

LIFE

Literature for ENYGO

Reviews covering publications from September 30, 2022 – March 31, 2023

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Dear Colleagues,

We present you LiFE 17, encompassing reviews of the most noteworthy articles across 28 topics in gynaecological oncology published between September 30, 2022, and March 31, 2023.

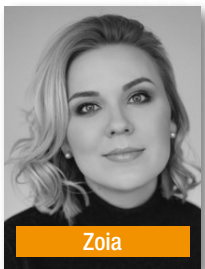
The LiFE Team warmly welcomes our two new LiFE contributors, Tibor Zwimpfer (Switzerland/Australia) and Monika Sobočan (Slovenia), expanding our team to 31 members from 20 countries worldwide. We express our gratitude to all ENYGO/ESGO members who use LiFE to enhance their knowledge in the field, and we extend our appreciation for the ongoing support from the *International Journal of Gynecological Cancer*.

We trust that you will find this Report both informative and beneficial for your daily practice. Please remember to share the report link with your colleagues and on social media. If you have an interest in joining the LiFE team, kindly email adminoffice@esgo.org.

ENYGO takes this opportunity to check the ESGO website to explore all possibilities the society provides you with.

Yours sincerely,
LiFE Editors

Zoia Razumova
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Medical treatment of primary ovarian cancer

Ilker Selçuk

A study by Pfisterer et al. evaluated the efficacy of extended use of bevacizumab in newly diagnosed stage IIB-IV epithelial ovarian cancer patients (AGO-OVAR 17). Patients were randomly assigned 1:1 to primary platinum-based chemotherapy with simultaneous bevacizumab (15mg/kg q3w) and maintenance for a duration of 15 (22 cycles, 464 patients) or 30 (44 cycles, 463 patients) months. Patient characteristics were well-balanced between the groups. On the other hand, BRCA mutation status was not known. Median progression-free survival (PFS) was 24.2 versus (vs) 26.0 months (m) with standard (15m) and extended use of bevacizumab (30m), respectively. The overall survival was not different among the groups, 54.3m and 60.0m, respectively, $p = 0.68$. Serious adverse events (AEs) were a slight increase for grade ≥ 3 hypertension (20% vs 25%) and proteinuria (2% vs 4%), but there were no significant differences. The rate of intestinal fistula and thromboembolic events were similar. Bevacizumab use for an extended period did not improve survival outcomes, and 15m of usage remains the standard. [1]

Copeland et al. (GOG-212) evaluated the role of single-agent taxane in newly diagnosed epithelial ovarian cancer patients with a complete clinical response after first-line platinum-based chemotherapy. In this three-arm study, 1:1:1, patients were distributed to surveillance (S, 387p), paclitaxel (P, 384p) 135mg/m² q4wx12m, or paclitaxel poliglumex (PP, 386p) 135mg/m² q4wx12m. The PFS was 13.4, 18.9, and 16.3m for S, P, and PP, respectively. Median OS was 58.3, 56.8, and 60.0m, respectively; not significantly different among the groups. Grade ≥ 3 sensory neuropathy was significantly more frequent in patients treated with maintenance taxane. In the 6m after treatment period, the deficits were significantly increased in patients using P or PP (more with PP). Maintenance of paclitaxel or paclitaxel poliglumex did not improve OS in patients with newly diagnosed ovarian cancer. However, the PPS period was improved by the taxane maintenance therapy. [2]

Gonzalez-Martin presented the second PFS results of olaparib plus bevacizumab maintenance therapy in newly diagnosed advanced high-grade epithelial

ovarian cancer patients (PAOLA-1). Patients in response after first-line platinum-based chemotherapy with bevacizumab were enrolled randomly 2:1 to olaparib (300mg twice daily) or placebo up to 24m, and in addition, bevacizumab was administered to all patients up to 15m. After a median follow-up of 35.5 and 36.5m, respectively, the median second PFS was 36.5m vs 32.6m, for the olaparib+bevacizumab and placebo+bevacizumab groups, respectively, HR: 0.78, $p=0.0125$. As an important note, 27% ($n = 72$) of patients in the placebo plus bevacizumab group received PARP inhibitor as the first subsequent therapy; the maintenance olaparib plus bevacizumab provided a continuing significant improvement in PFS. [3]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Optimal treatment duration of bevacizumab as front-line therapy for advanced ovarian cancer: AGO-OVAR 17 BOOST/GINECO OV118/ENGOT Ov-15 open-label randomized Phase III Trial	Pfisterer J et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/36332161/
2	Phase III randomized trial of maintenance taxanes versus surveillance in women with advanced ovarian/tubal/peritoneal cancer: A Gynecologic Oncology Group O212:NRG Oncology Study	Copeland LJ et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/35759733/
3	Maintenance olaparib plus bevacizumab in patients with newly diagnosed advanced high-grade ovarian cancer: Main analysis of second progression-free survival in the phase III PAOLA-1/ENGOT-ov25 trial	Gonzalez-Martin A et al.	Eur J Cancer	https://pubmed.ncbi.nlm.nih.gov/36067615/



Medical treatment of recurrent ovarian cancer

Seda Şahin Aker

Cueva et al. reported the effectiveness and safety of niraparib for platinum-sensitive recurrent ovarian cancer (OC) patients. Three hundred sixteen patients were enrolled in this retrospective study. The median niraparib duration was 7.8 months (0.2–39.4) while in the ISD group, the median treatment was higher (8.3 vs 5.9 months). Median progression-free survival (PFS) was 8.6 months. One- and two-year overall survival (OS) rates were 86% and 65%. Adverse events (AEs) were reported in 88% of patients, the most common being thrombocytopenia, asthenia/fatigue, and anaemia. Dose interruptions or reductions were less frequent in the ISD group. The strength of the study was its large sample size, while the main limitations concerned the retrospective design and the reported proportion of incomplete data. [1]

The INOVATYON/ ENGOT-ov5 study evaluated the efficacy of trabectedin/PLD (TP) on the platinum-free interval (TFlp) and OS in the recurrent OC. In all, 617 patients were enrolled in the study. Patients with a TFlp of six–12 months were randomised to receive carboplatin/PLD (CP), or TP followed by platinum therapy at relapse. The median age was 64 years, and the median TFlp was 8.3 months. The median OS was 21.4 for CP versus 21.9 months for TP (p = 0.197). Median PFS was significantly higher in the CP group (9.0 vs 7.5 months, p = 0.003). The

common AEs were neutropenia, gastrointestinal and hepatic dysfunction. Grade 3–5 AEs occurred mostly in the TP group (37.1% vs 69.7%). The limitation of this study was the absence of quality-of-life assessment and information on BRCA status. [2]

Zhang et al. performed a systematic review and meta-analysis to clarify the efficacy and side effects of pazopanib combined with chemotherapy (CT) in treating OC. Five clinical trials and 518 patients were included in this study. Two hundred eighty-two patients were in the pazopanib combined with the CT group, while 236 were in the CT-alone group. Pazopanib plus CT significantly improved the overall response rate (ORR) (p = 0.017) but did not exhibit an advantage in disease control rate (DCR) (p = 0.075). AEs occurred mostly in the combination group. [3]

The GEICO study analysed the efficacy and safety of rucaparib in the treatment of OC. Fifty-one patients were enrolled in the study, with 18 in the maintenance group (MG) and 33 in the treatment group (TG). Median PFS was 10.6 months in the PS group and 2.2 months in the PR group. In the MG, AEs occurred in 89% of patients versus 85% in TG. In MG, the most common AEs were nausea, fatigue, and ALT/AST increase; in TG, anaemia and thrombocyto-

penia were the most common. The weakness of this study was the heterogeneity of the population and the differences in BRCA testing. The main strength of the study was the large population. [4]

Yang et al. reported the efficacy and safety of apatinib plus chemotherapy in patients with recurrent PROC. One hundred and five patients were enrolled in the study. Fifty-four patients received CT, and 51 patients received apatinib plus CT. The median PFS and OS were significantly different, specifically 5.5 (3.4–7.6) and 21.4 (16.2–26.6) months in the combination group vs 3.8 (3.0–4.6) and 14.8 (11.9–17.7) months in the CT group. (PFS, p = 0.008; OS, p = 0.012). The objective response rate was 37.3% in the combination group vs 14.8% (p = 0.009), and the disease control rate was 80.4% in the combination group vs 61.1% in the CT group (p = 0.030). The main limitation of this study was the single-centre, retrospective character. [5]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Real-world safety and effectiveness of maintenance niraparib for platinum-sensitive recurrent ovarian cancer: A GEICO retrospective observational study within the Spanish expanded-access programme	Cueva JF et al.	European Journal of Cancer	https://pubmed.ncbi.nlm.nih.gov/36706655/
2	INOVATYON/ ENGOT-ov5 study: Randomized phase III international study comparing trabectedin/pegylated liposomal doxorubicin (PLD) followed by platinum at progression vs carboplatin/PLD in patients with recurrent ovarian cancer progressing within 6-12 months after last platinum line	Colombo N et al.	British journal of cancer	https://pubmed.ncbi.nlm.nih.gov/36759720/
3	The efficacy and safety of pazopanib plus chemotherapy in treating recurrent or persistent ovarian cancer: A systematic review and meta-analysis	Zhang Y et al.	Am J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/36877187/
4	Rucaparib in recurrent ovarian cancer: real-world experience from the rucaparib early access programme in Spain – A GEICO study	Yubero A et al.	BMC Cancer	https://pubmed.ncbi.nlm.nih.gov/36348385/
5	Efficacy and safety of apatinib combined with liposomal doxorubicin or paclitaxel versus liposomal doxorubicin or paclitaxel monotherapy in patients with recurrent platinum-resistant ovarian cancer	Yang H et al.	J Obstet Gynaecol Res	https://pubmed.ncbi.nlm.nih.gov/36988159/



Surgical treatment of primary and recurrent ovarian cancer

Ilker Kahramanoglu and Patriciu Achimas-Cadariu

Lee et al. performed a large, retrospective study to assess the utility of diagnostic laparoscopy for selecting primary debulking surgery (PDS). Six hundred and fourteen patients were analysed. In group 1, 192 patients had treatment decisions guided by laparoscopic findings, while 422 patients in group 2 relied on computed tomography results. Group 1 had a lower suboptimal cytoreduction rate after PDS compared to Group 2 (2% vs 11.1%, respectively). Additionally, Group 1 had fewer non-high-grade serous carcinoma patients undergoing neoadjuvant chemotherapy (9.1% in Group 1 and 15.4% in Group 2). Group 1 also experienced lower postoperative morbidity (5.2% vs 10.4%) without impacting overall survival. The retrospective design and selection bias because of the lack of an activated protocol-based triage are the main limitations of this study. [1]

In a multicentre, retrospective cohort study, Wohrer et al. compared the outcomes of PDS and interval debulking surgery (IDS) in stage III–IV epithelial ovarian cancer. Data from 513 patients were analysed, and 167 pairs were formed using propensity score. The study found no significant difference in overall

survival between groups (HR = 0.38, p = 0.32). Similarly, recurrence-free survival was comparable with a median of 26 months in both groups. The maximal cytoreduction rate was also similar (85% in PDS and 81.4% in IDS groups, p = 0.76). The PDS group had significantly higher rates of postoperative morbidity, such as gastrointestinal tract resections, stoma creation, and longer hospital stays. Its retrospective nature was the main limitation of this study. [2]

A retrospective single-institution study analysed 112 patients with platinum-sensitive relapsed (PSR) ovarian cancer with regards to the value of positron emission tomography/computed tomography (PET/CT) in predicting no residual disease (NRD) after secondary cytoreductive surgery (SCS), in comparison with currently established models (MSK criteria, iMODEL, AGO score). Patients with ≤2 lesions by PET/CT were more likely to have NRD (OR = 4.36; 95% CI = 1.07–17.7; p = 0.039), with 48 (92.3%) having achieved NRD, with an accuracy of 81.2% for this threshold. In comparison, NRD was achieved after fulfilling the MSK criteria, iMODEL and AGO Score in 89.1%, 88.1%, and 85.9%, respectively.

