**Table S1: Summary of recommendations**

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| **Guidelines statement** | **LoE** | **GoR** | **Consensus** |
| **1. Which surveillance should be used for asymptomatic women?**  **Recommendations:** |  |  |  |
| 1.1 There is no evidence for endometrial cancer screening in the general population | II | A | 100% yes (37 voters) |
| 1.2 Unopposed oestrogen treatment should not be started or should be discontinued in women with a uterus *in situ* | III | A | 100% yes (37 voters) |
| 1.3 Routine surveillance in asymptomatic women with obesity, PCOS, diabetes mellitus, infertility, nulliparity or late menopause is not recommended | III | B | 100% yes (37 voters) |
| 1.4 For women with AGCT, if hysterectomy has not been performed, endometrial sampling is recommended. If this shows no evidence of (pre)malignancy, no further screening for endometrial malignancies is required | IV | B | 100% yes (37 voters) |
| 1.5 In patients with epithelial ovarian cancer undergoing fertility-sparing treatment, endometrial sampling is recommended at the time of diagnosis | IV | B | 100% yes (37 voters) |
| 1.6 Routine screening for endometrial cancer in asymptomatic tamoxifen users is not recommended | III | B | 94.6% (35) yes, 5.4% (2) abstain (37 voters) |
| 1.7 Surveillance of the endometrium by gynaecological examination, transvaginal ultrasound and aspiration biopsy starting from the age of 35 years (annually until hysterectomy) should be offered to all LS mutation carriers | IV | B | 97.3% (36) yes, 2.7% (1) abstain (37 voters) |
| 1.8 Prophylactic surgery (hysterectomy and bilateral salpingo-oophorectomy), preferably using a minimally invasive approach, should be discussed at the age of 40 as an option for LS mutation carriers to prevent endometrial and ovarian cancer. All pros and cons of prophylactic surgery must be discussed | IV | B | 100% yes (37 voters) |
| **2. What work-up and management scheme should be undertaken for fertility-preserving therapy in patients with AH/EIN and grade 1 EEC?**  **Recommendations:** |  |  |  |
| 2.1 Patients with AH/EIN or grade 1 EEC requesting fertility-preserving therapy must be referred to specialised centres | V | A | 100% yes (37 voters) |
| 2.2 In these patients, D&C with or without hysteroscopy must be performed | IV | A | 97.3% (36) yes, 2.7% (1) abstain (37 voters) |
| 2.3 AH/EIN or grade 1 EEC must be confirmed/diagnosed by a specialist gynecopathologist | IV | A | 100% yes (37 voters) |
| 2.4 Pelvic MRI should be performed to exclude overt myometrial invasion and adnexal involvement. Expert ultrasound can be considered as an alternative | III | B | 100% yes (37 voters) |
| 2.5 Patients must be informed that fertility-sparing treatment is a non-standard treatment and the pros and cons must be discussed. Patients should be willing to accept close follow-up and be informed of the need for future hysterectomy | V | A | 97.3% (36) yes, 2.7% (1) abstain (37 voters) |
| 2.6 For patients undergoing fertility-preserving therapy, MPA (400-600 mg/day) or MA (160-320 mg/day) is the recommended treatment. However, treatment with LNG-IUD with or without GnRH analogues can also be considered | IV | B | 100% yes (37 voters) |
| 2.7 In order to assess response, D&C, hysteroscopy and imaging at 6 months must be performed. If no response is achieved after 6 months, standard surgical treatment should be performed | IV | B | 100% yes (37 voters) |
| 2.8 In case of complete response, conception must be encouraged and referral to a fertility clinic is recommended | IV | B | 100% yes (37 voters) |
| 2.9 Maintenance treatment should be considered in responders who wish to delay pregnancy | IV | B | 100% yes (37 voters) |
