LiFE report
Literature for ENYGO

LiFE | Literature for ENYGO

Reviews covering publications from March 31, 2024 – September 30, 2024

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Supported by ESGO

Issue No. 1 (19) July 2025

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Dear Colleagues,

The 19th edition of the LiFE Report (Literature of ENYGO) marks another milestone in our ongoing mission to foster collaboration, education, and innovation among young gynecologic oncologists across Europe and beyond. This edition is the result of months of dedicated work, coordination, and passion from a truly international team. With the invaluable contributions of 7 editors and 52 authors from around the world, we are proud to present a publication that reflects the diversity, expertise, and commitment of the ENYGO community.

It has been a true honour and privilege to lead this project. I would like to express my gratitude for the trust placed in me to coordinate this edition. The opportunity to work alongside such a talented and passionate group of professionals has been both inspiring and humbling.

This edition continues the tradition of excellence established by previous issues, offering a rich collection of articles, reviews, and insights into the latest developments in gynecologic oncology. The collaborative spirit that defines ENYGO is evident in every page, and it is thanks to the tireless efforts of our contributors that this vision has come to life. Special thanks must be expressed towards Founders and former Editors-in-Chief: Kamil Zalewski, Michael Halaska, Kristina Lindemann, and Zoia Razumova—whose leadership and dedication laid the foundation for the continuity and growth of the LiFE Report. Their legacy continues to guide and inspire us.

We are also thrilled to welcome our new editors: Elko Gliozheni, Chrysoula Margioula-Siarkou, David Viveros, and Tibor Andrea Zwimpfer. Their fresh perspectives and enthusiasm have already made a significant impact, and we look forward to their continued contributions in shaping the future of the LiFE Report. Equally, we extend a warm welcome to our new authors, whose names and work will be featured throughout this edition. Your voices bring new energy and insight to our publication, and we are excited to have you as part of the ENYGO family.

Finally, this project would not have been possible without the support and coordination of Helena Opolecka and Tereza Cicakova, ESGO Officers responsible for the administration of the LiFE Report. Their behind-the-scenes work ensured that every detail was managed with precision and care, and we are deeply grateful for their dedication. Acknowledgements must also go to Jonathan Wolfe for his proofreading and to Tomas Grünwald for his graphic design work.

As we celebrate the release of this 19th edition, we also look ahead with optimism and ambition. The LiFE Report remains a platform for learning, sharing, and connecting, and we are committed to nurturing its growth in the years to come. We are very grateful to everyone who made this edition possible. Together, we continue to build a stronger, more connected community of young gynecologic oncologists.

On behalf of the Editorial Team,

Joanna Kacperczyk-Bartnik, LiFE19 Editor-in-Chief

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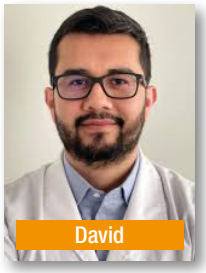
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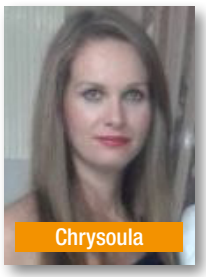
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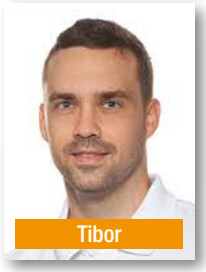
Tibor

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Medical (chemo and radiotherapy) treatment of primary ovarian cancer

Ilker Selçuk and Emmanouela Aliki Almperi

The FLAMES study was a multicentre, double-blind, randomized phase III trial evaluating senaparib, a PARP inhibitor, as maintenance therapy in advanced epithelial ovarian cancer (EOC) following response to first-line, platinum-based chemotherapy. A total of 404 patients were randomized (2:1) to receive senaparib (100 mg) or placebo. In the interim analysis, median progression-free survival (PFS) was not reached in the senaparib group compared to 13.6 months in the placebo group (HR=0.43, 95% CI 0.32–0.58; p<0.0001). The benefit was consistent between the subgroups, BRCA1/BRCA2 mutation or homologous recombination (HR) positive status. Grade ≥3 treatment-related adverse events were reported in 66% of patients receiving senaparib versus 20% in the placebo group. Senaparib demonstrated significant PFS improvement with a manageable safety profile, supporting its use as maintenance therapy in advanced ovarian cancer. [1]

