Epithelial Ovarian Cancer

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*

Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (Gynecologic Oncology Clinical Trials). Other comorbidities are taken into consideration prior to treatment selection.

CLINICAL PRESENTATION

- Pelvic mass
- Ascites
- Abdominal distention
- Abdominal/ pelvic pain
- Early satiety
- Urinary frequency

INITIAL EVALUATION

- Pelvic ultrasound
- CA 125
- Chest x-ray
- CT chest, abdomen, and pelvis with IV/PO contrast if concern for malignancy
- Other tumor markers if indicated[1]
- Colonoscopy if indicated
- Family history with referral to genetic counseling[2] and testing[3] as indicated
- Lifestyle risk assessment[4]

Consider laparoscopic assessment for disease resectability and biopsy to confirm diagnosis if carcinomatosis present by CT imaging and patient is medically stable for surgery

Able to achieve optimal resection ≤ 1 cm?

PRIMARY TREATMENT

Yes

- Hysterectomy/BSO[5] with comprehensive staging[6] **or**
- If Stage I, consider fertility sparing surgery (See Fertility Sparing Treatment algorithm) and Oncofertility consult[7] (See Fertility Preservation algorithm)
- If Stage II - IV, cytoreductive surgery

No

- Neoadjuvant chemotherapy[8] for 3 to 6 cycles
- Consider clinical trial[9]

Response?

Yes

Interval cytoreductive surgery

No

See Page 5 for relapsed/ progression treatment

END OF PRIMARY TREATMENT EVALUATION

- CT chest, abdomen, and pelvis with IV/PO contrast
- CA 125
- Consider laparoscopy

See Page 2 for treatment by stage[6]

Diagnosis by previous surgery or biopsy

- Chest x-ray
- CA 125
- CT chest, abdomen and pelvis with IV/PO contrast
- Genetic counseling[2] and testing[3] for high grade non-mucinous epithelial ovarian cancer, including primary peritoneal cancer and fallopian tube cancer

Incomplete surgery **and/or** staging?

Yes

No

[1] Consider MD Anderson approved biomarkers
[2] See Genetic Counseling algorithm to assess criteria for referral
[3] Consider both germline and somatic mutation testing (including HRD testing if *BRCA* germline or somatic mutation are negative). Consider testing at initial diagnosis or at the time of surgery.
[4] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

BSO = bilateral salpingo-oophorectomy

[5] If Stage I and patient desires fertility preservation, consider unilateral salpingo-oophorectomy (USO) and staging
[6] See Appendix A: The International Federation of Gynecology and Obstetrics (FIGO) Staging
[7] Refer to Reproductive Endocrinologists
[8] See Appendix B: Chemotherapy Regimens
[9] See Gynecologic Oncology Clinical Trials

Department of Clinical Effectiveness V9
Approved by the Executive Committee of the Medical Staff on 02/23/2021

