

Supplementary Table S1 - Summary of recommendations

1. How to determine the site of origin of extrauterine high-grade serous carcinomas?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|-----|-----|--|
| Recommendation 1.1: a large majority of extrauterine HGSCs arise in the fallopian tube from STIC. SEE-FIM sectioning of both fallopian tubes should be carried out in all cases of extrauterine HGSC where the tubes are grossly normal, and also in risk-reducing prophylactic surgery specimens. | III | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 1.2: extrauterine HGSC can only be assigned as ovarian in origin if both fallopian tubes are grossly normal, and histologically contain no mucosal disease following examination using a SEE-FIM protocol. | III | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 1.3: cases in which HGSC is present in the endometrium and the tube/ovary are very likely to represent a primary at one site with metastasis to the other; these are very unlikely to represent synchronous independent neoplasms. | V | A | Yes: 97.5% (39) No: 2.5% (1) Abstain: 0% (0) |
| Recommendation 1.4: the distinction between primary endometrial and primary tubal/ovarian HGSC requires assessment of a constellation of pathological features; negative WT1 staining favours an endometrial primary, but this is not always definitive. | V | A | Yes: 92.5% (37) No: 0% (0) Abstain: 7.5% (3) |
| Recommendation 1.5: the use of uniform criteria is important in site assignment in extrauterine HGSC for cancer registry and epidemiological reasons. The use of ICCR and CAP guidelines is recommended. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 1.6: correct and uniform use of site assignment criteria is particularly important for accurate staging of early HGSC. | III | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 1.7: STIC should count as a disease site for staging purposes; for example, a case with a STIC and HGSC confined to the ovary should be staged as stage IIA fallopian tube HGSC. | IV | A | Yes: 95% (38) No: 0% (0) Abstain: 5% (2) |
| Recommendation 1.8: true primary peritoneal HGSC is extremely rare. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 1.9: multifocal origin of extrauterine HGSC is exceptionally rare and thus HGSC currently staged as IB should be considered as stage IIA. | IV | A | Yes: 95% (38) No: 5% (2) Abstain: 0% (0) |

2. How to identify tumours that will respond to targeted therapies, including poly(adenosine diphosphate-ribose) polymerase inhibitors and immune checkpoint inhibitors?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|---|
| Recommendation 2.1: there are no validated predictive molecular biomarkers of bevacizumab benefit. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 2.2: PARP inhibitors have greatest activity in patients with <i>BRCA1/2</i> mutations. | I | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 2.3: testing for <i>BRCA1/2</i> mutations is recommended for all patients with non-mucinous ovarian cancer. | I | A | Yes: 95% (38) No: 0% (0) Abstain: 5% (2) |
| Recommendation 2.4: testing for mutations in other HR genes, in particular <i>RAD51C/D</i> , <i>BRIP1</i> and <i>PALB2</i> , should be considered. | III | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 2.5: current assays of HR function cannot be used to exclude patients from PARP inhibitor therapy. | I | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 2.6: moderate-strong ER staining may be a predictor of response to hormone therapy. | III | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 2.7: there are currently no prospectively validated predictive biomarkers of response to immune checkpoint inhibitors that are specific to ovarian cancer. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |

3. How to identify patients with acquired/intrinsic resistance to chemotherapy?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|-----|-----|---|
| Recommendation 3.1: there are no validated predictive markers of primary platinum refractory or resistant disease. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 3.2: defects in HR repair are associated with improved outcome/PFS following platinum-based chemotherapy. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 3.3: the time elapsed since last platinum chemotherapy represents a continuum of probability of response to further chemotherapy. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |

4. Can we develop accurate and sensitive circulating and tissue biomarkers both of response and relapse?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|-----|-----|---|
| Recommendation 4.1: the CA-125 criteria for response and progression as agreed by GCIG have utility in routine practice but should be used in combination with radiological and clinical assessment. | III | A | Yes: 97.5% (39) No: 0% (0) Abstain: 2.5% (1) |
| Recommendation 4.2: the role of CA-125 as a marker of response and progression in non-HGSC is less clear. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 4.3: the use of CA-125 in assessing response and progression to targeted therapies is not yet proven; thus, radiological and clinical assessment should be used. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 4.4: HE4 should not be used routinely to assess response and progression due to conflicting results. | IV | A | Yes: 97.5% (39) No: 0% (0) Abstain: 2.5% (1) |
| Recommendation 4.5: quantification of circulating cfDNA has not been established as a tool to assess response and relapse. | IV | A | Yes: 97.5% (39) No: 0% (0) Abstain: 2.5% (1) |
| Recommendation 4.6: pathological CRS after NACT may provide an objective and reproducible prognostic measure of outcome in HGSC. | IV | A | Yes: 82.5% (33) No: 12.5% (5) Abstain: 5% (2) |

5. What are the morphological criteria useful in separating borderline from invasive ovarian neoplasia?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|-----|-----|--|
| Recommendation 5.1: destructive stromal invasion is no longer necessary for carcinoma diagnosis (carcinomas may exhibit expansile invasion). | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 5.2: according to the 2014 WHO classification, extraovarian invasive implants in association with an sBOT are synonymous with extraovarian LGSC. The WG does not support this terminology because it may be misleading for clinical management. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 5.3: in the 2014 WHO classification, the micropapillary variant of sBOT is also termed non-invasive LGSC but the WG does not support this terminology because it may be misleading for clinical management. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 5.4: microinvasion (<5mm) can be seen in borderline tumours but these cases should still be regarded as borderline for classification and management purposes. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 5.5: the term implant should not be used in the context of mBOTs; extraovarian disease in association with a mBOT should be considered as metastasis (from ovary or another organ). | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 5.6: borderline endometrioid tumours can be differentiated from grade I endometrioid carcinoma using similar criteria as used to differentiate atypical hyperplasia from grade I endometrioid carcinoma in the uterine corpus. | V | A | Yes: 97.5% (39) No: 0% (0) Abstain: 2.5% (1) |

6. Are there exceptions to the standard surgical management for early-stage ovarian carcinoma?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|--|
| Recommendation 6.1: laparotomy is the standard surgical approach to treat and stage patients with apparent early-stage ovarian carcinoma. | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 6.2: minimally invasive surgery can be carried out for restaging. | IV | B | Yes: 75% (30) No: 12.5% (5) Abstain: 12.5% (5) |
| Recommendation 6.3: whatever the approach used, rupture of an intact tumour with spillage of cancer cells at the time of surgery must be avoided. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 6.4: peritoneal restaging surgery is mandatory even if it does not alter the indication for adjuvant chemotherapy. | V | B | Yes: 92.5% (37) No: 2.5% (1) Abstain: 5% (2) |
| Recommendation 6.5: peritoneal restaging should be considered in cases of incidentally detected, apparently isolated STIC lesions. | IV | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 6.6: the standard surgical staging of apparent early EOC includes systematic LN dissection of the pelvic and the para aortic regions up to the left renal vessel origin. | IV | A | Yes: 77.5% (31) No: 22.5% (9) Abstain: 0% (0) |
| Recommendation 6.7: LN dissection for restaging purposes may be avoided if the nodal status does not alter the patient management. | V | B | Yes: 95% (38) No: 0% (0) Abstain: 5% (2) |

7. What are the limits of fertility-sparing surgery (cancer and borderline ovarian tumour)?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|---|
| Recommendation 7.1: FSS can be safely offered to all stage IA and IC1 low-grade ovarian carcinomas. | IV | B | Yes: 94.74% (36) No: 2.63% (1) Abstain: 2.63% (1) |
| Recommendation 7.2: there is no place for ovarian preservation for invasive EOC greater than fully staged FIGO stage I. | V | A | Yes: 94.9% (37) No: 0% (0) Abstain: 5.1% (2) |