Adding PET/CT to the MSK/iMODEL/AGO score increased the NRD rates but lowered their accuracy. The retrospective design and small number of cases were the main limitations of this study. [3]

A single institution study retrospectively investigated the impact of BRCA1/2 mutational status on survival outcomes in 262 patients with PSR epithelial ovarian cancer treated between 2007 and 2021. In all, 34.7% of patients were germline or somatic BRCA1/2 mutation carriers, and, in comparison with the wild-type group, no significant differences were observed regarding the rate of secondary CRS and maintenance therapy. Additionally, no differences in PFS (p = 0.120) or OS (p = 0.400) were noted between the two groups. Subgroup analysis showed that PFS was not influenced by BRCA status in patients that did (p = 0.074) or did not receive (p = 0.222) SCS. Similarly, PFS was not influenced by BRCA status in patients that received bevacizumab maintenance (p = 0.992). The main limitations were the small sample size and lack of analysis of survival outcomes. [4]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Role of diagnostic laparoscopy in deciding primary treatment in advanced-stage ovarian cancer	Lee YJ et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36562129/
2	Prognostic impact of cytoreductive surgery conducted with primary intent, versus cytoreductive surgery after neoadjuvant chemotherapy, in the management of patients with advanced epithelial ovarian cancers: a multicentre, propensity score-matched study from the FRANCOGYN group	Wohrer H et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/37165717/
3	The value of PET/CT for cytoreductive surgery selection in recurrent ovarian carcinoma	Nunes RL et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36731894/
4	Effect of BRCA1/2 mutational status on survival outcomes according to secondary cytoreductive surgery and maintenance therapy in platinum-sensitive relapsed ovarian cancer: A real-world evidence study	Kim SI et al.	Cancer Res Treat	https://pubmed.ncbi.nlm.nih.gov/35879854/



Borderline ovarian tumours

Anton Ilin

Some types of cancers have common ethological factors, for example, hereditary, viral, or environmental. Therefore, the risk of second malignancy could be elevated in certain cases. Understanding such hazard risks may help to refine the screening algorithm. Hannibal et al. conducted the biggest nationwide cohort study evaluating the relevance between borderline ovarian tumours (BOTs) and non-ovarian cancers. Five thousand patients were included (2,506 serous and 2,493 mucinous) with up to 41 years of follow-up. It was found to have no association with breast or colorectal cancer. Simultaneously, when compared to the general female population rates, women diagnosed with serous

BOTs exhibited higher rates, specifically in malignant melanoma (SIR = 1.9; 95% CI: 1.3-2.6), thyroid cancer (SIR = 3.0; 95% CI: 1.4-5.4), and myeloid leukaemia (SIR = 3.2; 95% CI: 1.5-5.8). Similarly, those with mucinous BOTs experienced increased rates of lung cancer (SIR = 1.7; 95% CI: 1.3-2.1), pancreatic cancer (SIR = 1.9; 95% CI: 1.2-2.9), and myeloid leukaemia (SIR = 2.3; 95% CI: 0.9-4.7). [1]

Current evidence regarding fertility-sparing surgery for young patients with BOTs allows the saving of the uterus without negative oncological outcomes. For postmenopausal patients, we may offer hysterectomy in addition to bilateral salpingo-oophorectomy and omentectomy. In the study performed by

Raimondo et al., 98 patients participated, with 44 assigned to hysterectomy and 54 to no hysterectomy. Analysis revealed no significant differences in the five- and ten-year disease-free survival and overall survival rates between both groups (97.7% (95% CI: 84.9–99.7), 92.3% (95% CI: 69.7–98.2), and 86.8% (95% CI: 74.3–93.5) 86.8% (95% CI: 74.3–93.5), respectively). These findings suggest that hysterectomy does not influence survival rates in patients with BOT and may not be needed for consideration at the surgical staging. [2]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Risk of nonovarian cancer in a nationwide-based study of nearly 5000 women with borderline ovarian tumors in Denmark	Hannibal CG et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/36366853/
2	The impact of hysterectomy on oncological outcomes in postmenopausal patients with borderline ovarian tumors: A multicenter retrospective study	Raimondo D et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36387131/



Treatment of ovarian sex cord stromal and germ cell tumours

Paul Kubelac

An analysis of the AGO study group CORSETT database included 262 malignant sex cord-stromal cell tumours (SCST) treated between 2000 and 2014 with mixed input of retro- and prospective data. Over 80% of cases were stage I disease and adjuvant chemotherapy was offered to 18.7% of granulosa-cell tumour (GCT) and 8.3% of Sertoli-Leydig cell tumour (SLCT). With a median follow-up of 78.2 months, 46% of SCST relapsed treated mainly with secondary debulking surgery (>90%). The study showed that most SCST patients had laparoscopic surgery for stage I disease and lymph-node staging was usually omitted in this cohort, given the routine clinical practice in that period. Negative prognostic factors for disease recurrence were advanced FIGO stage, lymph node involvement and intra-operative capsule rupture ($p < 0.05$). Adjuvant chemotherapy did not influence relapse and, despite high recurrence rates, median PFS was 80.4 months in all GCT and was not reached in SLCT patients. Median overall survival was not reached in both groups. Study limitations include unknown accuracy of the database given clinical data input by different

investigators, patients lost to follow-up, and a very low misclassification rate of tumour samples (5.8%), as well as lack of differentiation between juvenile and adult GCT. [1]

A study by Liu et al. based on previous work sought to validate the modified versions of the male International Germ Cell Cancer Collaborative Group prognostic model (mIGCCCG) in a new cohort of female patients with germ cell tumours (GCTs). The combined cohort included 183 female patients with GCTs seen at a large single institution between 1990–2020, with similar characteristics between the original ($n = 93$) and final validation cohort ($n = 90$).

In a multivariate analysis, higher stage, older age, non-dysgerminoma histology were associated with worse PFS and OS ($p < 0.05$). The 162 patients who received chemotherapy, preoperative and pre-chemotherapy mIGCCCG models were significantly correlated with PFS and OS ($p < 0.001$ for all groups; higher risk patients had worse outcomes). The mIGCCCG risk model also suggested added benefit over conventional risk factors and the authors

concluded that the female-specific mIGCCCG classification system effectively stratifies patients and should be incorporated into clinical trials and clinical decision-making. Study limitations include its retrospective design, single institution data, incomplete tumour marker data for the 16% of patients in the pre-chemotherapy group and 34% of patients in the preoperative group, sample size, and the fact it does not address the value of intensification of chemotherapy in intermediate- and poor-risk patients or de-escalation for good risk patients. [2]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Treatment and survival of patients with malignant ovarian sex cord-stromal cell tumours: An analysis of the Arbeitsgemeinschaft für Gynäkologische Onkologie (AGO) study group CORSETT database	Klar M et al.	Journal of Surgical Oncology	https://pubmed.ncbi.nlm.nih.gov/36975108
2	Predicting outcomes in female germ cell tumors using a modified International Germ Cell Cancer Collaborative Group classification system to guide management	Liu YL et al.	Gynecologic Oncology	https://pubmed.ncbi.nlm.nih.gov/36669327



Emerging molecular-targeted therapies or early preclinical trials in ovarian cancer

Richárd Tóth

Davidson et al. conducted the TRIO-15 trial, an investigator-initiated, multi-centre, open-label, phase II trial to determine the safety and efficacy of ganitumab in recurrent platinum-sensitive ovarian cancer. Ganitumab is a fully human monoclonal antibody against the insulin-like growth factor 1 receptor (IGF1R), inhibiting binding of insulin-like growth factor 1 and 2 (IGF 1 and 2). The IGF pathway, which is important in ovarian follicular growth, is regulated by three ligands, three receptors, and six binding proteins. In this study, ganitumab was investigated as single agent in patients with non-measurable recurrence in imaging studies and/or biochemical recurrence confirmed by elevated CA125 levels. Patients older than 18 with relapsed epithelial ovarian cancer more than six months after completion of prior platinum-based chemotherapy were enrolled

Imaging studies were performed in every nine weeks and physical exams with CA125 determination were performed on day 1 of every cycle to assess progression. The primary endpoint of the study was objective response rate (ORR); secondary endpoints were clinical benefit rate (CBR), progress-free (PFS), and

overall survival (OS). ORR was defined as percentage of patients who achieved complete or partial response, while CBR was ORR and the group of patients who had stable disease for at least 24 months. Molecular analysis was performed to assess levels of circulating IGF1, IGFBP3 (IGF binding protein 3), and GH (growth hormone). Among the 61 participants, the median age was 62 and a majority had ECOG 0 status.

In all, 68.9% of the patients had papillary serous while 73.8% had poorly differentiated histology. All patients received one prior line of chemotherapy. Median relapse-free interval was 19 months. BRCA data was not collected. ORR was seen in five (8.2%) patients, of whom three had partial, two had complete response. Clinical benefit was found in 49 (80.3%) patients. The median PFS was 2.0 months and median OS was 21 months. The most common adverse events were fatigue (36.1%), hypertension (34.4%), and hypersensitivity (8.2%). Grade 1/2 hyperglycaemia, anaemia, neutropenia, and thrombocytopenia were observed in 30.4%, 19.7%, 18.0%, and 14.8% of the cases, respectively. Dose reduction was needed in four patients.

IGF1R blockade did not elevate the levels of GH, IGF1, or IGFBP3. There was no difference between biomarker levels of responders and non-responders. No correlation was found between changes in CA125 levels and intratumoural IGF1, IGF2, IGF1R, IGF2R, and IGFBP3 expression. Post-hoc additional molecular analysis was performed in one case with disease stabilisation for 12 months. In this patient, investigators found BRCA 1 mutation in exon 11 and an amplification in the IGFR1 coding region, suggesting its role in therapy response, although it is not clear which contributes to this result.

Ganitumab did not demonstrate significant activity in this setting. The authors suggest that the use of one highly selective ligand might be insufficient to block such a complex pathway. In conclusion, ganitumab did not meet its primary endpoint and the authors do not suggest further investigation in unselected groups of ovarian cancer patients. [1]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Results of TRIO-15, a multicenter, open-label, phase II study of the efficacy and safety of ganitumab in patients with recurrent platinum-sensitive ovarian cancer	Davidson TM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36709663/



Medical (chemo and radiotherapy) treatment of primary uterine cancer

Radwa Hablase

Two phase III, randomised, double-blinded, placebo-controlled trials investigated the safety and efficacy of adding immune checkpoint inhibitors to first-line standard chemotherapy for primary advanced, metastatic, and recurrent endometrial cancers. [1, 2]

In the Ruby Trial, 495 patients were randomised to dostarlimab + carboplatin-paclitaxel or placebo + carboplatin-paclitaxel. Among them, 118 were mismatch repair-deficient, microsatellite instability-high tumours (dMMR/MSI-H) and had a median follow-up of 24.8 months. Progression-free survival (PFS), stratified by MMR status in the dostarlimab arm was 61.4% (CI: 46.3–73.4) for dMMR/MSI-H, 28.4% (CI: 21.2–36.0) for proficient MMR (MMRp), and 36.1% (CI: 29.3–42.9) overall, compared to 15.7% (CI: 7.2–27.0), 18.8% (CI: 12.8–25.7), and 18.1% in the placebo group, respectively. The dostarlimab regimen demonstrated a 72% lower progression risk in dMMR-MSI-H tumours (HR 0.28; 95% CI: 0.16–0.50; $p < 0.001$) and a similar, albeit smaller, clinical benefit in patients without DNA repair deficiencies. The overall survival, despite not reaching a statistical significance, favoured combination treatment with 71.3% overall, 83.3% in dMMR/MSI-H, and 67.7% in MMRp, compared to 56%, 58.7%, and 55.1% in the placebo group, respectively. [1]

Eskander et al. excluded carcinosarcomas and randomly assigned 816 patients to pembrolizumab or placebo with paclitaxel plus carboplatin. The median follow-up was 12 months for the 225 dMMR patients and 7.9 months for MMRp group. The risk of disease progression or death was 70% lower in the dMMR arm with pembrolizumab regimen. In the dMMR group, PFS was 74% with pembrolizumab versus 38% with placebo (HR 0.30; 95% CI: 0.19–0.48; $p < 0.001$). For MMRp, pembrolizumab yielded a median PFS of 13.1 months, compared to 8.7 months with placebo (HR 0.54; 95% CI: 0.41–0.71; $p < 0.001$). [2]

Pembrolizumab and dostarlimab safety profiles were consistent with individual components of each regimen. Both trials saw early and sustained efficacy curve separation. Neither trial explored immune checkpoint inhibitors as first-line monotherapy, and the pembrolizumab trial had a short follow-up duration.