| 2.10 Patients not undergoing hysterectomy should be re-evaluated clinically every 6 months | IV | B | 97.3% (36) yes, 2.7% (1) abstain (37 voters) |
| 2.11 After completion of childbearing, a hysterectomy and salpingo-oophorectomy should be recommended. The preservation of the ovaries can be considered depending on age and genetic risk factors | IV | B | 100% yes (37 voters) |
| **3. Which (molecular) markers can help distinguish endometrial (pre)cancers from mimics?**  **Recommendations:** |  |  |  |
| 3.1 In cases of uncertainty, low threshold referral to a specialised gynaecopathologist is recommended | V | A | 100% yes (37 voters) |
| 3.2 PTEN and PAX-2 by IHC is recommended to distinguish AH/EIN from benign mimics. Other markers that can be used in this context are MLH1 and ARID1a by IHC | IV | B | 100% yes (37 voters) |
| 3.3 IHC is not recommended to distinguish APA from AH/EIN | V | B | 100% yes (37 voters) |
| 3.4 p53 by IHC is recommended to distinguish SEIC from its mimics | IV | A | 100% yes (37 voters) |
| 3.5 A panel of markers must be used in cases where endocervical cancer is suspected. This panel should include at least ER, Vimentin, CEA and P16 by IHC, and needs to be assessed in the histologic and clinical context. In addition, HPV analysis can be considered | IV | B | 100% yes (37 voters) |
| 3.6 WT-1 by IHC is the recommended marker to determine the origin of serous cancer | IV | A | 100% yes (37 voters) |
| 3.7 Morphology (and not IHC) should be used to distinguish AH/EIN from EEC | IV | A | 100% yes (37 voters) |
| **4. How does the medical condition influence surgical treatment?**  **Recommendations:** |  |  |  |
| 4.1 Mandatory work-up must include: Family history; general assessment and inventory of comorbidities; geriatric assessment, if appropriate; clinical examination, including pelvic examination; transvaginal or transrectal ultrasound; and complete pathology assessment (histotype and grade) of an endometrial biopsy or curettage specimen | V | A | 100% yes (37 voters) |
| 4.2 Extent of surgery should be adapted to the medical condition of the patient | V | A | 100% yes (37 voters) |
| 4.3 In clinical stage I, grade 1 and 2: At least one of the three following tools should be used to assess myometrial invasion if LND is considered: Expert ultrasound and/or MRI and/or intra-operative pathological examination | IV | A | 100% yes (37 voters) |
| 4.4 Other imaging methods (thoracic, abdominal and pelvic CT scan, MRI, PET scan or ultrasound) should be considered to assess ovarian, nodal, peritoneal or metastatic disease | IV | C | 94.6% (35) yes, 2.7% (1) abstain, 2.7% (1) no (37 voters) |
| 4.5 There is no evidence for the clinical usefulness of serum tumour markers, including CA 125 | IV | B | 91.9% (34) yes, 5.4% (2) abstain, 2.7% (1) no (37 voters) |
| 4.6 Standard surgery is total hysterectomy with bilateral salpingo-oophorectomy without vaginal cuff | IV | A | 100% yes (37 voters) |
| 4.7 Ovarian preservation can be considered in patients younger than 45 years old with grade 1 EEC with myometrial invasion <50% and no obvious ovarian or other extra-uterine disease | IV | B | 100% yes (37 voters) |
| 4.8 In cases of ovarian preservation, salpingectomy is recommended | IV | B | 100% yes (37 voters) |
| 4.9 Ovarian preservation is not recommended for patients with cancer family history involving ovarian cancer risk (e.g. BRCA mutation, LS, etc.). Genetic counselling/testing should be offered | IV | B | 100% yes (37 voters) |
| 4.10 Minimally invasive surgery is recommended in the surgical management of low- and intermediate-risk endometrial cancer | I | A | 100% yes (37 voters) |
| 4.11 Minimally invasive surgery can be considered in the management of high-risk endometrial cancer | IV | C | 100% yes (37 voters) |
