LiFE report
Literature for ENYGO

LiFE | Literature for ENYGO

Reviews covering publications from March 31, 2023 – March 31, 2024

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Dear Colleagues,

We are delighted to present the 18th edition of LiFE, featuring comprehensive reviews of the most noteworthy articles in gynaecological oncology published between March 31, 2023, and March 31, 2024, across 33 diverse topics.

The LiFE Team is excited to welcome our new contributors, 7 (Esra Bilir, Christian Braun, Andrea Rosati, Filip Karuga, Grzegorz Chmielewski, Andrej Cokan, Dimitry Utkin), expanding our team to 37 members from 18 countries around the world. Their contributions are invaluable in helping us provide you with high-quality, relevant content that can impact your daily practice. We are also grateful to all ENYGO/ESGO members who use LiFE to enhance their knowledge in the field. Together, we can advance the field of gynaecological oncology and improve patient outcomes worldwide. Additionally, we extend our sincere appreciation to the *International Journal of Gynecological Cancer* for their ongoing support.

We trust that you will find this report informative and beneficial for your daily practice. Please share the report link with your colleagues and on social media. If you are interested in joining the LiFE team and contributing to our collective efforts, we warmly invite you to contact us at adminoffice@esgo.org.

Furthermore, ENYGO/ESGO cordially invites you to the 26th ESGO Congress, which will be held from February 20-23, 2025, in the historic city of Rome, Italy. We look forward to seeing you there!

Yours sincerely,
LiFE Editors

Zoia Razumova
Joanna Kacperczyk-Bartnik
Stamatios Petousis
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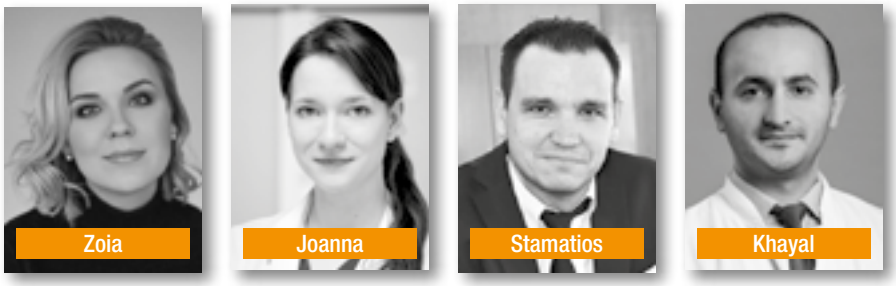

On behalf of the entire editorial board and the contributing authors, we would like to express our deepest gratitude for the exceptional leadership and commitment during tenure of Dr Zoia Razumova as Editor-in-Chief of LiFE Report. For many years, her dedication, expertise, and vision have significantly shaped the success and role of LiFE Report in advancing the field of gynecologic oncology.

LiFE Report is a project providing a vital platform for early-career researchers and clinicians passionate about gynecologic oncology. Efforts of the leaving Editor-in-Chief, the Founders of the project and all current and previous contributors, have fostered an environment of collaboration and mentorship, allowing emerging voices in the field to share their insights.

Invaluable contributions by Dr Zoia Razumova have set a standard of excellence that will continue to inspire our growth for years to come. We are truly grateful for her leadership, guidance, and the legacy she leaves behind.

Dear Zoia, as you transition to new endeavors, we wish you continued success and fulfilment. It has been an honour working with you, and we hope to stay in touch as as your dedication to the field leaves a lasting mark.

On behalf of the LiFE Report Team,

Joanna Kacperczyk-Bartnik

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Medical treatment of primary ovarian cancer

Ilker Selçuk

The final overall survival (OS) results of the PAOLA-1/ENGOT-ov25 trial were published after a median follow-up of 61 months with 55% data maturity. In this trial, newly diagnosed advanced-stage, high-grade ovarian cancer patients who responded to first-line, platinum-based chemotherapy plus bevacizumab were randomized 2:1 (535 vs. 267 patients) to olaparib (300 mg twice daily, up to 24 months) plus bevacizumab (15 mg/kg every three weeks for 15 months) or placebo plus bevacizumab. The trial included patients regardless of surgical or biomarker status; about 50% had upfront surgery and 40% had residual postoperative disease. Median OS was 56.5 vs. 51.6 months in the intention-to-treat population (HR=0.92, 95% CI 0.76-1.12, p=0.4118). Notably, 19.6% of patients in the olaparib arm and 45.7% in the placebo arm received a subsequent PARP inhibitor. In homologous recombination deficiency (HRD)-positive patients, five-year OS rates were 65.5% vs. 48.4%, with a median of 75.2 vs. 57.3 months (HR=0.62, 95% CI 0.45-0.85). In HRD-positive tumours, the OS benefit was independent of BRCA status. Median OS was not reached in the olaparib group compared to 52 months in HRD-positive, BRCA-negative patients (HR=0.71, 95% CI 0.45-1.13). In HRD-negative tumours, five-year OS rates were 25.7% vs. 32.3% (median OS: 36.8 vs. 40.4 months, HR=1.19, 95% CI 0.88-1.63). Median progression-free survival (PFS) in HRD-positive patients was 46.8 vs. 17.6 months (HR=0.41, 95% CI 0.32-0.54). No new safety signals were reported. [1]

The PRIMA/ENGOT-OV26/GOG-3012 trial involved newly diagnosed advanced-stage ovarian cancer patients with a complete or partial response after first-line, platinum-based chemotherapy, randomized to niraparib or placebo in a 2:1 ratio (487 vs. 246 patients). After a median follow-up of 41 months, 9.2% in the niraparib arm and 33.3% in the placebo arm received subsequent PARP inhibitors. For HRD patients, median PFS was 24.5 months in the niraparib arm vs. 11.2 months in the placebo arm (HR=0.52). In BRCA-mutated HRD patients, median PFS was 31.5 vs. 11.5 months (HR=0.45, 95% CI 0.32-0.64), while in BRCA wild-type HRD patients, it was 19.4 vs. 10.4 months. In HR-proficient patients, PFS was 8.4 vs. 5.4 months. Niraparib showed benefits across high-risk subgroups, including those with partial responses to chemotherapy, neoadjuvant therapy, or stage IV disease. OS data remains immature, and no new safety signals were noted. [2]

The IMagyn050/GOG 3015/ENGOT-Ov39 trial evaluated atezolizumab, an immune checkpoint inhibitor, combined with carboplatin-paclitaxel and bevacizumab in patients with advanced ovarian cancer. Patients with primary cytoreductive surgery who had residual disease or received neoadjuvant chemotherapy with interval surgery were randomized 1:1 (651 vs. 650 patients) to atezolizumab or placebo. In PD-L1 positive patients, median OS was not estimable in the atezolizumab arm vs. 49.2 months in the placebo arm (p=0.13, HR=0.83, 95% CI 0.66-1.06). In the intention-to-treat population, median OS was 50.5 vs. 46.6 months (HR=0.92, 95% CI 0.78-1.09), with no significant OS improvement in any subgroup. About half of the patients received subsequent systemic treatment. Atezolizumab did not significantly improve survival outcomes in ovarian cancer. [3]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Olaparib plus bevacizumab first-line maintenance in ovarian cancer: final overall survival results from the PAOLA-1/ENGOT-ov25 trial	Ray-Coquard I et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/37211045/
2	Progression-free survival and safety at 3.5 years of follow-up: results from the randomised phase 3 PRIMA/ENGOT-OV26/GOG-3012 trial of niraparib maintenance treatment in patients with newly diagnosed ovarian cancer	González-Martín A et al.	Eur J Cancer	https://pubmed.ncbi.nlm.nih.gov/37263896/
3	Overall survival and patient-reported outcome results from the placebo-controlled randomized phase III IMagyn050/GOG 3015/ENGOT-OV39 trial of atezolizumab for newly diagnosed stage III/IV ovarian cancer	Pignata S et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37625235/

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Medical (chemo and radiotherapy) treatment of recurrent ovarian cancer

Seda Şahin Aker and Stamatios Petousis

Arend et al. published a placebo-controlled, double-blind randomised controlled trial (RCT) evaluating the 1:1 effectiveness of the addition of ofranergene obadenovec (ofra-vec) to standard chemotherapy on a weekly basis for recurrent platinum-resistant ovarian cancer patients. The authors observed no significant difference in median overall survival (OS) (13.7 months vs. 13.14 months), while the objective response rate (ORR) was also similar between the two groups. The safety profiles were also observed to be comparable. The authors concluded that the addition of ovra-vec to paclitaxel did not significantly improve survival outcomes. A limitation of the study might be the non-stratification of patients based on homologous recombination deficiency (HRD) and BRCA status. However, this is one of several published reports regarding the ofra-vec medication regimen. [1]

Another important study on the issue of recurrent ovarian cancer patients was conducted by Pujade-Lauraine et al. The authors published the results of OReO-ENGOT-ov38, a randomized double-blind RCT. The study included relapsed platinum-sensitive ovarian cancer patients who had already received one prior line of treatment with PARP inhibitor therapy. Rechallenge with olaparib in this category of patients indicated significantly improved survival outcomes, with a median progression-free survival (PFS) of 4.3 months with olaparib vs. 2.8 months with placebo. Results were also consistent in the non-BRCA mutated group. The authors concluded that, in this category of patients, rechallenge with olparib resulted in significant PFS improvement independent of BRCA status. However, this improvement is limited and characterized as modest, therefore requiring further research or more targeted paper selection to optimize the results. [2]

Kurtz et al. reported on ATALANTE/ENGOT-ov29, a double-blind RCT in which recurrent ovarian cancer patients were assigned in a 2:1 ratio to atezolizumab vs. placebo. The study included only platinum-sensitive ovarian cancer patients. The authors reported that after three years, the PFS difference between atezolizumab and placebo did not reach statistical significance in the intention-to-treat population, nor in the PD-L1 positive population. The immature OS also did not reach statistical significance, at 35.5 months for atezolizumab vs. 30.6 months for placebo (95% CI 0.65-1.01). Furthermore, no significant difference was observed regarding grade 3 or higher adverse outcomes. In conclusion, the ATALANTE study did not reach statistical significance; however, the study is ongoing. Further research of biopsy samples is required to better understand the immunological background of patients presenting with late relapse. [3]

Peipert et al. published the results of patient-reported outcomes of ARIEL3, a placebo-controlled RCT in which patients with recurrent ovarian cancer were stratified to rucaparib maintenance vs placebo. The authors reported that the addition of rucaparib was correlated with an increased likelihood of the deterioration of patient-reported outcomes. Results were consistent in both BRCA and HRD mutated populations. Based on the outcomes of the study, the authors concluded that patients should be informed of the increased rates of adverse side effects of PARP inhibitors, which may outweigh any clinical benefit. A basic limitation of the study might be the inevitably subjective manner of outcome reporting, which is based not on a numeric measurable outcome but on a purely patient-reporting scale. [4]

Lastly, Colombo et al. published the results of a double-blind RCT in which patients were allocated to either trabectedin/PLD (TP) or carboplatin/PLD for treatment of relapse. The authors concluded that no significant difference was observed in the median OS between the two groups, while grade 3-5 adverse reactions were significantly increased in the TP group. Therefore, the patients concluded that carboplatin/PLD should remain the standard of care in those presenting with recurrence, while TP should be considered as an alternative treatment for patients presenting with persistent platinum side-effects. [5]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Ofranergene obadenovec (ofra-vec, VB-111) with weekly paclitaxel for platinum-resistant ovarian cancer: Randomized controlled phase III trial (OVAL Study/GOG 3018)	Arend RC et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37906726/
2	Maintenance olaparib rechallenge in patients with platinum-sensitive relapsed ovarian cancer previously treated with a PARP inhibitor (OReO/ENGOT-ov38): A phase IIIb trial	Pujade-Lauraine E et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/37797734/
3	Atezolizumab combined with bevacizumab and platinum-based therapy for platinum-sensitive ovarian cancer: Placebo-controlled randomized phase III ATALANTE/ENGOT-ov29 trial	Kurtz J-E et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37643382/
4	Patient-reported outcomes of maintenance rucaparib in patients with recurrent ovarian carcinoma in ARIEL3, a phase III, randomized, placebo-controlled trial	Peipert JD et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37262961/
5	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.	Br J Cancer	https://pubmed.ncbi.nlm.nih.gov/36759720/

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Surgical treatment of primary and recurrent ovarian cancer

Ilker Kahramanoglu

The OVHIPEC-1 trial, a randomized, controlled phase III study, investigated the impact of adding hyperthermic intraperitoneal chemotherapy (HIPEC) to interval cytoreductive surgery in patients with stage 3 epithelial ovarian cancer who were not candidates for primary cytoreduction. Aronson et al. reported final survival analysis from the OVHIPEC-1 study after 10 years of follow-up. Patients receiving HIPEC had significantly better progression-free survival (PFS) (14.3 months vs. 10.7 months, HR=0.63, 95% CI 0.48-0.83, p=0.0008) and overall survival (OS) (44.9 months vs. 33.3 months, HR=0.70, 95% CI 0.53-0.92, p=0.011) compared to those undergoing surgery alone. This study presents the first long-term survival analysis of HIPEC in patients with ovarian cancer. [1]

Nagao et al. conducted a multi-institutional observational study (GOTIC-019) involving 940 women with FIGO stage 3-4 epithelial ovarian cancer. The study compared the outcomes of patients undergoing NAC followed by interval debulking surgery (IDS) versus those undergoing primary debulking surgery (PDS) followed by adjuvant chemotherapy. The results indicated that NAC followed by IDS did not improve OS compared to PDS, particularly in patients with FIGO stage 3C disease, with NAC associated with shorter OS (48.1 vs. 68.2 months, HR=1.34, p = 0.06). Complete cytoreductive surgery was associated with significantly longer median PFS and OS in the PDS group compared to the NAC followed by IDS group (PFS: 21.5 months vs. 43.1 months, HR=1.47, 95% CI 1.23-1.76, p<0.0001; OS: did not reach the median vs. 57.2 months, HR=1.44, 95% CI:1.21-1.72, p<0.0001). The authors concluded that easy acceptance of NAC in advanced epithelial ovarian cancer should be avoided. However, there are several shortcomings of this study. First, among the 152 patients receiving primary surgery, 59 were placed in the NAC group due to not achieving the pre-planned surgical goals, potentially underestimating survival data in this cohort despite matching methods. Second, differences in chemotherapy regimens may have affected outcomes, with the NAC group receiving more dose-dense TC therapy and the PDS group more likely receiving bevacizumab. Lastly, the matching process might not have fully accounted for differences, such as the higher likelihood of high-grade serous carcinoma (HGSC) in the NAC cohort and potential stage misclassification in the PDS cohort. [2]

A population-based retrospective analysis conducted in France by Prost et al. examined the correlation between the volume of ovarian cancer surgeries performed at hospitals and patient outcomes. Analysing data from 8,429 patients treated between 2012 and 2016, the study found that patients who underwent surgery at high-volume centres (≥20 cases/year) had significantly better 5-year OS than those treated at low-volume centres (<20 cases/year) (63% vs. 60%, p=0.02). Multivariate analysis revealed that OS was significantly higher in low-volume hospitals (10-19 cases/year) compared to very low-volume hospitals (<10 cases/year), with survival rates of 63% vs. 59% (p<0.01). Similarly, the analysis showed a significant difference in OS between very high-volume hospitals (≥30 cases/year) and very low-volume hospitals (<10 cases/year), with rates of 63% vs. 59% (p<0.01). Additionally, recurrence-free survival (RFS) was less favourable in very low-volume hospitals (<10 cases/year) compared to other hospitals (HR=1.14, 95% CI 1.05-1.23).The study emphasizes the limited but significant clinical benefits associated with higher surgical volumes, suggesting that centralizing ovarian cancer surgeries in high-volume hospitals could improve patient outcomes, though challenges in accessibility and capacity should be considered. Retrospective design is the main limitation of this study. [3]

Praiss et al. investigated postoperative complications of 83 patients with recurrent platinum-sensitive ovarian cancer who were enrolled in a phase II trial randomized to HIPEC or no HIPEC. Among the patients analysed, 40% experienced grade ≥3 complications, while 60% had grade <3 complications. The most common severe complications were anaemia (27.7%) and abdominal infections (6%). Patients with grade ≥3 complications faced a slight delay in initiating postoperative chemotherapy (34 days vs. 31 days, p=0.017), but this did not significantly impact PFS (11.2 months vs. 14.9 months, p=0.186) or OS (46.9 months vs. 68.2 months, p=0.053). The study concludes that while severe postoperative complications can delay chemotherapy, they do not significantly affect long-term oncologic outcomes. This study benefits from using prospective data from the original phase II clinical trial, but it is an unplanned exploratory analysis and was not powered to evaluate differences in time to initiation of chemotherapy, PFS, and OS. [4]

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No	Title	Authors	Journal	Link to abstract
1	Cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy in patients with advanced ovarian cancer (OVHIPEC-1): Final survival analysis of a randomised, controlled, phase 3 trial	Aronson SL et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/37708912/
2	Neoadjuvant chemotherapy followed by interval debulking surgery for advanced epithelial ovarian cancer: GOTIC-019 study	Nagao S et al.	Int J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37140771/
3	Impact of ovarian cancer surgery volume on overall and progression-free survival: A population-based retrospective national French study	Prost P et al.	Ann Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/38393461/
4	Morbidity after secondary cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy for ovarian cancer: An analysis of a randomized phase II trial	Praiss AM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36804618/

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Borderline ovarian tumours

Anton Ilin

Borderline ovarian tumours (BOTs) pose unique challenges in oncogynaecology due to their borderline nature and varied risk factors associated with treatment and outcomes. This review compiles recent research findings to offer a detailed understanding of the associations between fertility treatments and BOTs, the risk of secondary primary malignancies in BOT survivors, the potential diagnostic utility of microRNAs (miRNAs), and the risk of non-ovarian cancers in BOT patients.

Kristensen et al. conducted an extensive cohort study to examine the link between fertility treatments and the incidence of BOTs among infertile women. The study followed 146,891 women aged 20-45 in Denmark between 1995 and 2017. Using national registry data, the researchers evaluated the impact of various fertility drugs on the development of BOTs. Over a median follow-up period of 11.3 years, 144 women were diagnosed with BOTs. The analysis revealed no significant correlation between the use of fertility drugs such as clomiphene citrate, gonadotropins, gonadotropin-releasing hormone modulators, human chorionic gonadotropin, and progesterone and the risk of BOTs. This lack of association held true for both serous and mucinous subtypes of BOTs. The study underscores the importance of extended follow-up periods to conclusively determine the long-term effects of fertility treatments. [1]

Wang et al. investigated whether survivors of BOTs are at increased risk of developing secondary primary malignancies. The study used data from the Surveillance, Epidemiology, and End Results (SEER) program to conduct a retrospective analysis. The study cohort included 3,661 BOT patients diagnosed between 1977 and 2000, with a median follow-up of nearly two decades. The analysis found that the risk of secondary primary malignancies in BOT survivors was not significantly higher than in the general population, with a standardized incidence ratio (SIR) of 0.88. Notably, higher risks were associated with mucinous BOTs, age over 50, and lack of lymph node dissection. Lymphadenectomy and age emerged as strong predictors of secondary primary malignancy risk, suggesting that BOT survivors do not face an increased overall risk of secondary malignancies. [2]

Dolivet et al. explored the potential of miRNAs as diagnostic biomarkers for differentiating between mucinous borderline and malignant ovarian tumours. Given the rarity and poor prognosis of mucinous ovarian carcinoma, early and accurate diagnosis is crucial. The researchers compared miRNA expression profiles in malignant and borderline tumour samples. They identified distinct patterns of miRNA expression, with 10 miRNAs down-regulated and five up-regulated in malignant tumours. A combination of 14 miRNA ratio pairs was found to accurately distinguish between malignant and borderline tumours, suggesting that miRNA signatures could significantly improve the precision of histological diagnoses and inform surgical and therapeutic decision-making. [3]

Dobilas et al. conducted a national cohort study in Sweden to assess the risk of non-ovarian cancers in women diagnosed with BOTs. The study tracked 4,998 women with serous and mucinous BOTs diagnosed between 1995 and 2018. The findings indicated an elevated risk for several non-ovarian cancers, including those of the colon, rectum, small intestine, cervix, endometrium, pancreas, upper aerodigestive tract, lung, kidney, and bladder. Additionally, women with serous BOTs showed an increased risk of thyroid cancer. These results suggest that BOT patients have higher risks for various non-ovarian malignancies, potentially pointing to shared etiological factors. [4]

Si et al. conducted a systematic review and meta-analysis to clarify the controversial link between infertility drug exposure and the risk of borderline ovarian tumours. The analysis included 10 studies published from 1990 to 2021, covering a total of 2,779,511 women. The pooled data revealed a significant association between infertility drug use and an increased risk of BOTs, with an odds ratio (OR) of 1.56. Specifically, the combination of clomiphene citrate and gonadotropins showed a notable increase in risk. However, no dose-dependent relationship was found between the number of assisted reproduction technology cycles and BOT risk. Interestingly, successful pregnancies among infertile women appeared to mitigate this risk. [5]

Collectively, these studies deepen our understanding of the complexities surrounding borderline ovarian tumours. The findings highlight the non-significant association between fertility drugs and BOTs, normal secondary primary malignancy risks in BOT survivors, the diagnostic potential of miRNA signatures, and the increased risk of non-ovarian cancers in BOT patients. Ongoing long-term research and the development of advanced diagnostic tools are essential for improving patient outcomes and guiding clinical practices in oncogynaecology.