In the final analysis of the phase III PRIMA/ENGOT-OV26/GOG-3012 trial, overall survival (OS) outcomes and long-term safety in newly diagnosed advanced EOC patients receiving niraparib as a first-line maintenance therapy after response to platinum-based chemotherapy was evaluated. The median follow-up was 73.9 months. The five-year PFS rate numerically favoured niraparib (overall 22% vs 12%), particularly in the HR deficiency (HRD) population (35% vs 16%), where it was twice as high as placebo. Myelodysplastic syndromes/acute myeloid leukaemia occurred in <2.5% of patients, and no new safety signals emerged. Niraparib demonstrated consistent long-term safety but did not improve OS (HR=1.01, 95% CI 0.84-1.23; p=0.8834). It should be stressed that subsequent PARP therapy was received by 37.8% and 48.4% of placebo patients in the overall and HRD populations, respectively, whereas this ratio was 11.7% and 15.8% in the niraparib group. [2]

In the post hoc analysis of the PRIMA phase III trial, factors associated with long-term PFS (≥2 years) in the 487 advanced EOC patients treated with niraparib as first-line maintenance therapy were examined. In total, 31% achieved PFS of ≥2 years. Logistic regression analysis identified significant predictors of extended PFS, including BRCA1/2 mutation or HRD status, FIGO stage III (versus IV), and having no or one baseline non-target lesions (versus ≥2). These findings suggest that genomic and clinical characteristics may predict prolonged therapeutic benefit, although further research is needed. [3]

Wu, et al. conducted a randomized study involving 100 post-primary surgery Chinese women with stage III/IV EOC, fallopian tube, or primary peritoneal cancer and assessed the efficacy and safety of bevacizumab use as first-line treatment combined with carboplatin and paclitaxel (CP). After a median follow-up of 20.9 months (0.0-28.6) and 21.0 (2.5-33.2) months, respectively, the median PFS was significantly longer with bevacizumab + CP (22.6 months) compared to placebo + CP (12.3 months) (HR=0.30, 95% CI 0.17–0.53). In the subgroup analysis, bevacizumab provided favourable outcomes both in the optimally and suboptimally debulked stage III patients. Treatment-related grade 3/4 adverse events occurred in 94% of the bevacizumab group versus 68% of the placebo group. These findings confirm bevacizumab's PFS benefit, supporting its use in this population. [4]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Senaparib as first-line maintenance therapy in advanced ovarian cancer: a randomized phase 3 trial	Wu X, et al.	Nat Med	https://pubmed.ncbi.nlm.nih.gov/38750351/
2	Niraparib first-line maintenance therapy in patients with newly diagnosed advanced ovarian cancer: final overall survival results from the PRIMA/ENGOT--OV26/GOG-3012 trial	Monk BJ, et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/39284381/
3	Predictors of long-term progression-free survival in patients with ovarian cancer treated with niraparib in the PRIMA/ENGOT-OV26/GOG-3012 study	Graybill WS, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38950925/
4	First-line bevacizumab plus chemotherapy in Chinese patients with stage III/IV epithelial ovarian cancer, fallopian tube cancer or primary peritoneal cancer: a phase III randomized controlled trial	Wu X, et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38872480/

Medical (chemotherapy and radiotherapy) treatment of recurrent ovarian cancer

Seda Şahin Aker, Ștefania Petrescu and Tibor Zwimpfer

Recurrent ovarian cancer poses a significant therapeutic challenge, necessitating innovative approaches to improve survival outcomes. The disease's heterogeneous nature and frequent resistance to standard treatments underscore the importance of exploring novel therapeutic strategies. This report synthesizes key findings from four major studies exploring advanced medical treatment approaches for both platinum-sensitive and platinum-resistant recurrent ovarian cancer.