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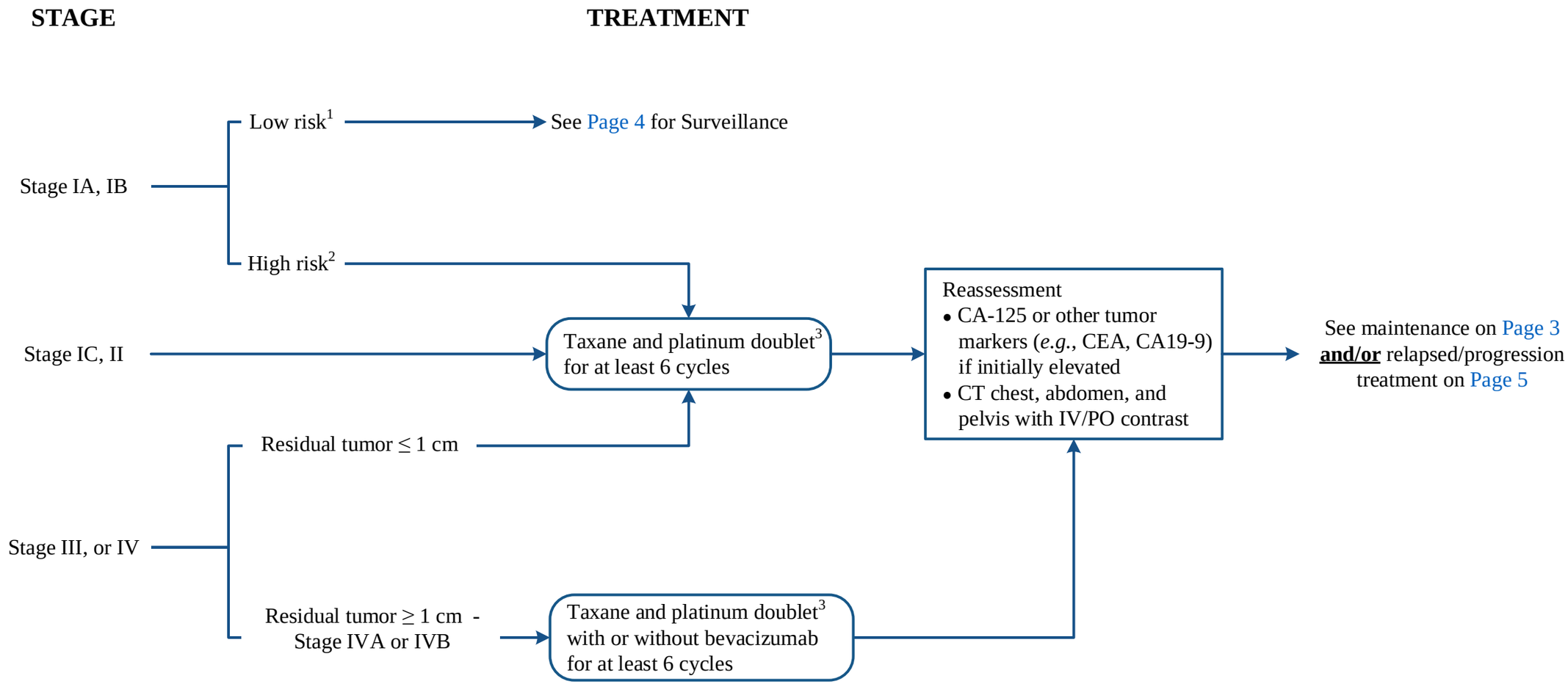

[1] Low risk – Grade 1 endometrioid or low grade serous histology
[2] High risk – Grade 2 or 3 endometrioid, high grade serous, clear cell, or carcinosarcoma
[3] See Appendix B: Chemotherapy Regimens

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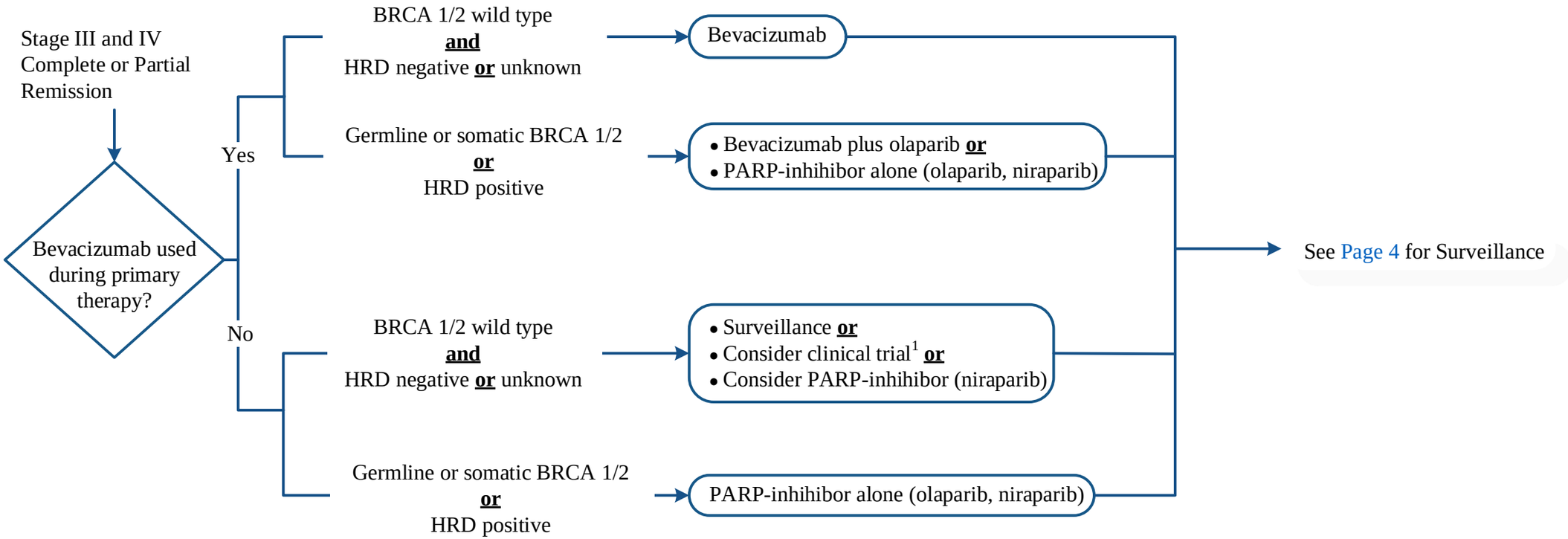
MAINTENANCE TREATMENT