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No	Title	Authors	Journal	Link to abstract
1	Risk of borderline ovarian tumours after fertility treatment: Results from a Danish cohort of infertile women	Kristensen AK et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38382167/
2	Do survivors of borderline ovarian tumours have susceptibility to secondary primary malignancies? A SEER population-based study	Wang J et al.	Int J Gyanecol Obstet	https://pubmed.ncbi.nlm.nih.gov/38205842/
3	Synergy of the microRNA ratio as a promising diagnosis biomarker for mucinous borderline and malignant ovarian tumours	Dolivet E et al.	Int J Mol Sci	https://pubmed.ncbi.nlm.nih.gov/37958997/
4	Risks of non-ovarian cancers in women with borderline ovarian tumour: a national cohort study in Sweden	Dobilas A et al.	BMC Cancer	https://pubmed.ncbi.nlm.nih.gov/37807065/
5	Effects of infertility drug exposure on the risk of borderline ovarian tumours: A systematic review and meta-analysis	Si M et al.	Biomedicines	https://pubmed.ncbi.nlm.nih.gov/37509474/

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Treatment of ovarian sex cord stromal and germ cell tumours

Paul Kubelac

A retrospective cohort analysis of 26 patients who underwent 51 complete surgical cytoreductions for relapsed granulosa cell tumours of the ovary over 20 years at two ESGO-accredited centres assessed the effectiveness of adjuvant systemic therapy. The study found no statistically significant differences in disease-free survival (DFS) among patients who received adjuvant chemotherapy (n=21, DFS 57 months), hormonotherapy (n=10, DFS 36 months), or no systemic treatment (n=20, DFS 57 months; p=0.616). Independent predictive factors for subsequent recurrences included extra-pelvic and/or multifocal tumour dissemination. However, factors such as advanced age, high BMI, repeated recurrences, initial surgical procedures and outcomes, first-line treatment modalities, interval time to recurrence, and the presence of ascites, nodal, or peritoneal involvement at recurrence did not show prognostic value. The authors concluded that maximal cytoreductive surgery remains the cornerstone of treatment for relapsed granulosa cell tumours. This study was a multicentric analysis that included patients over a period of two decades; however, its limitations reside in the small sample size and retrospective design. Hence, the adjuvant treatment decision was at the physician's discretion based on local protocols, missing data on treatment toxicities and quality of life. [1]

A study from the MD Anderson Rare Gynecologic Malignancy Registry, which included 149 patients, evaluated the role of serial cytoreductive surgery in recurrent adult-type ovarian granulosa cell tumours compared to systemic therapy alone. Secondary cytoreductive surgery significantly improved progression-free survival (PFS) (multivariate HR=0.42, p=0.03) and overall survival (OS) (multivariate HR=0.28, p=0.004). Similarly, tertiary cytoreductive surgery was associated with better PFS (HR=0.43, p=0.001), although quaternary cytoreductive surgery did not significantly improve PFS (HR=0.74, p=0.27). The study concluded that cytoreductive surgery could enhance survival in recurrent disease if tumour resection is feasible. This was a large study conducted over five decades, with extensive follow-up. However, its retrospective design may lead to selection bias. Hence, patients with unresectable disease or poor surgical candidates were excluded. Additionally, given the long time span, the study was limited by temporal changes in treatment strategies. [2]

A study conducted by 13 centres within the French Rare Malignant Gynecological Tumors Network included 469 patients with malignant sex cord-stromal tumours (SCSTs), 75% of whom had adult granulosa cell tumours. The study evaluated the impact of adjuvant chemotherapy following upfront surgery between 2011 and 2015. Adjuvant chemotherapy was administered to 14.7% of patients but did not significantly affect PFS in stage I (HR=1.02, p=0.9) or stage II (HR 0.76, p=0.6) disease. The five-year PFS was 72% for the chemotherapy group versus 74% for the control group. The BEP chemotherapy regimen did not demonstrate superiority in terms of PFS compared to other chemotherapy options (HR=0.88, p=0.7). All stage III and IV patients received adjuvant chemotherapy, precluding a comparative analysis. Following a first relapse, surgical treatment (HR=0.41, p=0.002) and the completeness of tumour debulking (HR=3.6, p=0.004) were significant predictors of improved outcomes in multivariate analysis, while chemotherapy had no significant impact on PFS. After a second relapse, only surgery remained a significant predictor for PFS (HR=0.43, 95% CI 0.23-0.8). This was a large multicentric study with long follow-up. However, its limitations reside in its retrospective design, with no data on performance status or comorbidities, which is commonly seen in this rare patient population given the difficulties of organizing a randomized trial. [3]

A comparative analysis from the Malignant Germ Cell International Consortium included 42 Brazilian children with ovarian immature teratoma who underwent surgery, of whom 13 received postoperative chemotherapy. The study found no differences in PFS or OS based on receipt of chemotherapy. This Brazilian cohort was compared with 98 patients from the US/UK cohort, showing no differences in event-free survival (EFS) or OS across all stages, despite 87% of stage II-IV Brazilian patients receiving adjuvant chemotherapy compared to 13% of US/UK patients. Although patient data was captured from clinical trials, study limitations included differences between trials in staging, risk stratification, treatment plans, lack of central pathology review, incomplete data on treatment at relapse, and a short follow-up for long-term toxicities. [4]

Another retrospective single-institution study examined the role of adjuvant chemotherapy in 74 patients diagnosed with stage I immature teratoma over four decades. After fertility-sparing surgery, 12% received adjuvant chemotherapy. No significant differences in recurrence rates were observed with respect to initial stage (IA-IB: 10%, IC: 28.6%, p=0.087), tumour grade (grade 1: 7.1%, grade 2: 14.3%, grade 3: 22.2%, p=0.39), or receipt of chemotherapy (no adjuvant chemotherapy: 13.9%, adjuvant chemotherapy: 11.1%, p=1.00). The five-year DFS was 87% in the surveillance group and 90% in the chemotherapy group, with overall survival at 100% in both groups. Although this was one of the largest single-centre case series reported with pure ovarian immature teratoma and homogenous treatment, study limitations include the retrospective design, small sample size and a low number of patients with high-risk disease, limited rate of events, and a low percentage of complete surgical staging. [5]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Effectiveness of adjuvant systemic therapy following complete cytoreductive surgery in patients with recurrent granulosa cell tumours of the ovary	Yumru Celiksoy H et al.	Sci Rep	https://pubmed.ncbi.nlm.nih.gov/38200105/
2	Serial cytoreductive surgery and survival outcomes in recurrent adult-type ovarian granulosa cell tumors	How JA et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/38191019/
3	Impact of surgery and chemotherapy in ovarian sex cord-stromal tumors from the multicentric Salomé study including 469 patients: A TMRG and GINECO group study	Hanvic B et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37210929/
4	Adjuvant chemotherapy does not improve outcome in children with ovarian immature teratoma: A comparative analysis of clinical trial data from the Malignant Germ Cell International Consortium	Vieira AGS et al.	Pediatr Blood Cancer	https://pubmed.ncbi.nlm.nih.gov/37243320/
5	Outcome of patients with stage I immature teratoma after surveillance or adjuvant chemotherapy	Marino G et al.	Front Oncol	https://pubmed.ncbi.nlm.nih.gov/38371620/

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

Richárd Tóth

Hinchcliff et al. conducted a randomized phase II trial investigating tremelimumab and durvalumab in patients with platinum-resistant (PR) ovarian cancer. A total of 38 patients received sequential therapy: 3 mg/kg of tremelimumab every four weeks, up to four doses or until disease progression, followed by 1.5 g of durvalumab every four weeks for up to nine doses. An additional 23 patients were treated with a combination of durvalumab (20 mg/kg) and tremelimumab (1 mg/kg) every four weeks. The primary endpoint was immune-related progression-free survival (PFS), while secondary endpoints included toxicity, overall response rate (ORR), overall survival (OS), and clinical benefit rate. There was no significant difference between the arms in terms of median PFS (1.84 vs. 1.87 months) or OS (10.61 vs. 7.26 months), with both comparable to historical data. Grade 3 or higher immune-related adverse events (AEs) occurred in 23.7% and 30.4% of patients in the sequential and combination arms, respectively. Symptom burden, quality of life, and health status were worse in the combination arm, although not statistically significant. [1]

The same agents were evaluated in the KGOG 3045 study, a multicentric, open-label phase II trial. This trial included 58 recurrent ovarian cancer patients without homologous recombination deficiency. Patients with high PD-L1 expression were enrolled in arm A and received durvalumab (1,500 mg every four weeks for up to 24 months) along with single-agent chemotherapy (six cycles of topotecan or weekly paclitaxel). Those with low PD-L1 expression were assigned to one of three additional arms: arm B received durvalumab with single-agent chemotherapy plus four cycles of 75 mg tremelimumab every four weeks; arm C received durvalumab with four cycles of weekly paclitaxel plus a one-time dose of 300 mg tremelimumab ; and arm D received durvalumab with single-agent chemotherapy.
The primary endpoint was ORR, with secondary endpoints including PFS, OS, duration of response, time to response, disease control rate, and safety. The median follow-up was 8.3 months, and patients received an average of four cycles. The ORR was 27.6%, with a disease control rate of 60.3% and two complete responses. Median time to response was 11.2 weeks, and the duration of response was 24.2 weeks. No significant differences in PFS or OS were found between the arms. Treatment-related AEs of any grade were observed in 86.2% of patients, with 56.9% experiencing grade 3-4 AEs. In a multivariate analysis, the addition of tremelimumab was associated with improved PFS, though higher rates of immune-related AEs were observed. [2]

The GINECO group conducted an open-label, single-arm phase II study on the combination of bevacizumab, olaparib, and durvalumab in patients with relapsed ovarian cancer. Patients could have previously received either bevacizumab or olaparib, but not both together, and none had received durvalumab. Olaparib (300 mg) was administered orally twice daily, while a bevacizumab biosimilar (FKB238, 15 mg/kg) and durvalumab (1.12 g) were given once every three weeks until progression, unacceptable toxicity, or withdrawal of consent, for up to two years. The primary objective was to assess efficacy, measured by the rate of non-progressive disease at three months for PR patients and six months for platinum-sensitive (PS) patients. Secondary objectives included CA-125 decline, PFS, OS, tumour response, and safety. The study included 74 patients, of whom 41 were PR. The median administered doses were nine for bevacizumab , durvalumab, and olaparib. Of the patients, 89% had a primary ovarian tumour, 96% had serous histology, and 24% had a BRCA mutation. Median follow-up was 15.4 months, with a three-month PFS of 69.8% for PR patients and a six-month PFS of 43.8% for PS patients.
All patients experienced at least one AE, with the most common being asthenia, nausea, anaemia, diarrhoea, arthralgia, and dyspnoea. Grade ≥3 AEs occurred in 26% of patients, with four experiencing grade 4 events. Biomarker analyses revealed that higher tumour inflammation signature (TIS) scores, especially when combined with the KELIM-B score, predicted better survival outcomes. Higher TIS was associated with improved PFS and OS. [3]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Randomized phase 2 trial of tremelimumab and durvalumab in combination versus sequentially in recurrent platinum-resistant ovarian cancer	Hinchcliff EM et al.	Cancer	https://pubmed.ncbi.nlm.nih.gov/38009662/
2	Durvalumab with or without tremelimumab plus chemotherapy in HRR non-mutated, platinum-resistant ovarian cancer (KGOG 3045): A phase II umbrella trial	Kim SI et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38246047/
3	Bevacizumab, olaparib, and durvalumab in patients with relapsed ovarian cancer: A phase II clinical trial from the GINECO group	Freyer G et al.	Nat Commun	https://pubmed.ncbi.nlm.nih.gov/38443333/

Medical (chemo and radiotherapy) treatment of primary uterine cancer

Radwa Hablase

The randomised phase III DUO-E trial (NCT04269200) investigated the addition of durvalumab to carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced and recurrent endometrial cancer. A total of 718 patients were randomly assigned into three treatment arms, with 241 receiving carboplatin/paclitaxel plus durvalumab placebo followed by placebo maintenance (control arm); 238 receiving carboplatin/paclitaxel plus durvalumab followed by maintenance durvalumab plus olaparib placebo (durvalumab arm); and 239 receiving carboplatin/paclitaxel plus durvalumab followed by maintenance durvalumab plus olaparib (durvalumab + olaparib arm). The primary endpoint was progression-free survival (PFS), and secondary endpoints included overall survival (OS), patient-reported outcomes, and safety. Prespecified exploratory subgroup analyses of PFS were conducted based on treatment arm, microsatellite instability, and PD-L1 status. The durvalumab and durvalumab + olaparib arms demonstrated statistically significant PFS benefits over the control arm (HR=0.71, 95% CI 0.57-0.89, p=.003 and HR=0.55, 95% CI 0.43-0.69, p<.0001, respectively). These benefits were observed in both the mismatch repair deficient (dMMR) and mismatch repair proficient (pMMR) subgroups, as well as the PD-L1–positive subgroup. The overall incidence of grade 3 or higher adverse events (AEs) in the control, durvalumab, and durvalumab + olaparib arms was 56.4%, 54.9%, and 67.2%, respectively. OS interim analysis supported the primary endpoint results. A strength of the trial was the wider inclusion of Asian patients compared to the RUBY trial, while a weakness was the small proportion of stage III patients due to the requirement for measurable disease. [1]

The updated efficacy and safety report from the 309/KEYNOTE-775 trial (NCT03517449) compared the combination of lenvatinib and pembrolizumab to the physician's choice of chemotherapy (doxorubicin or paclitaxel) in patients with advanced or recurrent endometrial cancer. Results showed continued OS benefits, despite 10.0% of the pMMR population and 8.7% of all-comers in the chemotherapy arm subsequently receiving lenvatinib plus pembrolizumab. No new safety signals were identified. A total of 827 patients were randomized, with results stratified by MMR status, comprising approximately 700 patients in the pMMR group. The overall median follow-up duration was 14.7 months (18.7 months in the lenvatinib plus pembrolizumab arm and 12.2 months in the chemotherapy arm). A limitation of this trial is the relatively short follow-up period, which may imply that responses are still evolving. While the protocol-defined criteria for efficacy analyses were met, safety and efficacy monitoring continues. [2]

The phase III Lunchbox trial compared sequencing cisplatin with irradiation (chemoRT) followed by carboplatin and paclitaxel versus a sandwich approach of carboplatin and paclitaxel followed by irradiation and then carboplatin and paclitaxel in advanced and high-risk early-stage endometrial cancer. The trial was unfunded and closed early due to slow patient accrual, with only 48 participants recruited over seven years. Of the recruited patients, 42 were eligible for futility analysis. The three-year recurrence-free survival and overall survival OS rates were not statistically significant between the two groups: 85.7% (95% CI 62-95) and 88.4% (95% CI 61-97) in the chemoRT arm versus 73.4% (95% CI 43-89) and 80.9% (95% CI 51-93) in the sandwich arm (p=0.58 and p=0.55, respectively). This study's strength lies in its prospective, multi-institutional comparison of standard treatments for advanced endometrial cancer. Limitations include lack of funding, slow patient accrual, and selection bias, affecting generalizability. [3]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line Treatment for advanced endometrial cancer: The phase III DUO-E trial	Westin SN et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37864337/
2	Lenvatinib plus pembrolizumab in previously treated advanced endometrial cancer: Updated efficacy and safety from the randomized phase III study 309/KEYNOTE-775	Makker V et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37058687/
3	Lunchbox trial: A randomized phase III trial of cisplatin and irradiation followed by carboplatin and paclitaxel versus sandwich therapy of carboplatin and paclitaxel followed by irradiation then carboplatin and paclitaxel for advanced endometrial carcinoma	Barlin JN et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38052110/

Medical (chemo and radiotherapy) treatment of recurrent uterine cancer

Stamatios Petousis

Liang et al. have published a systematic review and meta-analysis of the impact of PD-1 inhibitor therapy in patients with advanced or recurrent uterine cancer. The authors concluded that therapy resulted in significantly improved overall survival (OS) (HR=0.65, 95% CI 0.59-0.72, p<.001) and progression-free survival (PFS) (HR=0.59, 95% CI 0.49-0.70, p<.001) compared with controls, without a significant increase of grade 3 or higher adverse effects. This is the first study to assess the impact of PD-1 therapy, demonstrating significant benefits and reviewing five randomised controlled trials (RCTs). This study is limited in that it includes only endometrial and cervical cancer patients, though the authors state that subgroup analysis indicated a beneficial impact on all types of cancers. [1]

Bartoletti et al. published a meta-analysis of the addition of anti-PD1 or anti PD-L1 agents to platinum-based chemotherapy for advanced or recurrent endometrial cancer. The authors reported a beneficial effect to PFS of adding immune checkpoint inhibitors to chemotherapy (pooled HR=0.63, 95 % CI 0.52-0.76, p<.001). They noted that in mismatch repair deficient (dMMR) patients, optimal benefit was observed only when anti-PD1 agents were administered. Subgroup analysis of the proficient mismatch repair (pMMR) population was derived from only three RCTs, with the authors limiting the meta-analysis to PFS even though OS would also be of interest to consider. Still, this is just one of a few quality meta-analyses clearly demonstrating the beneficial impact of immunotherapy agents for advanced or recurrent cases of endometrial cancer. [2]

Yonemori et al. published East Asia subgroup analysis results from the 309/KEYNOTE-775 study regarding the use of levatinib plus pembrolizumab versus chemotherapy in patients with advanced or recurrent endometrial cancer. The authors concluded that PFS was significantly improved in the pMMR and all-comer populations of the subgroup receiving this treatment combination. However, they also reported treatment-related adverse events in 97% and 96%, respectively, for these two populations. The authors concluded that levatinib and pembrolizumab resulted in a clinically meaningful benefit, with acceptable safety, for this category of patients. A limitation of this study is that it represents only an exploratory analysis of evaluated outcomes in patients of East Asia; however, this robust and well-designed trial indicates a significant benefit of immunotherapy in patients with advanced/recurrent endometrial cancer. [3]

Vergote et al. reported on an interesting RCT investigating the therapeutic role of oral selinexor as maintenance treatment after chemotherapy in advanced or recurrent endometrial cancer. The authors did not observe any significant benefit of PFS between patients receiving selinexor (5.7 months) versus placebo (3.8 months). However, the significance level for PFS was reached in the audited analysis, and the rate of grade 3 adverse events was lower than 10%. This is the first published RCT on this medication to examine its potential benefit, with the authors concluding that the results show promise toward prolonging time until first and second relapse, even though further research is needed to achieve further clarity and statistical significance. [4]

Finally, Mekker et al. published updated efficacy and safety results from the well-known and important phase III 309/KEYNOTE-775 study. In total, 827 advanced-stage endometrial cancer patients were recruited to receive lenvatinib plus pembrolizumab versus chemotherapy. OS, PFS, and objective response rate were all significantly improved in both pMMR and all-comer patients receiving the combination of lenvatinib plus pembrolizumab, with a 30-35% increase in OS (pMMR HR=0.70, 95% CI 0.58-0.83; all-comer HR=0.65, 95% CI 0.55-0.77) and 40-44% increase in PFS (pMMR HR=0.60, 95% CI 0.50-0.72; all-comer HR=0.56, 95% CI 0.48-0.66). There were no significant safety issues indicated. This is the first and largest trial to clearly demonstrate the supremacy of lenvatinib plus pembrolizumab over conventional chemotherapy in advanced-stage endometrial cancer patients, leading to a great shift in the management of advanced-stage endometrial cancer patients. [5]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Impact of programmed cell death protein 1 inhibitor therapy on the survival of patients with advanced or recurrent uterine cancers: A meta-analysis	Liang K-W et al.	Front Immunol	https://pubmed.ncbi.nlm.nih.gov/38562939/
2	Incorporation of anti-PD1 or anti PD-L1 agents to platinum-based chemotherapy for the primary treatment of advanced or recurrent endometrial cancer: A meta-analysis	Bartoletti M et al.	Cancer Treat Rev	https://pubmed.ncbi.nlm.nih.gov/38422895/
3	Analysis of East Asia subgroup in study 309/KEYNOTE-775: Lenvatinib plus pembrolizumab versus treatment of physician's choice chemotherapy in patients with previously treated advanced or recurrent endometrial cancer	Yonemori K et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38302725/
4	Oral selinexor as maintenance therapy after first-line chemotherapy for advanced or recurrent endometrial cancer	Vergote I et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37669480/
5	Lenvatinib plus pembrolizumab in previously treated advanced endometrial cancer: Updated efficacy and safety from the randomized phase III study 309/KEYNOTE-775	Mekker V et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37058687/

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Surgical treatment of primary and recurrent uterine cancer

Houssein El Hajj

Three studies evaluated minimally invasive surgery (MIS) in endometrial cancer (EC), focusing on different techniques and outcomes. Sia et al. conducted a retrospective analysis comparing MIS and laparotomy in stage I serous carcinoma [1]. Of 391 patients, 242 underwent MIS (65% robotic-assisted surgery [RAS]) and 149 laparotomy. MIS was associated with lower lymphovascular space invasion, fewer nodes removed, and lower paraaortic dissection rates, with no statistical differences in five-year progression-free survival (PFS) and overall survival (OS) rates (58.7% vs. 59.8% and 65.2% vs. 63.5%). Lim et al. compared RAS and conventional laparoscopy surgery (CLS) in early-stage endometrioid EC [2], including 1,728 patients (1,389 RAS, 339 CLS), finding no significant differences between the two groups in recurrence rates (9.5% vs. 7.4%, p=0.3), five-year PFS (88.5% vs. 91.0%, p=0.3), or five-year OS (92.5% vs. 92.4%, p=0.7). RAS was associated with an 18-minute increase in operative times (p<0.001) but lower conversion rates and higher same-day discharge rates. Kang et al. conducted a randomized controlled trial (RCT) comparing laparoendoscopic single-site surgery (LESS) and CLS in early-stage EC [3]. They included 107 patients (53 LESS and 54 CLS), finding no significant differences in operation time, resected lymph nodes, or complication rates. After a median follow-up time of 34 months, PFS rates were 96.2% and 98.1% (p=0.55) and OS rates were 98.1% and 100.0% (p=0.31) in the LESS group and the CLS group, respectively. The study concluded that LESS is a safe alternative for early-stage EC. [1-3]

Kadoch et al. investigated the impact of body mass index (BMI) on RAS outcomes in 1,329 patients, finding no differences in post-anaesthesia care unit stay (p=0.105), hospital stay (p=0.497), or postoperative complications across BMI groups (8-9.5%, p=0.761). However, BMI≥40 had slightly higher median blood loss (30 mL vs. 20 mL) and longer operative times (288 min vs. 270 min; p<0.001) [4].