A phase II trial, MITO END-3, evaluated the combination of avelumab with standard first-line chemotherapy. One hundred twenty-five patients were included, with a median follow-up of 23.3 months. In the dMMR subgroup, the PFS at 24 months was 50% in the experimental group versus 13% in the standard arm. In the MMRp subgroup,

rates were 17% versus 21% in the experimental and standard arms, respectively. The authors concluded that survival benefits were MMR status driven. They acknowledged that focusing on a priori subgroup analysis rather than interpreting primary endpoint results is one of the trial's key limitations. [3]

Trabectedin's efficacy as second- or third-line chemotherapy for advanced ovarian or uterine carcinosarcomas was assessed in a phase II single-arm trial. Although the overall response rate was 11.9% lower than the prespecified $\geq 18.6\%$, the trial concluded that the drug confers modest clinical benefits in line with other available options in these settings. The trial lacked a comparator arm and included a small sample size. [4]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Dostarlimab for primary advanced or recurrent endometrial cancer	Mirza et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/36972026/
2	Pembrolizumab plus chemotherapy in advanced endometrial cancer	Eskander et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/36972022/
3	Carboplatin and paclitaxel plus avelumab compared with carboplatin and paclitaxel in advanced or recurrent endometrial cancer (MITO END-3): a multicentre, open-label, randomised, controlled, phase 2 trial	Pignata et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/37052965/
4	Efficacy and safety of trabectedin for the treatment of advanced uterine or ovarian carcinosarcoma: Results of a phase II multicenter clinical trial (MITO-26)	Lorusso et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36220670/



Medical (chemo and radiotherapy) treatment of recurrent uterine cancer

Stamatios Petousis

Oaknin et al. described the beneficial impact of dostarlimab in addition to standard chemotherapy in primary advanced or recurrent endometrial cancer patients. This was also a prospective RCT recruiting 494 patients to either dostarlimab or placebo addition to the standard chemotherapy schema of carboplatin and paclitaxel. At 24 months from randomisation they observed a 72% reduction in the risk of recurrence regarding the population of patients with mismatch repair-deficient (dMMR), microsatellite instability-high (MSI-H) tumours, while the relative reduction in the overall population was 36%, still statistically significant. The main objective of this study might be considered respectively with

the previous RCT the co-inclusion of both primary and recurrent patients. However, this was a breakthrough RCT demonstrating the beneficial impact of dostarlimab especially for dMMR, MSI-H tumours. More data about the outcomes of different patient subpopulations will be presented in the upcoming months. [1]

An interesting systematic review and meta-analysis was performed regarding the potential therapeutic role of progestins for advanced and recurrent endometrial cancer patients. Results from 26 studies with a total of 1,639 patients were included. The overall response rate was 30%, the clinical benefit rate

52%, while the response rate was significantly increased in progesterone-positive patients compared with progesterone-negative. Severe toxicity occurred only in 6.5%. The main limitation of the study was the fact that risk of bias was moderate or high for all included studies, while there was no study included with low risk of bias. [2]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Dostarlimab for primary advanced or recurrent endometrial cancer	Oaknin A et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/35064011/
2	The effect of progestin therapy in advanced and recurrent endometrial cancer: A systematic review and meta-analysis	van Weelden WJ et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/36264251/



Surgical treatment of primary and recurrent endometrial cancer

Houssein El Hajj

In their systematic review and meta-analysis, Raffone et al. aimed to identify predictive factors for failed mapping of sentinel lymph nodes in patients with endometrial cancer who underwent sentinel lymph node biopsy. The study analysed data from six studies involving 1,345 patients. The results indicated that several factors were associated with failed mapping of sentinel lymph nodes. These factors included a dose of indocyanine green less than 3 mL (OR 1.77, $p = 0.02$), advanced stage of cancer (FIGO stage III–IV) (OR 1.89, $p = 0.01$), presence of enlarged lymph nodes (OR 4.11, $p < 0.0001$), and lymph node involvement (OR 1.71, $p = 0.022$). The main strength of the study is the good quality of included studies. One of the limitations is differently defined surgeons' expertise among the studies. [1]

Two recent studies focused on lymphadenectomy (LND) in early-stage endometrial cancer patients and evaluated its impact on survival and recurrence.

Lay et al. retrospectively compared the survival outcomes of combined pelvic and para-aortic lymphadenectomy versus pelvic lymphadenectomy alone in FIGO stage I–II grade 3 endometrioid and non-endometrioid endometrial cancers. After a median follow-up of 45 months, they found no significant difference in recurrence-free survival (RFS) and overall survival (OS) between the two approaches. In multivariate analysis, certain prognostic factors were

associated with worse RFS, such as age ≥ 60 years (HR 2.20, $p = 0.006$) and LVSI (HR 2.79, $p < 0.001$), while non-endometrioid histology was associated with worse OS (HR 3.18, $p = 0.005$). Subgroup analysis did not demonstrate any beneficial effects of combined lymphadenectomy on survival outcomes. The strength of this study is the high number of included consecutive cases ($n = 804$). One of its limitations is the high percentage of patients with low-risk endometrial cancer (72.8%). [2].

On the other hand, Kim R. et al. assessed the clinical significance and extent of LND in intermediate- to high-risk early-stage endometrial cancer [3]. The study analysed a large cohort of 804 patients, of whom 82.5% underwent LND, and 62.3% underwent pelvic and para-aortic LND. After a median follow-up of 69.8 months, LVSI and LNM were independent risk factors for recurrence in the whole cohort (HR = 3.0, $p = 0.024$ and HR = 2.8, $p = 0.020$, respectively), however lymph nodes metastasis (LNM) rates varied significantly based on the risk group (1.2% in low-risk, 20.1% in intermediate-risk, and 30.0% in high-risk group). LNM was observed in both the pelvic and para-aortic regions, with similar rates below (11.1%) and above (12.5%) the inferior mesenteric artery (IMA). Importantly, on multivariate analysis, LNM was identified as an independent risk factor for recurrence in intermediate- to

high-risk endometrial cancer (HR 2.63, $p = 0.047$). Therefore, the study suggests that nodal assessment should include evaluation up to the infra-renal level, particularly for staging high-risk early-stage endometrial cancer. [3]

When comparing these two studies, Lay et al. did not observe a survival benefit with combined pelvic and para-aortic lymphadenectomy and implied that LND may not be necessary in specific cases, while Kim et al. highlighted the clinical significance of LNM as an independent risk factor for recurrence and emphasised the importance of comprehensive nodal assessment, particularly in high-risk patients. Neither study analysed molecular classification results and both might include possible bias due to retrospective design.

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No	Title	Authors	Journal	Link to abstract
1	Predictive factors of sentinel lymph node failed mapping in endometrial carcinoma patients: a systematic review and meta-analysis	Raffone A et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36914172/
2	Role of systematic lymphadenectomy in patients with intermediate to high-risk early stage endometrial cancer	Kim NR et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36562131/
3	Does para-aortic lymphadenectomy improve survival in pathologically diagnosed early-stage grade 3 endometrioid and non-endometrioid endometrial cancers? A retrospective cohort study in Korea and Taiwan	Lay IL et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35995599/



Uterine sarcoma

Marcin Bobiński

Schram et al. published results of a phase IIb clinical trial which aimed to evaluate the effectiveness of combination of avelumab and talazoparib in patients with pathogenic BRCA1/2 or ATM alterations, regardless of tumour type. The authors indicated the objective response (lasting more than 24 months) in all enrolled LMS cases. The results seem to be promising, although the main limitation is that this trial included only three cases of uterine leiomyosarcomas and the results obtained in other histological subtypes were less positive since neither the BRCA1/2 nor ATM cohort met the prespecified overall response rate of 40%. [1]

Zhou et al. reported on the usefulness of tumour-informed ctDNA for disease monitoring among patients treated for LMS. The results obtained in the analysis indicated that undetectable ctDNA may

suggest a lower likelihood of relapse, but ctDNA positivity may indicate progressive disease. This led to the conclusion that utilising this method may allow for closer monitoring and earlier clinical intervention in relapse. The limitation of the study is its retrospective design and the small number cases enrolled (34 LMS). [2]

Du et al. presented a new nomogram predicting the survival benefit of radiotherapy for patients with uterine sarcomas. This tool was based on analysis of the SEER database that retrospectively included 2,871 uterine sarcoma cases. The nomogram based tool indicated the high-risk group in which radiotherapy showed significant (17 months) overall survival benefit. Even though this approach is very interesting, the usefulness of this method requires prospective validation to prove its practical value. [3]

The results of the prospective intergroup real-world registry for gynaecological sarcoma (REGSA-NOGGO RU1), were widely awaited. The registry covered 723 cases from 120 German, Austrian, and Swiss centres. Authors followed the therapeutic strategies applied to uterine and breast sarcomas of STUMPs. The results showed high heterogeneity in the approach, including surgical procedures [application of lymphadenectomy (9.5%), omentectomy (12.7%), morcellation (11.4%)] as well as medical treatment [(hormonal treatment (9.9%), radiotherapy (6.6%)). The analysis led to the conclusion that such heterogeneity is the result of an insufficient number of high-quality trials indicating the effectiveness of particular therapeutic strategies. [4]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Avelumab plus talazoparib in patients with BRCA1/2- or ATM-altered advanced solid tumors: Results from JAVELIN BRCA/ATM, an open-label, multicenter, phase 2b, tumor-agnostic trial	Schram AM et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih.gov/36394867/
2	Feasibility of Longitudinal ctDNA Assessment in Patients with Uterine and Extra-Uterine Leiomyosarcoma	Zhou M et al.	Cancers	https://pubmed.ncbi.nlm.nih.gov/36612153/
3	A nomogram-based overall survival stratification to identify uterine sarcoma patients without distant metastases who may benefit from adjuvant radiotherapy	Du J et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36469973/
4	Treatment strategies in patients with gynecological sarcoma: Results of the prospective intergroup real-world registry for gynecological sarcoma in Germany (REGSA-NOGGO RU1)	Roser E et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36631151/



Emerging molecular-targeted therapies or early preclinical trials in endometrial cancer

Jakub Dobroch

Rubinstein et al. published the results of a phase II clinical trial on durvalumab alone (arm 1) or in combination with tremelimumab (arm 2) in advanced and recurrent endometrial cancer (EC). The purpose was to analyse the efficacy of both monotherapy and combined regimens using immune checkpoint inhibitors. A subgroup of mismatch repair deficient

(MMRd) EC was selected in both arms. Eighty-two patients were enrolled in the study and divided randomly into groups. After a 24-week follow-up, an overall response rate (ORR) of 10.8% was observed for arm 1 and 5.3% for arm 2. Each patient achieving partial (PR) or complete response (CR) had an MMRd tumour. A higher immune-related toxicity rate

was noticed in the combined therapy group. The primary endpoints of the study have not been reached. The authors highlighted the necessity of further research on immunotherapy resistance mechanisms, especially in MMR-proficient patients. [1]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Durvalumab with or without tremelimumab in patients with persistent or recurrent endometrial cancer or endometrial carcinosarcoma: A randomized open-label phase 2 study	Rubinstein MM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36512912/



Medical treatment of primary and recurrent cervical cancer

Khayal Gasimli

Early-stage cervical cancer

Hu et al. presented the outcomes of a randomised controlled trial (RCT) investigating the application of preoperative neoadjuvant chemotherapy (NACT) in patients with stage IB3 and IIA2 cervical cancer. The Kaplan-Meier analysis unveiled no significant differences in five-year progression-free survival (PFS) rates (80.5% vs 83.8%, $p = 0.320$) and overall survival (OS) rates (85.8% vs 87.8%, $p = 0.319$) between the NACT and primary surgery cohorts, respectively. Remarkably, there were even no relevant survival differences among NACT patients based on their treatment response subgroups (complete response [CR] vs partial response [PR] vs stable disease [SD]/progressive disease [PD]). Notably, deep cervical invasion emerged as the sole statistically significant factor influencing OS within the NACT group ($p = 0.046$). Furthermore, within the primary surgery group, patients with intermediate or high-risk factors experienced greater benefits and improved PFS from adjuvant chemotherapy compared to radiation. It is essential to acknowledge that the study exhibits selection biases. [1]