8. Should all stage I carcinomas receive adjuvant chemotherapy and, if not, which ones?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|---------|--------|---|
| <p>Recommendation 8.1: adjuvant chemotherapy should be offered to patients with early-stage ovarian cancer (stage I-IIA) with the exception of fully staged patients with the following:</p> <ul style="list-style-type: none"> • Low-grade serous IA • Grade 1 and 2 endometrioid IA • Grade 1 and 2 mucinous IA (expansile invasion) | II | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| <p>Recommendation 8.2: adjuvant chemotherapy is not recommended in the management of incidentally detected isolated STIC lesions.</p> | V | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| <p>Recommendation 8.3: the benefit of adjuvant chemotherapy is uncertain for patients with the following cancers and should be discussed on an individual patient basis:</p> <ul style="list-style-type: none"> • Clear cell carcinoma stage IA and IB/IC1 • Grade 1 and 2 endometrioid IB/IC • Low-grade serous IB/IC • Grade 1 and 2 mucinous IC (expansile invasion) • Mucinous IA (infiltrative invasion) | III | C | Yes: 92.5% (37) No: 7.5% (3) Abstain: 0% (0) |
| <p>Recommendation 8.4: for patients with early-stage disease requiring adjuvant chemotherapy, acceptable treatment regimens are:</p> <ul style="list-style-type: none"> • carboplatin alone • carboplatin/paclitaxel | I II | A A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| <p>Recommendation 8.5: for patients receiving single-agent adjuvant carboplatin, 6 cycles are recommended.</p> | I | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| <p>Recommendation 8.6: for patients receiving carboplatin and paclitaxel, a minimum of 3 cycles is recommended except for the high-grade serous subgroup or stage IC (any histological type), for whom 6 cycles are recommended.</p> | II | B | Yes: 77.5% (31) No: 0% (0) Abstain: 22.5% (9) |

9. Are non-serous borderline ovarian tumours managed according to the same standard as serous borderline ovarian tumours?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|---|
| <p>Recommendation 9.1: preservation of at least part of one ovary and the uterus is the standard approach in young patients with BOTs.</p> | III | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| <p>Recommendation 9.2: unilateral salpingo-oophorectomy is recommended with mBOTs to decrease the risk of invasive recurrence after cystectomy.</p> | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| <p>Recommendation 9.3: cystectomy is an acceptable management in sBOTs to preserve fertility.</p> | III | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |

10. How should serous borderline ovarian tumours with extraovarian implant be managed?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|-----------|--------|--|
| Recommendation 10.1: peritoneal staging surgery is recommended for sBOTs. | III | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 10.2: the benefit of restaging is not clear but should be considered in patients with: <ul style="list-style-type: none"> sBOTs with micropapillary pattern sBOTs with incomplete visual exploration of the peritoneal cavity | IV III | B B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 10.3: there is no role for appendectomy in BOTs. | V | A | Yes: 85% (34) No: 0% (0) Abstain: 15% (6) |
| Recommendation 10.4: all peritoneal implants must be removed. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 10.5: there is no proven benefit of systematic LN dissection in stage II/III sBOTs. | IV | B | Yes: 97.5% (39) No: 0% (0) Abstain: 2.5% (1) |
| Recommendation 10.6: FSS could be considered in selected patients with stage II or III sBOTs. | V | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 10.7: adjuvant systemic treatment is not recommended for primary treatment of sBOTs with extraovarian invasive/non-invasive implants. | III | B | Yes: 92.5% (37) No: 0% (0) Abstain: 7.5% (3) |

11. How to select patients for primary debulking surgery or neoadjuvant chemotherapy?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|-----|-----|---|
| Recommendation 11.1: the selection of patients for primary debulking surgery or neoadjuvant treatment must be carried out in a specialist ovarian cancer centre, according to the ESGO Quality recommendations 2016 [1] in a multidisciplinary setting. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 11.2: complete tumour resection at upfront debulking is the most important prognostic factor for patients with advanced ovarian cancer and is the main goal of surgery. | IV | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 11.3: when complete surgery with no macroscopic visible disease appears feasible (both spread of disease and general condition of the patient), primary upfront debulking should be offered. | IV | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 11.4: diagnostic work-up with CT, (PET)-CT or diffusion-weighted whole-body MRI and expert ultrasound or diagnostic laparoscopy should be used to assess the extent of disease. | III | C | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 11.5: patients are not candidates for primary surgery (according to ESGO 2017 recommendations [2]) if the following spread of disease, among other factors, is present: <ul style="list-style-type: none"> • Diffuse deep infiltration of the root of small bowel mesentery • Diffuse carcinomatosis of the small bowel involving such large parts that resection would lead to a short bowel syndrome (remaining bowel <1.5 m) • Diffuse involvement/deep infiltration of <ul style="list-style-type: none"> • stomach/duodenum • head or middle part of pancreas • Involvement of coeliac trunk, hepatic arteries, left gastric artery • Central or multisegmental parenchymal liver metastases • Multiple parenchymal lung metastases (preferably histologically proven) • Non-resectable LNs • Brain metastases | III | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |

12. What is the current role of bevacizumab in first-line treatment?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|--|
| Recommendation 12.1: bevacizumab (15 mg/kg or 7.5 mg/kg every 3 weeks for maximum of 15 months) improves PFS in patients with stage III-IV ovarian cancer and should be considered in addition to carboplatin and paclitaxel. | I | A | Yes: 97.5% (39) No: 0% (0) Abstain: 2.5% (1) |
| Recommendation 12.2: bevacizumab in the neoadjuvant setting can be considered, although additional improvement in efficacy is not proven with level I evidence. | II | B | Yes: 97.5% (39) No: 2.5% (1) Abstain: 0% (0) |
| Recommendation 12.3: bevacizumab can be safely administered in the neoadjuvant setting before and after IDS providing the interval between surgery and administration is at least 4-6 weeks. | II | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |

13. Should weekly regimens be used in first line?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|---|
| Recommendation 13.1: incorporation of weekly chemotherapy into first-line treatment for women with EOC does not improve PFS or OS in the population of western countries. | I | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 13.2: the schedule of weekly chemotherapy with carboplatin (AUC2) and paclitaxel (60 mg/m ²) shows better QoL and reduced toxicity (e.g. alopecia, neuropathy) compared with the standard 3-weekly schedule and can be considered. | I | B | Yes: 95% (38) No: 0% (0) Abstain: 5% (2) |
| Recommendation 13.3: weekly chemotherapy cannot be regarded as a substitute for bevacizumab. | V | B | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |
| Recommendation 13.4: 3-weekly carboplatin/paclitaxel remains the standard-of-care chemotherapy of first-line ovarian cancer treatment. | I | A | Yes: 100% (40) No: 0% (0) Abstain: 0% (0) |

14. Is there a place for intraperitoneal chemotherapy and hyperthermic intraperitoneal chemotherapy?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|--|
| Recommendation 14.1: i.p. chemotherapy is not a standard of care as first-line treatment. | I | A | Yes: 95% (38) No: 0% (0) Abstain: 5% (2) |
| Recommendation 14.2: HIPEC is not a standard of care as first-line treatment. | II | A | Yes: 95% (38) No: 0% (0) Abstain: 5% (2) |

15. Is the standard of management of non-high-grade serous epithelial ovarian cancer different?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|--|
| Advanced (FIGO III and IV) non-high-grade serous ovarian cancer in first line | | | |
| Recommendation 15.1: primary debulking surgery with no macroscopic residual disease is of pivotal importance due the low chemosensitivity in low-grade serous, mucinous and clear cell ovarian carcinoma. | IV | A | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |
| Recommendation 15.2: even debulking with residual disease <1 cm in low-grade serous ovarian cancer may improve survival when complete cytoreduction is not feasible. | IV | C | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |
| Recommendation 15.3: carboplatin in combination with paclitaxel is the standard chemotherapy. Addition of bevacizumab should be considered. | I | B | Yes: 97.4 (37) No: 0% (0) Abstain: 2.6% (1) |
| Recommendation 15.4: maintenance antioestrogen therapy after chemotherapy can be considered in low-grade serous ovarian cancer. | IV | C | Yes: 92.1% (35) No: 0% (0) Abstain: 7.9% (3) |
| Recurrent non-high-grade serous ovarian cancer in first line | | | |
| Recommendation 15.5: secondary debulking surgery should be considered with the aim of no macroscopic residual disease. | I | B | Yes: 100% (37) No: 0% (0) Abstain: 0% (0) |
| Recommendation 15.6: in low-grade serous, low-grade endometrioid, mucinous and clear cell ovarian carcinoma, chemotherapy is an option but the magnitude of benefit is uncertain. | IV | B | Yes: 100% (37) No: 0% (0) Abstain: 0% (0) |
| Recommendation 15.7: antioestrogen therapy can be considered in low-grade serous ovarian cancer and low-grade endometrioid ovarian carcinoma. | IV | B | Yes: 97.3% (36) No: 0% (0) Abstain: 2.7% (1) |