Two studies provide valuable insights into the applications and outcomes of sentinel lymph node (SLN) dissection and lymph node dissection (LND) in EC. In the SENTIREC-endo study, Bjørnholt et al. conducted a national multicentre prospective evaluation that included 627 women (458 low-risk and 169 intermediate-risk) to investigate the risks and benefits of SLN. The SLN detection rate was 94.3%, and the overall incidence of nodal metastases was 9.3% (4.4% in low-risk and 22.5% in intermediate-risk). Ultrastaging identified 62% of metastases. Postoperative and intraoperative complication rates were 8% and 0.3%, respectively. SLN did not impact the risk of lymphedema (5.2%) or swelling (5.8%). Holtzman et al. analysed 189 high-risk EC patients (23.7% SLN and 73.7% LND). There was no significant difference in the three-year PFS rate (71%, p=0.91), unadjusted HR (1.11), or adjusted HR (1.04) for recurrence in the SLN versus LND groups. The three-year OS was higher in the LND group (95.1% vs. 81.1%, p=0.009), with an unadjusted HR for death of 3.74 for the SLN group versus the LND group (p=0.009). However, after adjusting for age, adjuvant therapy, and surgical approach, the HR decreased to 2.90 and was no longer statistically significant (p=0.06). [5, 6]

Three studies evaluated intraoperative factors' impact on surgery. Saini et al. evaluated intraoperative tumour spillage (ITS) in 1,057 patients treated with MIS. They found that 20% of recurrences had ITS compared to 4% of nonrecurrent controls, with an increased recurrence risk of 5.6 times in case of ITS, when adjusted for tumour size, myoinvasion, and adjuvant treatment. Laskov et al. retrospectively evaluated the impact of intrauterine manipulators in 699 patients. They found that manipulators were associated with increased positive cytology (8.8% vs. 4.4%, p=0.02). After a median follow-up of 44 months, they found no difference in total recurrence rate (p=0.8); however, vaginal vault recurrence was higher in the manipulator group (4.5% vs. 1.3%, p=0.007). Among low-risk patients not receiving adjuvant treatment, the manipulator group had higher recurrence rates (8.3% vs. 3%, p=0.023) and worse DFS (p=0.01). After adjusting for other variables, manipulator use did not significantly affect overall recurrence risk or survival. In their systematic review, Zorzato et al. included 14 studies with 5,019 patients. Manipulator use was associated with a pooled recurrence HR of 1.52 (p=0.05; chi-square p=0.22). When considering only RCTs, the pooled recurrence HR was 1.48 (p=0.62; chi-square p=0.08). The HR for OS was 1.07 (p=0.79; chi-square p=0.17). [7-9]

Zhang et al. and Kanno et al. studied the impact of surgery on stage IVB EC survival. Zhang et al. used the SEER database to analyse 1,978 patients diagnosed between 2004 and 2016, revealing that cancer-directed surgery (CDS) significantly prolonged overall survival, especially in patients under age 60 and those with T1 and T2 invasions. Their findings suggest that surgery, including palliative hysterectomy, should be considered even in advanced stages to improve survival outcomes. Kanno et al. retrospectively reviewed 67 patients, comparing survival outcomes between those who had surgery either before or after chemotherapy and those who received only chemotherapy. They found that complete intra-abdominal cytoreductive surgery (R0 resection) markedly extended median survival to 44 months in the preceding surgery group and 27 months in the chemotherapy followed by surgery group, compared to significantly shorter survival with residual disease (R1 resection) or chemotherapy alone. Both studies highlight the potential survival benefits of aggressive surgical approaches in managing advanced EC, particularly when complete resection is achievable. Zhang et al. emphasize the broader application of CDS across different patient profiles, while Kanno et al. focus on the timing and extent of cytoreductive surgery in conjunction with chemotherapy. These findings collectively suggest that surgical intervention, tailored to individual patient conditions and complemented by chemotherapy, can significantly enhance survival in stage IVB EC. [10, 11]

These studies offer valuable data but face limitations. Sia et al. and Lim et al.'s large sample sizes strengthen outcomes, but retrospective designs add bias. Kang et al.'s RCT offers rigor but has a small sample and short follow-up. Kadoch et al. and Holtzman et al. offer insights into BMI and high-risk groups but are limited by retrospective designs. Bjørnholt et al.'s multicentre prospective study strengthens SLN findings but focuses on low/intermediate risk. Saini et al and Laskov et al. highlight intra-operative issues but face design limitations. Zorzato et al.'s meta-analysis aggregates large data but struggles with heterogeneity, while Zhang et al. and Kanno et al. provide insights on cytoreductive surgery limited by retrospective design and sample size.

Surgical treatment of primary and recurrent endometrial cancer

Houssein El Hajj

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No	Title	Authors	Journal	Link to abstract
1	Laparoscopy with or without robotic assistance does not negatively impact long-term oncologic outcomes in patients with uterine serous carcinoma	Sia TY et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37267674/
2	Oncologic outcomes of robot-assisted laparoscopy versus conventional laparoscopy for the treatment of apparent early-stage endometrioid adenocarcinoma of the uterus	Lim YH et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37980770/
3	Laparo-endoscopic single-site versus conventional laparoscopic surgery for early-stage endometrial cancer: A randomized controlled non-inferiority trial	Kang O-J et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37105060/
4	The impact of body mass index on robotic surgery outcomes in endometrial cancer	Kadoch E et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38368813/
5	The SENTIREC-endo study: Risks and benefits of a national adoption of sentinel node mapping in low and intermediate risk endometrial cancer	Bjørnholt SM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36893488/
6	Outcomes for patients with high-risk endometrial cancer undergoing sentinel lymph node assessment versus full lymphadenectomy	Holtzman S et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37270906/
7	Intra-operative tumor spillage in minimally invasive surgery for endometrial cancer and its impact on recurrence risk	Saini A et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37356313/
8	The impact of intrauterine manipulators on outcome and recurrence patterns of endometrial cancer patients undergoing minimally invasive surgery	Laskov I et al.	J Womens Health (Larchmt)	https://pubmed.ncbi.nlm.nih.gov/38170184/
9	Intrauterine manipulator during hysterectomy for endometrial cancer: A systematic review and meta-analysis of oncologic outcomes	Zorzato PC et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/37704174/
10	Survival benefit of surgical treatment for patients with stage IVB endometrial cancer: A propensity score-matched SEER database analysis	Zhang Y et al.	J Obstet Gynaecol	https://pubmed.ncbi.nlm.nih.gov/37170930/
11	Efficacy of intra-abdominal cytoreductive surgery in advanced endometrial cancer with distant metastasis	Kanno M et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37477100/

Uterine sarcoma

Marcin Bobiński

The STATICE trial investigated the efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing advanced or recurrent uterine carcinosarcoma. The results showed high objective response rates (ORRs) (54.5% for HER2-high and 70% for HER2-low groups). Median progression-free survival (PFS) was 6.2 months for HER2-high and 6.7 months for HER2-low expression, with overall survival (OS) reaching 13.3 months in HER2-high patients. Adverse events, including grade 3 toxicities, were consistent with prior studies and manageable. Strengths include promising efficacy regardless of HER2 status; limitations involve a small sample size and limited follow-up. [1]

The SARCUT study examined prognostic factors in 683 patients with uterine sarcomas across multiple institutions. Findings revealed that incomplete tumour removal, advanced stage, and tumour persistence significantly impacted survival, particularly in leiomyosarcoma, endometrial stromal sarcoma, and undifferentiated sarcoma. Adenosarcoma prognosis was strongly linked to the FIGO stage at diagnosis. Key risk factors for relapse included lymphovascular invasion and receiving adjuvant chemotherapy. Strengths include a large sample size and international scope, while limitations stem from its retrospective nature and heterogeneity in treatment approaches. [2]

The study by Knipprath-Mészáros et al. assessed the Basel sarcoma score in differentiating uterine myomas from sarcomas using six sonographic criteria in 545 patients. The score showed high negative predictive value of 99.8%, meaning it effectively rules out sarcomas in patients with low scores. The sensitivity and specificity were 93.8% and 97.9%, respectively, for sarcomatous masses. Strengths include its simplicity and potential use in routine sonographic examinations. However, caution is advised for patients with scores above 1, as false positives are possible. [3]

The results of the phase II study by Ingham et al. evaluated the efficacy of olaparib and temozolomide for advanced uterine leiomyosarcoma. Among 22 patients, the ORR was 27%, with a median PFS of 6.9 months. Hematologic toxicity, including neutropenia, was common but manageable. The study identified a link between homologous recombination deficiency (HRD) and prolonged PFS. This combination therapy met its primary endpoint and showed promise for patients with pretreated advanced uterine leiomyosarcoma, especially those with HRD. However, the small sample size and toxicity issues limit the broader applicability of the findings. [4]

Toyohara et al. aimed to develop an artificial intelligence (AI) system (AutoDiag) to aid in diagnosing uterine sarcomas using MRI data from 342 patients. The AI system employed a deep neural network to automatically detect tumour sites and classify them as sarcomas. Results showed high diagnostic performance, with an accuracy of 92.44%, sensitivity of 92.25%, and specificity of 92.50%, comparable to human radiologists. This technology holds promise for improving diagnostic precision and workflow efficiency in clinical settings. However, further external validation and testing on larger cohorts are necessary. Additionally, real-world applications need refinement to handle more diverse cases and imaging variations. The study highlights the potential of AI in transforming diagnostic processes, although limitations include the need for ongoing model improvements and wider adoption. [5]

Garcia et al. analysed the impact of perioperative factors on recurrence risk and survival in 390 patients with uterine leiomyosarcoma. The key findings indicated that incomplete cytoreduction significantly increased recurrence and decreased OS. Tumour persistence, margin involvement, and the use of adjuvant chemotherapy and radiotherapy were also associated with poorer outcomes. Complete cytoreduction emerged as the most important factor for improving disease-free and OS rates. The results suggest that minimizing residual tumour burden and carefully considering adjuvant treatments are crucial for improving patient prognosis. [6]

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No	Title	Authors	Journal	Link to abstract
1	Trastuzumab deruxtecan for human epidermal growth factor receptor 2-expressing advanced or recurrent uterine carcinosarcoma (NCCH1615): The STATICE trial	Nishikawa T et al.	J Clin Onc	https://pubmed.ncbi.nlm.nih.gov/36977309/
2	Prognostic factors in patients with uterine sarcoma: The SARCUT study	Zapardiel I et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37192761/
3	High negative prediction for the Basel sarcoma score: Sonographic assessment of features suspicious of uterine sarcoma	Knipprath-Mészáros AM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37210928/
4	Phase II study of olaparib and temozolomide for advanced uterine leiomyosarcoma (NCI Protocol 10250)	Ingham M et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37467452/
5	The automatic diagnosis artificial intelligence system for preoperative magnetic resonance imaging of uterine sarcoma	Toyohara Y et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38246183/
6	Impact of perioperative characteristics on the recurrence risk and survival of patients with uterine leiomyosarcoma	Garcia M et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37485666/

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Emerging molecular-targeted therapies or early preclinical trials in uterine tumours

Jakub Dobroch

Efficacy of trastuzumab deruxtecan (T-DXd) was assessed in a phase II study of multiple HER2-expressing solid tumours, including endometrial cancer (EC) (n=40). Objective response rate (ORR) was set as a primary endpoint in the analysis. Prescribed dose totalled 5.4 mg/kg every 3 weeks. Out of examined cohorts, patients with EC demonstrated the highest rate of ORR (57.5%). The result was even more distinct in the subgroup with stronger HER2 expression. The majority of recruited patients suffered from a recurrent disease. Progression-free survival (PFS) in the EC group was 11.1 months and OS was 26 months. The most common adverse event was nausea. Grade 3 or more severe complications occurred in 35.0% of patients from the EC cohort. T-DXd in a prescribed dose turned out to be promisingly effective in HER2-positive EC patients. Further investigation in a randomized setting is required. [1]

Efficacy and safety of another anti-HER2 agent, zanidatamab, which binds two different HER2 epitopes, was assessed in a phase II study. It included 16 patients with metastatic EC or carcinosarcoma. Partial response was achieved only in one of the patients, while clinical benefit rate (CBR) was 37.5%. Low efficacy of the examined agent might be associated with HER2-downregulation assessed by FISH and immunohistochemistry caused by prior treatment regimens. [2]

Lurbinectedin monotherapy (3.2 mg/m2 every three weeks) was administered to 73 EC patients in a phase II basket trial. The research included either early stage, locally advanced, or metastatic cases representing all major pathological and molecular subtypes. The majority of participants underwent previous anticancer treatment. Only 11.3% of patients achieved ORR. Median PFS and OS were 2.6 and 9.2 months, respectively. Patients with a p53abn mutation had significantly worse OS (6.6 months vs. 16.1 in the p53-wt group). The safety profile of lurbinectedin was assessed as predictable and manageable. The authors concluded that further research on this anti-transcription agent should consider combination with cytostatic therapy. [3]

A four-arm phase II study including 241 participants was performed to assess the clinical outcome of sapanisertib (a selective dual inhibitor of mTORC1/2) in recurrent EC patients. Enrolled women were divided into four study groups. The first received weekly paclitaxel, the second paclitaxel and sapanisertib (4 mg on days 2-4, 9-11, 16-18, and 23-25), the third sapanisertib monotherapy (30 mg weekly), and the fourth sapanisertib with TAK-117 (a PI3K inhibitor). Results in the third and fourth arm were distinctly worse than in arms including paclitaxel. The primary endpoint of PFS was 3.7 versus 5.6 months in the paclitaxel monotherapy group vs. the paclitaxel-sapanisertib group (HR=0.82, p=0.139). Statistical significance was not reached in OS analysis (14.6 vs. 13.7 months). CBR, which includes complete response, partial response, and stable disease, reached 57.5% vs. 80.2 in the first arm vs. the second arm. This effect was even more noticeable in endometrioid histology EC (55% vs. 84%). Adverse events (overall and grade ≥3) were visibly more common in the combined treatment group, although they were most often entirely manageable. The authors recommended further investigation of sapanisertib efficacy in combination with cytostatic agents, especially in endometrioid EC. [4]

One-hundred twenty patients with advanced and recurrent EC were enrolled in a phase II study on the efficacy of olaparib and cediranib either in monotherapy or combined treatment. Cediranib is an angiogenesis inhibitor and olaparib is a poly-ADP-ribose polymerase inhibitor commonly prescribed in maintenance therapy of OC. Participants were randomly assigned to three study arms. The primary endpoint, PFS, was 2.0 months for olaparib monotherapy, 3.8 months for cediranib alone, and 5.5 months for combined therapy. No statistical significance nor primary endpoint was reached. The authors concluded that the combination of olaparib and cediranib demonstrated modest clinical efficacy. Toxicity rates were predictable and comparable between examined groups. [5]

Another phase II study was conducted on efficacy of theONC201 molecule in patients with advanced, recurrent endometrial and breast cancer. ONC201 leads to nonapoptotic cell death through an alteration of mitochondrial function. Out of 22 patients recruited to the study, 10 suffered from endometrial cancer. Both clinical outcome and molecular effects on mitochondria by tissue sampling before and after treatment were assessed. In the EC group, six patients were eligible for final assessment and only two of them achieved any clinical benefit, which was stable disease. Although the safety profile of ONC201 was assessed as acceptable, the clinical outcome of the prescribed dose (625 mg by mouth weekly) was generally poor. Analysis of taken tissue samples revealed no mitochondrial damage caused by ONC201. [6]

Patients suffering from recurrent EC, platinum-resistant ovarian cancer (OC), and triple-negative breast cancer were recruited to a phase I study on mirvetuximab soravtansine (MIRV), a conjugated cytostatic-antibody drug combined with gemcytabine. Patients were assessed towards a MIRV target, folate receptor alpha expression. Maximal tolerated dose was set on 6 mg/kg of adjusted ideal body weight. Twenty patients diagnosed with aforementioned cancers were recruited. Despite promising efficacy in ovarian cancer patients, the authors concluded that with regard to frequent haematological toxicity, there are more effective combination therapies including MIRV available. [7]

Efficacy of the novel agent DKN-01 was investigated in a phase II basket study either in monotherapy or in combination with weekly paclitaxel in EC and platinum-resistant OC patients. Specimens were genetically analysed for DKK-1 and other Wnt signalling alterations. EC patients with high DKK-1 expression showed better response in both mono and combined therapy arms. ORR was 25% versus 0%, and disease control rate was 62.5% versus 6.7% in the DKK-1-high and DKK-1-low groups, respectively. Further investigation of targeted treatment approach was recommended. [8]

Patients with recurrent or persistent clear cell OC and EC were recruited to a phase II study which investigated the effectiveness of dasatinib, a tyrosine kinase inhibitor. Expression of ARID1A gene alterations was assessed at the time of qualification to the study. Out of 28 evaluable patients, one achieved partial response, 28% stable disease, and 53.6% progressive disease. The efficacy of dasatinib was assessed as limited. The authors emphasized an urgency to conduct further studies on gynaecologic cancers of clear cell histology. [9]

Emerging molecular-targeted therapies or early preclinical trials in uterine tumours

Jakub Dobroch

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: Primary results from the DESTINY-PanTumor02 phase II trial	Meric-Bernstam F et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37870536/
2	A phase 2 trial of zanidatamab in HER2-overexpressed advanced endometrial carcinoma and carcinosarcoma (ZW25-IST-2)	Lumish M et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38262242/
3	Lurbinectedin in patients with pretreated endometrial cancer: Results from a phase 2 basket clinical trial and exploratory translational study	Kristeleit R net al.	Invest New Drugs	https://pubmed.ncbi.nlm.nih.gov/37556023/
4	A randomized phase 2 study of sapanisertib in combination with paclitaxel versus paclitaxel alone in women with advanced, recurrent, or persistent endometrial cancer	Han SN et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37839313/
5	NRG=GY012: Randomized phase 2 study comparing olaparib, cediranib, and the combination of cediranib/olaparib in women with recurrent, persistent, or metastatic endometrial cancer	Rimel BJ et al.	Cancer	https://pubmed.ncbi.nlm.nih.gov/38127487/
6	A single-arm, open-label phase II study of ONC201 in recurrent/refractory metastatic breast cancer and advanced endometrial carcinoma	Atkins SLP et al.	Oncologist	https://pubmed.ncbi.nlm.nih.gov/37279797/
7	A phase I study of mirvetuximab soravtansine and gemcitabine in patients with FRα-positive recurrent ovarian, primary peritoneal, fallopian tube, or endometrial cancer, or triple negative breast cancer	Cristea MC et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38262235/
8	DKK1 is a predictive biomarker for response to DKN-01: Results of a phase 2 basket study in women with recurrent endometrial carcinoma	Arend R et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37001446/
9	A phase 2 study of dasatinib in recurrent clear cell carcinoma of the ovary, fallopian tube, peritoneum or endometrium: NRG oncology/gynecologic oncology group study 0283	O'Cearbhaill RE et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37418832/

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

Khayal Gasimli

Tewari et al., in the KEYNOTE-826 trial, conducted a subgroup analysis to evaluate the survival efficacy of pembrolizumab in patients with a combined positive score (CPS) ≥1. The analysis considered various treatment types: with or without bevacizumab, with carboplatin or cisplatin, with or without prior RCT, and histologic type (squamous or non-squamous). Patients received pembrolizumab (200 mg, every three weeks) or placebo for 24 months with chemotherapy (paclitaxel plus cisplatin or carboplatin) with or without bevacizumab. The following hazard ratios for OS were observed: with bevacizumab (HR=0.63; 95% CI 0.47-0.87), without bevacizumab (HR=0.74, 95% CI 0.53-1.04), with carboplatin (HR=0.69, 95% CI 0.54-0.89), with cisplatin (HR=0.59, 95% CI 0.32-1.09), with prior RCT (HR=0.64, 95% CI 0.45-0.91), without prior RCT (HR=0.71, 95% CI 0.53-0.97), squamous histologic type (HR=0.61, 95% CI 0.47-0.80), and non-squamous histologic type (HR=0.76, 95% CI 0.47-1.23). The authors concluded that pembrolizumab, a PD-1 inhibitor, improves PFS and OS across all subgroups. The limitation of their study is the small sample size in several subgroups, which may result in random variation and requires careful interpretation of the findings. [1]

Vergote et al. published results from the innovaTV 205/GOG-3024/ENGOT-cx8 open-label, multicentre study, which investigated the recommended phase II dose and objective response rate (ORR) of tisotumab vedotin (TV), an antibody-drug conjugate, in combination with bevacizumab, pembrolizumab, or carboplatin in patients with R/M CC. ORRs were 54.5% for first-line TV plus carboplatin, 40.6% for first-line TV plus pembrolizumab, and 35.3% for second-/third-line TV plus pembrolizumab. The most common grade ≥3 AEs were anaemia, diarrhoea, nausea, and thrombocytopenia. TV demonstrated promising efficacy and tolerable safety. A limitation of this study is the small sample size in the combination arms, limiting definitive conclusions on efficacy. [2]

Friedman et al. examined the anti-tumour activity of neratinib, an irreversible pan-HER tyrosine kinase inhibitor, in HER2-mutated R/M CC patients. In this basket trial, 22 CC patients received neratinib (240 mg/day) after progression following platinum-based treatment. Responses included four partial responses (ORR 18.2%, 95% CI 5.2-40.3) and six cases of stable disease lasting ≥16 weeks (clinical benefit rate 45.5%, 95% CI 24.4-67.8). The most common AEs were diarrhoea, nausea, and constipation. Neratinib shows potential as an alternative therapy for HER2-mutated R/M CC patients, emphasizing the importance of sequencing for patient selection. This study faced limitations, including a small sample size and limited archival tissue access, hindering additional correlative studies. As part of the larger pan-cancer SUMMIT basket trial, the cervical cohort was single-arm without a comparator group. [3]

Monk et al. analysed patient-reported outcomes (PROs) for CC patients treated with pembrolizumab as a secondary endpoint in the KEYNOTE-826 study. They employed the EORTC Quality of Life-Core 30 (QLQ-C30), the CC module (QLQ-CX24), and the EuroQol-5 dimension-5 level (EQ-5D-5L) visual analogue scale. Among the 587 patients who received at least one treatment dose and completed at least one post-baseline PRO assessment, 69% completed the QLQ-C30 by week 30, with compliance exceeding 90% in both groups. The difference in least squares mean change in QLQ-C30 global health status/quality of life (GHS/QoL) score from baseline to week 30 was 1.0 point (95% CI 2.7-4.7) between the groups. Improved GHS/QoL was observed in 42% of the pembrolizumab group compared to 29% of the placebo group (p=0.0003). Pembrolizumab combined with chemotherapy, with or without bevacizumab, did not adversely affect QoL. A key limitation of this study was that PRO assessments were only collected up to the 30-day safety follow-up after treatment discontinuation, preventing them from evaluating health-related QoL beyond the treatment period. [4]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Pembrolizumab or placebo plus chemotherapy with or without bevacizumab for persistent, recurrent, or metastatic cervical cancer: Subgroup analyses from the KEYNOTE-826 randomized clinical trial	Tewari KS et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih.gov/38095881/
2	Tisotumab vedotin in combination with carboplatin, pembrolizumab, or bevacizumab in recurrent or metastatic cervical cancer: Results from the innovaTV 205/GOG-3024/ENGOT-cx8 study	Vergote I et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/37651655/
3	Targeting HER2-mutant metastatic cervical cancer with neratinib: Final results from the phase 2 SUMMIT basket trial	Friedman CF et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38211393/
4	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/

Radiotherapy of primary and recurrent cervical cancer

Erbil Karaman

Li et al. conducted a study on the outcomes of re-irradiation in patients with recurrent cervical cancer (CC), based on the experience of a single institution. The research suggests that re-irradiation can be a viable option for managing recurrent disease, particularly in terms of overall survival (OS) and progression-free survival (PFS) rates. The study reported a median OS of 14 months and a PFS of 9 months, highlighting its potential as a salvage therapy, especially for patients with limited treatment options. While the study significantly contributes to the discussion on managing recurrent CC, it is important to note that its findings are limited by the single-centre experience and the relatively small number of subjects involved. [1]