In another randomised, non-inferiority, multicentre trial conducted by Weng and colleagues, the efficacy of adjuvant chemotherapy paclitaxel+cisplatin alone was compared to concurrent chemoradiotherapy (external beam radiation therapy/brachytherapy+cisplatin) in patients with stage IB–IIA cervical cancer. Notably, the clinicopathological characteristics of both study cohorts were comparable, and the median follow-up duration was 72.1 months. The three-year survival analysis revealed indistinguishable PFS rates of 91.9% for both groups ($p = 0.846$), and OS rates of 95.6% and 93.7%, respectively ($p = 0.384$). Adjuvant chemotherapy, with its comparatively lower toxicity profile, presented as a promising alternative for patients in this disease stage. However, it's important to acknowledge that the study included cases with varying risk factors and lacked patient stratification based on clinical stages or risk factors, thereby constraining the conclusiveness of the study. [2]

Metastatic and recurrent cervical cancer

Nishio et al. conducted a subgroup analysis within the broader context of the global KEYNOTE-826 study, revealing notably enhanced antitumour activity and well-manageable safety in the Japanese cohort when subjected to combinational treatment involving

pembrolizumab and cisplatin (+/-bevacizumab), in contrast to the placebo group. The response and tolerability outcomes were in alignment with those observed in the global cohort. [3]

In a phase III non-inferiority randomised controlled trial, Yang et al. investigated the antitumour efficacy and safety profiles of nedaplatin-based radiochemotherapy against cisplatin-based regimens in patients with stage IB–IVA cervical cancer. The disparities in overall survival (OS) (30.5 vs 28.5 months, $p = 0.058$) and haematological toxicity did not attain statistical significance. Notably, the administration of nedaplatin led to significantly fewer gastrointestinal adverse events (AE) but resulted in elevated levels of liver transferases and bilirubin. The study is subject to pertinent limitations, including its single-centre design, the comparison of statistically distinct patient cohorts despite randomisation, a relatively short follow-up duration, incomplete chemotherapy cycles, and heterogeneous treatments in cases with advanced stages. [4]

Tewari et al. presented the conclusive survival analysis from a phase III randomised controlled trial, comparing the combination of topotecan and paclitaxel versus cisplatin-paclitaxel with or without bevacizumab in patients with recurrent, metastatic cervical cancer (CC). The study's primary endpoints encompassed overall survival (OS) and the severity of adverse events (AE). The applied treatment regimens followed a q3w schedule until disease progression, complete response, or the onset of unacceptable toxicity. The outcomes demonstrated no statistically significant survival advantages for the topotecan combination, with or without bevacizumab (median OS 13.8 vs 16.3 months, $p = 0.28$ and 16.2 vs 17.5 months, $p = 0.34$, respectively). Adverse event rates were observed at comparable frequencies across both therapy arms. [5]

Quality of life (QoL)

In the interim, findings pertaining to patient-reported quality of life (PRO) and physical functioning (PF) have emerged from the treatment of recurrent cervical cancer patients with cemiplimab within the context of the EMPOWER Cervical-1 phase III randomised controlled trial. The authors unveiled a notable enhancement in PRO (8.49, $p < 0.05$) and PF (8.35, $p < 0.05$) within the cemiplimab-treated group compared to the chemotherapy-treated group. It's worth noting that the EORTC QLQ-C30 question-

naire was employed for this assessment, which does introduce limitations given its generic psychometric nature designed for cancer diseases and not tailored specifically for cervical cancer. [6]

Monk et al. presented patient-reported outcomes (PROs) from a quality-of-life analysis among patients enrolled in the KEYNOTE-826 trial. In this context, the QLQ-C30 questionnaire was completed by 69% of individuals in the pembrolizumab arm and 57% in the placebo group. The observations unveiled a change in QLQ-C30 Global Health Status-Quality of Life (GHS-QoL) scores, with -0.3 points in the pembrolizumab group and -1.3 points in the placebo group. Furthermore, a noteworthy proportion of patients (42% in pembrolizumab vs 29% in placebo) exhibited improvements in GHS-QoL during the trial ($p = 0.0003$). Importantly, the introduction of pembrolizumab alongside chemotherapy for cervical cancer did not exert an impact on patients' quality of life. [7]

Medical treatment of primary and recurrent cervical cancer

Khayal Gasimli

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No	Title	Authors	Journal	Link to abstract
1	Neoadjuvant chemotherapy for patients with international federation of gynecology and obstetrics stages IB3 and IIA2 cervical cancer: a multicenter prospective trial	Hu Y et al.	BMC Cancer	https://pubmed.ncbi.nlm.nih.gov/36471257/
2	Adjuvant chemotherapy versus adjuvant concurrent chemoradiotherapy after radical surgery for early-stage cervical cancer: a randomized, non-inferiority, multicenter trial	Weng D et al.	Front Med	https://pubmed.ncbi.nlm.nih.gov/36422763/
3	Pembrolizumab plus chemotherapy in Japanese patients with persistent, recurrent or metastatic cervical cancer: Results from KEYNOTE-826	Nishio S et al.	Cancer Sci	https://pubmed.ncbi.nlm.nih.gov/35792064/
4	A phase III randomized, controlled trial of nedaplatin versus cisplatin concurrent chemoradiotherapy in patients with cervical cancer	Yang X et al.	ESMO Open	https://pubmed.ncbi.nlm.nih.gov/35994789/
5	Final survival analysis of topotecan and paclitaxel for first-line treatment of advanced cervical cancer: An NRG oncology randomized study	Tewari KS et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36898292/
6	Health-related quality of life with pembrolizumab or placebo plus chemotherapy with or without bevacizumab for persistent, recurrent, or metastatic cervical cancer (KEYNOTE-826): a randomised, double-blind, placebo-controlled, phase 3 trial	Monk BJ et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/36878237/
7	EMPOWER CERVICAL-1: Effects of cemiplimab versus chemotherapy on patient-reported quality of life, functioning and symptoms among women with recurrent cervical cancer	Oaknin A et al.	Eur J Cancer	https://pubmed.ncbi.nlm.nih.gov/35922251/

Radiotherapy of primary and recurrent cervical cancer

Erbil Karaman

Gao et al. studied the efficacy of stereotactic body radiotherapy boost with CyberKnife(CK-SBRT) and compared it with high-dose-rate(HDR) intracavitary/interstitial brachytherapy(IC/ISBT) in patients with locally advanced cervical cancer (CC). The study included 20 patients with locally advanced cervical cancers. The BT plan of these patients was compared with the CK plan based on the same CT images. They divided the therapy plans according to the two types, with high-risk planning target volume (HR-TPV) defined by the high-risk clinical target volume (HR-CTV) without and with a 5mm margin, which were named CyberKnife-Clinical Target Volume(CK-CTV) plan and CyberKnife Planning Target Volume(CK-PTV) plan, respectively. The outcomes showed that target coverage was preferable with the CK plan than with the BT plan, as the D95%, D98%, Homogeneity index (HI) and Conformity index(CI) of the CK-CTV plan and CK-PTV plan were higher than those of the BT plan. The authors concluded that CK-SBRT can reach better target coverage, dose sparing for organs at risks and radiobiological effectivity in comparison with IC/ISBT. The main limitation of this study was that CT images with applicators were used to generate CK plans, which is not in line with the actual treatment situation by CK. [1]

Aoshika et al. conducted a retrospective study that included 236 cases with CC, and they investigated the local control (LC), overall survival (OS), and late toxicity in patients treated with Computerized Tomography-based adaptive brachytherapy in combination with whole-pelvic (WP)-and central shielding (CS)-external beam radiotherapy(EBRT). The three-year LC rates for T1b2, T2a, T2b, T3b, and T4 were 100%, 100%, 97.3%, 86.9%, and 91.7%, respectively. Regarding toxicity, grade 3 and 4 gastrointestinal and genitourinary toxicities were 3.8% and 1.7%, respectively.

The authors concluded that a combination of WP- and CS-EBRT and CT-based IGBT therapy showed good LC results with a decreased number of toxicities for cases with small- or medium-sized lesions. The main limitation of this study was that it is a retrospective study and there were few local recurrences which may have potential bias on the outcomes. [2]

A retrospective study by Meng et al. investigated image-guided intensity modulated radiotherapy (IG-IMRT) on a specific group of stage FIGO IIIC1 cervical cancer patients. They evaluated the efficacy, toxicity, and prognosis of 502 patients. The study included both 2D and 3D brachytherapy. The median follow-up time was 42.1 months. The three-year and five-year estimated OS, DFS, LC, LRC were 81.7% and 75.5%, 71.4% and 68.6%, 89.9% and 89.9%, 86.1% and 84.3%, respectively. Pelvic recurrences were observed in 21 cases (4.2%). Toxicity including grade 3 or greater gastrointestinal and genitourinary were 2.7% and 0.8%, respectively. The study showed that cases with stage IIIC1 were well tolerated with low toxicity and excellent survival with treatment of IG-IMRT. [3]

A prospective phase I/II clinical trial conducted a study that investigated the feasibility and effectivity of hybrid use of intracavitary and interstitial brachytherapy (HBT) in locally advanced cervical cancer. In total, 125 patients enrolled and proceeded into the registration. Cases with tumour size > 5cm and stage IB2-IVA were included. The primary outcome of phase II was two-year pelvic progression-free survival (PPFS) higher than 64% with the standard treatment. The median follow-up was 37.3 months and the 2-PPFS for the studied group was 80.7%. This prospective study showed the effectiveness of HBT and the primary endpoint of the study was reached. [4]

The SENTICOL I-II trial analysis reported by Kissel et al. compared the effect of preoperative brachytherapy plus radical surgery versus primary radical surgery in patients with stage FIGO IB2 with tumour sizes of 2 and 4cm. In all, 104 cases were included: 55 underwent primary radical surgery alone while 49 cases received preoperative radiotherapy and subsequently underwent radical surgery. The results showed the preoperative radiotherapy group were more likely to have no residual tumours (71.4% vs 25.5%, $p < 0.0001$) and this patient group was more likely defined as low-risk according to the Sedlis criteria, in which it is described as a tumour size less than 2cm, no LVSI and depth of stromal invasion less than 10mm (83.3% vs 51.2%, $p < 0.0001$). Adjuvant treatment was required less frequently in cases of preoperative brachytherapy. However, cases with preoperative radiotherapy showed more complications after the operation with grade 3 and more (24.5% vs 9.1%, $p = 0.03$). Cases with preoperative brachytherapy were observed to have better five-year disease free survival (DFS) with comparison to cases that underwent radical operation alone, 93.6% and 74.4% respectively. This analysis showed the better histopathological results with R0 margin were reached after operation in patients with preoperative brachytherapy and this resulted with a better five-year DFS in IB2 cervical cancer. [5]

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No	Title	Authors	Journal	Link to abstract
1	Stereotactic body radiotherapy boost with the CyberKnife for locally advanced cervical cancer: Dosimetric analysis and potential clinical benefits	Gao J et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/36291951/
2	Results of computer tomography-based adaptive brachytherapy in combination with whole-pelvic- and central-shielding-external beam radiotherapy for cervical cancer	Aoshika T et al.	Brachytherapy	https://pubmed.ncbi.nlm.nih.gov/359227196/
3	Image-guided intensity-modulated radiotherapy in patients with FIGO IIIC1 cervical cancer: efficacy, toxicity and prognosis	Meng Q et al.	J Cancer	https://pubmed.ncbi.nlm.nih.gov/37151392/
4	Phase I/II prospective clinical trial for the hybrid of intracavitary and interstitial brachytherapy for locally advanced uterine cervical cancer	Murakami N et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36603849/
5	Impact of preoperative brachytherapy followed by radical hysterectomy in stage IB2 (FIGO 2018) cervical cancer: An analysis of SENTICOL I-II trials	Kissel M et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36758421/



