requiring cytoreductive surgery be referred to higher levels of care.

***Limited-resource settings and enhanced-resource settings.*** Complete cytoreductive surgery for patients with stage III or IV ovarian cancer should be performed by a gynecologic oncologist, general gynecologist, or general surgeon with experience in cancer surgery. Patients should be referred to the highest-level cancer center for optimal surgical management. Access to perioperative supportive services for complex surgical patients may be necessary to optimize surgical outcomes and minimize morbidity.

### Surgery after neoadjuvant chemotherapy (Recommendation 2.2.2-2.2.3)

Recommendations on interval cytoreductive surgery after NACT are available in Table 6 and Appendix Figures A3 and A9.

***Discussion.*** Patients with stage III/IV disease with bulky disease may benefit from NACT if a gynecologic oncologist or surgical oncologist reviews the case and deems the patient's disease as unresectable or unlikely to achieve complete cytoreduction. Additional patients appropriate for NACT consideration include those with poor PS or at high surgical risk assessed by a surgical specialist. Research is underway on assessing response to NACT using validated scoring tools and nomograms, although reviewing this literature is outside this guideline's scope.[30] According to the ASCO and SGO guideline on NACT in stage IIIC and IV, only patients with response to chemotherapy or stable disease following three to four cycles of platinum-based chemotherapy benefit from interval cytoreductive surgery.[15] The goal of surgery is the same as primary surgery to achieve optimal tumor cytoreduction to $< 1$ cm, ideally to no visible disease (R0). For patients whose tumor progresses during chemotherapy, interval surgery is not indicated as it offers no added survival benefit. Options for these patients include alternative chemotherapy regimens, clinical trials, and/or discontinuation of active cancer therapy and initiation of end-of-life care. In general, in the setting of progressive disease, there is little role for surgery, and it is not typically advised, unless for palliation (eg, relief of bowel obstruction).

***Basic-resource settings.*** This guideline recommends that patients at this level should be referred to higher levels of care, otherwise patients should be managed with supportive and palliative care interventions.

***Limited-resource settings.*** Treatment response following NACT should be evaluated by an MDT and guided by imaging, tumor marker analysis, and physical examination. Response to NACT may be indicative of a greater likelihood of benefit from interval cytoreductive surgery. Patients with disease response or stable disease benefit from interval cytoreductive surgery to achieve tumor cytoreduction $< 1$ cm, ideally to no visible disease (R0) where feasible, otherwise achieve tumor cytoreduction to $< 1$ cm.

Options for patients with progressive disease with NACT are palliative systemic therapies, enrollment in clinical trials, single-agent therapies, or discontinuation of all therapies and pursuit of end-of-life care. There is a laimited role for surgery in patients with poor response to chemotherapy. The decision for additional treatment in patients with progressive disease with NACT should be endorsed by the MDT, weighing the risks and benefits in patients with poor survival outcomes.

***Enhanced-resource settings.*** The same recommendations apply as in limited settings, with added capacity for more aggressive cytoreductive procedures by experienced and specialized surgeons and/or gynecologic oncologists.

## OVERARCHING CLINICAL QUESTION C

What is the optimal adjuvant and/or systemic therapy for stages I-IV EOC?

Recommendations on adjuvant and systemic therapy are in Appendix Figures A3 and A10 and Table 6.

### Adjuvant chemotherapy following surgery in patients with stage I EOC (Recommendations 3.1.1-3.1.5)

***Discussion.*** Stage I ovarian cancer is potentially curable; early and accurate treatment is fundamental to optimizing survival outcomes. Adjuvant chemotherapy may follow any attempt at best possible surgical staging and debulking. Clinicians should use information from surgical staging to guide adjuvant chemotherapy decisions and define disease prognosis. Since patients with previously presumed early-stage ovarian cancer may be upstaged,[27,28] women who were previously deemed not likely to require adjuvant chemotherapy may qualify for adjuvant therapy given known benefit for OS.[31] Patients with stage I ovarian cancer who are incompletely staged or completely staged with residual disease experience survival benefit from adjuvant chemotherapy. Adjuvant chemotherapy should not replace additional surgery where feasible.

The OS for stage I EOC is high, although a subset of women is at a higher risk of relapse. Adjuvant chemotherapy does not improve survival for women with stage IA or IB low-grade (grade 1) endometrioid, serous, or mucinous ovarian carcinoma. This subset of patients is classified as having low-risk early-stage EOC. The risk of relapse is increased with incompletely staged and any grade disease; clear cell, while not normally graded, is considered a high-grade, high-risk histology, and these subsets of patients benefit in improved OS with adjuvant chemotherapy. The international standard-of-care recommendation for adjuvant chemotherapy is a taxane plus platinum doublet on an every-three-weekly schedule (once every 3 weeks) for a total of six cycles; clinicians may use other platinum-based doublets, although there are no data showing noninferiority or superiority to platinum plus taxane doublets. Data exist on the use of three versus six cycles of treatment with nonsignificant difference in survival outcome, although six