Williamson et al. examined the outcomes of a high-dose-rate brachytherapy regimen delivered in three fractions to patients with CC. Their analysis showed that the three-fraction (3F) regimen yielded promising clinical outcomes, with a two-year OS rate of 85% and a local control rate of 90%. However, the study also noted a higher incidence of grade 3-4 toxicities, particularly gastrointestinal and genitourinary, affecting 15% and 10% of patients, respectively. These findings underscore the need to balance therapeutic efficacy with the management of potential side effects in CC treatment. By comparing two different fractionation schedules (3F vs. longer fractionation [LF]), the study provides valuable insights into optimizing treatment protocols, suggesting that a shorter regimen may be equally effective. However, the retrospective nature of the study and the smaller number of patients in the 3F group (32 patients) compared to the LF group (118 patients) may affect the robustness of the conclusions. [2]

Barbera et al. assessed the impact of advancements in external beam radiation therapy and brachytherapy techniques on survival outcomes and long-term toxicities in locally advanced CC. The study highlighted that with advanced techniques, such as image-guided brachytherapy, the five-year OS rate improved to 78%, compared to 65% with conventional methods. Additionally, the study reported a reduction in severe late toxicities from 18% to 10%, demonstrating the effectiveness of these technological advancements in enhancing patient outcomes while minimizing adverse effects. [3]

Ross et al. evaluated the outcomes of a newly implemented MRI-based brachytherapy program for CC, focusing on its impact on patient survival and treatment-related toxicities. The introduction of MRI-guided brachytherapy resulted in a two-year OS rate of 80% and a significant reduction in severe toxicities, with only 8% of patients experiencing grade 3-4 complications. These data suggest that MRI-based brachytherapy offers improved precision and reduced toxicity, making it a valuable tool in the treatment of CC. [4]

Zhang et al. explored the use of a novel hybrid brachytherapy technique, FINITO (freehand interstitial needles in addition to tandem and ovoid), for locally advanced CC. Their findings indicated that the FINITO technique improves dose distribution and tumour coverage, leading to a two-year OS rate of 82% and a local control rate of 88%. The study also reported manageable toxicity levels, with 12% of patients experiencing grade 3-4 toxicities. This innovative approach shows promise for improving outcomes in complex CC cases, particularly when conventional brachytherapy techniques are insufficient. However, the study's generalizability is limited by the lack of long-term follow-up data and the small sample size. [5]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Re-irradiation for recurrent cervical cancer: A single institutional experience	Li J et al.	Clin Transl Radiat Oncol	https://pubmed.ncbi.nlm.nih.gov/37876912/
2	Outcomes from a 3-fraction high-dose-rate brachytherapy regimen for patients with cervical cancer	Williamson CW et al.	Brachytherapy	https://pubmed.ncbi.nlm.nih.gov/36631374/
3	Locally advanced cervical cancer: How the improvement in techniques in external beam radiotherapy and brachytherapy impacts on survival outcomes and long-term toxicities	Barbera F et al.	Radiol Med	https://pubmed.ncbi.nlm.nih.gov/37640897/
4	Evaluating outcomes and toxicities for a newly implemented MRI-based brachytherapy program for cervical cancer	Ross DH et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38492475/
5	Utilizing a novel hybrid brachytherapy technique FINITO (freehand interstitial needles in addition to tandem and ovoid) for locally advanced cervical cancer	Zhang YH et al.	Brachytherapy	https://pubmed.ncbi.nlm.nih.gov/37722989/

ENYGO ESGO European Network of Young Gynae Oncologists
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Surgical treatment of primary and recurrent cervical cancer

Chrysoula Margioula-Siarkou and Georgia Margioula-Siarkou

Plante et al. conducted a randomized, multicentre, noninferiority trial to compare oncological outcomes between patients diagnosed with low-risk cervical cancer (CC), with tumours of ≤2 cm and limited stromal invasion, who underwent radical hysterectomy (n=350) or simple hysterectomy (n=350). There was no statistically significant difference in three-year pelvic recurrence rate (90% CI -1.62-2.32), but the incidence of urinary incontinence was significantly lower in patients treated with simple hysterectomy, both within (p=0.048) and beyond four weeks (p=0.03) after surgery. The main limitation of the study is the limited number of disease recurrences or deaths during the follow-up period that led to subsequent wide confidence intervals around hazard ratios. Consequently, the authors concluded that simple hysterectomy is non-inferior to radical hysterectomy for patients with low-risk CC, regarding three-year pelvic recurrence rate. [1]

The 4C study by Piedimonte et al., a multicentre retrospective cohort study of 956 patients with stage IA1 with lymphovascular space invasion to IB2 (FIGO 2018) CC treated with radical hysterectomy, aimed to correlate surgical margin status with surgical approach (robotic/laparoscopic, abdominal and combined laparoscopic-assisted vaginal/vaginal) and survival outcomes. The most notable limitations of the study are its retrospective design and the small number of events in the positive margin group. The authors reported no significant association between surgical approach and margin status (p=0.27). The risk of death in univariate analysis was significantly higher (p=0.017) in cases of close (<3mm, n=65) and positive (n=38) surgical margins, but close/positive margin status did not significantly affect five-year overall survival (OS) (p=0.3) and five-year recurrence free survival (RFS) (p=0.47), leading the authors to conclude that close or positive margins after radical hysterectomy, regardless of surgical approach, can attribute to higher risk of death. [2]

Bizzari et al. performed an international, multicentre, retrospective study from the Surveillance in Cervical CANcer (SCCAN) collaborative cohort, including 1,257 patients with stage IB1 and IIA1 (FIGO 2009) CC treated with open type B/C1/C2 radical hysterectomy according to Querleu-Morrow classification, to investigate whether surgical radicality affected survival outcomes. Although there was no significant difference in five-year OS (p=0.78) between patients undergoing non-nerve-sparing (n=374) versus nerve-sparing radical hysterectomy (n=883), five-year disease free survival (DFS) was significantly improved in the non-nerve-sparing group (p=0.047), especially for the subgroup of patients with tumours between 21 mm and 40 mm (p=0.016). Regarding limitations of the study, it is of retrospective design, it did not document the depth of stromal infiltration, pretreatment suspicious parametrial involvement, and perioperative morbidity outcomes, and there was no standardized assessment of metastatic disease and practice patterns to recognize recurrences. In conclusion, type C2 radical hysterectomy offers a significantly improved DFS in patients with early-stage CC with tumours measuring 21-40 mm. [3]

The COBRA-R study by Kim et al., a retrospective multicentre study, was designed to assess the impact of preceding conization in survival outcomes in a population of 1,254 patients with negative node, parametrial and margin status stage IB1 (FIGO 2009) CC patients who received primary type C radical hysterectomy. After propensity score matching and subcategorization per surgical approach, the three-year DFS was significantly increased (p=0.007) only for the subgroup of patients with tumours >2cm, who received minimally invasive surgery (MIS) radical hysterectomy with prior conization, regardless of tumour histology, compared to patients with matched characteristics who did not receive conization. Regarding limitations, the retrospective nature of the study, the potentially insufficient number of patients with tumours ≤2 cm, exclusion of high-risk patients, and the omission of investigation of quality-of-life issues and cost-effectiveness of conization should be taken into consideration. The authors concluded that conization before MIS radical hysterectomy could reduce recurrence rates in patients with early-stage CC and tumours >2 cm. [4]

The SUCCOR Nodes study by Gómez et al., a multicentre, retrospective study of 1,048 patients with stage IB1 (FIGO 2009) CC that underwent radical hysterectomy with lymph node assessment, was developed to identify potential associations between method of surgical node assessment and administration of adjuvant therapy. Patients who underwent only systematic lymphadenectomy (n=836) received significantly more frequently adjuvant treatment (p=0.02), compared to those staged by sentinel lymph node biopsy (SLNB) and lymphadenectomy (n=212), but the latter group was in significantly higher risk of relapse (HR=2.49, p=0.056) and death (HR=3.49, p=0.042). Notable limitations of the study are its retrospective design, the use of inverse probability weighting based on propensity score to construct a weighted cohort, and the possibility of residual confounding. The study concluded that patients with stage IB1 CC are less likely to receive adjuvant therapy if nodal metastasis was identified by combination of SLNB and lymphadenectomy. [5]

The GORILLA-1003 study by Kong et al., a multicentre, retrospective cohort study that enrolled 722 patients with IA1 with lymphovascular space invasion, IA2, and IB1 (FIGO 2018) CC treated with MIS radical hysterectomy, aimed to identify clinicopathological factors that may contribute to disease recurrence. Considerable limitations of the study are its retrospective design, the lack of comparison to an open surgery group, and the tailoring of adjuvant treatment not according to guidelines, which may have affected the reported survival outcomes. The authors detected three risk factors associated with disease recurrence — residual disease in the remaining cervix (p=0.025) after prior conization, intracorporeal colpotomy (p=0.003), and positive resection margin (p=0.044) on vaginal cuff — and consequently concluded that patients with CC and tumours ≤2 cm may be vulnerable to peritoneal recurrences when treated with MIS radical hysterectomy if protective measures to prevent tumour dissemination are not used. [6]

Di Donato et al. designed a multicentre, retrospective study to compare surgical and survival outcomes in a population of 150 patients with stage IA1-IB1 (FIGO 2018) CC who underwent either MIS (n=50) or abdominal radical hysterectomy (n=100). The authors reported no significant differences in the rates of intra-operative (p=0.257), severe (grade 3+), and post-operative complications (p=0.497), as well as 10-year DFS (p=0.812) and 10-year OS (p=0.995), between the groups undergoing MIS and open radical hysterectomy. The main limitations of the study are its retrospective nature and the potential allocation biases in terms of choice of surgical approach. The authors conclusively state that for patients with low-risk, early-stage CC, the MIS approach does not seem to negatively influence morbidity rates and survival outcomes. [7]

Kim et al. performed a multicentre, retrospective cohort study of 498 patients with stage IB1 (FIGO 2009) CC with no preoperative suspicion of lymph node metastasis of parametrial involvement who were treated with laparoscopic (n=299) or abdominal (n=199) radical hysterectomy to compare oncological outcomes between the two groups. Both three-year progression free survival (PFS) (p=0.615) and five-year OS (p=0.439) were similar between patients who received laparoscopic and open surgery, while five-year PFS rates were also not significantly different between the groups, in

Surgical treatment of primary and recurrent cervical cancer

Chrysoula Margioula-Siarkou and Georgia Margioula-Siarkou

case lymph node disease (p=0.169) or parametrial invasion (p=0.893) were detected on pathological examination. Main limitations of the study are the retrospective design, selection bias due to the favourable characteristics of the study population, and the small sample sizes, especially for patients with incidental identification of risk factors. In conclusion, the laparoscopic approach is likely not associated with worse survival outcomes in early-stage CC cases, even if high-risk factors are postoperatively detected, given that appropriate adjuvant treatment is offered. [8]

Chen et al. published a retrospective, population-based cohort study that included 18,519 patients aged 18-49 with FIGO stage I CC who underwent local excision (n=3149), hysterectomy (n=12984), or other primary treatment (n=2386), with the objective of comparing survival outcomes between fertility-sparing and classic surgical approaches. Overall, five-year OS and five-year disease specific survival (DSS) were similar between patients who underwent local excision and hysterectomy, but if age and stage were taken into consideration, both survival outcomes were significantly worse in the local excision group for patients older than 40 years (OS: p<0.001, DSS: p<0.001) and for patients with stage IB disease (OS: p<0.001, DSS: p<0.001). Regarding the limitations of the study, the descriptive and retrospective design, the lack of a comprehensive risk adjustment, and missing information about clinicopathological characteristics and fertility outcomes are the most outstanding. The authors conclusively suggest that for patients <40 years of age and with stage IA CC, fertility-sparing surgery could be offered without significantly compromising oncological safety. [9]

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No	Title	Authors	Journal	Link to abstract
1	Simple versus radical hysterectomy in women with low-risk cervical cancer	Plante M et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/38416430/
2	Surgical margin status in relation to surgical approach in the management of early-stage cervical cancer: A Canadian cervical cancer collaborative (4C) study	Piedimonte S et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37146436/
3	Survival associated with extent of radical hysterectomy in early-stage cervical cancer: A subanalysis of the Surveillance in Cervical CANcer (SCCAN) collaborative study	Bizzari N et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/37336255/
4	Conization before radical hysterectomy in patients with early-stage cervical cancer: A Korean multicenter study (COBRA-R)	Kim SI et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37105062/
5	SUCCOR nodes: May sentinel node biopsy determine the need for adjuvant treatment?	Gómez AB et al.	Ann Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/37208571/
6	Is minimally invasive radical surgery safe for patients with cervical cancer ≤2 cm in size? (MISAFE): Gynecologic Oncology Research Investigators coLLborAtion study (GORILLA-1003)	Kong T-W et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37515926/
7	Ten-year outcomes following laparoscopic and open abdominal radical hysterectomy for "low-risk" early-stage cervical cancer: A propensity-score based analysis	Di Donato V et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37149905/
8	Survival outcomes of laparoscopic versus open radical hysterectomy in early cervical cancer with incidentally identified high-risk factors	Kim NR et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37229880/
9	Local excision as a viable alternative to hysterectomy for early-stage cervical cancer in women of reproductive age: A population-based cohort study	Chen Y et al.	Int J Surg	https://pubmed.ncbi.nlm.nih.gov/37074037/

Medical treatment of primary and recurrent cervical cancer

Monika Sobočan and Zoia Razumova

Gass et al. conducted the AGO-Zervix-1 trial to compare topotecan with paclitaxel versus topotecan with cisplatin in patients with recurrent or metastatic cervical cancer. The trial enrolled 173 patients, reporting median progression-free survival (PFS) of 4.4 months in the paclitaxel arm and 4.2 months in the cisplatin arm. Median overall survival (OS) was 9.6 months in the paclitaxel group versus 12 months in the cisplatin group (HR=1.21, 95% CI 0.90-1.63). Haematological toxicities, including leukopenia, were more frequent in the cisplatin group. Despite these differences, quality-of-life scores remained comparable between the arms. These findings reinforce the importance of regimen selection based on individual patient profiles and tolerability. [1]

Oaknin et al. evaluated atezolizumab combined with bevacizumab and chemotherapy in the phase III BEATcc trial for metastatic, persistent, or recurrent cervical cancer. A total of 410 patients were randomly assigned, with a median PFS of 13.7 months in the atezolizumab arm versus 10.4 months in the control arm (HR=0.62, 95% CI 0.49-0.78; p<0.0001). Median OS was also significantly improved, reaching 32.1 months with atezolizumab versus 22.8 months in the control arm (HR=0.68, 95% CI 0.52-0.88; p=0.0046). Notable adverse events included grade ≥3 diarrhoea and rash in the atezolizumab arm, though toxicity was deemed manageable. These results suggest a dual immune-angiogenic approach could enhance treatment efficacy in advanced cervical cancer. [2]

Monk et al. assessed the role of durvalumab with chemoradiotherapy for locally advanced cervical cancer in the phase III CALLA trial. Among 770 patients, PFS was 24.3 months with durvalumab and 24.1 months with placebo (HR=0.95, 95% CI 0.73-1.24). Despite no statistically significant benefit, durvalumab demonstrated a tolerable safety profile, with the most frequent immune-related adverse events being hypothyroidism (9.7%) and pneumonitis (2.3%). These findings highlight the challenges of enhancing outcomes in locally advanced disease using immunotherapy. [3]

Mileshkin et al. examined the addition of adjuvant chemotherapy to cisplatin-based chemoradiotherapy for locally advanced cervical cancer in the OUTBACK trial. Among 926 patients, five-year OS was 72% in the adjuvant chemotherapy group versus 71% in the chemoradiotherapy-only group (HR=0.90, 95% CI 0.70-1.17; p=0.81). Adverse events, including grade ≥3 neutropenia (20%) and anaemia (18%), were more frequent in the adjuvant chemotherapy group. The lack of a survival advantage and increased toxicity suggest that adjuvant chemotherapy may not benefit unselected patients. [4]

Lorusso et al. investigated pembrolizumab in combination with chemoradiotherapy for newly diagnosed, high-risk, locally advanced cervical cancer in the phase III ENGOT-cx11/GOG-3047/KEYNOTE-A18 trial. Among 1,060 patients, PFS at 24 months was 68% in the pembrolizumab group compared to 57% in the placebo group (HR=0.70, 95% CI 0.5-–0.89; p=0.002). The median OS had not been reached in either group at the time of analysis. Grade 3 or higher adverse events occurred in 75% of the pembrolizumab group, with the most common being anaemia, diarrhoea, and elevated liver enzymes. The study highlights pembrolizumab's immunomodulatory effect in conjunction with chemoradiotherapy for high-risk patients. [5]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Primary results of the AGO-Zervix-1 study: A prospective, randomized phase III study to compare the effects of paclitaxel and topotecan with those of cisplatin and topotecan in the treatment of patients with recurrent and persistent cervical cancer	Gass P et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38490057/
2	Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): A randomised, open-label, phase 3 trial	Oaknin A et al.	Lancet	https://pubmed.ncbi.nlm.nih.gov/38048793/
3	Durvalumab versus placebo with chemoradiotherapy for locally advanced cervical cancer (CALLA): A randomised, double-blind, phase 3 trial	Monk BJ et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/38039991/
4	Adjuvant chemotherapy following chemoradiotherapy as primary treatment for locally advanced cervical cancer versus chemoradiotherapy alone (OUTBACK): An international, open-label, randomised, phase 3 trial	Mileshkin LR et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/37080223/
5	Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): A randomised, double-blind, phase 3 clinical trial	Lorusso D et al.	Lancet	https://pubmed.ncbi.nlm.nih.gov/38521086/

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

María de los Reyes Oliver and Rubén M. Betoret

Li et al. conducted a meta-analysis of 162 studies, finding a prevalence of HPV DNA of 39.1% in vulvar cancer and of 76.1% in vulvar intraepithelial neoplasia (VIN). Worldwide, p16INK4a positivity was 34.1% in vulvar cancer and 65.7% in VIN. Double positivity, which is proposed as a better prognostic marker in vulvar cancer patients based on previous findings in HPV-related neck tumours, appeared in 19.6% of vulvar cancer and 44.2% of VIN, emphasizing the role of HPV vaccination in preventing vulvar neoplasia. [1]

Being that PD-L1 expression is a possible clinical response predictor in other cancers, Baandrup et al. conducted a meta-analysis of 19 studies that found a pooled PD-L1 prevalence of 83.4% in vulvar cancer, without significant variation regarding tumour stage or HPV status. [2]

Zach et al. designed a prospective study to extend the indications for sentinel lymph node (SLN) biopsy in squamous cell carcinoma of the vulva (SCCV), selecting women with tumours >4 cm or multifocal tumours. In a cohort of 53 patients, detection rates varied from 94.1% to 100% per patient and 84.1% to 85.3% per groin, with a negative predictive value of 100% achieved, providing initial data that might widen the indication of SLN technique if confirmed by further studies. [3]

Following publication of the GROINSS-V-I study, negative SLN biopsy is considered a safe procedure to omit inguinofemoral lymphadenectomy in early stage SCCV, with groin recurrence of around 2.3% being reported after a median follow-up of 35 months. Warmerdam et al. evaluated the correlation of complete SLN biopsy (removal of all SLNs visualized on lymphoscintigraphy) versus successful SLN biopsy (removal of at least one SLN per groin, with remaining tissue showing less than 10% radioactivity when compared to the most radioactive SLN). The authors found no statistically significant differences between the two groups in a retrospective study of 171 women in terms of groin recurrence, with a rate of 2.6% after a median follow-up of 47.0 months in SLN-negative patients, which is consistent with previous literature. [4]

Guijarro-Campillo et al. conducted a prospective multicentre study to assess the performance of indocyanine green (ICG) tracer as compared to the gold-standard technetium-99 (Tc-99) nanocolloid in the detection of SLN in vulvar cancer. An overall detection rate of 85.3% was described for Tc-99 and 82.7% for ICG, with a sensitivity of 91.08% and positive predictive value of 94.8% for the latter. No differences between tracers were found in subgroups regarding size of tumour (>2-4 cm), obese patients (body mass index >30), or midline lesions, showing the potential of ICG as a promising detection method in early SCCV. [5]

While pelvic exenteration is associated with important postoperative morbidity, it may be the only curative option for some patients with advanced or recurrent vulvar cancer. Valstad et al. present a single-centre retrospective analysis of 30 patients undergoing pelvic exenteration, showing that acceptable oncologic outcomes are achievable (90-day mortality of 3% and 63% grade 3 complications; five-year OS of 50%) with careful patient selection and surgical centralization. [6]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Prevalence of human papillomavirus DNA and p16INK4a positivity in vulvar cancer and vulvar intraepithelial neoplasia: A systematic review and meta-analysis	Li Z et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/36933562/
2	PD-L1 expression in vulvar cancer: A systematic review and meta-analysis	Baandrup L et al.	Histopathology	https://pubmed.ncbi.nlm.nih.gov/38084642/
3	Time to extend the indication for sentinel node biopsy in vulvar cancer? Results from a prospective nationwide Swedish study	Zach D et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37918956/
4	Sentinel lymph node procedure in early-stage vulvar cancer: Correlation of lymphoscintigraphy with surgical outcome and groin recurrence	Warmerdam DHM et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/37572588/
5	Accuracy of ICG compared with technetium-99 for sentinel lymph node biopsy in vulvar cancer	Guijarro-Campillo AR et al.	Eur J Obstet Gynecol Reprod Biol	https://pubmed.ncbi.nlm.nih.gov/38183845/
6	Pelvic exenteration for vulvar cancer: Postoperative morbidity and oncologic outcome – a single center retrospective analysis	Valstad H et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/37349160/

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Screening and prevention of gynaecological cancer

Catarina Pardal

Primary HPV testing is the preferred approach to cervical cancer screening in many countries, but its moderate specificity leads to excessive colposcopy referrals and unnecessary distress in patients. Many potential prognostic tests have been evaluated as triaging strategies, with methylation markers having shown some success for prevalent disease. In this study, the authors aimed to evaluate the potential for long-term prediction of ≥ cervical intraepithelial neoplasia (CIN)3 with the S5 DNA methylation classifier (which tests for methylation on the host tumour suppressor gene EPB41L3 and of the viral late genes L1 and L2 of HPV16, HPV18, HPV31, and HPV33) among high-risk HPV-positive women in the ARTISTIC screening trial cohort. This case-control study compared S5 DNA methylation tests in archived high-risk, HPV-positive, liquid-based samples from 343 women with ≥CIN2 to 800 high-risk HPV-positive controls and concluded that S5 methylation was higher in HPV-positive samples ≥CIN3+. The S5 classifier could discriminate between high-risk, HPV-positive women who developed ≥CIN3 and high-risk HPV-positive controls on average five years before diagnosis (with no relation to cytology at baseline). However, S5 testing is based on pyrosequencing, which is not suitable for routine diagnostic tests, and therefore an automated test that could be produced at a reasonable cost would be necessary to use this marker as a screening tool. [1]