Surgical treatment of primary and recurrent cervical cancer

Chrysoula Margioulou-Siarkou and Georgia Margioulou-Siarkou

Slama et al. performed the FERTility Sparing Surgery retrospective multicentre study to evaluate the oncological outcomes of 733 patients with FIGO 2018 stage IA1 and positive lymphovascular space invasion or with stage ≥ IA2 cervical cancer of any histological type and tumour grade, who underwent any type of fertility-sparing surgery. Recurrence was diagnosed in 7% of the patients (n = 51), with the risk of recurrence being significantly increased in patients with tumour size > 2cm, irrespectively of the radicality of surgery (HR 2.982) However, it was not significantly different between patients with tumour size ≤ 2cm treated with radical trachelectomy versus conisation or simple trachelectomy (p = 0.957), regardless of lymphovascular space invasion. The main limitations of the study are its retrospective design and the subsequent potential selection bias, as well as geolocation bias in procedures and outcomes, caused by differences in the number of patients registered at each participating institution. Consequently, the authors concluded that fertility-sparing surgery increases the risk of recurrence for patients with tumour size > 2cm, while nonradical and radical procedures have similar oncological outcomes in patients with tumour size ≤ 2cm. [1]

The 4C study by Aubrey et al., a multicentre retrospective cohort study of 238 patients with cervical cancer and no residual disease on subsequent hysterectomy specimen after initial cervical conisation,

analysed the differences in five-year recurrence-free survival (RFS) and overall survival (OS) rates between patients treated with minimally invasive (MIS, n = 122), abdominal (AH, n = 103) and laparoscopically assisted vaginal hysterectomy (VLH, n = 13). The most notable limitations of the study are its retrospective design, the low event rate of recurrence and potential missed recurrences due to differences in follow up among participating centres, the lack of a centralised pathology review or detailed information on the excisional specimens and potential procedural differences between institutions regarding surgical approach. No statistically significant differences were reported regarding both five-year RFS (MIS/VLH 97.7%, AH 95.8%, p = 0.23) and five-year OS (MIS/VLH 98.9%, AH 97.4%, p = 0.10), leading the authors to the conclusion that surgical approach does not significantly affect survival outcomes in patients with no residual cervical cancer on hysterectomy specimens. [2]

The SUCCOR quality study by Boria et al., a retrospective cohort study on 838 patients with FIGO 2009 stage IB1, FIGO 2018 stage IB1 and IB2 cervical cancer treated with radical hysterectomy, investigated the association between survival outcomes and compliance with European Society of Gynaecological Oncology (ESGO) surgery quality indicators. Both risk of relapse (HR 0.39) and risk of death (HR 0.43) were significantly lower for patients

who underwent surgery in high compliance centres. However, the latter did not remain significantly decreased when adjustments for conisation, surgical approach, use of manipulator surgery, and adjuvant therapy were applied. The limitations of the study include its retrospective design, the lack of an external audit of data at the time of collection, the lack of structured compliance evaluation for some of the included data, and the potential bias created by corresponding with only one person per centre. Conclusively, the authors noted that high adherence with ESGO quality indicators is associated with improved survival outcomes. [3]

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No	Title	Authors	Journal	Link to abstract
1	Analysis of risk factors for recurrence in cervical cancer patients after fertility-sparing treatment: The FERTility Sparing Surgery retrospective multicenter study	Slama J et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/36427596/
2	Oncologic outcomes of surgically treated cervical cancer with no residual disease on hysterectomy specimen: A 4C (Canadian Cervical Cancer Collaborative) working group study	Aubrey C et al.	Curr Oncol	https://pubmed.ncbi.nlm.nih.gov/36826114/
3	SUCCOR quality: validation of ESGO quality indicators for surgical treatment of cervical cancer	Boria F et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36583728/



Emerging molecular-targeted therapies or early preclinical trials in cervical cancer

Monika Sobočan

Xia et al. conducted a phase II trial with a multicentre, open-label, single-arm design to evaluate the effectiveness of camrelizumab, either as a standalone treatment or in combination with famitinib, among individuals diagnosed with metastatic or recurrent cervical squamous cell carcinoma. A total of 33 participants underwent 1–2 lines of systemic therapy for recurring or metastatic conditions, each receiving an intravenous dose of 200mg camrelizumab on the first day of a three-week cycle, along with orally administered famitinib at a daily dose of 20mg.

During the concurrent administration of famitinib, participants underwent a median of 16 camrelizumab lines spanning 43 weeks. All individuals experienced treatment-related adverse events, notably anaemia (66.7%), decreased platelet count (66.7%), and decreased white blood cell count (60.6%). Adverse events of grade 3 or higher impacted 78.8% of patients, encompassing anaemia (78.8%), decreased neutrophil count (21.2%), decreased white blood cell count (15.2%), hypertension (15.2%), and hypertriglyceridemia (12.1%). Treatment-related adverse events prompted the interruption of camrelizumab in 30.3% of patients, famitinib interruption

in 75.8%, and famitinib dose reduction in 51.5%. Three patients (9.1%) with camrelizumab and five patients (15.2%) with famitinib had to discontinue treatment. Immune-related adverse events were observed in 36.4% of patients, with hypothyroidism (24.2%) being the most prevalent.

The amalgamation of camrelizumab and famitinib demonstrated favourable results, manifesting a considerable proportion of objective responses (39.4%) in individuals previously subjected to treatment. In all, 75.9% of patients had a reduction in tumour size. The response exhibited durability, with a 12-month likelihood of response duration reaching 74.1% and a progression-free survival of 10.3 months. Although median overall survival was immature, the 12-month overall survival probability was 77.7%. Adverse events related to this combination treatment were manageable and tolerable. [1]

In a multicentre, open-label study, a phase I/II trial investigated the objective response rate of the recommended phase II dose of the oral Chk1 inhibitor in solid tumours. The study included 134 patients with solid tumours characterised by high genomic

instability, such as high-grade serous ovarian cancer, small cell lung cancer, soft tissue sarcoma, anogenital cancer, or cervical cancer. Among the 77 patients treated with a phase II dose of the oral Chk1 inhibitor (500mg) combined with low-dose gemcitabine (250 mg/m²), 12 had cervical cancer. Therapy discontinuation was low, and the overall objective response rate across all solid tumours was 10.8%. The most common toxicities reported were nausea (63.3%), diarrhoea (55.0%), and vomiting (56.7%). [2]

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No	Title	Authors	Journal	Link to abstract
1	A multicenter phase 2 trial of camrelizumab plus famitinib for women with recurrent or metastatic cervical squamous cell carcinoma	Xia L et al.	Nat Commun	https://pubmed.ncbi.nlm.nih.gov/36481736/
2	A phase I/II trial of oral SRA737 (a Chk1 Inhibitor) given in combination with low-dose gemcitabine in patients with advanced cancer	Jones R et. al.	Clin Cancer Res	https://pubmed.ncbi.nlm.nih.gov/36378548/



Treatment of primary and recurrent vulvar and vaginal cancer including rare vulvo-vaginal malignancies

María de los Reyes Oliver and Rubén M. Betoret

Radiological staging workup

Preoperative lymph-node (LN) staging of vulvar cancer remains a challenging topic. Fragomeni et al. developed the "Morpho node Predictive Model", based on the machine learning method, which predicts LN inguinal metastases according to the results of a preoperative inguinal ultrasound. The presented model was characterised by excellent predictive ability for LN involvement, even superior to the subjective assessment of experienced ultrasound examiners. However, multicentre prospective studies are needed to externally validate it on a larger population. [1]

Lymph node evaluation

A retrospective analysis of data from the National Cancer Database was performed by Bercow et al. to evaluate possible factors associated with LN evaluation of 5,685 patients with T1b and T2 vulvar squamous cell carcinoma (SCC). In addition, they assessed the outcome of these patients depending on the evaluation (n = 3,756) or not (n = 1,929) of LN. Older age (≥80 years), black race, and care at low-volume hospitals were associated with lower odds of LN evaluation. Older individuals who did not undergo LN evaluation had significantly worse overall

survival than those with pathologically negative LNs. In contrast, overall survival was similar to those with pathologically positive LNs. Potential bias of the study is associated with missing data, lack of cancer-specificity mortality, and potential unmeasured patient confounding factors that may influence the decision to perform an LN evaluation. [2]

Pascoal et al. conducted a retrospective observational cohort study to assess the feasibility of sentinel lymph node biopsy (SLNB) by scar injection after prior excision of vulvar cancer and the long-term outcomes of this procedure. Data from 173 groins in 97 patients were analysed. The detection rate did not differ whether the groin was assessed following tumour (n = 122, 94%) or scar (n = 40, 93%) injection. Scar injection was not associated with recurrence or death. Limitations of the study are associated with its retrospective nature, the small size of some subgroups, and the fact that lymphadenectomy was not performed in all patients. [3]

In a prospective study, Rundle et al. evaluated Indocyanine green near infrared (ICG-NIR) techniques as a SLN tracer in apparently early-stage vulvar cancer, both as a single agent and as ICG-99mTc-nanocolloid combination, compared to traditional blue-dye-99mTc-nanocolloid. All successfully

mapped SLN were identified with the combination of ICG-NIR and 99mTc-nanocolloid compared to 69% with blue-dye-99mTc-nanocolloid. These results suggest that ICG, specifically in combination with 99mTc, is more likely to achieve successful SLN identification than a combination with blue-dye and should be incorporated as a standard protocol. Potential bias results from small subgroups sizes, and concomitant administration of all three tracers. [4]

Molecular pathways

Several potentially targetable molecular pathways have emerged as being involved in the tumorigenesis of SCC, melanoma, and Vulvar Paget's disease (VPD). Deb et al. conducted an extensive systematic literature review of molecular and genetic characteristics of vulvar neoplasms [5]. Caruso et al. published a systematic review of VPD and its treatment strategies, emphasizing new emerging molecular targets, such as HER2 and PD-L1. [6]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Evaluating the risk of inguinal lymph node metastases before surgery using the morphonode predictive model: A prospective diagnostic study in vulvar cancer patients	Fragomeni SM et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/36831462/
2	Guideline-discordant care in early-stage vulvar cancer	Bercow AS et al.	Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/36357957/
3	Inguinofemoral sentinel lymph node biopsy by scar injection in vulvar cancer: an assessment of feasibility and long-term outcomes	Pascoal E et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36332935/
4	A comparison of ICG-NIR with blue dye and technetium for the detection of sentinel lymph nodes in vulvar cancer	Rundle S et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/36207232/
5	Molecular features of preinvasive and invasive vulvar neoplasms	Deb PQ et al.	J Low Genit Tract Dis	https://pubmed.ncbi.nlm.nih.gov/36083687/
6	Vulvar Paget's disease: A systematic review of the MITO Rare Cancer Group	Caruso G et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/36980691/



Screening of gynaecological cancer

Catarina Pardal

Using data from a Finnish large-scale randomised HPV screening trial (ISRCTN23885553), the authors compared the performance (sensitivity and specificity of CIN II+ detection, colposcopy referral rate, precancer lesions prevalence) of five different HPV with cytology triage algorithms: two HPV Persistence Algorithms (HPV-positive cytology-negative would maintain one or two follow-up tests) and three Decisive Cytology Algorithms (follow-up and referral decisions based on cytology positivity despite the persistence of HPV, would maintain one or two follow-up tests). Cytology-alone algorithm and HPV-alone algorithm were used as references. The HPV-alone algorithm was associated with high colposcopy referral rate and showed the highest sensitivity (94%) but lowest specificity (93%). The cytology-alone algorithm had a low sensitivity (69%) with a high specificity (99%) and a lower colposcopy referral rate. In the HPV with cytology triage algorithms with no follow-up if negative cytology, the sensitivities were 65–82% and the specificities 98–99%. Between the five HPV with cytology triage algorithms studied, the best sensitivity/specificity balance was achieved by HPV Persistence Algorithm with two repeated follow-up tests. The most important study limitations were the potentially missed

regressive CIN II+ lesions in HPV-positive cytology-negative (no colposcopy evaluation) that might have interfered with algorithm performance, and HPV testing in individuals under 30 years old (currently not recommended) that may have altered prevalence of CIN II+ lesions. [1]