16. What is a reasonable monitoring and follow-up strategy following treatment of ovarian cancer?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|-----|-----|---|
| Recommendation 16.1: follow-up should be offered, and the value should be discussed individually with patients, as there is uncertainty about the benefit of early diagnosis and treatment of recurrent disease. | II | C | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |

17. What is the place of surgery for recurrent disease?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|---|
| Recommendation 17.1: complete cytoreductive surgery followed by systemic treatment improves PFS and extends benefit to the next line of treatment in selected patients with first recurrence of ovarian cancer; OS data are not yet mature. Patients eligible for cytoreductive surgery should be informed about this option. | I | A | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |
| Recommendation 17.2: complete cytoreductive surgery in second or later recurrence may provide benefit in selected patients and specialised centres. | V | A | Yes: 100% (37) No: 0% (0) Abstain: 0% (0) |
| Recommendation 17.3: in recurrent ovarian cancer, HIPEC added to cytoreductive surgery has not been proven to be beneficial in appropriately designed prospective studies. | IV | A | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |
| Recommendation 17.4: MBO should be managed on an individual basis. There is a lack of evidence for optimal management and a need for clinical trials to evaluate medical, endoscopic and surgical approaches. | V | A | Yes: 100% (37) No: 0% (0) Abstain: 0% (0) |

18. How should molecularly targeted therapy be integrated into the management of recurrent ovarian cancer?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|---|
| Recommendation 18.1: bevacizumab in combination with platinum-based second-line chemotherapy (gemcitabine or paclitaxel) followed by bevacizumab maintenance has proven benefit with respect to tumour response rate and PFS, and could be recommended. | I | A | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |
| Recommendation 18.2: bevacizumab in combination with second or third-line non-platinum chemotherapy (weekly paclitaxel, PLD, topotecan) has proven benefit with respect to tumour response rate and PFS, has been associated with improvement in QoL and could be recommended. | I | A | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |
| Recommendation 18.3: PARP inhibitors (olaparib, niraparib and rucaparib) when given as maintenance therapy following a response to platinum-based second or higher line of treatment have proven benefit with respect to PFS and could be recommended. The benefit is greatest in, but is not limited to, patients with a <i>BRCA</i> mutation. | I | A | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |
| Recommendation 18.4: PARP inhibitors (rucaparib*, olaparib) are active as monotherapy in patients with a <i>BRCA</i> mutation and could be considered <i>*In Europe, only rucaparib is licensed by the EMA as a monotherapy for patients with 'platinum-sensitive' disease.</i> | III | B | Yes: 100% (38) No: 0% (0) Abstain: 0% (0) |