The Onclarity trial evaluated the performance of extended HPV genotyping plus cytology triage for detection of ≥CIN2 and ≥CIN3 in women undergoing routine cervical cancer screening to establish ≥CIN2/3 risk strata and determine the corresponding clinical performance characteristics (sensitivity and ratio of colposcopies-to-disease detected). Seven risk strata were obtained using a combination of extended genotyping and cytology results. For ≥CIN3 ROC analysis, the optimal cutoff for sensitivity versus specificity was approximated between HPV16-negative and HPV18/31-positive and with any cytology group (≥CIN3 sensitivity = 85.9% and colposcopy-to-≥CIN3 = 7.4) and HPV16/18/31-negative but HPV33/58/52-positive with NILM cytology (≥CIN3 sensitivity = 94.5% and colposcopy-to-≥CIN3 = 10.8). A secondary objective of the study was to compare the diagnostic performance of extended genotyping with combined cytology to HPV16/18 primary screening plus p16/Ki-67 dual staining (DS) previously published from the IMPACT trial. HPV16/18 with DS triage showed a sensitivity of 94.3%, with a colposcopy-to-≥CIN3 ratio of 11.4. Therefore, extended genotyping with reflex cytology for selected HPV genotypes performs similarly to HPV primary screening plus DS for detection of ≥CIN3, with the advantage of analysis on self-collected specimens and application of different risk thresholds in different geographic regions, where risk tolerances may differ. [2]

A cohort study examined the overall performance of stand-alone artificial intelligence (AI slide reviewing without cytologist support) at distinguishing between negative and positive cases of abnormal cervical squamous cells and assessed whether cytologist-in-the-loop artificial intelligence (CITL-AI) could improve the diagnostic accuracy of detecting these abnormal cervical squamous cells compared with standard cytology screening without AI assistance. Stand-alone AI showed an overall sensitivity of 89.4% and specificity of 66.4% in distinguishing between negative and positive cases, as well as 10.6% of false negative cases (94.7% of which were atypical squamous cells of undetermined significance). CITL-AI had superior sensitivity and specificity compared with junior cytologists (81.6% vs. 53.1% and 78.9% vs. 66.2%, respectively; both with p<.001). For senior cytologists, CITL-AI specificity increased slightly from 89.9% to 91.5% (p=0.029); however, sensitivity did not significantly increase (p=0.450). CITL-AI was able to reduce cytologists' workload by 37.5%, while improving diagnostic accuracy, especially compared with less-experienced cytologists. These findings need to be further validated through prospective studies. [3]

ALDO (Avoiding Late Diagnosis of Ovarian Cancer), a UK pilot surveillance programme for women with BRCA1/2 declining risk-reducing surgery (bilateral salpingo-oophorectomy), aimed to establish 'real-world' performance of the Risk of Ovarian Cancer Algorithm (ROCA, a multimodal screening algorithm that assesses serial CA-125 results, and trans-vaginal sonography as a second-line test) at increasing earlier-stage ovarian cancer diagnosis and potential clinical benefits compared with no surveillance. The authors concluded that the ROCA test had similar performance in a 'real-world 'setting as in research trials (e.g., the UK Collaborative Trial of Ovarian Cancer Screening) with proven cost-effectiveness. While bilateral salpingo-oophorectomy remains the recommended management, ROCA-based surveillance may be considered for women with pathogenic BRCA 1/2 mutations who decline/defer risk-reduction surgery. [4]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Long-term prediction by DNA methylation of high-grade cervical intraepithelial neoplasia: Results of the ARTISTIC cohort	Gilham C et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/38507581/
2	Risk stratification of HPV-positive results using extended genotyping and cytology: Data from the baseline phase of the Onclarity trial	Stoler MH et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37149907/
3	Improving the accuracy and efficiency of abnormal cervical squamous cell detection with cytologist-in-the-loop artificial intelligence	Xue P et al	Mod Pathol	https://pubmed.ncbi.nlm.nih.gov/37059230/
4	The Avoiding Late Diagnosis of Ovarian Cancer (ALDO) project: A pilot national surveillance programme for women with pathogenic germline variants in BRCA1 and BRCA2	Philpott S et al.	J Med Genet	https://pubmed.ncbi.nlm.nih.gov/36319079/

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

Joanna Kacperczyk-Bartnik

In a systematic review and meta-analysis by Albright et al., the authors analysed treatments and outcomes for high-risk gestational trophoblastic neoplasia (GTN) across 35 studies from 20 countries, involving 2,276 patients. Results showed that 99.7% of patients received chemotherapy, 35.8% had surgery, and 4.9% underwent radiotherapy. Mortality was 10.9%, with a 79.7% complete response to primary chemotherapy. Modern chemotherapy regimens like EMA/CO or EMA/EP were linked to better survival and response rates. Ultra-high-risk disease and GTN following term pregnancies showed higher mortality rates. Overall, relapse rates were between 3% and 6%. The study's strengths begin with its extensive search strategy, screening more than 1,100 unique results and ultimately including 35 distinct studies. These studies represent data from 20 countries across five continents, providing a comprehensive and diverse global perspective on high-risk GTN. All the included studies were retrospective and observational, leading to potential variations in follow-up duration and completeness. [1]

The study by Winter et al. evaluated the use of carboplatin as second-line treatment for low-risk, methotrexate-resistant GTN in the UK. Despite adjustments in carboplatin dosing, only 36% of patients achieved complete human chorionic gonadotropin (hCG) response. All non-responders were successfully treated with multiagent chemotherapy. The study concludes that carboplatin is not effective enough for this purpose and suggests the need for new strategies to reduce reliance on more toxic chemotherapy regimens, while maintaining the 100% overall survival. A key limitation of this study is its retrospective cohort design and relatively small sample size. [2]

A retrospective study by Bolze et al. reviewed 80 patients with gestational choriocarcinoma who normalized their hCG levels after tumour removal without chemotherapy. The study was conducted across 11 international centres between 1981 and 2017, with follow-up until 2023, with none of the patients experiencing recurrence after a median follow-up of 50 months. Most patients had a low-risk score, and the median time to hCG normalization was 48 days. The findings suggest that expectant management may be safe for highly selected patients without the need for additional oncological treatment. The strengths of this study include its multicentre, international design and the participation of recognized expert centres specializing in trophoblastic diseases. The main limitation includes the retrospective nature of the study. [3]

The study by de Codt et al. evaluated the feasibility of hysteroscopic resection for managing hydatidiform mole (HM) in a case series of 36 patients from 2007 to 2019. Histological analysis revealed partial HM in 28 patients (77.8%) and complete HM in eight patients (22.2%). Complications included one case of uterine perforation and 10 instances of glycine resorption. Follow-up ultrasounds indicated retained products of conception in 16.7% of patients. The findings suggest that hysteroscopic resection is a viable option for managing molar pregnancy, warranting further comparative studies with traditional methods. The retrospective nature of the study limits the strength of its findings. However, presenting hysteroscopic resection as a novel approach to treating molar pregnancy, with minimal adverse events, could pave the way for more rigorous studies. [4]

The study by Braga et al. evaluates the efficacy of immunotherapy for treating GTN after methotrexate resistance, presenting four Brazilian cases. A systematic review of 12 studies found a 46.7% complete remission rate for avelumab and an 86.7% rate for pembrolizumab. Immunotherapy showed effectiveness, particularly for high-risk GTN, with both therapies being well-tolerated, and successful pregnancies following treatment. The primary limitation of this review is the infrequency of GTN cases treated with immunotherapy, resulting in the inclusion of mostly case reports in this systematic review. [5]

The TROPHIMMUN trial evaluated the efficacy of avelumab in patients with gestational trophoblastic tumours (GTTs) resistant to polychemotherapy. In cohort B, seven patients received avelumab but only one achieved hCG normalization, leading to treatment discontinuation. The remaining six patients showed resistance to avelumab, resulting in the study being halted for futility. Adverse events were mostly grade 1-2, with fatigue being the most common. The findings highlight the need for innovative treatment approaches for patients resistant to polychemotherapy. The reported outcomes have several limitations, primarily due to the early termination of cohort B, which resulted in a very small sample size of only seven patients treated. [6]

Immune checkpoint immunotherapy targeting PD-1/PD-L1 has proven effective for treating GTN, including multidrug-resistant and ultra-high-risk cases. Data from 133 patients treated with checkpoint inhibitors, of which 85 achieved complete remission, is analysed in a study by Baas et al. While treatment was generally well tolerated, future research should focus on earlier intervention, combination therapies, and effects on fertility. High costs remain a concern for treatment accessibility. [7]

The study by Parker et al. aimed to increase the ease of use of the FIGO scoring system for predicting chemotherapy resistance in GTN by developing streamlined two-factor models and visual decision aids (nomograms). Using datasets from two UK centres, three models were created, showing comparable performance to FIGO without significant discordance. Models M2 and M3 are prioritized for further validation, while M1 offers practical application in resource-limited settings. Future research should focus on prospective validation with larger cohorts. [8]

The study by Golfier et al. reviews the successes and areas for improvement in gestational trophoblastic disease (GTD) care through national and international collaborations. While most women in high-income countries have access to effective GTD treatment, those in lower-income countries face challenges. Establishing expert centres is crucial for optimizing management protocols and outcomes, emphasizing the need for collaboration and support in under-resourced areas. [9]

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

Joanna Kacperczyk-Bartnik

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No	Title	Authors	Journal	Link to abstract
1	Treatments and outcomes in high- risk gestational trophoblastic neoplasia: A systematic review and meta-analysis	Albright BB et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/36648416/
2	Efficacy analysis of single-agent carboplatin AUC4 2-weekly as second-line therapy for methotrexate-resistant (MTX-R) low risk gestational trophoblastic neoplasia (GTN)	Winter MC et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37327541/
3	Chemotherapy is not needed when complete evacuation of gestational choriocarcinoma leads to hCG normalization	Bolze P et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/38350264/
4	Hysteroscopic management of molar pregnancy: A series of 36 cases	De Codt M et al.	Rare Tumors	https://pubmed.ncbi.nlm.nih.gov/37035475/
5	Immunotherapy in the treatment of chemoresistant gestational trophoblastic neoplasia: Systematic review with a presentation of the first 4 Brazilian cases	Braga A et al.	Clinics (Sao Paulo)	https://pubmed.ncbi.nlm.nih.gov/37523979/
6	Avelumab in patients with gestational trophoblastic tumors with resistance to polychemotherapy: Cohort B of the TROPHIMMUN phase 2 trial	You B et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36401942/
7	Immunotherapy for gestational trophoblastic neoplasia: A new paradigm	Baas IO et al.	Gynecol Obstet Invest	https://pubmed.ncbi.nlm.nih.gov/37703867/
8	PREDICT-GTN 2: Two-factor streamlined models match FIGO performance in gestational trophoblastic neoplasia	Parker VL et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38091775/
9	From national to international collaboration in gestational trophoblastic disease: Hurdles and possibilities	Golfier F et al.	Gynecol Obstet Invest	https://pubmed.ncbi.nlm.nih.gov/37827125/

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Pathology of gynaecological cancers

Nicolas Samartzis and Dimitrios Rafail Kalaitzopoulos

The European Society of Gynaecological Oncology (ESGO), the European Society for Medical Oncology (ESMO), and the European Society of Pathology (ESP) conceived a consensus paper on ovarian cancer following the consensus conference in June 2022 in Valencia, Spain. This comprehensive article presents the consensus recommendations along with supporting evidence for each. The article primarily focuses on pathology and molecular biology, early-stage disease, advanced-stage (including older or frail patients), and recurrent disease. [1]

Chowdhury et al., identified a 64-protein signature capable of predicting a subset of high-grade serous ovarian cancers (HGSOCs) refractory to initial platinum-based therapy. A sample size of 242 HGSOCs, including both chemo-sensitive and refractory cases, were used. The proteomic landscape revealed five distinct clusters of HGSOC, suggesting different mechanisms of refractoriness and potential therapeutic targets. The main limitation of the study was that the predictor model identifies only 35% of refractory cases. Further, the lack of germline DNA in the study made it challenging to characterize somatic mutations. Lastly, tumour heterogeneity may affect the accuracy of the test results. However, these findings could provide a basis for new diagnostic opportunities in predicting chemo-resistant HGSOCs. [2]

The studies by Wang et al. and Wepy et al. address the topic of endometriosis-associated epithelial ovarian neoplasia in large-scale studies and what has been demonstrated to date. The first study employed Mendelian randomization to investigate the correlation between endometriosis and ovarian cancer using the genetic dataset of a genome-wide association study (GWAS) of endometriosis and epithelial ovarian cancer. The analysis showed a significant association between the two diseases, with an odds ratio (OR) of 1.23. Specifically, endometriosis was strongly associated with endometrioid carcinoma (OR=1.49), clear cell carcinoma (OR=2.56), and low malignant potential tumours (OR=1.28). The strength of the study was the methodology, which is less likely to be affected by confounding variables than conventional observational studies. However, the study group used only summarized data from the GWAS, which cannot further assess the pathogenetic mechanism leading to a malignant transformation of endometriosis. The second study aimed to refine the understanding of atypical endometriosis according to histological and molecular features. Among 4,598 cases of endometriosis, the authors identified 36 atypical cases. Immunohistochemistry revealed wild-type p53 in 100% of the cases, retained PMS2/MSH6 in 100% of the cases, and positive oestrogen and progesterone receptors in 97% and 76% of the cases, respectively. One-quarter (25%) of the cases showed synchronous/subsequent tubo-ovarian neoplasia, of which 84% exhibited genomic alterations similar to those found in endometriosis-related tumours, especially with synchronous ipsilateral neoplasia. The authors concluded that it is crucial to report atypical endometriosis, as it appears to increase the risk of endometriosis-related epithelial neoplasia. However, the relatively low prevalence of atypical endometriosis in benign cases of endometriosis limits its usefulness as a sole predictor of malignant transformation risk. [3, 4]

The 2023 updated FIGO staging of endometrial cancer summarizes advancements in understanding the disease's pathology and molecular features since 2009. This revision aims to better define prognostic groups and guide treatment decisions. The new staging system includes subclassifications based on histological types, tumour extent, and molecular characteristics, such as POLEmut, mismatch repair deficiency, and p53abn status. In the revised FIGO classification, the four stages (I to IV) have been updated. The main influence of molecular subtyping is that the detection of p53abn or POLEmut in stages I and II can lead to upstaging or downstaging of the disease. [5]

Cytological examination during surgery for endometrial cancer is easily accessible and involves low additional costs. Zhang et al. demonstrated in a multicentric retrospective study that positive peritoneal cytology was significantly associated with decreased progression-free survival (PFS) and overall survival (OS). Specifically, in the intermediate- and high-intermediate-risk groups, positive peritoneal cytology significantly correlated with poorer survival outcomes. These findings indicate that peritoneal cytology status and ESGO/ESP risk classification should be considered together for risk stratification. The study's strength is the large sample size of 6,313 patients. However, its main limitation is the retrospective design, which necessitates confirmation through prospective studies. [6]

No specific molecular profile (NSMP) endometrial carcinomas represent a heterogenous group of tumours. The study from Jamieson et al. focused on identifying factors that could help further stratify the outcomes in this group. Among 1,110 NSMP endometrial cancer oestrogen receptor (ER) and low-grade demonstrated exceptionally favourable outcomes, while high-risk NSMPs (grade 3 and/or ER-negative) had significantly poorer outcomes (five-year disease-specific death rate of 1.6% vs. 22.9% for low- and high-risk NSMP, respectively). It must be mentioned that this study has several limitations, including low inter-observer reproducibility, especially in the histological assignment of high-grade tumours, as reported in previous studies. Other limitations include the retrospective nature of the study and the use of older samples, which could lead to antigen degradation and interfere with ER assessment. However, the findings highlight the importance of subclassifying NSMP endometrial cancer to identify low-risk cases. This could help direct endometrial cancer management within NSMP tumours and form the framework for clinical algorithms or prospective clinical trials, assessing the safety of de-escalation of therapy for patients with low-risk NSMP endometrial cancer, in contrast to more intense adjuvant treatments for those with high-risk NSMP endometrial cancer. [7]

Pathology of gynaecological cancers

Nicolas Samartzis and Dimitrios Rafail Kalaitzopoulos

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No	Title	Authors	Journal	Link to abstract
1	ESGO-ESMO-ESP consensus conference recommendations on ovarian cancer: Pathology and molecular biology and early, advanced and recurrent disease	Ledermann JA et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/38307807/
2	Proteogenomic analysis of chemo-refractory high-grade serous ovarian cancer	Chowdhury S et al.	Cell	https://pubmed.ncbi.nlm.nih.gov/37541199/
3	Endometriosis and epithelial ovarian cancer: A two-sample Mendelian randomization analysis	Wang L et al.	Sci Rep	https://pubmed.ncbi.nlm.nih.gov/38082154/
4	Atypical endometriosis: Comprehensive characterization of clinicopathologic, immunohistochemical, and molecular features	Wepy C et al.	Int J Gynecol Pathol	https://pubmed.ncbi.nlm.nih.gov/37043650/
5	FIGO staging of endometrial cancer: 2023	Berek JS et al.	Int J Gynecol Obstet	https://pubmed.ncbi.nlm.nih.gov/37337978/
6	Prognostic significance of positive peritoneal cytology in endometrial carcinoma based on ESGO/ESTRO/ESP risk classification: A multicenter retrospective study	Zhang Y et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37442025/
7	Grade and estrogen receptor expression identify a subset of no specific molecular profile endometrial carcinomas at a very low risk of disease-specific death	Jamieson A et al.	Mod Pathol	https://pubmed.ncbi.nlm.nih.gov/36788084/

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Treatment of pre-invasive gynaecological neoplasia

Elko Gliozheni

In the cross-sectional study by Liu et al., characteristics of the vaginal microbiota in women with various grades of cervical intraepithelial neoplasia (CIN) were examined using high-throughput 16S rRNA sequencing. The study found that as CIN grade increased, Lactobacillus and Pseudomonas detection rates decreased, while Gardnerella, Dialister, and Prevotella rates increased. High-grade CIN was also linked to altered metabolic pathways. Limitations include the study's cross-sectional design, which limits causal inference, and the focus on a single population (Chinese cohort), which may affect generalizability. [1]

In the systematic review and meta-analysis by Inayama et al., the efficacy and safety of imiquimod for treating CIN and vaginal intraepithelial neoplasia (VAIN) were evaluated. Imiquimod was associated with a significantly higher likelihood of disease regression (pooled OR=4.05) compared to placebo or no treatment. The study found that while local and systemic side effects were common, treatment discontinuation was rare. The evidence for imiquimod effectiveness in VAIN was limited. Major limitations include variability in study quality and a small number of studies for VAIN. [2]

In the study by Tossas et al., the influence of the vaginal microbiome (VMB) on CIN risk was examined across different racial groups using 16S rRNA sequencing of 3,050 predominantly Black women. The research found that VMB profiles varied, with 51% of participants having suboptimal profiles. Among non-Latina Black women, the risk of CIN3 was double that of non-Latina white women, but this association was significant only with an optimal VMB. Conversely, CIN3 risk was elevated for white women with suboptimal VMB. The study limitations include the focus on a predominantly Black cohort, which may impact the generalizability of the findings. [3]

In the systematic review and meta-analysis by Van de Sande et al., the efficacy of topical imiquimod for treating high-grade CIN was assessed. The study included five trials with 463 participants. Imiquimod achieved a 55% rate of histological regression to ≤CIN1, compared to 29% for placebo and 93% for surgical treatment. The odds of regression with imiquimod were significantly higher than with placebo (OR=4.17), but lower than with surgical treatment (OR=14.81). HPV clearance rates were also lower with imiquimod (53.4%) compared to surgery (66%). Limitations include variability in study quality and treatment protocols. [4]

In the study by Deng et al., a predictive model for residual lesions after loop electrosurgical excision procedure (LEEP) in CIN3 patients was developed. The retrospective analysis of 436 CIN3 patients identified post-LEEP follow-up HPV, TCT, and gland involvement as independent risk factors for residual lesions. A nomogram model was created with a high consistency index (C-index 0.975), indicating strong predictive ability. The study limitations include its retrospective nature and reliance on data from a single surgical approach, which may impact broader applicability. [5]

In the prospective observational study by Chen et al., the efficacy of HPV prophylactic vaccination post-conization for preventing CIN recurrence was evaluated. Out of 421 patients who underwent LEEP for CIN2+, 148 received the Gardasil vaccine, while 273 did not. The vaccinated group had significantly lower HPV infection rates and a reduced CIN2+ recurrence rate (2.03%) compared to the non-vaccinated group (10.62%). Logistic regression identified no vaccination as a major risk factor for recurrence (OR=12.35). The study limitations include the lack of randomization, which emphasized the need for more controlled trials. [6]

In the nonrandomized intervention study by Tranberg et al., the value of a catch-up HPV test for women aged 65-69 in Denmark was assessed. The study compared HPV screening in 11,192 women with no prior HPV testing to standard care (cervical cytology) in 33,387 women. The HPV intervention group showed a significantly higher detection rate of CIN2+ lesions (3.9 per 1,000 women) compared to the cytology group (0.3 per 1,000). Although the catch-up HPV test was more effective in detecting CIN2+, it required more colposcopies per CIN2+ case detected (11.6 vs. 10.1). Limitations include the nonrandomized design, potential selection bias, and limited follow-up duration. Despite these issues, the study suggests catch-up HPV testing could enhance cervical cancer prevention in older women. [7]

In a retrospective study, Stuebs et al. evaluated the accuracy of colposcopic findings and the progression of untreated CIN2/3 in 655 pregnant women. Colposcopy accuracy was 89.2%, with higher regression rates for CIN2/3 post-vaginal delivery. Limitations include retrospective design and single-centre setting, which may limit generalizability. Despite high colposcopy accuracy, the study suggests experienced examiners' role in outcomes and emphasizes the impact of delivery mode on CIN regression. [8]

Chu et al. conducted a comparative study on the diagnostic efficacy of colposcopic-directed biopsy and four-quadrant biopsy in detecting high-grade CIN. The study involved 1,311 women from three clinics. Four-quadrant biopsies showed higher detection rates (86.4%) compared to colposcopic-directed biopsies (50.8%). Even in cases with normal or unsatisfactory colposcopy, four-quadrant biopsies detected 22.9% of high-grade CIN. The authors suggest that four-quadrant biopsies are valuable for women with abnormal smears or positive HPV tests. Limitations include potential selection bias and the retrospective nature of the study. [9]