In order to increase cervical cancer detection in women who do not attend routine screening, the authors designed a prospective randomised study that evaluated the feasibility of an "opt-in" self-sampling test for high-risk HPV detection. From a total of 5,350 women invited to HPV self-sampling, 792 returned a self-taken sample, of which 22 (2.8%) gave an invalid result with more expression in the oldest age group of 65- to 69-year-old women. A high proportion (20.5%) of the samples were high-risk HPV positive, with HPV-16 and HPV-18/45 detection relatively low (21.3%). The subsequent cytology determined colposcopy referral in high-risk HPV positive cases, and the overall HSIL detection rate was 0.9% (7 cases), while it was 0.5% among participants in routine screening, highlighting the quality of the self-taken sample as well the higher compliance of this women for the cervical cancer screening. [2]

WID-qEC test is a three-marker DNA methylation-based test (ZSCAN12 and GYPCin genes) developed for endometrial cancer detection. In this case-control and hospital-based cohort study, the authors investigated whether it could also identify women with cervical cancer and if it was superior to cytology for cervical and endometrial cancer diagnosis. In the case-control setting (n = 51), the WID-qEC test sensitivity and specificity for cervical cancer detection was 100% and 92.9% and amongst the hospital-cohort setting (n = 330) was 100% and 82.5%, respectively. In comparison, cytology had worst performance, with a sensitivity of 33.3% and a specificity of 96.9%, suggesting that WID-qEC test detects both endometrial and cervical cancer with higher accuracy. The main study limitation was its small sample size. [3]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Alternative cytology triage strategies for primary HPV screening	Vahteristo M et al.	Gynecologic Oncology	https://pubmed.ncbi.nlm.nih.gov/35963790/
2	Human papillomavirus self-sampling with mRNA testing benefits routine screening	Tarkkanen J et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/35716139/
3	The WID-qEC test: Performance in a hospital-based cohort and feasibility to detect endometrial and cervical cancers	Schreiberhuber L et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/36056582/



Gestational trophoblastic disease management (pathology, diagnosis, follow-up, pregnancies)

Joanna Kacperczyk-Bartnik

Diagnosis

In a systematic review and meta-analysis by Newhouse et al., the authors evaluated the diagnostic value and accuracy of ultrasound examination in the diagnostic process of hydatidiform moles. Meta-analysis results showed that sensitivity of ultrasound for the diagnosis of this condition is 52.2% with specificity of 92.6%. Heterogeneity and different diagnostic criteria for detection of hydatidiform moles among the studies were the main limitations of this meta-analysis. [1]

Another diagnostic approach was presented by Ravn et al. The authors performed a short tandem repeat analysis of specimen collected from fifteen women with suspected molar pregnancies between the 6th and 13th gestational weeks. It was possible to obtain circulating gestational trophoblasts from blood in 87% of women above the 10th gestational week. Short tandem repeat profiles in circulating gestational trophoblasts were equal to the profiles of DNA collected from chorionic villi. The strength of

the proposed method is its non-invasiveness. The main limitation seems to be that it was not possible to capture circulating gestational trophoblasts in all examined patients. [2]

Assisted reproductive technology

Braga et al. presented the results of a single institution retrospective cohort study from a referral centre comparing the characteristics of hydatidiform mole in patients with the history of intracytoplasmic sperm injection (ICSI) for in vitro fertilization (n = 31) and patients after spontaneous conception (n = 4,895). It was observed that women after ICSI were diagnosed with singleton molar pregnancy at an earlier gestational week (7th vs 10th, p < 0.01), presented fewer medical complications at diagnosis, and developed fewer cases of singleton postmolar gestational trophoblastic neoplasia (7.7% vs 20.8%) compared to women after spontaneous conception. The main limitation of the study is the possibility of bias due to its retrospective design. [3]

Educational online tool

Frijstein et al. published the results of a multicentre randomised controlled trial enrolling 69 patients with newly diagnosed gestational trophoblastic disease. Patients received direct (n = 33) or delayed (n = 36) access to an online tool which was an information source about the disease. Patients with direct access presented a higher level of knowledge about the medical condition; however, their perception of the disease, levels of anxiety, depression, and distress were comparable with the control group. Patients were satisfied with the tool (92%) but the study results could be affected by access to other sources of information about gestational trophoblastic disease available online. [4]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	The diagnostic value and accuracy of ultrasound in diagnosing hydatidiform mole: A systematic review and meta-analysis of the literature	Newhouse I et al.	Radiography (Lond)	https://pubmed.ncbi.nlm.nih.gov/35785640/
2	Diagnosis of hydatidiform moles using circulating gestational trophoblasts isolated from maternal blood	Ravn K et al.	Placenta	https://pubmed.ncbi.nlm.nih.gov/36889013/
3	Presentation, medical complications and development of gestational trophoblastic neoplasia of hydatidiform mole after intracytoplasmic sperm injection as compared to hydatidiform mole after spontaneous conception - a retrospective cohort study and literature review	Braga A et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36706644/
4	Evaluation of a web-based intervention for patients with gestational trophoblastic disease: a randomized controlled trial	Frijstein M et al.	Gynecol Obstet Invest	https://pubmed.ncbi.nlm.nih.gov/36682348/



Cancer in pregnancy

Michael J. Halaska

Konishi et al. analysed short-term surgical outcomes for 260 patients with PABC matched with non-PABC patients, finding more total mastectomy and axillary dissection but less reconstruction surgeries. On the other hand, similar complication rates and hospital stays were described. [1]

Two reports dealt with long-term follow-up of children exposed to maternal cancer in utero. Greiber et al. found 690 children using a national health registry and found no difference in child mortality, congenital malformation, or somatic or psychiatric diseases. Similar findings were described in a subgroup of children exposed to chemotherapy in utero. Van Assche analysed 151 nine-year-old children exposed to maternal cancer in utero using an INCIP database and a detailed and standardised psychological examination. A decrease of 1.6 points of IQ score was found for each gestational week of

premature delivery. Another association was found with maternal education and maternal death but no association with type of treatment. [2,3]

Maggen et al. evaluated an INCIP group of 201 patients with regards to birth weight and the influence of chemotherapy administered during pregnancy. The longer and later chemotherapy was given the higher risk of lower birth weight was found. [4]

A population-based study from Sweden evaluated a cohort of 208 patients with breast cancer found during pregnancy and 672 post-partum breast cancer patients. A higher risk of spontaneous preterm birth was found. Risks of other pregnancy complications were similar to non-PABC patients, such as neonatal mortality and malformations. Postpartum breast cancer was only associated with increased incidence of bleeding during pregnancy. [5]

On et al. collected 37 cases of rituximab used for NHL. One first-trimester death and two missed abortions were observed. Post-delivery, five children experienced respiratory, cardiac, or haematologic problems. [6]

As MRI is commonly used during pregnancy, the topic of the impact of gadolinium contrast agent on a fetus was evaluated by Winterstein et al. in a cohort of 5,991 patients. No difference in the risk of death and ICU admission was found between gadolinium-exposed and non-exposed children. [7]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Surgical and obstetric outcomes of breast cancer surgery during pregnancy: a nationwide database study in Japan	Konishi T et al.	Breast Cancer Res Treat	https://pubmed.ncbi.nlm.nih.gov/35917051/
2	Long-term morbidity and mortality in children after in utero exposure to maternal cancer	Greiber IK et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/35797496/
3	Cognitive and behavioral development of 9-year-old children after maternal cancer during pregnancy: A prospective multicenter cohort study	Van Assche IA et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/36634293/
4	Impact of chemotherapy during pregnancy on fetal growth	Maggen C et al.	J Matern Fetal Neonatal Med	https://pubmed.ncbi.nlm.nih.gov/36202393/
5	Risk of obstetric and perinatal complications in women presenting with breast cancer during pregnancy and the first year postpartum in Sweden 1973-2017: A population-based matched study	Lundberg FE et al.	Acta Obstet Gynecol Scand	https://pubmed.ncbi.nlm.nih.gov/36959086/
6	Treatment of lymphoma with rituximab and chemotherapy during pregnancy	On S et al.	Leuk Lymphoma	https://pubmed.ncbi.nlm.nih.gov/35856478/
7	Risk of fetal or neonatal death or neonatal intensive care unit admission associated with gadolinium magnetic resonance imaging exposure during pregnancy	Winterstein AG et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/36241080/



Pathology of gynaecological cancers

Nicolas Samartzis and Dimitrios Rafail Kalaitzopoulos

Endometrial cancer

Bruce et al. analysed 2,927 endometrioid endometrial cancer patients with whole exome and transcriptome sequencing and found that 5.5% were HER-2 positive. Those had increased immune checkpoint gene expression, immune cell infiltration, increased MAPK pathway activation scores, and worse overall survival. These findings could represent a potential benefit of targeted therapies as well as immunotherapies in these patients. A strength of this study is that it represents one of the biggest populations studied for HER-2 in endometrioid uterine cancer and the associated molecular landscape. The therapeutic effect of anti-HER-2 or MAPK targeted immunotherapies was not a subject of this study. [1]

Canet-Hermida et al. prospectively assessed microsatellite instability in endometrial aspirates in 93 Lynch syndrome carriers and compared it to 25 sporadic endometrium cancer and 30 women with benign gynaecologic disease. In Lynch syndrome carriers, elevated MSI scores were detected in aspirates from premalignant and malignant lesions and normal endometrium, correlating with MMR protein loss. As tissue collection was obtained with endome-

trial aspiration, sample bias should be considered as a limitation. This technique may also not be possible in every case due to cervical stenosis, especially in postmenopausal patients. [2]

Diniz et al. found that MMR status was independently related to lymph node metastasis in endometrioid uterine cancer in an overall sample of 332 women who underwent sentinel lymph node mapping with or without systematic lymphadenectomy. MMR deficiency was noted in 20.8% of cases and was correlated to presence of lymphovascular space invasion ($p = 0.032$), being an independent risk factor for lymph node metastasis (OR 2.76, 95% CI: 1.36–5.62). Further prospective studies could help to investigate and confirm these results. [3]

Ovarian cancer

Asangba et al. investigated the microbiome in ovarian cancer and found an enrichment of several microbial taxa. The accumulation of these species was associated with worse outcomes. This may therefore serve as potential indicator for predicting patients' responses to treatment, apart from the potential use as an early detection of ovarian cancer.

Given its small number of a total of 64 cases (ovarian cancer and control), further larger size studies are warranted. [4]

Wieser et al. examined the mRNA expression of seven angiogenic genes (VEGF, VEGFR2, PDGFA, PDGFB, PDGFRA, PDGFRB, KIT) in a cohort of 195 ovarian cancer cases and found an association with worse clinical outcome. They proposed an angiogenesis score with four different categories (zero, low, medium, and high) with prognostic value. A strength of the study was that a broad range of different angiogenetic markers was explored. However, the relatively small number of cases should be taken as a limitation. [5]

Funnell et al. used single-cell whole-genome sequencing in high-grade ovarian cancer and triple negative breast cancer and showed that cell-to-cell structural variation is influencing the phenotype and evolutionary diversity of cancer cells. This study contributes to a comprehensive understanding of the genomic diversity of cancer cells in high-grade ovarian cancer. [6]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	HER2+ endometrioid endometrial cancer possesses distinct molecular and immunologic features associated with a more active immune microenvironment and worse prognosis	Bruce SF et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37003074/
2	Highly Sensitive Microsatellite Instability and Immunohistochemistry Assessment in Endometrial Aspirates as a Tool for Cancer Risk Individualization in Lynch Syndrome	Canet-Hermida J et al.	Mod Pathol	https://pubmed.ncbi.nlm.nih.gov/36918055/
3	Can mismatch repair status be added to sentinel lymph node mapping algorithm in endometrioid endometrial cancer?	Diniz TP et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36580755/
4	Diagnostic and prognostic potential of the microbiome in ovarian cancer treatment response	Asangba AE et al.	Sci Rep	https://pubmed.ncbi.nlm.nih.gov/36639731/
5	An angiogenic tumor phenotype predicts poor prognosis in ovarian cancer	Wieser V et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36758419/
6	Single-cell genomic variation induced by mutational processes in cancer	Funnell T et al.	Nature	https://pubmed.ncbi.nlm.nih.gov/36289342/