19. What defines platinum resistance and how does that influence subsequent treatment?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|---|------|-----|---|
| Recommendation 19.1: there are currently no molecular biomarkers to predict platinum response. <ul style="list-style-type: none"> • <u>Resistance to platinum</u> in recurrent ovarian cancer is a therapy-oriented definition: <ul style="list-style-type: none"> ○ Proven platinum resistance: progression during platinum therapy ○ Assumed/expected platinum resistance: early symptomatic relapse with low probability of response to platinum; these patients should be treated with sequential non-platinum therapy adding bevacizumab if indicated. • <u>Sensitivity to platinum</u> in recurrent ovarian cancer is a therapy-oriented definition: <ul style="list-style-type: none"> ○ Proven platinum sensitivity: response to platinum; these patients can receive maintenance PARP inhibitors ○ Assumed/expected platinum sensitivity: previous response to platinum without early symptomatic relapse; these patients should be treated with platinum-based therapy adding bevacizumab or followed by maintenance PARP inhibitor therapy, if indicated. This group includes those who did not receive prior platinum or those who received adjuvant platinum post-surgery without any evaluable residual disease to assess chemotherapy response. | I-IV | A | Yes: 85.7% (30) No: 11.4% (4) Abstain: 2.9% (1) |
| Recommendation 19.2: platinum re-challenge following treatment with a non-platinum regimen (monotherapy or combination) could be considered if a patient had not progressed during prior platinum therapy. | IV | A | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |
| Recommendation 19.3: early palliative care should be integrated into the management of patients with recurrent ovarian cancer. | V | A | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |
| Recommendation 19.4: incorporating HRQoL tools in the care of patients with a low probability of response to platinum may identify patients for whom subsequent therapy is futile, and this information should be discussed with the patient. | III | A | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |

20. How long should therapy be continued in recurrent disease?

| Recommendations | LoE | GoR | Consensus (Nb voters) |
|--|-----|-----|--|
| Stopping chemotherapy | | | |
| Recommendation 20.1: for platinum-based chemotherapy, 6 cycles are recommended. More or fewer cycles have not been shown to be beneficial, and consideration should be given to the toxicity. | V | B | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |
| Recommendation 20.2: for non-platinum chemotherapies, treatment may be continued as long as there is clinical benefit and treatment is well-tolerated. | V | B | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |
| Stopping bevacizumab | | | |
| Recommendation 20.3: recommended length of treatment remains unclear. Treatment is usually continued until disease progression. The continuation of bevacizumab beyond progression has not been evaluated in the recurrent setting. | V | B | Yes: 97.1% (33) No: 2.9% (1) Abstain: 0% (0) |
| Stopping maintenance PARP inhibitors | | | |
| Recommendation 20.4: recommended length of treatment remains unclear. Despite an increase in TFST demonstrated for olaparib and niraparib, the benefit of continuing treatment beyond progression has not been demonstrated conclusively to date. | III | A | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |
| Recommendation 20.5: PROs and HRQoL should be integrated into the decision-making and the evaluation of treatment efficacy in all patients with recurrent ovarian cancer. | V | A | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |
| Recommendation 20.6: follow-up of QoL and symptoms should be integrated into routine practice. | V | A | Yes: 100% (34) No: 0% (0) Abstain: 0% (0) |

CA-125, cancer antigen 125; CAP, College of American Pathologists; cfDNA, circulating cell-free DNA; CRS, chemotherapy response score; CT, computed tomography; ESGO, European Society of Gynaecological Oncology; EMA, European Medicines Agency; EOC, epithelial ovarian cancer; ER, oestrogen receptor; FIGO, International Federation of Obstetrics and Gynaecology; FSS, fertility-sparing surgery; GCIG, Gynaecological Cancer InterGroup; HE4, human epididymis protein 4; HGSC, high-grade serous carcinoma; HIPEC, hyperthermic intraperitoneal chemotherapy; HR, homologous recombination; HRQoL, health-related quality of life; ICCR, International Collaboration on Cancer Reporting; IDS, interval debulking surgery; i.p., intraperitoneal; LGSC, low-grade serous carcinoma; LN, lymph node; MBO, malignant bowel obstruction; mBOT, mucinous BOT; MRI, magnetic resonance imaging; OS, overall survival; PARP, poly(adenosine diphosphate-ribose) polymerase; PET, positron emission tomography; PFS, progression-free survival; PLD, PEGylated liposomal doxorubicin; PRO, patient-reported outcome; QoL, quality of life; sBOT, serous BOT; SEE-FIM, Sectioning and Extensively Examining the FIMbriated End; STIC, serous tubal intraepithelial carcinoma; TFST, time to first subsequent therapy; WG, working group; WHO, World Health Organization; WT1, wild-type 1.

References

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