Treatment of pre-invasive gynaecological neoplasia

Elko Gliozheni

Relevant articles retrieved March 31, 2023 – March 31, 2024

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1	Characteristics of vaginal microbiota in various cervical intraepithelial neoplasia: A cross-sectional study	Liu Y et al.	J Transl Med	https://pubmed.ncbi.nlm.nih.gov/37974192/
2	Imiquimod for cervical and vaginal intraepithelial neoplasia: A systematic review and meta-analysis	Inayama Y et al.	Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/37411024/
3	Does the vaginal microbiome operate differently by race to influence risk of precervical cancer?	Tossas KY et al.	J Womens Health (Larchmt)	https://pubmed.ncbi.nlm.nih.gov/36897755/
4	The efficacy of topical imiquimod in high-grade cervical intraepithelial neoplasia: A systematic review and meta-analysis	Van de Sande AJM et al.	Int J Gynaecol Obstet	https://pubmed.ncbi.nlm.nih.gov/37350560/
5	A predictive model for residual lesions after LEEP surgery in CIN III patients	Deng L et al.	Front Med (Lausanne)	https://pubmed.ncbi.nlm.nih.gov/38148909/
6	The efficacy of human papillomavirus prophylactic vaccination after conization in preventing cervical intraepithelial neoplasia recurrence: A prospective observational study in China	Chen M et al.	Eur J Obstet Gynecol Reprod Biol	https://pubmed.ncbi.nlm.nih.gov/37159990/
7	Value of a catch-up HPV test in women aged 65 and above: A Danish population-based nonrandomized intervention study	Tranberg M et al.	PLoS Med	https://pubmed.ncbi.nlm.nih.gov/37410699/
8	Management of cervical intraepithelial neoplasia in pregnant women	Stuebs FA et al.	Anticancer Res	https://pubmed.ncbi.nlm.nih.gov/37352006/
9	The value of four-quadrant cervical biopsy in women with different colposcopic impressions	Chu MM et al.	Diagnostics (Basel)	https://pubmed.ncbi.nlm.nih.gov/37510128/

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Treatment of elderly patients with gynaecological cancers

Alex Mutombo

In a retrospective cohort study of 64 patients aged 80-99 years with stage I endometrioid endometrial cancer (EC) who underwent hysterectomy with or without lymph node dissection between 2006 and 2018, AlAshqar et al. found that women with a combined age-adjusted Charlson Comorbidity Index score of ≥7 had an eightfold higher risk of postoperative infections and were 45% less likely to survive at three years (aRR=0.55, 95% CI 0.004-0.87; p=0.039) compared to women with a score of <7. [1]

In another study, using the SEER-Medicare database to evaluate the risk of several gastrointestinal (GI) diagnoses among EC patients aged 66 years and older, Anderson et al. reported that, compared to matched women without a history of cancer, those with EC had an increased risk of GI symptoms after the index date, including constipation, abdominal pain, and faecal incontinence, as well as other GI diagnoses (e.g., bowel obstruction: HR=5.72, 95% CI 5.47-5.98; ileus: HR=7.22, 95% CI 6.89-7.57). These findings underscore the need for surveillance of these conditions during follow-up. [2]

In a study by Ghanem et al., which estimated the five-year recurrence-free survival for 706 patients with FIGO stage I uterine endometrioid carcinoma who underwent surgical lymph node evaluation, only age ≥60 years and high tumour grade were found to be independent predictors of recurrence. [3]

Quick et al., evaluating changes in physical function in EC patients aged 70 years and older, reported that women who received adjuvant treatment (137 patients) experienced greater declines in physical function than those who did not receive adjuvant therapy (150 patients), particularly those who underwent chemotherapy. [4]

Wakkerman et al. conducted a study to determine whether older age was a causal prognostic factor for oncological outcomes in women with EC or whether other risk factors become more common with age. Using data from 1,801 women in the randomized PORTEC-1, PORTEC-2, and PORTEC-3 trials, the study showed that advanced age was associated with more aggressive tumour features and was independently and causally related to worse oncological outcomes. [5]

Cai et al. evaluated treatment modalities offered to older patients and their impact on overall survival. Among 5,055 patients with high-grade serous ovarian cancer and 3,584 patients with advanced-stage (IIIC and IV) disease, very elderly patients (≥75 years) received less complex surgical treatments and lower rates of chemotherapy compared to younger counterparts, resulting in worse overall survival. [6]

Lastly, in a study assessing survival and the impact of comorbidities in women aged 80 years and older with FIGO IA vulvar squamous cell carcinoma, Schuurman et al. observed that the vast majority of both older (91%) and younger (<80 years, 99%) patients received surgical treatment. However, older patients with ≥2 comorbidities had poorer overall survival compared to those with one or no comorbidities (p<0.01). [7]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Surgical and oncologic outcomes in surgically treated women 80 years and older with endometrioid endometrial cancer as a function of their comorbidities	AlAshqar A et al.	Gynecol Oncol Rep	https://www.ncbi.nlm.nih.gov/pubmed/37636496
2	Gastrointestinal outcomes among older women with endometrial cancer	Anderson C et al.	Gynecol Oncol	https://www.ncbi.nlm.nih.gov/pubmed/37354788
3	Recurrence risk stratification for women with FIGO stage I uterine endometrioid carcinoma who underwent surgical lymph node evaluation	Ghanem AI et al.	Am J Clin Oncol	https://www.ncbi.nlm.nih.gov/pubmed/37679878
4	Changes in physical function in older women with endometrial cancer with or without adjuvant therapy	Quick AM et al.	J Cancer Surviv	https://www.ncbi.nlm.nih.gov/pubmed/37668940
5	Prognostic impact and causality of age on oncological outcomes in women with endometrial cancer: A multimethod analysis of the randomised PORTEC-1, PORTEC-2, and PORTEC-3 trials	Wakkerman FC et al.	Lancet Oncol	https://www.ncbi.nlm.nih.gov/pubmed/38701815
6	Disparities in treatment modalities and survival among older patients with high-grade serous ovarian cancer	Cai Y et al.	BMC Womens Health	https://www.ncbi.nlm.nih.gov/pubmed/38326784
7	Vulvar squamous cell carcinoma in women 80 years and older: Treatment, survival and impact of comorbidities	Schuurman MS et al.	Gynecol Oncol	https://www.ncbi.nlm.nih.gov/pubmed/37951042

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Fertility sparing treatment in gynaecological malignancies

Charalampos Theofanakis

A systematic review and meta-analysis by Murakami et al. assessed progestin retreatment for recurrent endometrial intraepithelial neoplasia (EIN), atypical endometrial hyperplasia (AH), and endometrial cancer (EC). Thirty-two studies including 365 patients (270 treated with progestin retreatment and 95 with hysterectomy) showed complete remission (CR) in 81.1% of those on progestin. However, progestin retreatment posed a higher recurrence risk than hysterectomy. Despite recurrence, 14% of the women conceived, suggesting that progestin retreatment offers a pregnancy possibility. The authors propose that repeat progestin therapy is viable for recurrent EIN, AH, and EC patients. This study's systematic review and meta-analysis design strengthened data reliability but faced limitations, including a lack of phase III trials, varying study methodologies, missing side-effect data, and a mixed population with differing progestin regimens. [1]

A randomised controlled trial by Chen et al. assessed DEAR weight management in obese patients undergoing fertility-sparing treatment for EC or AH. Seventy-two patients (body mass index [BMI] >25 kg/m^2) were divided into DEAR and self-managed groups. The DEAR group showed significantly lower median weight, BMI, lipid accumulation, body fat, visceral fat area, and improved glycolipid indices compared to controls ($p<0.05$). Complete remission was also higher in the DEAR group (88.46% vs. 57.14%; $p<0.05$), though remission time was similar between groups. Lack of long-term follow-up and absence of diverse patient demographics may limit generalizability and understanding of sustained outcomes. [2]

A systematic review and meta-analysis by Adamyan et al. evaluated the combined use of metformin and progestin-based treatment for atypical endometrial hyperplasia (AEH) and early endometrial cancer (EEC). Analysing nine studies with 1,104 patients, the study found a significant improvement in complete remission rates for AEH with metformin. Secondary analysis showed higher pregnancy rates (RR=1.28) but no significant change in live birth rates. The authors concluded that, while combined therapy is effective, the ideal fertility-sparing treatment for EC has not yet been determined and further clinical trials are needed. Study limitations include varied designs, lack of phase III trials, short follow-ups, potential publication bias, limited side-effect data, and inconsistent metformin dosing. [3]

A retrospective analysis by Plaikner et al. assessed 31 patients with cervical cancer FIGO 2018 stages IB2, IB3, and IIA1 who underwent pelvic lymphadenectomy, neoadjuvant chemotherapy, and radical vaginal trachelectomy. Lymphadenectomy was completed in all patients except one (sentinel) with a median of 33 (range: 11-47) pelvic lymph nodes. Chemotherapy regimens varied across patients. Residual tumour was histologically confirmed in 17 specimens (55%). Fertility was preserved in 27 patients (87%); two patients underwent adjuvant chemoradiation after radical vaginal trachelectomy due to high-risk histological features and two other patients underwent radical hysterectomy with adjuvant chemoradiation therapy following neoadjuvant chemotherapy. Of 18 (67%) patients who attempted pregnancy, 13 became pregnant (72%), with 12 live births in 10 women. After a median follow-up of 94.5 months (range: 6-183) three recurrences (11.1%) were detected and one patient (3.7%) died of the disease. The authors stated that this fertility-sparing approach could be offered to patients with tumours greater than 2 cm, but it is associated with higher recurrence and death rates compared to standard protocols. Study limitations include its retrospective design, small sample size, lack of a control group, and potential biases in patient selection and treatment protocols. [4]

A retrospective multicentre study by Slama et al. included 733 patients from 44 institutions and 13 countries with FIGO 2018 stage IA1 with positive lymphovascular space invasion (LVSI) or ≥IA2 cervical cancer who underwent any type of fertility-sparing procedure. After a median follow-up of 72 months, 51 patients (7%) experienced recurrence, of whom 19 (2.6%) died of disease. The most common sites of recurrence were the cervix (53%) and pelvic nodes (22%). The recurrence risk in patients with tumours ≤2 cm in size did not differ between patients who underwent radical trachelectomy and those who underwent less radical surgery (p=.957), regardless of tumour size subcategory (<1 or 1-2 cm) or LVSI. Study limitations include its retrospective design, potential selection bias, and variations in treatment protocols across participating institutions. [5]

A multicentre study by Zimmermann et al. evaluated minimally invasive fertility-sparing surgery (FSS) versus radical surgery (RS) regarding oncological safety and reproductive outcomes in 80 patients with FIGO stage I/II ovarian cancer. Progression-free survival [150 (3-150) and 150 (5-150) months; p=0.61] and overall survival [36 (3-150) and 50 (1-275) months; p=0.65] were similar between groups. Eight (25.8%) women became pregnant after FSS, resulting in seven (22.5%) deliveries. The authors stated that laparoscopic FSS appears applicable and oncologically safe for patients with early-stage ovarian cancer. Retrospective design limits findings. [6]

A retrospective study by Piątek et al. included 146 patients with germ cell tumours (n=84) and sex cord-stromal tumours (n=62), who underwent fertility-sparing surgery. Adjuvant chemotherapy was administered to 86 (58.9%) patients, while most cases (133 out of 146) were staged FIGO I. Five- and ten-year disease-free survival rates were 91% and 83%, respectively. Cumulative birth incidence rates at 36, 60, and 120 months post-treatment were 13.24%, 20.75%, and 42.37%, respectively. Age, not chemotherapy, influenced childbearing chances, highlighting the need for close follow-ups. Study limitations include its retrospective design. [7]

A retrospective study by Ayhan et al. assessed the long-term oncologic and obstetric outcomes of 68 patients with epithelial ovarian cancer who underwent fertility-sparing surgery. Disease recurrence occurred in 15 (22.1%) patients. Five-year disease-free and overall survival rates were 75.6% and 83.3%, respectively, with FIGO stage significantly affecting overall survival (p=0.001). Twelve (80%) pregnancies reached term and resulted in 15 live births. Chemotherapy administration and surgical intervention (cystectomy or unilateral salpingo-oophorectomy) showed no difference in pregnancy results (p=0.806 and p=0.066, respectively). Fertility preservation is considered safe for early-stage epithelial ovarian cancer patients. Limitations include the study's retrospective design, small sample size, and potential selection bias affecting generalizability. [8]

Fertility sparing treatment in gynaecological malignancies

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No	Title	Authors	Journal	Link to abstract
1	Effects of a fertility-sparing re-treatment for recurrent atypical endometrial hyperplasia and endometrial cancer: A systematic literature review	Murakami I et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36929578/
2	DEAR model in overweight endometrial cancer patients undergoing fertility--sparing treatment: A randomized controlled trial	Chen Y et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38422947/
3	Metformin and progestins in women with atypical hyperplasia or endometrial cancer: Systematic review and meta-analysis	Adamyan L et al.	Arch Gynecol Obstet	https://pubmed.ncbi.nlm.nih.gov/38503850/
4	Fertility sparing therapy in women with lymph node negative cervical cancer >2cm: Oncologic and fertility outcomes of neoadjuvant chemotherapy followed by radical vaginal trachelectomy	Plaikner A et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37696645/
5	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/
6	Laparoscopic fertility-sparing surgery for early ovarian malignancies	Zimmermann JSM et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/37894466/
7	Obstetric results after fertility-sparing management of non-epithelial ovarian cancer	Piątek S et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/37627198/
8	Oncologic and obstetric outcomes of early-stage epithelial ovarian cancer patients who underwent fertility-sparing surgery: A retrospective study	Ayhan A et al.	Int J Gynaecol Obstet	https://pubmed.ncbi.nlm.nih.gov/36825554/

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Prevention and management of surgical complications

Anastasia Prodromidou

The study by Ejaredar et al. evaluated the effect of implementation of a surgical site infection prevention bundle (SSIPB) in gynaecologic oncology patients within an Enhanced Recovery After Surgery (ERAS) pathway. Pre- and post-intervention clinical outcomes were compared (n=259 vs. n=387). A significant reduction in infection rates ($p<0.001$) was observed in the SSIPB group, which remained when analysing wound infections, urinary tract infections, and intra-abdominal abscesses. The hospital stay was also significantly shorter in the SSIPB group. The study's main advantage is the large patient cohort. However, the nonrandomized design makes it difficult to confirm whether improvements were solely due to the SSIPB. [1]

The retrospective study by De Jong et al. evaluated the prevalence and risk factors for symptomatic lymphoceles following robotic-assisted pelvic lymphadenectomy in cervical and endometrial cancer patients. A total of 387 cases were included. A 9.6% incidence of symptomatic lymphoceles was recorded, with smoking being the only significant risk factor for lymphocele formation derived from the entire cohort. The study emphasizes the need to manage risk factors of lymphocele formation. Limitations involve the retrospective nature of the study and the heterogeneity in study populations including both cervical and endometrial cancer, which may affect generalizability and introduce biases. [2]

The study by Kincaid et al. is a retrospective analysis of the impact of preoperative steroid use and perioperative glycaemic control on postoperative complications in gynaecologic oncology surgical populations with diabetes. The incidence of at least one postoperative complication among the 225 patients included was 47.6%. Perioperative hyperglycaemia (blood glucose ≥180 mg/dL) resulted in significantly increased complication rates ($p<0.01$), while preoperative steroid use did not. The study highlights the significance of optimizing glycaemic control to prevent postoperative complications, with the authors indicating the safety of preoperative steroid administration to reduce postoperative nausea, vomiting, and pain. Despite the study population being derived from a tertiary centre, the potential referral of patients to a local hospital in case of complications may interfere the evaluation of complication incidence. [3]

Knisely et al. retrospectively compared the use of apixaban with enoxaparin for postoperative venous thromboembolism (VTE) prophylaxis in 452 gynaecologic cancer patients undergoing laparotomy (n=348 vs. n=104, respectively). The outcomes demonstrated significantly lower 30-day VTE rates with apixaban (0.6% vs. 6.2%, $p=0.006$), with no significant difference in major bleeding between the groups. The findings of the study indicate the safety and efficacy of apaxiban, which could be applicable as standard of care for the prevention of VTE. However, the study's retrospective design and selection bias, along with the fact that the enoxaparin group included patients with significantly increased body mass index, emphasize the need for further study in the field. [4]

The systematic review and meta-analysis by Lavikainen et al. assessed the risks of VTE and major bleeding in gynaecologic cancer surgeries with and without thromboprophylaxis. The analysed indices included 188 studies with 398,167 patients, reporting outcomes from 37 surgical procedures. The VTE risk varied significantly among procedures and patients' risk factors from 0.1% to 33.5% for low-and high-risk VTE patients, respectively. Similarly, bleeding rates requiring intervention ranged from <0.1% to 1.3% among surgeries. The main conclusion of the study is that for many procedures including ovarian cancer (OC) surgery, total hysterectomy with lymphadenectomy and trachelectomy, the benefits of thromboprophylaxis in preventing VTE outweigh the risks of bleeding. However, for lower-risk procedures, decisions should be individualized based on patient risk factors. The study emphasizes the need for personalized thromboprophylaxis to balance VTE prevention with bleeding risks. [5]

The study by Vázquez-Vicente is a retrospective analysis of intra- and post-operative complications between open and minimally invasive radical hysterectomy in patients with early-stage cervical cancer using data from the SUCCOR database. A total of 1,156 patients (n=633 and n=523 for open and minimally invasive, respectively) were analysed. Despite the superiority of minimally invasive approach in terms of blood loss and hospital stay, no significant difference in overall complications was observed between the two approaches. However, open surgery was associated with more bladder dysfunction and wound complications, while minimally invasive surgery had higher vaginal bleeding, vaginal cuff dehiscence, and ureteral fistula rates. Despite its retrospective nature, which precludes reaching firm results, the study emphasizes that open radical hysterectomy remains an oncologically safe option with distinct complication profiles. [6]

The retrospective analysis of 60,017 patients operated on by gynaecologic oncologists revealed that preoperative anaemia resulted in a significantly elevated risk of complications, including infections, thromboembolic events, and the need for intraoperative blood transfusion. OC patients and those with advanced disease presented with the highest rates of preoperative anaemia. The study highlights the importance of screening and treating anaemia preoperatively to reduce perioperative morbidity. However, the retrospective design, the potential missing data on neoadjuvant chemotherapy, and the inclusion of those who received preoperative blood transfusion in the non-anaemia group could potentially affect the study's conclusions. [7]

The prospective analysis by Pergialiotis et al. examined the Prognostic Nutritional Index (PNI) as a predictor of post-operative infectious morbidity in gynaecological cancer patients. It involved 208 patients and found that decreased PNI scores were significantly associated with higher infection rates. The study highlights PNI's role in predicting complications, showing better performance than traditional markers like post-operative white blood cells. The use of the PNI score seems to be of critical clinical importance in identifying high-risk patients for targeted interventions, but larger studies are needed to validate findings across different populations. [8]

The study by Mohammad et al. retrospectively evaluated 892 patients who underwent primary debulking surgical procedures for stage IIIC/IV OC and compared the effectiveness of three complication-reporting scales: the Contracted Accordion Scale, the Expanded Accordion Scale, and the Clavien-Dindo Scale. The complications were graded within 30 days of surgery, with length of stay, 90-day mortality, and delayed chemotherapy initiation examined. The Expanded Accordion and Clavien-Dindo scales provided a more refined assessment of complication severity compared to the Contracted Accordion Scale, highlighting the clinical importance of their use in recoding outcomes after OC surgeries. [9]

Prevention and management of surgical complications

Anastasia Prodromidou

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No	Title	Authors	Journal	Link to abstract
1	Implementation of a surgical site infection prevention bundle in gynecologic oncology patients: An enhanced recovery after surgery initiative	Ejaredar M et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38430815/
2	Symptomatic lymphocele after robot-assisted pelvic lymphadenectomy as part of the primary surgical treatment for cervical and endometrial cancer: A retrospective cohort study	De Jong A et al.	J Minim Invasive Gynecol	https://pubmed.ncbi.nlm.nih.gov/38171478/
3	Impact of steroid use and glycemic control on postoperative complications in diabetic gynecologic oncology patients undergoing laparotomy	Kincaid K et al.	Gynecol Oncol Rep	https://pubmed.ncbi.nlm.nih.gov/38404909/
4	Efficacy, safety, and feasibility of apixaban for postoperative venous thromboembolism prophylaxis following open gynecologic cancer surgery at a comprehensive cancer center	Knisely A et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38368180/
5	Risk of thrombosis and bleeding in gynecologic cancer surgery: Systematic review and meta-analysis	Lavikainen LI et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/37827272/
6	SUCCOR morbidity: Complications in minimally invasive versus open radical hysterectomy in early cervical cancer	Vázquez-Vicente D et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38669163/
7	Characterization of pre-operative anemia in patients undergoing surgery by a gynecologic oncologist and association with post-operative complications	Foley OW et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37423639/
8	Prognostic Nutritional Index as a predictive biomarker of post-operative infectious morbidity in gynecological cancer patients: A prospective cohort study	Pergialiotis V et al.	Nutr Cancer	https://pubmed.ncbi.nlm.nih.gov/38369888/
9	Comparison of the Contracted Accordion, Expanded Accordion, and Clavien-Dindo complication grading scales after ovarian cancer cytoreduction	Mohammad A et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36750269/

Nutrition and perioperative care

Begoña Díaz de la Noval and Zoia Razumova

Laan et al. demonstrated the profound impact of malnutrition on survival in cervical cancer patients undergoing radiotherapy. Among 294 patients, 45% developed malnutrition during treatment, which was associated with a worse three-year overall survival (77% vs. 89%; p=0.001). Despite this high prevalence, only 45% of malnourished patients received dietary support. This study highlights the urgent need for systematic nutritional screening and timely dietary interventions to enhance survival and quality of life in this vulnerable population. [1]

Niu et al. conducted a meta-analysis evaluating the prognostic nutritional index (PNI) as a marker of outcomes in cervical cancer patients. Across nine studies involving 2,508 patients, a low PNI was significantly associated with worse overall survival (HR=2.98) and progression-free survival (HR=2.43). Additionally, low PNI correlated with adverse clinicopathological features, such as lymph node metastasis (OR=1.53) and larger tumour size (OR=1.73). These results establish the PNI as a robust prognostic tool, advocating for its integration into clinical decision-making to tailor nutritional interventions. [2]

Boitano et al. investigated the use of mobile health technology to enhance perioperative care in gynaecologic oncology patients. Their study evaluated 682 women enrolled in a patient engagement platform that provided personalised preoperative education and postoperative monitoring. Participants experienced shorter hospital stays (2.9 vs. 3.6 days; p<0.01) and lower 30-day readmission rates (4.3% vs. 8.6%; p<0.01) compared to controls. This innovative approach demonstrates the potential of leveraging technology to improve perioperative outcomes and patient satisfaction. [3]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Malnutrition is associated with poor survival in women receiving radiotherapy for cervical cancer	Laan J et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38233092/
2	Prognostic and clinicopathological effect of the pro gnostic nutritional index (PNI) in patients with cervical cancer: A meta-analysis	Niu Z et al.	Ann Med	https://pubmed.ncbi.nlm.nih.gov/38039954/
3	Use of a mobile health patient engagement technology improves perioperative outcomes in gynecologic oncology patients	Boitano TKL et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37742507/

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Follow-up after gynaecological malignancies