Treatment of pre-invasive gynaecological malignancies

Elko Gliozheni

Liu et al. conducted a study to compare the safety of cervical conisation (CC) alone versus hysterectomy for patients with adenocarcinoma in situ (AIS) of the cervix. The study found that CC with negative margins is an effective and safe option for AIS patients, with low rates of residual disease and recurrence. Hysterectomy did not significantly influence the risk of residual disease or recurrence. The large number of included patients is this study's strength (n = 453). The main limitation is its retrospective design. [1]

Bruno et al. conducted a retrospective study to evaluate the regression rate of cervical intraepithelial neoplasia (CIN) 3 diagnosed with a biopsy by studying the histological result of the cone removed by a loop electrosurgical excision procedure (LEEP). The study found that there is a 15.8% spontaneous regression rate of CIN3, which is strongly associated with a biopsy-cone interval of more than 11 weeks. Age and HPV genotype were not significant predictors of regression. The authors concluded

that waiting at least 11 weeks from the biopsy before qualifying the woman to LEEP could prevent unnecessary LEEP procedures, considering also that it takes years before the neoplastic transformation from CIN3 to carcinoma takes place. The study presents limitations due to its retrospective design; however, its strength is the entry criterion of CIN3 unlike other similar studies, which accepted CIN2 or CIN3 for this purpose. [2]

Schwameis et al. conducted a prospective phase II study which aimed to investigate the efficacy of a single application of 85% trichloroacetic acid (TCA) in treating cervical intraepithelial neoplasia (CIN) 1/2. A total of 102 patients with CIN 1/2 were treated with 85% TCA, and the results showed high histologic complete remission rates of 75.5% and 78.4% three and six months after treatment, respectively. HPV clearance rates were also observed, suggesting that TCA could be an effective non-surgical treatment approach for CIN. Data integrity and pro-

spective design are strengths of this study. A study limitation is that it presented no new knowledge about patients with CIN3, who require treatment the most. [3]

Wu et al. conducted a retrospective study analysing predictors of residual disease in patients who underwent hysterectomy following a LEEP for CIN3. Positive endocervical curettage (ECC), positive margin of LEEP samples, type II or III transformation zone, and infection with high-risk HPV types were found to be significant predictors of residual disease. Incomplete data about endocervical cytology after LEEP and retrospective design are the limitations of this study. [4]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Comparison of the safety between cervical conization and hysterectomy for patients with cervical adenocarcinoma in situ	Liu J et al.	J Gynecol Oncol	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9807369/
2	Spontaneous regression of cervical intraepithelial neoplasia 3 in women with a biopsy—cone interval of greater than 11 weeks	Bruno M et al	BMC Cancer	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9578209/
3	TRICIN: A phase II trial on the efficacy of topical trichloroacetic acid in patients with cervical intraepithelial neoplasia	Schwameis R et al.	Cancers (Basel)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9740961/
4	Clinical predictors of residual disease in hysterectomy following a loop electrosurgical excision procedure for cervical intraepithelial neoplasia grade 3	Wu Q et al.	BMC Pregnancy Childbirth	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9793502/



Treatment of elderly patients with gynaecological cancers

Alex Mutombo

So et al. conducted a retrospective study to evaluate survival rates and surgical outcomes in patients 65 and older with gynaecologic cancers between 2005 and 2020. The most patients were treated for ovarian cancer (OC), followed by endometrial cancer (EC), cervical cancer, and leiomyosarcoma. Their mean age was 70 (65–83) years; 80.9% of patients were young-old (those aged less than 75 years) and 19.1% were old-old (those aged 75 years and above). Nineteen patients experienced postoperative complications while four patients died within six months after surgery; three died because of disease progression. They found no difference in survival between the two groups. They concluded that older patients showed good outcomes and tolerable postoperative complications. However, the retrospective nature of the study, the fact that only patients who underwent surgery were included, and the small-scaled sample originating from a single hospital constituted limitations for this study. [1]

Park et al. used the SEER database to evaluate non-cancer related factors that influence the receipt of adjuvant radiotherapy after a hysterectomy for an early stage endometrial cancer in a series of 25,654

older women aged 66 years and above. Diagnosis and procedure codes were used to identify adjuvant radiotherapy claims filed for the seven-month period following hysterectomy. They found that Asian-American and Pacific Islander patients (PR 0.84; 95% CI: 0.73–0.97), women treated outside the Northeast region or those residing in rural areas (PR 0.75; 95% CI: 0.71–0.79), women with high probability of predicted of frailty (PR 0.67; 95% CI: 0.55–0.81), women who did not receive lymph node assessment (PR 1.43; 95% CI: 1.34–1.51 and women treated by a non-gynaecologic oncologist or outside of a large academic hospital were less likely to benefit from adjuvant radiotherapy. A limitation of the study is related to its retrospective nature with the possibility of several biases. [2]

Ogura et al. conducted a retrospective study to examine whether the geriatric nutritional risk index (GNRI) could influence the prognosis of older patients with epithelial ovarian cancer. They used data of 75 epithelial ovarian cancer patients who underwent surgical treatment at a single hospital from 2010 to 2015. Patients were divided into two groups based on the GNRI cut-off value calculated using the re-

ceiver operating characteristic curve. The calculated GNRI was 97.3. The survival rate was 61.9% for the group of patients with an index value > 97.3, and 39.4% for patients with an index value < 97.3 at 48 months ($p < 0.001$). At multivariate analysis, the GNRI was the only variable to show a significant influence on prognosis ($p = 0.0481$). In conclusion, this study shows the future possibilities of the clinical utility of GNRI in the creation of treatment strategies for EOC in developed countries. Limitations of the study included the single-centre retrospective design with differences in the patients' background data and the inability to assess differences in standard chemotherapy, maintenance therapy, and BRCA gene mutations. [3]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Surgical treatment outcomes of gynecologic cancer in older patients: A retrospective study	So K et al.	J Clin Med	https://www.ncbi.nlm.nih.gov/pubmed/37048601
2	Patient characteristics and health system factors associated with adjuvant radiation therapy receipt in older women with early-stage endometrial cancer	Park J et al.	J Geriatr Oncol	https://www.ncbi.nlm.nih.gov/pubmed/36088216
3	Clinical utility of the geriatric nutritional risk index before surgical intervention for epithelial ovarian cancer patients: A retrospective study	Ogura S et al.	J Clin Med Res	https://www.ncbi.nlm.nih.gov/pubmed/36406943



Fertility-sparing treatment in gynaecological malignancies

Charalampos Theofanakis

Endometrial cancer

A retrospective study by Liu et al. assessed the body mass index (BMI) interval as an independent risk factor for treatment efficacy in young patients with endometrial atypical hyperplasia (EAH) and endometrioid endometrial cancer (EEC). The study included 286 patients (209 with EAH and 77 with EEC) treated with progestins. Analysis compared cumulative complete response (CR) rate, recurrence rate (RR) and fertility outcomes, in comparison to different weight or metabolic statuses. Underweight and overweight/obese status significantly decreased the cumulative 16-week and 32-week CR rate ($p = 0.004$, $p = 0.022$, respectively). The highest 16-week CR rate was observed at a BMI of 21–22 kg/m² in the overall population ($p = 0.033$). Obesity (HR 0.37, 95% CI: 0.15–0.90, $p = 0.029$) and PCOS (HR 0.55, 95% CI: 0.31–0.99, $p = 0.047$) were associated with a lower 16-week CR rate. Hyperuricaemia (HR 0.66, 95% CI: 0.45–0.99, $p = 0.043$) was associated with a lower 32-week CR rate. The 16-week and 32-week CR rate ($p = 0.036$, $p = 0.008$, respectively) were significantly lower in patients exhibiting both obesity and hyperuricaemia. This is the first study to show that underweight status

has an adverse impact on fertility-sparing therapy; however, the small number of underweight patients (14) and the retrospective character of the analysis are study limitations. The authors concluded that the optimal fertility-sparing treatment (FST) efficacy was observed at BMI of 21–22 kg/m² in EAH/EEC and that hyperuricaemia was an independent risk factor for long-term treatment outcomes. [1]

Cervical cancer

A systematic review by Ronsini et al., focussed on fertility-sparing treatment options for patients with early-stage cervical cancer with tumour size above 2cm. Twenty-six studies with 691 patients were included in this study, in which surgery-based FST showed an RR of 0–42.9%. Papers regarding FST based on the neoadjuvant chemotherapy (NACT) approach showed a CR rate of 21.4–84.5%, and an RR of between 0 and 22.2%. The authors demonstrated the heterogeneity of various clinical approaches in early-stage cervical cancer patients with tumours ≥ 2 cm. The fact that this study analyses all patients with ECC ≥ 2 cm represents both its high and low points. Surgical treatment options including minimally invasive or vaginal approach showed higher

RR, while lack of standard protocols for NACT makes it ever harder to set an optimal standard course of treatment strategy for these patients. [2]

A systematic review by Yong et al. assessed the possible variations between reported outcomes of women who were offered fertility-sparing surgery for cervical cancer. Analysis identified 104 studies with 9,535 patients. Most studies reported on oncological outcomes (97/104), followed by fertility and pregnancy (86/104), postoperative complications (74/104), intra-operative complications (72/104), and quality of life (5/104). Significant variation and heterogeneity were reported, with only 12% being good quality and 87% being of poor quality. The authors concluded that an agreed Core Outcome Set is necessary for future studies to effectively unify reported outcomes that are measurable and relevant to patients, clinicians, and researchers. [3]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Effects of weight status and related metabolic disorders on fertility-sparing treatment outcomes in endometrial atypical hyperplasia and endometrial cancer: a retrospective study	Liu S et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/36291808/
2	Fertility-sparing treatment for early-stage cervical cancer ≥ 2 cm: a problem with a thousand nuances-a systematic review of oncological outcomes	Ronsini C et al.	Ann Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/36064991/
3	Variation in outcome reporting in studies of fertility-sparing surgery for cervical cancer: a systematic review	Yong N et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/36367451/



Prevention and management of surgical complications

Anastasia Prodromidou

According to the systematic review and meta-analysis by Jansen et al. on the laparotomic approach, the decreased number of excised lymph nodes and the additional performance of para-aortic lymph node dissection resulted in an elevated risk of lymphocele formation in patients who had lymph node dissection due to cervical and endometrial cancer. More specifically, the dissection of a mean number of less than 21 lymph nodes was associated with a significantly increased rate of lymphoceles compared to those with a mean number of resected nodes >21 (19% vs 5%, $p = 0.002$). [1]

The use of vacuum-assisted wound closure (VAWC) for the primary closure of abdominal fascia was evaluated after cytoreductive surgery (CRS) in patients with epithelial ovarian cancer (OC) by Mercadel et al. The total of the cases that required VAWC achieved primary closure of the fascia ($n = 19$ patients, 100%). The indications for VAWC application were gastrointestinal perforation, intestinal ischemia, necrotic enterocolitis, anastomotic leakage, and ab-

dominal haemorrhage for the prevention of abdominal compartment syndrome. The authors concluded that the use of VAWC resulted in a decrease in early post-operative morbidity and mortality. [2]

Wang et al. aimed to detect the risk factors for developing postoperative complications in patients who had major surgery for gynaecologic oncologic indications. Patients with prolonged hospital stays were more likely to be diagnosed with a postoperative Clavien-Dindo complication grade \geq II (OR 1.474, $p = 0.0084$). Moreover, a hospital stay of more than four days was associated with an elevated risk of developing 30-day grade II-IV complications after discharge compared to hospitalisation for four days or less. In addition, a prolonged hospital stay led to a significantly increased risk of 30-day readmission ($p = 0.0046$). [3]

According to the prospective study by Kengsakul et al., both Clavien-Dindo complication and Comprehensive Complication Index (CCI) complication

assessment tools were found to have comparable diagnostic performance for the prediction of postoperative outcomes after CRS in patients with advanced OC. However, CCI presented an improved performance in discrimination of prolonged hospitalisation compared to the Clavien-Dindo classification ($p < 0.001$). This was not observed when admission to intensive care unit, 30-day readmission and time to chemotherapy > 42 days were compared among the two classification systems ($p = 0.25$, $p = 0.22$, and $p = 0.90$, respectively). [4]

