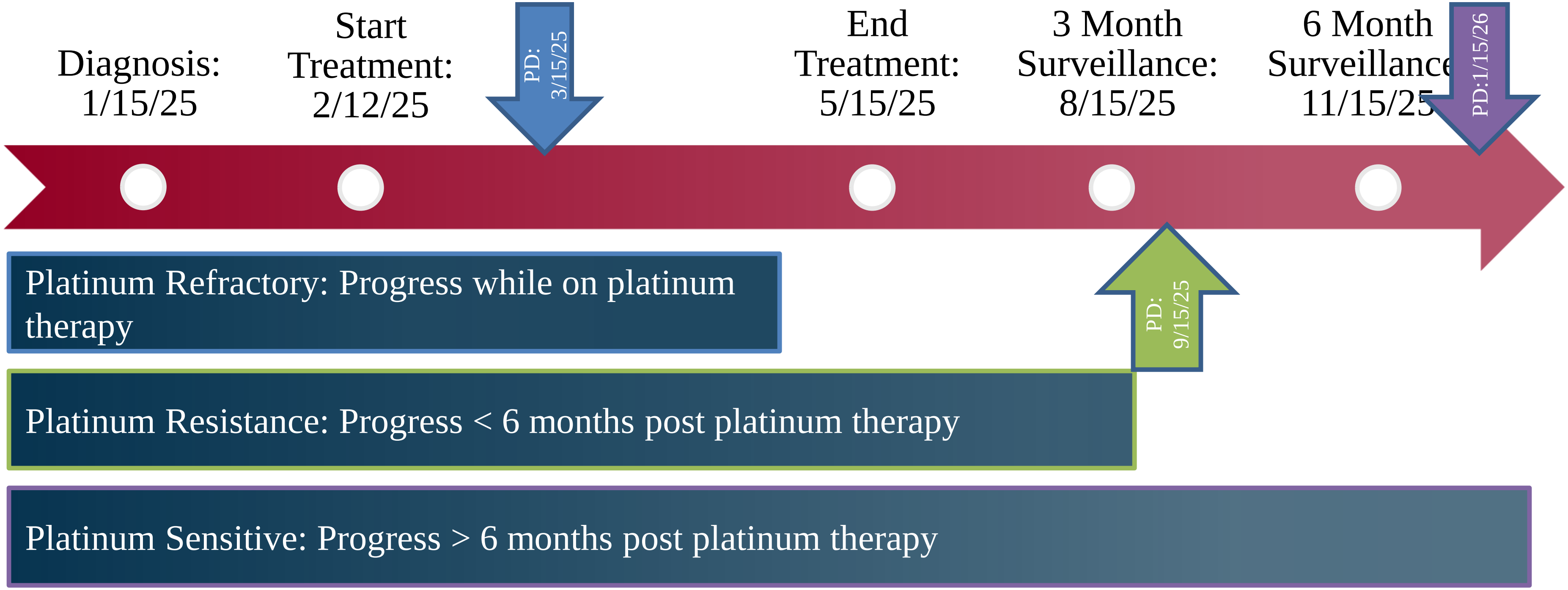
Diagnosis → Start Treatment → End Treatment → 3 Month Surveillance → 6 Month Surveillance

Platinum Refractory: Progress while on platinum therapy

Platinum Resistance: Progress < 6 months post platinum therapy

Platinum Sensitive: Progress > 6 months post platinum therapy

Platinum Therapy Response



Cervical Treatment

Upfront

- Stage 1A1: Loop Electrosurgical Excision Procedure (Leep)/ Colposcopy/Cold Knife Cone (CKC) or total hysterectomy +/- BSO
- Stage 1A2, 1B2, IIa: Radical hysterectomy
- Stage IIB-IVa: Concurrent chemoradiotherapy +/- Pembro (PD-L1 status)
- Stage IVB: Cisplatin or Carbo/Taxol +/- Bev +/- Atezolizumab

Recurrent

- Carbo/Taxol +/- Bev +/-Pembro
- Tisotumab Vedotin

Poll 4

Does CCRT count as systemic therapy?

Yes or No

Endometrial Treatment

Upfront Setting

- Treatment Naïve ⟶ surgery ⟶ carbo/taxol +/- bevacizumab (Avastin) maintenance +/- IO
- Neoadjuvant (NACT) ⟶ surgery ⟶ Adjuvant therapy

Recurrence

- Carbo/Taxol +/- Bev +/- IO
- Lenvatinimb + Pembrolizumab (aka Len Pem)
- Everolimus + Letrozole (aka Rad Let)

Further Treatment Information Resources

- Refer to NCCN guidelines
  - https://www.nccn.org/home
- For More SOC Chemo Info
  - UptoDate
  - Chemocare.com

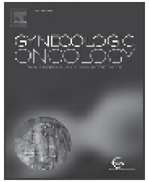
Imaging Standards

Gynecologic Oncology 146 (2017) 3–10

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Society Position Statements/White Papers

An update on post-treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncology (SGO) recommendations

Ritu Salani [a,*], Namita Khanna [b], Marina Frimer [c], Robert E. Bristow [d], Lee-may Chen [e]

[a] Department of Obstetrics & Gynecology, The Ohio State University, Columbus, OH, United States
[b] Department of Gynecology & Obstetrics, Emory University, Atlanta, GA, United States
[c] Department of Obstetrics & Gynecology, Hofstra Northwell School of Medicine, New Hyde Park, NY, United States
[d] Department of Obstetrics & Gynecology, University of California Irvine, Los Angeles, CA, United States
[e] Department of Obstetrics & Gynecology, University of California San Francisco, San Francisco, CA, United States

HIGHLIGHTS

- Surveillance strategies for gynecologic cancer vary based on stage and recurrence risk.
- Review of symptoms, physical exam, and education are the most effective methods in surveillance.

Cervical Imaging

Upfront

- PET/CT Whole body + Pelvis MRI PRE CCRT and PET/CT Whole Body after CCRT completion (6 weeks post)

Recurrence

- PET/CT Whole Body Prior to treatment and EOT

Endometrial Imaging

Upfront

- CT CAP or MRI Pelvis pre-op

Adjuvant

- CT CAP Pre-surgery/after 6 cycles carbo and taxol

Neoadjuvant

- CT CAP Pre-chemo/after 3 cycles carbo and taxol/after 6 cycles

Maintenance / Surveillance

- CT CAP as clinically indicated

Recurrence

- CT CAP after 3 month of treatment/after 6 months/EOT

Ovarian Imaging

Adjuvant

- CT CAP Pre-surgery/after 6 cycles carbo and taxol

Neoadjuvant

- CT CAP Pre-chemo/after 3 cycles carbo and taxol/after 6 cycles

Maintenance / Surveillance

- CT CAP as clinically indicated

Recurrence

- CT CAP after 3 month of treatment/after 6 months/EOT

Any questions?