[1] See Gynecologic Oncology Clinical Trials

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Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (Gynecologic Oncology Clinical Trials). Other comorbidities are taken into consideration prior to treatment selection.

SURVELLIANCE

Surveillance to include the following:

- Review of symptoms (pain, persistent headache, shortness of breath, bleeding, discharge, chronic cough, and change in bowel or bladder habits)
- Pelvic exam during clinic visits
- CA-125 or other tumor markers if initially elevated
- Pap test is *not* recommended
- Routine diagnostic imaging is *not* recommended

Recommended surveillance schedule:

- Year 1: Every 3 months
- Year 2: Every 3-4 months
- Year 3-5: Every 6 months

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Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (Gynecologic Oncology Clinical Trials). Other comorbidities are taken into consideration prior to treatment selection.

RELAPSED/PROGRESSION TREATMENT

- Progression or no response on primary chemotherapy[1] **or**
- Relapse < 6 months after stopping platinum-based chemotherapy[1] (taxane and platinum resistant)

→
- Consider supportive care for selected patients
- Salvage chemotherapy/biotherapy[1] with or without bevacizumab
- Hormonal therapy
- NGS, *MSI* by PCR, and HLA testing for primary tumor
- Clinical trial[2]

Relapse ≥ 6 months after stopping platinum-based chemotherapy[1]

→ Serially rising CA 125 →
- Delay until clinical or radiologic relapse or treat as clinically indicated
- BRCA testing, if not already performed
- HRD tumor testing if germline BRCA testing negative
- NGS, *MSI* by PCR, and HLA testing for primary tumor
- Clinical trial[2]
- Consider supportive care for selected patients

→ Clinical or radiologic relapse → Consider cytoreductive surgery **or** radiation therapy in selected patients →
- Platinum-based doublet with or without bevacizumab[1] plus bevacizumab maintenance therapy **or**
- Platinum doublet followed by PARP inhibitor maintenance therapy[1]
- BRCA testing, if not already performed
- HRD tumor testing if germline BRCA testing negative
- NGS, *MSI* by PCR, and HLA testing for primary tumor
- Clinical trial[2]
- Consider supportive care for selected patients

HRD = homologous recombination deficiency
MSI = microsatellite instability
HLA = human leukocyte antigen

[1] See Appendix B: Chemotherapy Regimens
[2] See Gynecologic Oncology Clinical Trials

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APPENDIX A: The International Federation of Gynecology and Obstetrics (FIGO) Staging

Stage	Description
I	Tumor confined to ovaries or fallopian tube(s) IA: Tumor limited to one ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings IB: Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings IC: Tumor limited to one or both ovaries or fallopian tubes, with any of the following: IC1: Surgical spill IC2: Capsule ruptured before surgery or tumor on ovarian fallopian tube surface IC3: Malignant cells in ascites or peritoneal washings
II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer IIA: Extension and/or implants on uterus and/or fallopian tubes and/or ovaries IIB: Extension to other pelvic intraperitoneal tissues
III	Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes IIIA1: Positive retroperitoneal lymph nodes only (cytologically or histologically proven) (i) Metastasis up to 10 mm in greatest dimension (ii) Metastasis more than 10 mm in greatest dimension IIIA2: Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes IIIB: Macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes IIIC: Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)
IV	Distant metastasis excluding peritoneal metastases IVA: Pleural effusion with positive cytology IVB: Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