Sunaina Wadhwa and Zoia Razumova

Patel et al. described a survey conducted across 43 cancer centres in the UK to evaluate follow-up practices for endometrial cancer. The findings highlighted that 93% of centres have a standardised protocol, while the remaining 7% discharged patients following a single postoperative review. Patient-initiated follow-up was primarily adopted for patients who had undergone surgery alone, accounting for 68% of cases, while traditional face-to-face follow-up was common among those receiving adjuvant therapies. Molecular profiling to guide follow-up was used in only 13% of centres. Importantly, 93% of respondents expressed interest in a national standardised protocol to address these variations. [1]

González-Martín et al. emphasised the importance of personalised follow-up strategies for epithelial ovarian cancer in the recently updated European Society for Medical Oncology guidelines. Routine monitoring typically includes serum CA-125 levels, imaging, and symptom-driven assessments, particularly for high-grade serous carcinomas, where molecular testing plays a critical role. While CA-125 monitoring aids early recurrence detection, its role in improving survival remains debatable. The guidelines also recommend integrating genetic and molecular profiling to tailor follow-up based on individual risk factors. However, some recommendations are derived from older trials, limiting their relevance in modern contexts involving PARP inhibitors and secondary cytoreductive surgery. [2]

Rulanda et al. conducted the OPAL trial, comparing patient-initiated follow-up with hospital-based follow-up in 212 women with early-stage, low-to-intermediate-risk endometrial cancer. Over a 34-month follow-up period, there were no significant differences in fear of cancer recurrence or quality of life between the two groups. However, healthcare use was significantly reduced in the patient-initiated group, supporting its feasibility and acceptability in this population. The study underscores the potential of patient-initiated follow-up to reduce the burden on healthcare systems without compromising patient outcomes, though its applicability to high-risk populations remains unestablished. [3]

Wullaert et al. conducted a systematic review and meta-analysis assessing follow-up strategies for oncological patients, including those with gynaecological tumours. Three studies specifically focused on 565 patients treated for gynaecological cancers, with sample sizes ranging from 24 to 385. All were considered to have a low risk of bias. Two studies evaluated nurse-led follow-up approaches, while one investigated patient-initiated follow-up as the least intensive strategy. Results were mixed: two studies reported significant benefits favouring less intensive follow-up in terms of quality of life and emotional well-being, while one favoured more intensive follow-up due to reduced fear of cancer recurrence. These findings highlight the potential of tailored follow-up approaches but also underscore the need for further research to optimise strategies for different patient populations. [4]

Zachou et al. explored follow-up strategies for epithelial ovarian cancer in a Cochrane review. Nurse-led follow-up approaches demonstrated improvements in quality of life compared with conventional medical follow-up, while there was no survival advantage associated with routine CA-125 monitoring in asymptomatic patients. These findings reinforce the shift toward patient-centred follow-up while highlighting the need for further studies to confirm their efficacy in the context of modern therapeutic advancements. [5]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	National survey of current follow-up protocols for patients treated for endometrial cancer in the UK	Patel H et al.	Clin Oncol (R Coll Radiol)	https://pubmed.ncbi.nlm.nih.gov/38548582/
2	Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment, and follow-up	González-Martín A et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/37597580/
3	Patient-initiated follow-up in women with early-stage endometrial cancer: A long-term follow-up of the OPAL trial	Rulanda MC et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/37277320/
4	Oncological surgery follow-up and quality of life: Meta-analysis	Wullaert L et al.	Br J Surg	https://pubmed.ncbi.nlm.nih.gov/36781387/
5	Evaluation of follow-up strategies for women with epithelial ovarian cancer following completion of primary treatment	Zachou G et al.	Cochrane Database Syst Rev	https://pubmed.ncbi.nlm.nih.gov/37650760/

Quality of life in gynaecological cancers/palliative care

Engin Çelik

Cao A. et al. assessed the effect of exercise on chemotherapy-induced peripheral neuropathy (CIPN) in ovarian cancer patients. The Women's Activity and Lifestyle Study in Connecticut (WALC) randomized trial was conducted between May 2010 and March 2014. Ovarian cancer patients who were fluent in English, between 18 and 75 years of age, and diagnosed and treated for epithelial ovarian cancer were enrolled in the study. CIPN was measured with the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group/Neurotoxicity scale at baseline and after six months. Higher scores corresponded with more severe CIPN symptoms. In total, 144 patients were included in the study. In the exercise intervention arm (n=74), home-based, moderate-intensity aerobic exercise was encouraged by weekly telephone calls from an American College of Sports Medicine/American Cancer Society-certified cancer exercise trainer. In the study group, patients were recommended 150 minutes of aerobic exercise per week Participants self-reported about their activity. The control arm (n=70) received instructions restricted to ovarian cancer survivorship-related information and a weekly call from the staff member. The majority of participants were diagnosed at advanced stage (58.2%) and received carboplatin plus paclitaxel therapy (82%). Mean (SD) CIPN score at baseline was 8.4 (6.8) (exercise arm: 8.1 [5.6] vs. control arm: 8.8 [7.9]; p=.56). By the end of the intervention, 83.8% of participants achieved the exercise goal. Peripheral neuropathy was evaluated after intervention, with the CIPN score decreasing by 1.3 points (95% CI -2.3 to -0.2) in the exercise group but not changing in the control arm significantly (0.4 points; 95% CI -0.8 to 1.5). In univariate analysis, baseline CIPN score (p=0.38), counselling attendance (p=0.94), stage of disease (p=0.98), chemotherapy during study (p=0.91), administration of paclitaxel (p=0.73), age (p=0.51), body mass index (p=0.59), and time since diagnosis (p=0.51) were not associated with the effect of exercise. [1]

Marchetti et al. reported on the quality of life in a randomized SCORPİON trial (NCT01461850). Patients with high-tumour-load epithelial ovarian cancer at advanced stage were randomized into primary debulking surgery (PDS) and neoadjuvant chemotherapy (NACT) arms. One hundred seventy-one patients were included in the study and 143 patients (PDS:71 patients; NACT:72 patients) were evaluated in the secondary analysis of the trial. European Organisation for Research and Treatment of Cancer QLQ-C30 and QLQ-OV28 questionnaires were completed by participants at random, at fourth cycle of chemotherapy, or before interval debulking surgery at the sixth cycle and 12 months after diagnosis. There was no difference in the global quality of life at 12 months between the two groups (PDS: 57.53 [27], NACT: 62.72 [16] +4.7 (95 CI -4.99 to 14.4; p=0.34). In the longitudinal analysis across a 12-month period, global health scores were lower in the PDS group (NACT vs. PDS difference of 6.27, 95% CI 0.440-12.11, p=0.035). Insomnia (NACT vs. PDS difference of -11.55, 95% CI -19.18 to -3.92, p=0.003) and constipation (NACT vs. PDS difference of -10.08, 95% CI -18.88 to -1.27, p=0.025) symptoms were improved in the NACT arm. No differences were found in QLQ-OV28 at 12 months. [2]

Cao A. et al. investigated exercise adherence factors in ovarian cancer patients. The Women's Activity and Lifestyle Study in Connecticut (WALC) randomized trial enrolled 144 women with ovarian cancer between 2010 and 2014. In this study, the intervention group (n=74) was analysed for adherence to exercise and higher exercise duration. Home-based aerobic exercise with 150 minutes per week was set as a target. Weekly telephone calls from a certified cancer exercise trainer provided motivational support and educational lessons to ovarian cancer patients. The mean age of the study participants was 57 ± 8.8 years. All patients had epithelial ovarian cancer and 55.4% had advanced-stage disease. Multivariate analysis showed that patients without recurrence (OR=9.15, 95% CI 1.09-44.02, p=0.005) and higher presence at counselling sessions (OR=1.21, 95% CI 1.02-1.43, p=0.03) were associated with better exercise adherence. Increased weekly exercise time was associated with higher attendance of counselling sessions (4.86 ± 1.49 min; p<0.001) and higher baseline physical activity levels (0.38 ± 0.16 min; p= 0.02). According to the ROC curve analysis, an optimal cutoff of 18 sessions was appropriate for weekly counselling attendance. [3]

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No	Title	Authors	Journal	Link to abstract
1	Effect of exercise on chemotherapy-induced peripheral neuropathy among patients treated for ovarian cancer: A secondary analysis of a randomized clinical trial	Cao A et al.	JAMA Netw Open	https://pubmed.ncbi.nlm.nih.gov/37526937/
2	Quality of life in patients with advanced ovarian cancer after primary debulking surgery versus neoadjuvant chemotherapy: Results from the randomised SCORPION trial (NCT01461850)	Marchetti C et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/37334772/
3	Exercise adherence in a randomized controlled trial of exercise on quality of life in ovarian cancer survivors	Cao A et al.	J Cancer Surviv	https://pubmed.ncbi.nlm.nih.gov/36550261/

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Hereditary gynaecological cancer

Tibor A. Zwimpfer

The majority of ovarian cancers are diagnosed at an advanced stage and have a poor prognosis. In particular, tubo-ovarian high-grade serous carcinoma (HGSC) accounts for 70-80% of ovarian cancer deaths due to its typically late presentation and high relapse rate.

The Normal Risk Ovarian Screening Study (NROSS) (NCT00539162) evaluated a two-stage screening approach in postmenopausal women at average hereditary risk. In increasing CA125 levels were used to trigger transvaginal sonography (TVS). If the TVS was abnormal, surgery was performed. The NROSS trial was conducted over 21 years from 2001 to 2022 and enrolled 7,856 healthy postmenopausal women. The study showed that the two-step screening approach had a positive predictive value of 50% (17/34) and a sensitivity of 74% (17/23) for detecting ovarian and borderline cancers. Early-stage cancers were detected in 70% of cases. These results suggest that ovarian cancer can be detected at an early stage, regardless of the site of origin. However, these results, although promising, need to be treated with caution, as they differ from other ovarian cancer screening trials such as the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). The UKCTOCS randomized 202,638 postmenopausal women to a control group (101,314), a group with annual TVS (50,623), and a group (50,625) that was screened with annual CA125 followed by TVS, with none of these groups showing a significant reduction in ovarian cancer deaths. [1]

Another promising strategy is to focus on screening individuals at a high genetic risk for ovarian cancer who carry a pathogenic germline variant in BRCA1 or BRCA2 (gBRCApvar) and offer them risk-reducing salpingo-oophorectomy (RRSO). Women who inherit loss-of-function mutations in BRCA1 or BRCA2 genes have an inreased lifetime risk of developing ovarian cancer or breast cancer. gBRCApvar account for up to 17% of all HGSC. Genome-wide association studies (GWAS) have so far identified 52 variants in 40 genomic regions associated with epithelial ovarian cancer (EOC), with 19 of these regions showing the strongest association with HGSC. Now, an additional eight variants in seven genomic regions have been found by analyzing more than 22 million variants from 398,238 women from the Ovarian Cancer Association Consortium (OCAC), the Consortium of Investigators of Modifiers of BRCA1/BRCA2 (CIMBA), UK Biobank (UKBB), and FinnGen. The OCAC and CIMBA cohorts were used as discovery cohorts, UKBB for validation, and FinnGen for training. These results demonstrate that even in the well-studied EOC, and particularly in HGSC, there are more undetected rare pathogenic variants, and patients with these gBRCApvar may benefit from RRSO. RRSO has been shown to reduce the risk of HGSC by up to 96% when performed between the ages of 35 and 40 years for gBRCA1pvar carriers and between ages 40 and 45 years for gBRCA2pvar carriers. This has now been further supported by Stroot et al., who showed that 1.5% (24/1,624) of gBRCA1pvar and 0.6% (6/930) of gBRCA2pvar carriers had HGSC at RRSO. The fallopian tube was identified as the primary site in 73% of cases. In addition, Kotsopolous et al. showed in a longitudinal cohort study of 4,432 patients with a BRCA1 or BRCA2 sequence alteration and no history of cancer that oophorectomy was associated with reducued overall mortality (HR=0.32, 95% CI, 0.24-0.42, p<0.001). Taken together, timely RRSO is currently the most effective option for preventing ovarian cancer in gBRCApvar carriers, but further efforts should be made to find a screening method for early detection of ovarian cancer also in non-carriers. [2-4]

In endometrial cancer (EC), germline pathogenic variants (gPVs) have been identified in 10-15% of patients, including mismatch repair (MMR) genes and DNA repair genes such as BRCA1 and BRCA2. Gordhandas et al. conducted a germline assessment of more than 76 cancer susceptibility genes in 1,625 patients with EC, finding that 13% (n=216) had gPVs across 35 genes. Patients with gPVS were observed to be younger (p=0.002) and less obese (p=0.025) compared to those without gPVS. Sixty-three percent (47/75) of the gPVs in high-penetrance genes had biallelic alterations. High-penetrance genes predominantly included MMR and homologous recombination-related genes, which are likely drivers of cancer development in EC. The potential role of additional hysterectomy with RRSO to prevent EC in these cases requires further investigation, especially considering the recommendations to investigate this in gBRCApvar carriers. In addition, these findings could impact the efficacy of treatments in EC subgroups. Overall, these results emphasize familial testing members due to the established associations of these genes with other types of cancers. [5]

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No	Title	Authors	Journal	Link to abstract
1	Normal Risk Ovarian Screening Study: 21-year update	Han CY et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/38194613/
2	High-grade serous carcinoma at risk-reducing salpingo-oophorectomy in asymptomatic carriers of BRCA1/2 pathogenic variants: Prevalence and clinical factors	Stroot IAS et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/36809028/
3	Bilateral oophorectomy and all-cause mortality in women with BRCA1 and BRCA2 sequence variations	Kotsopoulos J et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih.gov/38421677/
4	Large-scale genome-wide association study of 398,238 women unveils seven novel loci associated with high-grade serous epithelial ovarian cancer risk	Barnes DR et al.	medRxiv	https://pubmed.ncbi.nlm.nih.gov/38496424/
5	Comprehensive analysis of germline drivers in endometrial cancer	Gordhandas S et al.	J Natl Cancer Inst	https://pubmed.ncbi.nlm.nih.gov/36744932/

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Organisation of gynaecological oncology services

Esra Bilir

The organization of gynaecological oncology services is becoming increasingly challenging due to the growing complexity of disease management, which now includes novel and personalized therapies. In our globalized world, additional challenges arise as patients seek treatment at internationally renowned centres, leading to communication barriers due to language differences and complications with insurance-related paperwork. Furthermore, the multidisciplinary nature of the care team — comprising scrub nurses, patient experience teams, ward nurses, residents, fellows, attending physicians, chemotherapy experts, radiotherapy specialists, radiologists, pathologists, and palliative-care experts — makes effective communication, both vertically and horizontally, even more critical. This also raises the question of institutional qualifications, where it is important to conduct audits to ensure compliance with international recommendations for the management of gynaecologic cancers. [1]

In 2015, a guideline was developed to optimize the organization of gynaecologic oncology services in a higher-resource setting, based on a systematic review and expert consensus. The recommendations emphasize subspecialist care within designated centres, multidisciplinary management, and collaboration across the healthcare system to improve patient access and treatment quality. [2]

A systematic review evaluating literature from 1996 to 2015 found that centralising gynaecologic oncology services, particularly for advanced-stage ovarian cancer, tends to improve patient outcomes due to better access to specialist care and multidisciplinary management. The review also identified 16 primary studies on the centralisation of gynaecologic oncology services across the UK (three studies), other parts of Europe (six studies), the US (five studies), and Canada (two studies), with only three studies evaluating all types of gynaecologic cancers. Further analysis of 16 additional studies focusing on survival outcomes by hospital and physician type, surgical outcomes by hospital and physician type, chemotherapy-related outcomes, and the organisation of gynaecologic pathology found that centralisation generally improves survival outcomes, particularly for advanced-stage ovarian cancer, and enhances surgical procedures such as lymphadenectomy and optimal debulking. Specialised gynaecologic oncologists and pathologists are more likely to provide accurate diagnoses, perform complete staging, and reduce the likelihood of repeat surgeries compared to generalists. However, some studies reported no significant differences in survival outcomes by hospital or physician type, indicating variability depending on the setting and specific practices. [3]

Gynaecologic oncology outpatients experience a high symptom burden regardless of cancer stage or site, with the highest symptoms reported in those who are younger, on treatment, or have a history of chronic pain, depression, or anxiety. A cross-sectional survey including 305 patients with gynaecologic cancers showed significant prevalence of moderate to severe symptoms, particularly fatigue and pain. The authors suggested that patients with these risk factors should be prioritized for referral to outpatient palliative care services. [4]

Another study analysed predictors for inpatient palliative care consultations in women with gynaecologic malignancies, finding that high disease burden and poor prognosis were key factors. Despite meeting America Society of Clinical Oncology guidelines, palliative care referrals are predominantly made late in the disease course, indicating a need for earlier integration of palliative care. [5]

A cross-sectional study including 66 multidisciplinary team members in gynaecologic oncology explored how team members perceive the role of specialist nurses, highlighting their crucial functions in contact, communication, coordination, support, and education. While specialist nurses are seen as central to patient care and team communication, there are concerns about over-dependence on them and potential issues related to large workloads. Team members without a specialist nurse felt it was a disadvantage for patient care, unless other experienced nurses were available. The study calls for clearer role definitions and standardized guidelines to avoid over-reliance and better define the specialist nurse's scope of practice. [6]

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No	Title	Authors	Journal	Link to abstract
1	Chapter 11: Communication, collaboration, clinical and personal audit	Bilir E et al.	ESGO Textbook of Gynaecological Oncology, 6th ed.	https://www.researchgate.net/publication/384289817_Communication_with_Colleagues_and_Clinical_Audit_Chapter_11_Communication_Collaboration_Clinical_and_Personal_Audit
2	An organizational guideline for gynecologic oncology services	Fung-Kee-Fung M et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/25756401/
3	The optimal organization of gynecologic oncology services: A systematic review	Fung-Kee-Fung M et al.	Curr Oncol	https://pubmed.ncbi.nlm.nih.gov/26300679/
4	Predictors of high symptom burden in gynecologic oncology outpatients: Who should be referred to outpatient palliative care?	Lefkowits C et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/24472408/
5	Predictors of palliative care consultation on an inpatient gynecologic oncology service: Are we following ASCO recommendations?	Lefkowits C et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/24594073/
6	“Our nurse is the glue for our team”: Multidisciplinary team members' experiences and perceptions of the gynaecological oncology specialist nurse role	Cook O et al.	Eur J Oncol Nurs	https://pubmed.ncbi.nlm.nih.gov/31358260/

Epidemiology

Christian Braun

In a study involving FIGO stage I EC treated at two cancer centres between 2009 and 2017, 2,815 cases were included. Of these, 47% had no myometrial invasion, 42% had <50% myometrial invasion, and 11% had ≥50% invasion. Rios-Doria et al. reported isolated vaginal recurrences in 2% of patients, primarily at the vaginal apex, while extravaginal recurrences occurred in 8%. Higher risks for extravaginal recurrence were observed in patients with uterine serous carcinoma and carcinosarcoma, grade 3 EC, lymphovascular space invasion (LVSI) positivity, and high-intermediate risk. The median recurrence time was 11 months for isolated vaginal recurrences and 20 months for extravaginal recurrences. The surgical approach did not impact recurrence rates. Adjuvant vaginal brachytherapy after primary surgery carried a 1-2% risk of isolated vaginal apex recurrence. [1]

Kim et al., in a retrospective cohort study of 162 EC patients treated between 2014 and 2018, identified L1CAM as an independent negative prognostic factor for PFS (HR=3.207), particularly in the p53 wild-type (p53wt) subgroup (aHR=4.906). The cohort was predominantly composed of early-stage (67.3%) and endometrioid-type cancers (86.4%), with L1CAM positivity observed in 9.9% of cases, most frequently in the p53-abnormal (p53abn) subgroup (50%) and 37.6% in the p53wt subgroup. L1CAM expression was significantly associated with worse PFS (five-year PFS rate: 35.3% vs. 72.5%, p=0.001), whereas other markers such as α-catenin and PD-L1 did not demonstrate significant prognostic value. [2]

Cucinella et al., in a multi-institutional international retrospective cohort study, compared low-risk EC (stage IA, endometrioid histology, grade 1 or 2) patients with sentinel lymph node (SLN)-isolated tumour cells (ITCs) who did not undergo adjuvant therapy, across 15 centres worldwide (2013-2019), with low-risk EC SLN-negative tumours from the Mayo Clinic (2013-2018). Patients with SLN-ITCs exhibited worse PFS (HR=4.47) and non-vaginal PFS (HR=5.66) compared to node-negative patients. However, OS did not differ significantly between the groups (log-rank p=0.80), and the median OS was not reached during the follow-up period. [3]

Siegenthaler et al. analysed 589 EC patients in a retrospective cohort study between February 2004 and February 2016, finding that LVSI significantly decreased PFS in patients with mismatch repair deficiency, p53abn, and EC of no specific molecular profile (NSMP), as well as OS in patients with p53abn and NSMP tumours. There was no significant impact on POLE-mutated EC. In patients with histologically confirmed node-negative EC, LVSI was not significantly correlated with PFS or OS, and multivariable Cox regression analysis, adjusting for stage and grading, also showed no significant association with PFS and OS. [4]

In a retrospective study of 139 EC patients treated at the University Hospital Frankfurt, Dokora-Friedrich et al. found that fractional curettage with an endocervical curettage (ECC) had a sensitivity of 70.9% and specificity of 73.8% for detecting pT2 EC. OS was 81.8 months for negative ECC, significantly longer than the 59.5 months for positive ECC (p=0.019). [5]

Van Kol et al. conducted a nationwide retrospective cohort study in the Netherlands on stage IB-IVA cervical cancer. For FIGO 2009 stage IB-IB1-IIA-IIA1 and stage IB2-IIA2-IIB with pelvic and/or para-aortic lymph node metastases, the five-year OS was 77% and 67%, compared with 92% and 74% for women without lymph node metastases. Survival rates for FIGO 2009 stage IIIA-IIIB-IVA with and without lymph node metastases were not significantly different (p=0.064). The authors hypothesized that tumour size and/or growth pattern might primarily influence survival in these cases. For FIGO 2018 stage IIIC (lymph node metastases), the five-year OS was 65%. Survival rates for stage IIIC diagnosed by imaging (IIICr) (five-year OS 61%) were significantly worse than for stage IIIC diagnosed by pathology (five-year OS 78%) (p<0.001). The authors suggested that the poorer prognosis for stage IIICr might be due to the fact that lymph node metastases must be of significant size to be detected by imaging, whereas pathological examination can identify smaller metastases, including micrometastases. [6]

In a study involving 10 institutions from Romania, the US, Canada, Italy, Sweden, and Japan (1992-2021), Praiss et al. analysed LVSI in a cohort of 670 patients with cervical squamous cell carcinoma. Multivariable analysis for PFS showed that extensive and focal LVSI had significantly worse outcomes compared to negative LVSI (HR=2.38 and HR=1.54). The difference in OS was not statistically significant. With a median follow-up of 5.7 years, the median OS had not been reached during the observation period. [7]

