

# Systemic Therapy for Metastatic Endometoid uterine AdenoCa



# Assessments



- **Histologic subtype** – Although histologic subtype does not predict response to chemotherapy, this provides prognostic insights, as *serous* and *clear cell* histologies are associated with worsened overall survival
- **Receptor testing for estrogen (ER) and progesterone (PR)**, which is particularly important for *endometrioid histologies*
- **Human epidermal growth factor receptor 2 (HER2) testing** by immunohistochemistry (IHC) for *serous* histology, with reflex testing for fluorescence in situ hybridization (FISH) in IHC 2+ results.
- **IHC for mismatch repair proteins or microsatellite instability testing**

# Chemotherapy-naïve patients



- ***Carboplatin and paclitaxel*** (typically continued until progression or unacceptable toxicity)
- Serous papillary tumors, the addition of [trastuzumab](#)

# Monitoring on treatment



- ***CT*** of the chest, abdomen, and pelvis every two to three cycles
- CA125 if elevated upfront

# Progression after prior chemotherapy



- MMR-deficient (dMMR) or microsatellite-instable (MSI) endometrial cancer, or with high tumor mutational burden (TMB;  $\geq 10$  mutations/megabase)
- Immune checkpoint inhibitor [pembrolizumab](#)

# Endocrine therapy



- I. Alternative to first- or second-line therapy
- II. later-line option for those who have progressed on chemotherapy- or immunotherapy-based options

# Endocrine therapy



1. Grade 1 or 2 endometrioid endometrial cancer
2. Positive expression of estrogen (ER) and progesterone (PR) receptors
3. Asymptomatic or minimally symptomatic disease

# Endocrine therapy



- Megestrol acetate alternating in sequence with tamoxifen



# Bevacizumab



- [Bevacizumab](#) (15 mg/kg intravenous [IV] every three weeks) both as a **single** agent and when **combined** with chemotherapy.
- Reasonable later-line option for those without contraindications (eg, poorly controlled hypertension).

# P13K/PTEN/AKT/mTOR pathway inhibitors



- [Temsirolimus](#) with or without [Bevacizumab](#)
- [Everolimus](#) with the aromatase inhibitor [letrozole](#)

# HER2-overexpressing tumors



- For those with metastatic serous endometrial cancer overexpressing human epidermal growth factor receptor 2 (HER2):
- Addition of [trastuzumab](#) to front-line chemotherapy, and continue until progression

# Thanks for your patient attention