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APPENDIX B: Chemotherapy Regimens

<table>
<tr><td>Adjuvant Therapy</td><td colspan="2">
• Paclitaxel 135 mg/m^2 IV over 3 hours on Day 1 with cisplatin 75-100 mg/m^2 IP on Day 2 and paclitaxel 60 mg/m^2 IP on Day 8 every 3 weeks for 6 cycles
• Paclitaxel 175 mg/m^2 IV over 3 hours with carboplatin AUC 5-6 IV over 1 hour every 3 weeks for 6 cycles
• Docetaxel 75 mg/m^2 IV over 1 hour with carboplatin AUC 5 IV over 1 hour every 3 weeks for 6 cycles
• Paclitaxel 80 mg/m^2 IV over 1 hour on Days 1, 8 and 15 with carboplatin AUC 5-6 IV over 1 hour on Day 1 every 3 weeks for 6 cycles
• Paclitaxel 175 mg/m^2 IV over 3 hours with carboplatin AUC 5-6 IV over 1 hour every 3 weeks for 6 cycles. Starting Day 1 of cycle 2 give bevacizumab 15 mg/kg IV over 30 minutes every 3 weeks
• Option for patients with mucinous ovarian cancer:
  ○ Oxaliplatin 130 mg/m^2 IV over 2 hours on Day 1 and capecitabine 850 mg/m^2 PO twice daily on Days 1 through 14 followed by 7 day rest period every 3 weeks
</td></tr>
<tr><td>Neoadjuvant Therapy</td><td colspan="2">
• Paclitaxel 175 mg/m^2 IV over 3 hours with carboplatin AUC 5-6 IV over 1 hour every 3 weeks for 3 to 6 cycles
• Docetaxel 75 mg/m^2 IV over 1 hour with carboplatin AUC 5 IV over 1 hour every 3 weeks for 3 to 6 cycles
• Paclitaxel 80 mg/m^2 IV over 1 hour on Days 1, 8 and 15 with carboplatin AUC 5-6 IV over 1 hour on Day 1 every 3 weeks for 3 to 6 cycles
• Paclitaxel 175 mg/m^2 IV over 3 hours with carboplatin AUC 5-6 IV over 1 hour and bevacizumab 15 mg/kg IV over 30 minutes every 3 weeks for 3 to 6 cycles. Bevacizumab should not be given in the cycle prior to surgery.
</td></tr>
<tr><td>Maintenance Therapy</td><td colspan="2">
• Bevacizumab 15 mg/kg IV over 30 minutes every 3 weeks for at least 1 year or until progression
• Approved PARP inhibitor therapy until progression (BRCA positive or HRD positive)
• Aromatase inhibitors (low grade serous ovarian cancer)
</td></tr>
<tr><td rowspan="3">Recurrence Therapy</td><td>Platinum Sensitive</td><td>Platinum Resistant</td></tr>
<tr><td colspan="2">All systemic chemotherapy agents[1] can be given alone or with bevacizumab</td></tr>
<tr><td>
• Paclitaxel and carboplatin
• Carboplatin and weekly paclitaxel
• Carboplatin and docetaxel
• Carboplatin and gemcitabine
• Carboplatin and gemcitabine
• Carboplatin and liposomal doxorubicin
• Carboplatin single agent
• Bi-weekly cisplatin and gemcitabine
• Approved PARP inhibitor therapy (BRCA positive)
</td><td>
• Docetaxel
• Oral etoposide
• Gemcitabine
• Liposomal doxorubicin
• Weekly paclitaxel
• Bi-weekly cisplatin and gemcitabine
• Approved PARP inhibitor therapy (BRCA positive or HRD positive) or aromatase inhibitor (low grade serous ovarian cancer)
• Oral cyclophosphamide
• Bevacizumab single agent
• Topotecan
• Vinorelbine
• Hormonal therapy
</td></tr>
</table>

[1] Excludes PARP inhibitors

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