Menon et al. conducted an exploratory analysis of the UK Collaborative Trial of Ovarian Cancer Screening, involving 202,562 postmenopausal women, comparing multimodal screening (MMS), ultrasound screening (USS), and no screening for ovarian cancer. Annual screening in the MMS group involved serum CA125 testing, with changes over time assessed using the risk of ovarian cancer algorithm (ROCA). ROCA categorized women into normal (annual screening), intermediate (repeat CA125 in three months), and elevated risk (repeat CA125 and transvaginal USS in six weeks). Women with high-grade serous cancer in the MMS group had longer survival than those in the no-screening group, with an absolute survival difference of 6.9% at 18 years (21% vs. 14%, p=0.042). The small survival benefit was attributed to early detection and treatment improvements. Higher rates of primary surgery (61% vs. 42%), no residual disease after debulking surgery (46% vs. 30%), and primary treatment involving surgery and chemotherapy (74% vs. 64%) were observed in the MMS group. [8]

Epidemiology

Christian Braun

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No	Title	Authors	Journal	Link to abstract
1	Isolated vaginal recurrence in women with stage I endometrial cancer	Rios-Doria E et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37864854/
2	Prognostic significance of L1CAM expression in addition to ProMisE in endometrial cancer	Kim J et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37236032/
3	Prognostic value of isolated tumor cells in sentinel lymph nodes in low risk endometrial cancer: Results from an international multi-institutional study	Cucinella G et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38088182/
4	Prognostic value of lymphovascular space invasion according to the molecular subgroups in endometrial cancer	Siegenthaler F et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37666529/
5	The clinical relevance of fractional curettage in the diagnostic management of primary endometrial cancer	Dokara-Friedrich ML et al.	Gynecol Obstet Invest	https://pubmed.ncbi.nlm.nih.gov/38471484/
6	The prognostic value of the presence of pelvic and/or para-aortic lymph node metastases in cervical cancer patients: The influence of the new FIGO classification (stage IIIC)	Van Kol KGG et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/36804623/
7	Extensive versus focal lymphovascular invasion in squamous cell carcinoma of the cervix: A comprehensive international, multicenter, retrospective clinico-pathologic study	Praiss AM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37541128/
8	Tumour stage, treatment, and survival of women with high-grade serous tubo-ovarian cancer in UKCTOCS: An exploratory analysis of a randomised controlled trial	Menon U et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/37657461/

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Diagnostic methods in gynaecological oncology

Andrea Rosati

Li et al. performed a meta-analysis evaluating the diagnostic accuracy of three non-invasive imaging methods — CT, MRI, and PET — in detecting ovarian cancer by analysing data from 61 studies involving 4,284 patients. The results showed that CT had a pooled sensitivity of 0.83, specificity of 0.69, and an area under the curve (AUC) of 0.84; MRI demonstrated a higher diagnostic accuracy, with a sensitivity of 0.95, specificity of 0.81, and an AUC of 0.90; and PET exhibited the highest diagnostic performance, with a sensitivity of 0.92, specificity of 0.88, and an AUC of 0.96. The study concluded that while all three imaging methods are effective in detecting ovarian cancer, hybrid imaging techniques like PET/MRI offer the highest accuracy, particularly in identifying metastatic ovarian cancer. [1]

Alcàzar et al. performed a systematic review of the literature and meta-analysis evaluating the effectiveness of ultrasound in assessing tumour spread in the abdomen of women with ovarian cancer, comparing it to surgical outcomes. The analysis included five studies with 822 women. While the overall study quality was good, patient selection had a high risk of bias. The pooled sensitivity and specificity for ultrasound varied across different anatomical areas. It performed well in detecting disease in the recto-sigmoid and greater omentum but showed low performance for the root of the mesentery. Ultrasound also demonstrated good accuracy in detecting ascites. However, due to limited data, the diagnostic performance for other areas like retroperitoneal lymph nodes, abdominal carcinomatosis, liver, or spleen could not be assessed. [2]

Tameish et al. aimed to compare the diagnostic performance of MRI and transvaginal ultrasound (TVS) in detecting myometrial invasion (MI) in patients with low-grade endometrioid endometrial carcinoma. A systematic review of databases from January 1990 to December 2022 identified 104 citations, with four studies meeting the inclusion criteria. The studies were assessed for bias using the QUADAS-2 tool and found to be of low risk. The meta-analysis showed that MRI had a pooled sensitivity of 65% and specificity of 85%, while TVS had a sensitivity of 71% and specificity of 76%. No significant differences were found between the two imaging techniques. The study concluded that both MRI and TVS have similar diagnostic performance in evaluating deep MI in women with low-grade endometrioid endometrial cancer, though further research is needed due to the limited number of studies available. [3]

Di Donato et al. investigated the use of MRI-based radiomics analysis to preoperatively predict molecular and clinicopathological prognostic factors in endometrial carcinoma. A systematic review of the literature identified 153 relevant articles, with 15 studies meeting the inclusion criteria, encompassing 3,608 patients. The pooled diagnostic accuracy of MRI for predicting high-grade endometrial carcinoma showed a sensitivity of 0.785 and specificity of 0.814. For deep myometrial invasion, sensitivity and specificity were 0.743 and 0.816, respectively. For lymphovascular space invasion, the values were 0.656 and 0.753, while for nodal metastasis, they were 0.831 and 0.736. The findings suggest that preoperative MRI-based radiomics is effective in predicting key prognostic factors in endometrial carcinoma. [4]

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No	Title	Authors	Journal	Link to abstract
1	Diagnostic performance of noninvasive imaging using computed tomography, magnetic resonance imaging, and positron emission tomography for the detection of ovarian cancer: A meta-analysis	Li X et al.	Ann Nucl Med	https://pubmed.ncbi.nlm.nih.gov/37422857/
2	Ultrasound for assessing tumor spread in ovarian cancer: A systematic review of the literature and meta-analysis	Alcàzar JL et al.	Eur J Obstet Gynecol Reprod Biol	https://pubmed.ncbi.nlm.nih.gov/38042117/
3	Transvaginal ultrasound versus magnetic resonance imaging for preoperative assessment of myometrial infiltration in patients with low-grade endometrioid endometrial cancer: A systematic review and head-to-head meta-analysis	Tameish S et al.	J Clin Ultrasound	https://pubmed.ncbi.nlm.nih.gov/37318272/
4	Magnetic resonance imaging-radiomics in endometrial cancer: A systematic review and meta-analysis	Di Donato V et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37094971/

Cancer in pregnancy

Filip Karuga and Grzegorz Chmielewski

The population-based cohort study by Lundberg et al. quantified the incidence of pregnancy-associated cancer using data from Swedish birth and cancer registers (1973-2017). Among 4,557,284 deliveries, 1,274 cases of cancer were diagnosed during pregnancy and 3,355 within one year post-delivery, with 50 cases per year during pregnancy and 110 cases per year post-delivery from 2015 to 2017. Malignant melanoma, breast cancer, and cervical cancer were predominant, accounting for 57% of cases during pregnancy and 53% post-delivery. The incidence of pregnancy-associated cancer increased over time. Smoking, non-immigrant background, and nulliparity partially contributed to this phenomenon. However, only high maternal age was a significant risk factor for increasing the incidence of cancers in pregnancy. The study's main limitation was no information about terminated pregnancies. [1]

The population-based retrospective cohort study by Cairncross et al. examined mortality and survival in premenopausal women with pregnancy-associated cancers diagnosed in three Canadian provinces from 2003 to 2016. Of 24,307 participants, 1,014 were diagnosed during pregnancy, 3,074 postpartum, and 20,219 remote from pregnancy. One-year survival was similar across groups, but five-year survival was lower for pregnancy-associated cancer patients. Women diagnosed during pregnancy had a higher mortality risk (aHR=1.79, 95% CI 1.51-2.13), as did those diagnosed postpartum (aHR=1.49, 95% CI 1.33-1.67). Increased mortality was noted for breast cancer (aHR=2.01, 95% CI 1.58-2.56), ovarian cancer (aHR=2.60, 95% CI 1.12-6.03), and stomach cancer (aHR=10.37, 95% CI 3.56-30.24) during pregnancy, and for brain cancer (aHR=2.75, 95% CI 1.28-5.90), breast cancer (aHR=1.61, 95% CI 1.32-1.95), and melanoma (aHR=1.84, 95% CI 1.02-3.30) postpartum. This study found that overall five-year mortality was increased in pregnancy-associated cancers, though not all cancer sites presented the same risk. The study's main limitation was no reported data on other risk factors that could influence mortality. [2]

The systematic review by Walters et al. aimed to evaluate the risk of adverse maternal and neonatal outcomes in pregnancy-associated cancer patients. Twenty-two relevant studies were identified from databases such as MEDLINE and Embase. The meta-analysis included 59,190 pregnancy-associated cancer cases out of 70,097,167 births. Key findings indicated increased risks for caesarean deliveries (RR=1.58, 95% CI 1.31-1.89), preterm birth (RR=3.07, 95% CI 2.37-3.98), venous thromboembolism (RR=6.76, 95% CI 5.08-8.99), and maternal death (RR=41.58, 95% CI 20.38-84.83). Conversely, the risk of instrumental delivery was reduced (RR=0.67, 95% CI 0.52-0.87). The lack of prospective and blinded data collection was the main limitation of this review. [3]

The single-group trial by Partidge et al. assessed the risk of breast cancer recurrence in women with hormone receptor-positive early breast cancer who temporarily stopped endocrine therapy to attempt pregnancy. It included women aged 42 or younger with stage I-III breast cancer, who had been on endocrine therapy for 18-30 months. Among 516 participants, the median age was 37 years, with 93.4% having stage I or II cancer. After 1,638 patient-years of follow-up, 44 breast cancer events were recorded, not exceeding the safety threshold. The three-year incidence of recurrence was similar between the treatment-interruption group (8.9%) and the control cohort (9.2%). The study concluded that temporary interruption of endocrine therapy to attempt pregnancy did not increase short-term recurrence risk. Short follow-up time (3.4 years) was the limitation of this trial. [4]

The multicentre, retrospective cohort study conducted by Lambertini et al. explored the incidence of pregnancy and disease-free survival in young women with BRCA1/BRCA2 variants post-breast cancer. Conducted across 78 global centres, the study included 4,732 participants diagnosed before age 40. Results showed a 22% cumulative pregnancy incidence at 10 years, with a median conception time of 3.5 years post-diagnosis. Among 659 pregnant participants, 6.9% had abortions and 9.7% experienced miscarriages. Term deliveries occurred in 91% of cases, with twins in 10.4%. Over a median follow-up of 7.8 years, pregnancy did not affect disease-free survival, and those who conceived had better breast cancer-specific and overall survival rates. The study included retrospective data from different health care systems, resulting in potential bias. [5]

The multicentre, international cohort study by Ferrigno Guajardo et al. evaluated obstetric and neonatal outcomes in breast cancer patients treated with taxanes during pregnancy. Among 103 participants, most received paclitaxel and anthracyclines sequentially. The median gestational age for taxane initiation was 28 weeks. Severe adverse events occurred in 6.8% of patients. Common complications included intrauterine growth restriction (8.5%) and preterm premature rupture of membranes (5.3%). The live birth rate was 97.9%, with a median delivery age of 37 weeks. Neonatal intensive care was required for 15.9% of infants, and 24.3% were small for gestational age. Congenital malformations were rare (2.2%). The findings support the safe use of taxanes during pregnancy when necessary. Retrospective data collection was the main limitation of this work. [6]

The study by Mills et al. addressed the management of life-threatening haematological malignancies in pregnancy, focusing on a systematic review of published data and a cross-sectional study of clinical trial protocols. The systematic review included 17 studies and 595 women treated with immunochemotherapy during pregnancy. Fourteen percent were treated in the first trimester, and 86% in the second and third trimesters. Maternal outcomes were broadly comparable to non-pregnant populations, and no increase in congenital malformations or perinatal mortality was observed with second- and third-trimester chemotherapy. The cross-sectional observational study analysed 68 trials on ClinicalTrials.gov for acute myeloid leukaemia, acute lymphocytic leukaemia, high-grade non-Hodgkin lymphoma, and Hodgkin lymphoma. Most protocols (97%) excluded pregnant women, with 69% not providing a rationale. This exclusion reflects historical concerns over foetal harm from anti-cancer therapy, prioritizing foetal safety over pregnant women's autonomy. The findings highlight the need for more rigorous evidence and inclusion of pregnant women in clinical trials to better inform treatment strategies. Excluding pregnant women and the lack of prospective data were the main limitations of the study. [7]

Cancer in pregnancy

Filip Karuga and Grzegorz Chmielewski

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	Risk factors for the increasing incidence of pregnancy-associated cancer in Sweden: A population-based study	Lundberg FE et al.	Acta Obstet Gynecol Scand	https://pubmed.ncbi.nlm.nih.gov/37694965/
2	Long-term mortality in individuals diagnosed with cancer during pregnancy or postpartum	Cairncross ZF et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih.gov/37022714/
3	Pregnancy-associated cancer: A systematic review and meta-analysis	Walters B et al.	Mayo Clin Proc Innov Qual Outcomes	https://pubmed.ncbi.nlm.nih.gov/38524280/
4	Interrupting endocrine therapy to attempt pregnancy after breast cancer	Partidge AH et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/37133584/
5	Pregnancy after breast cancer in young BRCA carriers: An international hospital-based cohort study	Lambertini M et al.	JAMA	https://pubmed.ncbi.nlm.nih.gov/38059899/
6	Taxanes for the treatment of breast cancer during pregnancy: An international cohort study	Ferrigno Guajardo AS et al.	J Natl Cancr Inst	https://pubmed.ncbi.nlm.nih.gov/38059798/
7	Immunochemotherapy for life-threatening haematological malignancies in pregnancy: A systematic review of the literature and cross-sectional analysis of clinical trial eligibility	Mills GS et al.	Lancet Haematol	https://pubmed.ncbi.nlm.nih.gov/37263722/

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Palliative care in gynaecological oncology

Andrej Cokan

Canaz et al. explored the effectiveness of CT-guided percutaneous gastrostomy (CT-PG) in palliating symptoms associated with malignant bowel obstruction in patients with advanced ovarian cancer. The study retrospectively analyzed 31 patients treated at the Charité Comprehensive Cancer Center, revealing that CT-PG was successfully performed in 81% of cases, particularly in patients where traditional endoscopic methods failed due to anatomical challenges. The procedure provided significant symptom relief in 80% of patients, allowing for improved quality of life and the potential for further chemotherapy in selected cases. The study underscores the utility of CT-PG as a safe and effective intervention for managing intractable symptoms in advanced ovarian cancer, highlighting its role as a crucial tool in the palliative care of these patients. However, the study notes limitations such as its retrospective design and the potential under-recognition of complications due to the terminal status of the patients. [1]

Moyett et al. investigated the prevalence and outcomes of malignant bowel obstruction (MBO) in patients with gynecologic cancers. The study, conducted at Duke University, retrospectively reviewed 179 patients admitted with MBO between 2016 and 2021. The findings indicate that MBOs, particularly in ovarian cancer patients, are associated with high mortality rates, with a 30-day mortality rate increasing significantly with higher Henry score (14.3% in 2–3 and 40.9% in 4–5 groups), a tool developed to predict short-term mortality in MBO cases. The study observed no significant difference in overall survival between surgical and medical management of MBOs, although the majority of cases were managed non-surgically. Patients with MBO at the time of cancer diagnosis had slightly better prognosis than those with MBO in recurrent settings, but survival outcomes remained poor overall (9.6 vs. 2.6 months). The study underscores the utility of the Henry score in predicting mortality and guiding palliative care discussions in managing gynecologic cancer patients with MBO. Limitations include the retrospective design and the small surgical cohort, which may impact the generalizability of the results. [2]

Vestergaard et al. examined the use of specialist palliative care (SPC) among patients with gynecological cancers in Denmark between 2010 and 2016. This nationwide registry-based study analyzed data from 4,502 patients, finding a significant increase in SPC utilization from 24.2% in 2010 to 50.7% in 2016. Factors such as younger age, higher comorbidity scores, residing outside the Capital Region, and immigrant status were associated with higher SPC utilization. The study also revealed that early access to SPC, particularly more than 30 days before death, was associated with a reduction in high-intensity end-of-life care interventions, including fewer chemotherapy sessions, radiotherapy, and hospital admissions close to death. These findings underscore the importance of timely SPC integration in the care of gynecological cancer patients to reduce aggressive end-of-life treatments and improve the quality of life. The study is limited by registry data that only records initial SPC encounters and does not capture details about the level or quality of SPC the patient received afterwards. [3]

A retrospective study by Mathew et al. analyzed data from 237,069 ovarian cancer patients in the U.S. between 2003 and 2019, using the CDC's WONDER database. The study observed a shift towards more deaths occurring at home and in hospice facilities, with a decline in hospital and nursing facility deaths. However, significant disparities were found among racial and ethnic minority groups, who were more likely to die in hospitals and less likely to die in hospice facilities compared to White patients. Additionally, individuals with lower educational levels were more likely to die in nursing facilities and less likely in hospice settings. These disparities suggest differences in access to palliative care and underscore the need for culturally sensitive end-of-life care and communication to better align care with patient preferences. Limitations include the retrospective design and that the study does not account for potential changes in healthcare policies or practices during the study period that could have influenced the trends observed. [4]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	CT Fluoroscopy-Guided Percutaneous Gastrostomy in the Palliative Management of Advanced and Relapsed Ovarian Cancer: The Charité Experiences and a Review of the Literature	Canaz E et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/37760510/
2	Understanding the spectrum of malignant bowel obstructions in gynecologic cancers and the application of the Henry score	Moyett JM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37182431/
3	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/
4	Trends in Location of Death for Individuals With Ovarian Cancer in the United States	Mathew AT et al.	Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/37944156/
5	Palliative care utilization across health sectors for patients with gynecologic malignancies in Ontario, Canada from 2006 to 2018	Mah SJ et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/37392530/

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Rehabilitation and social reintegration in gynaecological oncology

Dmitry Utkin

Gynaecological cancers are a major health concern for women worldwide, often leading to overlooked issues in sexual function and intimate relationships. Couple-based interventions, particularly through platforms like WeChat, offer a promising approach to addressing these challenges. A study by Li et al. involved 98 patient-partner dyads and tested an eight-week WeChat-based support programme for women with gynaecological cancer and their partners. The intervention included psychoeducation, skills training, and counselling, while the control group received general nutritional information. Results showed improvements in relationship satisfaction and quality of life (QoL) for both partners in the intervention group compared to the control group. However, sexual function did not significantly improve. While the intervention showed promise in enhancing relationship satisfaction and QoL, the lack of improvement in sexual function indicates the need for further research and refinement. Future studies should include multidisciplinary support to address the complex needs of these couples. [1]

A prospective cohort study by Daggez et al. investigated the effectiveness of prophylactic complex physiotherapy on lower extremity lymphoedema in gynaecological cancer patients. Data from 100 patients diagnosed with endometrial, ovarian, cervical, or vulvar cancer who underwent lymphadenectomy between July 2021 and June 2022 was analysed. Patients who accepted prophylactic physiotherapy received massage and exercise training, while those who declined were only informed. Results showed that 5% of patients in the physiotherapy group developed lymphedema, compared to 60% in the non-physiotherapy group. Additionally, the physiotherapy group reported significantly lower symptom scores. Prophylactic physiotherapy was associated with reduced lymphedema rates and improved patient-reported outcomes. This study's strengths include using both objective measurements and the Gynecologic Cancer Lymphedema Questionnaire to assess the effects of prophylactic physiotherapy. Limitations include a small sample size, lack of randomization, and infrastructure constraints (e.g., no sentinel lymph node mapping for all patients). Differentiating swelling from other factors also posed challenges. [2]

A retrospective study by Miralpeix et al. assessed the impact of an enhanced recovery after surgery (ERAS) programme combined with prehabilitation on post-operative outcomes in endometrial cancer patients undergoing laparoscopic surgery. A total of 128 patients were included, with 60 in the ERAS group and 68 in the prehabilitation group. The prehabilitation group had a significantly shorter hospital stay (one day) and earlier restart of a normal diet (3.6 hours) compared to the ERAS group. There were no significant differences in post-operative complications or readmission rates between the two groups. The study concluded that combining ERAS with prehabilitation improves recovery without increasing complications. This study, the first to assess the impact of prehabilitation and ERAS in endometrial cancer patients undergoing laparoscopy, has strengths such as a homogeneous population and reduced selection bias. However, it also has limitations, including a nonrandomized design, lack of data on program compliance and specific impacts, and limited external validity due to its single-centre nature. [3]

A study by Pozzar et al. explored the challenges faced by patients with peritoneal carcinomatosis and their caregivers during care transitions. It highlights the lack of preparation for managing complex care needs like ostomies and drains at home. Of 61 patients and 39 caregivers, most caregivers provided daily care, but few received proper training. Many patients assessed their conversations with healthcare providers about their prognosis and end-of-life care as inadequate. A significant portion experienced symptoms of depression and anxiety. Interviews revealed that the peritoneal carcinomatosis diagnosis is a turning point, underscoring the need for health system changes, including better training, advance care planning, and psychosocial support. This study has several limitations, including a sample of patients with new complex care needs who volunteered for a randomised controlled trial, which may not represent those ineligible or too ill to participate. The sample was also homogenous in race, ethnicity, and education, limiting generalizability. Ongoing work is testing a more diverse population. [4]

Gil-Ibanez et al. designed a prospective clinical trial (NCT05918770) aiming to assess the impact of systematic screening and early treatment for long-term side effects of gynaecological cancer treatment, such as lower limb lymphedema, anxiety, depression, sexual dysfunction, malnutrition, and sarcopenia, on patients' quality of life. Patients will be randomized into two groups: standard care or systematic screening every two months for two years. Quality of life will be assessed every four months. In the experimental group, positive screenings will trigger referrals to specialized units (rehabilitation, psycho-oncology, sexual health, or nutrition). The primary endpoint is self-reported quality of life, with 168 patients expected to be enrolled. Results are anticipated in May 2026. [5]

Relevant articles retrieved March 31, 2023 – March 31, 2024

No	Title	Authors	Journal	Link to abstract
1	The effectiveness of WeChat couple-based psychosocial support for gynaecological cancer: A randomised controlled trial	Li M et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/36648406/
2	Prophylactic complex physiotherapy in gynecologic cancer survivors: Patient-reported outcomes based on a lymphedema questionnaire	Daggez M et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37844965/
3	Prehabilitation in an ERAS program for endometrial cancer patients: Impact on post-operative recovery	Miralpeix E et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/36898697/
4	Experiences of patients with peritoneal carcinomatosis-related complex care needs and their caregivers	Pozzar RA et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38141533/
5	Side effects screening and early intervention to impact in quality of life of patients with gynecological cancers (HALIS study)	Gil-Ibanez B et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/37748803/

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