| 4.12 Vaginal hysterectomy with salpingo-oophorectomy can be considered in patients unfit for the recommended surgery and in selected patients with low-risk endometrial cancer | IV | C | 100% yes (37 voters) |
| 4.13 In medically unfit patients, RT or hormone treatment can be considered | IV | C | 100% yes (37 voters) |
| **5. What are the indications for and to what extent is lymphadenectomy indicated in the surgical management of endometrial cancer?**  **Recommendations:** |  |  |  |
| 5.1 Peritoneal cytology is no longer considered mandatory for staging | IV | A | 100% yes (37 voters) |
| 5.2 If a lymphadenectomy is performed, systematic removal of pelvic and para-aortic nodes up to the level of the renal veins should be considered | IV | B | 91.9% (34) yes, 2.7% (1) abstain, 5.4% (2) no (37 voters) |
| 5.3 SLND is still experimental, but large series suggest that it is feasible. SLND increases the detection of lymph nodes with small metastases and isolated tumour cells; however, the importance of these findings is unclear | IV | D | 100% yes (37 voters) |
| 5.4 Lymphadenectomy is a staging procedure and allows tailoring of adjuvant therapy | III | B | 100% yes (37 voters) |
| 5.5 Patients with low-risk endometrioid carcinoma (grade 1 or 2 and superficial myometrial invasion <50%) have a low risk of lymph node involvement, and two RCTs did not show a survival benefit. Therefore, lymphadenectomy is not recommended for these patients | II | A | 100% yes (37 voters) |
| 5.6 For patients with intermediate risk (deep myometrial invasion >50% or grade 3 superficial myometrial invasion <50%), data have not shown a survival benefit. Lymphadenectomy can be considered for staging purposes in these patients | II | C | 100% yes (37 voters) |
| 5.7 For patients with high risk (grade 3 with deep myometrial invasion >50%), lymphadenectomy should be recommended | IV | B | 73.0% (27) yes, 8.1% (3) abstain, 18.9% (7) no (37 voters) |
| 5.8 Lymphadenectomy to complete staging could be considered in previously incompletely operated high-risk patients in order to tailor adjuvant therapy | V | C | 100% yes (37 voters) |
| **6. How radical should the surgery be in different stages and pathological subtypes of endometrial cancer?**  **Recommendations:** |  |  |  |
| 6.1 Radical hysterectomy is not recommended for the management of stage II endometrial cancer | IV | B | 91.9% (34) yes, 8.1% (3) abstain (37 voters) |
| 6.2 Modified (type B) or type A radical hysterectomy should be considered only if required for obtaining free margins | IV | B | 100% yes (37 voters) |
| 6.3 Lymphadenectomy is recommended for clinical or intra-operative stage II endometrial cancer | IV | B | 97.3% (36) yes, 2.7% (1) abstain (37 voters) |
| 6.4 Complete macroscopic cytoreduction and comprehensive staging is recommended in advanced endometrial cancer | IV | A | 100% yes (37 voters) |
| 6.5 Multimodality management should be considered for the treatment of advanced endometrial cancer when surgery may significantly impair vaginal function | IV | B | 97.3% (36) yes, 2.7% (1) abstain (37 voters) |
| 6.6 In non-EEC (apparent stage I), lymphadenectomy is recommended | IV | B | 100% yes (37 voters) |
| 6.7 Staging omentectomy is not mandatory in clear-cell or undifferentiated endometrial carcinoma and carcinosarcoma | IV | C | 100% yes (37 voters) |
| 6.8 Staging omentectomy should be considered in serous carcinoma | IV | C | 94.6% (35) yes, 5.4% (2) abstain (37 voters) |
| **7. What is the current best definition of risk groups for adjuvant therapy?**  **Recommendations:** |  |  |  |
| **Low:** Stage I endometrioid, grade 1-2, <50% myometrial invasion, LVSI negative | I |  |  |
| **Intermediate:** Stage I endometrioid, grade 1-2, ≥50% myometrial invasion, LVSI negative | I |  |  |
| **High-intermediate:** |  |  |  |
| * Stage I endometrioid, grade 3, <50% myometrial invasion, regardless of LVSI status | I |  |  |