Wu, et al. conducted a final overall survival (OS) analysis of the NORA trial, assessing the impact of individualized niraparib dosing (IND) in patients with platinum-sensitive recurrent ovarian cancer. Their findings demonstrated a notable survival advantage, with patients receiving niraparib exhibiting an OS of 44.5 months compared to 37.3 months in the placebo group (HR=0.76, 95% CI 0.58–0.99; p=0.040). Median progression-free survival (PFS) was also significantly extended, reaching 18.3 months versus 5.4 months in the control arm (HR=0.48, 95% CI 0.36–0.64; p<0.0001). Importantly, IND led to a substantial reduction in severe thrombocytopenia (grade ≥3) from 33.9% to 14.7%, reinforcing the value of a personalized dosing strategy in minimizing toxicities while maintaining therapeutic efficacy. [1]

González-Martín, et al. conducted a phase III trial assessing the combination of atezolizumab with platinum-based chemotherapy, followed by niraparib maintenance, in platinum-sensitive recurrent ovarian cancer. Their analysis revealed a median PFS of 12.8 months in the atezolizumab group versus 10.5 months in the control arm (HR=0.74, 95% CI 0.58–0.94; p=0.011). Although OS data remain immature, early indications suggest a trend toward improved survival, particularly in patients harbouring BRCA mutations or homologous recombination deficiency (HRD). The results suggest that the addition of atezolizumab could potentiate anti-tumour immunity, highlighting the need for further research into the long-term benefits of combining immune checkpoint inhibitors with PARP inhibitors. [2]

Moore, et al. performed an integrated safety analysis of mirvetuximab soravtansine, an antibody-drug conjugate designed to target folate receptor alpha (FRα) in recurrent ovarian cancer. Among patients with FRα-high tumours, the treatment demonstrated a median PFS of 6.9 months, with an objective response rate of 31.7%. The most frequently reported adverse events included ocular toxicities (49%) and gastrointestinal symptoms (38%), though these were largely manageable with dose modifications. While OS data remain pending, preliminary findings underscore the potential of mirvetuximab as a viable option for biomarker-driven therapy, particularly in platinum-resistant cases where treatment alternatives remain limited. [3]

Lorusso, et al. conducted a phase III trial comparing trabectedin monotherapy with physician's choice chemotherapy in patients with BRCA-mutated or BRCAness recurrent ovarian cancer. Trabectedin achieved a median OS of 19.2 months versus 16.4 months in the control group (HR=0.85, 95% CI 0.68–1.07; p=0.170), and a median PFS of 7.3 months compared to 5.9 months (HR=0.79, 95% CI 0.63–0.99; p=0.042). With a favourable safety profile and distinct mechanism of action, trabectedin may offer a chemotherapy alternative, particularly in HRD-positive patients who may not respond optimally to standard regimens. [4]

These trials illustrate the dynamic and evolving treatment landscape in recurrent ovarian cancer. IND, atezolizumab-based combinations, mirvetuximab soravtansine, and trabectedin represent promising therapeutic options, particularly in biomarker-selected patient populations. The shift toward immune-based therapies, targeted agents, and individualized dosing strategies continues to refine the standard of care, emphasizing the necessity of precision medicine. Future research should focus on optimizing combination therapies, identifying predictive biomarkers, and improving long-term outcomes, ensuring that patients receive personalized, effective, and well-tolerated treatments.

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No	Title	Authors	Journal	Link to abstract
1	Niraparib maintenance therapy using an individualised starting dose in patients with platinum-sensitive recurrent ovarian cancer (NORA): final overall survival analysis of a phase 3 randomised, placebo-controlled trial	Wu X, et al.	EClinicalMedicine	https://pubmed.ncbi.nlm.nih.gov/38745967/
2	Atezolizumab combined with platinum and maintenance niraparib for recurrent ovarian cancer with a platinum-free interval >6 months: ENGOT-OV41/GEICO 69-O/ANITA phase III trial	González-Martín A, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/39292975/
3	Safety and tolerability of mirvetuximab soravtansine monotherapy for folate receptor alpha-expressing recurrent ovarian cancer: an integrated safety summary	Moore KN, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/39461270/
4	Single-agent trabectedin versus physician's choice chemotherapy in patients with recurrent ovarian cancer with BRCA-mutated and/or BRCAness phenotype: a randomized phase III rial	Lorusso D, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/38315944/

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Surgical treatment of primary and recurrent ovarian cancer