Relevant articles retrieved September 30, 2022 – March 31, 2023

No	Title	Authors	Journal	Link to abstract
1	Lymphocele following lymph node dissection in cervical and endometrial cancer: A systematic review and meta-analysis	Jansen A et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36738486/
2	Risk factors for catheter-associated urinary tract infections following radical hysterectomy for cervical cancer	Mercadel AJ et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/36863644/
3	Patient-reported symptoms at discharge and risk of complications after gynecologic surgery	Wang XS et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36600503/
4	Clinical validation and comparison of the Comprehensive Complication Index and Clavien-Dindo classification in predicting post-operative outcomes after cytoreductive surgery in advanced ovarian cancer	Kengsakul M et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36600504/



Nutrition and perioperative care

Begoña Díaz de la Noval

Thomson et al. presented initial findings from the Lifestyle Intervention in Ovarian Cancer Enhanced Survival (LIVES) study (NRG/GOG0225). LIVES is a multicentre phase III trial involving 1,205 stage II-IV ovarian cancer survivors, implementing a 24-month programme focused on modifying lifestyle factors including diet and physical activity to enhance progression-free survival. Participants enrolled within six months of successful first-line treatment receive remote intervention facilitated by trained health coaches through text messaging and email. The control group addresses general health topics. Primary outcomes include progression-free survival, with secondary outcomes encompassing quality of life and adherence to lifestyle changes. Study demographics reflect disease characteristics with elevated metabolic biomarkers and potential for improvement in lifestyle behaviours. The high adherence in the intervention group suggests motivation among ovarian cancer survivors to adopt healthier habits. [1]

The European Organization for Research and Treatment published the largest multicentre randomised control trial on the impact of blood transfusion in advanced epithelial OC (n = 612). The study demonstrated that peri-operative transfusions were not associated with changes in progression-free survival (p = 0.96) or overall survival (p = 0.97) but with increased peri-operative morbidity without

improved quality of life. Some limitations mentioned were the variability in transfusion protocols and the fact that transfusion was more common in complex primary debulking surgery, which limits a causative relationship. [2]

Narasimhulu et al. validated the Mayo triage algorithm in 625 patients post-debulking surgery for stage IIIC/IV advanced ovarian cancer. Complications were assessed using the modified Accordion classification, with high-risk patients identified retrospectively based on Mayo criteria. The algorithm found 20.3% to be high-risk, with a threefold increase in 90-day mortality (p = 0.02). While severe post-operative complications at 30 days showed no significant difference between high-risk and triage-appropriate groups (p = 0.17), those high-risk after a grade 3+ complication had a higher 90-day mortality (25.9% vs 10.0%; p = 0.05). The study's eight-year inclusion span and retrospective analysis are acknowledged limitations, impacting the completeness of morbidity and mortality data, especially with follow-up loss. [3]

Brasky et al. performed a meta-analysis investigating the association between dietary omega-3 fatty acids and the risk of endometrial cancer (EC). The study gathered data from 12 prospective cohort studies involved in the Epidemiology of the Endometrial

Cancer Consortium, encompassing a sample of 7,212 cases and 26,031 controls. The findings suggested that a greater dietary intake of long-chain omega-3 polyunsaturated fatty acids (LCn3PUFA) was associated with a 9% increased risk of EC (95% CI: 1.01–1.19; p = 0.04). Though heavier women (BMI ≥ 25kg/m²) had an increased risk of EC (95% CI: 1.05–1.29; p = 0.004), no association was found among BMI < 25kg/m² (95% CI: 0.87–1.15; p = 0.875), race, or EC grade. The study had a high statistical power and the largest number of patients to date. Still, some risk factors for EC were not considered (such as family history of EC and history of oestrogen-only hormone therapy), caloric intake or dietary supplementation was not considered, and control of the confounding bias through stratification by race was not possible. [4]

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No	Title	Authors	Journal	Link to abstract
1	Lifestyle intervention in ovarian cancer enhanced survival (LIVES) study (NRG/GOG0225): recruitment, retention and baseline characteristics of a randomized trial of diet and physical activity in ovarian cancer survivors	Thomson CA et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36608382/
2	Transfusion use and effect on progression-free, overall survival, and quality of life in upfront treatment of advanced epithelial ovarian cancer: evaluation of the European Organization for Research and Treatment EORTC-55971 Cohort	Prescott LS et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36356982/
3	Validation of a risk-based algorithm to reduce poor operative outcomes after complex surgery for ovarian cancer	Narasimhulu DM et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36517075/
4	Dietary omega-3 fatty acids and endometrial cancer risk in the epidemiology of Endometrial Cancer Consortium: an individual-participant meta-analysis	Brasky TM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36934308/



Follow-up after gynaecological malignancies

Sunaina Wadhwa

There is a variation observed in the diagnosis, treatment, and follow-up of patients with endometrial cancer across different Asian countries. To enhance clinical outcomes and standardise the care of endometrial cancer patients, the European Society for Medical Oncology and a group of Asian experts have proposed guidelines for management specific to the pan-Asian region.

There is a lack of evidence supporting intensive, clinician-led, hospital-based follow-up evaluations for endometrial cancer patients, leading to a lack of consensus on appropriate surveillance tests. It has been determined that clinical monitoring can be tailored based on a patient's risk factors. Results

from the multicentre phase III TOTEM trial based in Europe have refuted any survival benefits from intensive compared to minimal follow-up, including high-risk patients. Although follow-up strategies for the low-risk group have been slightly adjusted in the current guidelines to address Asian region-specific needs and issues, they are uniformly applied to the high-risk group.

For low-risk patients, the recommended surveillance includes evaluations at least every six months for the first two years, followed by yearly assessments until the fifth year. Each visit entails a physical and gynaecological examination. Notably, in contrast to the 2022 ESMO guidelines for the Western world,

remote follow-up can be integrated into hospital-based follow-up rather than relying solely on telephonic follow-up. [1]

PROS: This guideline, though drawn on data from Western and Asian trials, acknowledges the variations in clinical presentation, diagnostic practices, discrepancies in access to therapeutic alternatives, etc., worldwide.

CONS: Because of the heterogeneity in practices across the continents based on distinct recommendations, multicentric trials or study collaborations will be challenging in the future.

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No	Title	Authors	Journal	Link to abstract
1	Pan-Asian adapted ESMO clinical practice guidelines for the diagnosis, treatment and follow-up of patients with endometrial cancer	Koppikar S et al.	ESMO Open	https://pubmed.ncbi.nlm.nih.gov/36696825/



Quality of life in gynaecological cancers/Palliative care

Nadja Taumberger and Engin Çelik

Vestergaard et al. conducted a retrospective national study based on official registries in Denmark from 2010–2016 and included patients who died from gynaecological cancer in this period. The aim was to estimate the percentage of patients who received hospital-based specialist palliative care (SPC) and investigate if there was a correlation between the gynaecological cancer type, year of death, and other factors. They included 4,502 patients and saw an

overall increase in SPC from only around 24% in 2010 to more than 50% in 2016. Moreover, younger age, as well as more than three comorbidities and living outside the capital region, was associated with increased SPC utilization. In patients who used SPC, the risk of admission to the intensive care unit, as well as the risk for surgery in the last month before death, was decreased. This has been shown to be an important factor when it comes to improving quality

of life at the end of life. The authors concluded that SPC utilization in Denmark increased in the investigated period and that it is associated with less high-intensity end-of-life care, such as ICU admissions or surgery in the last two weeks before death. [1]

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No	Title	Authors	Journal	Link to abstract
1	Utilisation of hospital-based specialist palliative care in patients with gynaecological cancer: Temporal trends, predictors and association with high-intensity end-of-life care	Vestergaard AHS et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36905767/



Hereditary gynaecological cancer

Tibor A. Zwimpfer

The new clinical practice guidelines for risk reduction and screening in hereditary breast-ovarian cancer have been published. Patients with pathogenic BRCA1 mutations have the highest lifetime risk of ovarian cancer (OC) (40–60%), followed by BRCA2 (15–30%), RAD51C/D (10%), and BRIP1 (5–10%). Salpingo-oophorectomy remains the most effective strategy for OC risk reduction and is recommended for women with pathogenic BRCA1 and BRCA2 mutations who have completed childbearing at 35–40 and 40–45 years, respectively. It can also be considered for women with pathogenic BRIP1 or RAD51C/D and completed family planning at 45–50 years of age. Salpingectomy is not recommended for risk reduction outside of clinical trials. Individuals with an increased familial risk should be offered genetic testing and awareness should be raised. [1]

In a retrospective study of a total of 28,586 patients with potentially hereditary breast (n = 15,005), ovarian (n = 924), pancreatic (n = 2,364), and prostate cancer (n = 10,293), Clark et al. showed that the genetic testing frequency almost doubled from 11.5% in 2013 to 21.5% in 2019 (p < 0.001). OC showed the highest frequency with 39.5% compared to 27.4% for breast, 6% pancreatic, and 3.5% prostate cancer. The testing frequency more than doubled in OC, from 21.8% in 2013 to

46.3% in 2019 (p < 0.001). Additionally, patients with advanced (Stage II+III) compared to early OC were more likely to have undergone genetic testing (OR 2.01, 95% CI: 1.26–3.22; OR 1.76, 95% CI: 1.06–2.91, respectively). This also highlights that although there has been an increase in the frequency of genetic testing in recent years, there is still room for improvement. [2]

In their systematic review and meta-analysis, Mitric et al. investigated mismatch-repair deficiency (MMRd), microsatellite instability (MSI) and Lynch syndrome (LS) in OC. A total of 55 cohort, cross-sectional, and case series studies were included. Epithelial OC showed MMRd in 6%, high MSI in 13%, and LS in 2% of patients. MSH6 and MSH2 were the most frequently mutated genes. In detail, the serous subtype showed the lowest and the endometrioid the highest prevalence with MMRd 1% versus 12%, high MSI 9% versus 12%, and LS 1% versus 3%. This study showed that MMRd and LS testing should be considered in endometrioid and, where appropriate, in non-serous or non-mucinous epithelial OC. [3]

A subgroup analysis of the phase III PAOLA-1/ENGOT-ov25 trial investigated whether the mutation location of BRCA1 (n = 159) and BRCA2 (n = 74) in advanced high-grade OC show a benefit from

olaparib+bevacizumab maintenance therapy. A benefit of olaparib+bevacizumab therapy was shown regardless of BRCA status [BRCA1, HR = 0.26 (95% CI: 0.16–0.41); BRCA2, HR = 0.22 (0.09–0.54); interaction p = 0.64]. Furthermore, there was a trend for better treatment response in patients with BRCA1/2 mutation location on exon 11 [exon 11, HR = 0.2 (0.11–0.36); non-exon 11, HR = 0.41 (0.22–0.75), interaction p = 0.14]. Specifically, there was a significant advantage in patients with BRCA1 mutation on the DNA-binding-domain compared to other locations in BRCA1 [HR = 0.08 (0.02–0.28); interaction p = 0.03]. Patients with BRCA-mutated high-grade OC all showed a benefit with olaparib+bevacizumab maintenance therapy, but this benefit was particularly high in specific mutation locations of BRCA1/2. [4]

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No	Title	Authors	Journal	Link to abstract
1	Risk reduction and screening of cancer in hereditary breast-ovarian cancer syndromes: ESMO Clinical Practice Guideline	Sessa C et al.	Annals of Oncology	https://pubmed.ncbi.nlm.nih.gov/36307055/
2	Genetic testing among patients with high-risk breast, ovarian, pancreatic, and prostate cancers	Clark NM et al.	Annals of Surgical Oncology	https://pubmed.ncbi.nlm.nih.gov/36335273/
3	Mismatch-repair deficiency, microsatellite instability, and lynch syndrome in ovarian cancer: A systematic review and meta-analysis	Mitric C et al.	Gynecologic Oncology	https://pubmed.ncbi.nlm.nih.gov/36682091/
4	Association of location of BRCA1 and BRCA2 mutations with benefit from olaparib and bevacizumab maintenance in high-grade ovarian cancer: phase III PAOLA-1/ENGOT-ov25 trial subgroup exploratory analysis	Labidi-Galy SI et al.	Annals of Oncology	https://pubmed.ncbi.nlm.nih.gov/36564284/



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