| * Stage I endometrioid, grade 1-2, LVSI unequivocally positive, regardless of depth of invasion | II |  |  |
| **High:** |  |  |  |
| * Stage I endometrioid, grade 3, ≥50% myometrial invasion, regardless of LVSI status | I |  |  |
| * Stage II | I |  |  |
| * Stage III endometrioid, no residual disease | I |  |  |
| * Non endometrioid (serous or clear-cell or undifferentiated carcinoma, or carcinosarcoma) | I |  |  |
| **Advanced:** Stage III residual disease and stage IVA | I |  |  |
| **Metastatic:** Stage IVB | I |  |  |
| **8. What are the best evidence-based adjuvant treatment strategies for patients with low- and intermediate-risk endometrial cancer?**  **Recommendations:** |  |  |  |
| 8.1 In patients with low-risk endometrial cancer (stage I endometrioid, grade 1-2, <50% myometrial invasion, LVSI negative), no adjuvant treatment is recommended | I | A | 100% yes (37 voters) |
| 8.2 In patients with intermediate-risk endometrial cancer (stage I endometrioid, grade 1-2, ≥50% myometrial invasion, LVSI negative): |  |  | 100% yes (37 voters) |
| 1: Adjuvant brachytherapy is recommended to decrease vaginal recurrence | I | B |  |
| 2: No adjuvant treatment is an option, especially for patients aged <60 years | II | C |  |
| 8.3 In patients with high-intermediate-risk endometrial cancer (stage I endometrioid, grade 3, <50% myometrial invasion, regardless of LVSI status; or stage I endometrioid, grade 1-2, LVSI unequivocally positive, regardless of depth of invasion): |  |  |  |
| 1: Surgical nodal staging performed, node negative: |  |  | 100% yes (37 voters) |
| A. Adjuvant brachytherapy is recommended to decrease vaginal recurrence | III | B |  |
| B. No adjuvant therapy is an option | III | C |  |
| 2: No surgical nodal staging: |  |  | 100% yes (37 voters) |
| A. Adjuvant EBRT recommended for LVSI unequivocally positive to decrease pelvic recurrence | III | B |  |
| B. Adjuvant brachytherapy alone is recommended for grade 3 and LVSI negative to decrease vaginal recurrence | III | B |  |
| 3: Systemic therapy is of uncertain benefit; clinical studies are encouraged | III | C | 94.6% (35) yes, 5.4% (2) abstain (37 voters) |
| **9. What are the best evidence-based adjuvant treatment strategies for patients with high-risk endometrial cancer?**  **Recommendations:** |  |  |  |
| 9.1 In patients with high-risk endometrial cancer (stage I endometrioid, grade 3, ≥50% myometrial invasion, regardless of LVSI status): |  |  |  |
| 1: Surgical nodal staging performed, node negative: |  |  | 100% yes (37 voters) |
| A. Adjuvant EBRT with limited fields should be considered to decrease locoregional recurrence | I | B |  |
| B. Adjuvant brachytherapy may be considered as an alternative to decrease vaginal recurrence | III | B |  |
| C. Adjuvant systemic therapy is under investigation | II | C |  |
| 2: No surgical nodal staging: |  |  | 100% yes (37 voters) |
| A. Adjuvant EBRT is generally recommended for pelvic control and relapse-free survival | III | B |  |
| B. Sequential adjuvant chemotherapy may be considered to improve PFS and CSS | II | C |  |
| C. There is more evidence to support giving chemotherapy and EBRT in combination rather than either treatment modality alone | II | B |  |
| 9.2 In patients with high-risk, stage II endometrial cancer: |  |  |  |
| 1: Simple hysterectomy, surgical nodal staging performed, node negative: |  |  | 97.3% (36) yes, 2.7% (1) abstain (37 voters) |
| A. Grade 1-2, LVSI negative: Recommend vaginal brachytherapy to improve local control | III | B |  |
| B. Grade 3 or LVSI unequivocally positive: |  |  |  |
| i. Recommend limited field EBRT | III | B |  |
| ii. Consider brachytherapy boost | IV | C |  |
| iii. Chemotherapy is under investigation | III | C |  |
| 2: Simple hysterectomy, no surgical nodal staging: |  |  | 100% yes (37 voters |
| A. EBRT is recommended | III | B |  |
| B. Consider brachytherapy boost | IV | C |  |
| C. Grade 3 or LVSI unequivocally positive: Sequential adjuvant chemotherapy should be considered | III | B |  |
| 9.3 In patients with high-risk, stage III endometrial cancer and no residual disease: |  |  | 94.6% (35) yes, 5.4% (2) abstain (37 voters) |
| 1: EBRT is recommended to: |  |  |  |
| A. Decrease pelvic recurrence | I | B |  |
| B. Improve PFS | I | B |  |
| C. Improve survival | IV | B |  |
| 2: Chemotherapy is recommended to improve PFS and CSS | II | B |  |
| 3: There is more evidence to give chemotherapy and EBRT in combination than either alone in stage III disease: | II | B |  |
| A. IIIA: Chemotherapy AND EBRT to be considered |  |  |  |
| B. IIIB: Chemotherapy AND EBRT to be considered |  |  |  |
| C. IIIC1: Chemotherapy AND EBRT to be considered |  |  |  |
| D. IIIC2: Chemotherapy AND extended field EBRT to be considered |  |  |  |
| 9.4 In patients with high-risk, non-endometrioid cancers: |  |  |  |
| 1: Serous and clear cell after comprehensive staging: |  |  | 100% yes (37 voters) |
| A. Consider chemotherapy; clinical trials are encouraged | III | B |  |
| B. Stage IA, LVSI negative: Consider vaginal brachytherapy only without chemotherapy | IV | C |  |
| C. Stage ≥IB: EBRT may be considered in addition to chemotherapy, especially for node-positive disease | III | C |  |
| 2: Carcinosarcoma and undifferentiated tumours: |  |  | 94.6% (35) yes, 5.4% (2) abstain (37 voters) |
| A. Chemotherapy is recommended | II | B |  |
| B. Consider EBRT; clinical trials are encouraged | III | C |  |
| **10. Does surgery or RT have a role in advanced or recurrent endometrial cancer?**  **Recommendations:** |  |  |  |
| 10.1 For patients with advanced or recurrent disease, surgery is recommended only if optimal cytoreduction (no residual disease) can be achieved. In selected cases, palliative surgery is recommended to alleviate specific symptoms | IV | C | 100% yes (37 voters) |
| 10.2 Exenteration can be considered in selected patients with locally advanced tumours, and for isolated central local relapse after radiation, if clear margins are expected | IV | C | 100% yes (37 voters) |
| 10.3 Complete resection of distant oligometastases and pelvic or retroperitoneal lymph node relapse can be considered if technically possible according to localisation of disease | V | C | 100% yes (37 voters) |
| 10.4 Histological type should not influence the decision whether or not to proceed with surgery | IV | B | 100% yes (37 voters) |
| 10.5 RT with curative intent is indicated in patients with isolated vaginal relapse after surgery | III | A | 100% yes (34 voters) |
| 10.6 For vaginal or pelvic node recurrence, chemotherapy with RT could be considered in patients with high-risk features for systemic relapse | IV | C | 97.1% (33) yes, 2.9% (1) abstain (34 voters) |
| 10.7 Use of systemic therapy or surgery before RT for vaginal or pelvic node recurrence could be considered in certain patients | V | C | 100% yes (34 voters) |
| 10.8 Re-irradiation could be considered in highly selected patients using specialised techniques | V | C | 100% yes (34 voters) |
| 10.9 RT is indicated for palliation of symptoms related to local recurrence or systemic disease | IV | A | 100% yes (34 voters) |
| 10.10 RT may be indicated for primary tumours that are unresectable, or where surgery cannot be performed or is contraindicated for medical reasons | IV | B | 100% yes (34 voters) |
| **11. What are the optimal systemic therapies for advanced/recurrent disease?**  **Recommendations:** |  |  |  |
| 11.1 Hormone therapy is indicated in advanced or recurrent EEC | II | A | 100% yes (34 voters) |
| 11.2 Hormone therapy is more likely to be effective in grade 1 or 2 endometrioid tumours | IV | B | 100% yes (34 voters) |
| 11.3 Hormone receptor status should be determined before hormone therapy is initiated, as it is more likely to be effective in patients with positive PgR and ER status | III | B | 97.1% (33) yes, 2.9% (1) abstain (34 voters) |
| 11.4 Biopsy of recurrent disease could be considered as there may be differences in hormone receptor status in the primary and metastatic tumour | III | C | 100% yes (34 voters) |
| 11.5 Hormone therapy is the preferred front-line systemic therapy for patients with hormone receptor positive tumours – grade 1 or 2 and without rapidly progressive disease | V | A | 100% yes (34 voters) |
| 11.6 Progestogens (e.g. MPA 200 mg or MA 160 mg) are generally recommended | III | A | 100% yes (34 voters) |
| 11.7 Other hormonal agents to consider after progestins include tamoxifen, fulvestrant and aromatase inhibitors | III | C | 100% yes (34 voters) |
| 11.8 The standard of care is six cycles of 3-weekly carboplatin and paclitaxel. This is based on the preliminary communication of a randomised trial showing similar efficacy and less toxicity compared with cisplatin/doxorubicin/paclitaxel | I | A | 100% yes (34 voters) |
| 11.9 There is no standard of care for second-line chemotherapy | V | C | 100% yes (34 voters) |
| **12. What are the most promising targeted agents and which study designs should be used to evaluate their clinical benefit?**  **Recommendations:** |  |  |  |
| 12.1 PI3K/PTEN/AKT/mTOR pathway, PTEN, RAS-MAPK, angiogenesis (especially FGFR2 and VEGF/VEGFR), ER/PgR and HRD/MSI are altered in endometrial cancer and their relevance should be studied in clinical trials with targeted agents | III | B | 100% yes (34 voters) |
| 12.2 Drugs targeting PI3K/mTOR pathway signalling and angiogenesis have shown modest activity but no agent has been approved for clinical use, and further biomarker-driven studies are warranted | III | A | 100% yes (34 voters) |
| 12.3 Clinical trial designs for new, targeted therapy: | V | A | 100% yes (34 voters) |
| 1: Basket studies with multiple cohorts related to histological subtypes and/or molecular alterations are considered a priority |  |  |  |
| 2: Biomarker-driven clinical trials with biopsy at entry and sequential biopsies in trials with molecular end points are recommended |  |  |  |
| 3: PFS or PFS at a defined time-point are the preferred primary end points for early phase trials |  |  |  |
| 4: OS is the preferred primary end point in phase III trials, unless crossover is planned or expected |  |  |  |

AGCT, adult granulosa cell tumours; AH, atypical hyperplasia; APA, atypical polypoid adenomyoma; CAH, complex atypical hyperplasia; CEA, carcinoembryonic antigen; CSS, cancer-specific survival; CT, computed tomography; D&C, dilation and curettage; EBRT, external beam radiation therapy; EEC, endometrioid endometrial cancer; EIN, endometrial intraepithelial neoplasia; ER, oestrogen receptor; FGFR2, fibroblast growth factor receptor-2; GnRH, gonadotropin-releasing hormone; GoR, grade of recommendation; HPV, human papillomavirus; HRD, homologous recombination deficiency; IHC, immunohistochemistry; LNG-IUD, levonorgestrel intrauterine device; LoE, level of evidence; LS, Lynch syndrome; LVSI, lymphovascular space invasion; MA, megestrol acetate; MPA, medroxyprogesterone acetate; MRI, magnetic resonance imaging; MSI, microsatellite instability; mTOR, mammalian target of rapamycin; OS, overall survival; PCOS, polycystic ovary syndrome; PET, positron emission tomography; PFS, progression-free survival; PgR, progesterone receptor; RT, radiotherapy; SEIC, serous endometrial intraepithelial carcinoma; SLN, sentinel lymph node; VEGFR, vascular endothelial growth factor receptor; WT-1, Wilms tumour 1 gene