Ilker Kahramanoglu and Ayush Heda

The surgical management of ovarian cancer has seen substantial advancements, focusing on improving oncological outcomes while preserving quality of life. In early-stage epithelial ovarian cancer (EOC), fertility-sparing surgery (FSS) has emerged as a safe and effective alternative for young, selected patients with a strong desire for fertility preservation. Data from large population-based analyses indicate that FSS offers comparable cancer-specific survival (CSS) to radical comprehensive staging surgery (RCS) in stage I EOC, provided that tumour grade and stage are carefully considered. Tumour stage and grade remain the most important prognostic factors, with low-grade, stage I disease being the ideal candidate for FSS. Endometrial biopsy is strongly recommended before or during FSS to rule out synchronous malignancies. Regular surveillance, including imaging and tumour marker assessment, is mandatory for early detection of recurrence. [1]

For advanced-stage ovarian cancer, primary cytoreductive surgery (PCS) continues to be the cornerstone of treatment, particularly in BRCA-mutated high-grade serous ovarian cancer (HGSC). Long-term data showed that PCS significantly improves both overall survival (OS) and progression-free survival (PFS) compared with neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS). Specifically, the 10-year OS was nearly doubled in the PCS group (49% vs. 25%). Complete cytoreduction (R0) remains the most important determinant of survival, with suboptimal cytoreduction negatively impacting outcomes. PCS, although associated with higher surgical complexity, offers superior long-term benefits in appropriately selected patients. [2]

Minimally invasive surgery (MIS) has gained prominence in both early- and advanced-stage ovarian cancer. In early-stage disease, MIS is associated with survival outcomes comparable to laparotomy while offering significant perioperative advantages such as reduced blood loss, shorter hospital stay, and faster recovery. For advanced-stage disease, robotic interval debulking surgery (RIDS) following NACT is feasible in patients with limited disease burden (e.g., pelvic mass ≤8 cm). Studies showed that robotic surgery achieves high rates of R0 (47%) with minimal morbidity. However, MIS shows lower rates of complex procedures such as lymphadenectomy and multivisceral resections compared to laparotomy, warranting careful patient selection. [3,4] Despite these advancements, challenges remain. MIS is limited in achieving R0 in patients with extensive disease, emphasizing the need for surgeon expertise and appropriate patient selection. Similarly, while FSS is effective in carefully selected cases, it carries a risk of secondary malignancies, necessitating rigorous long-term follow-up.

The CHIPOR trial investigated hyperthermic intraperitoneal chemotherapy (HIPEC) in platinum-sensitive recurrent ovarian cancer. [5] Conducted across 31 international centres, 415 patients undergoing secondary cytoreductive surgery were randomized to receive HIPEC or not. Results showed a significant improvement in median overall survival (54.3 vs. 45.8 months; HR=0.73, p=0.024) with HIPEC, though PFS gains were modest. Subgroup analyses showed the greatest benefit in patients with CC-1 resection, non-high-grade serous histology, and a peritoneal cancer index (PCI) >5. However, patients with CC-0 resections or low tumour burden showed minimal benefit, limiting generalizability. HIPEC was associated with increased toxicity, particularly renal failure (10% vs. 1%), though quality of life was not adversely affected. These findings support HIPEC as a potential option for carefully selected patients, though its role in routine practice remains debated, especially in the setting of evolving systemic therapies. Future studies are needed to define its optimal use.

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Outcomes after fertility-sparing surgery of early-stage ovarian cancer: a nationwide population-based study	Lee C-Y, et al.	Cancer Med	https://pubmed.ncbi.nlm.nih.gov/38606892/
2	Primary cytoreductive surgery compared with neoadjuvant chemotherapy in patients with BRCA mutated advanced high grade serous ovarian cancer: 10 year survival analysis	Kim SR, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38548312/
3	MIRRORS: a prospective cohort study assessing the feasibility of robotic interval debulking surgery for advanced-stage ovarian cancer	Uwins C, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38561194/
4	Efficacy and safety of minimally invasive surgery versus open laparotomy for epithelial ovarian cancer: a systematic review and meta-analysis	Yokoi A, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/39142091/
5	Hyperthermic intraperitoneal chemotherapy for recurrent ovarian cancer (CHIPOR): a randomised, open-label, phase 3 trial	Classe J-M, et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/39549720/

Borderline ovarian tumours

Anton Ilin

Borderline ovarian tumors (BOTs) significantly affect ovarian reserve, influencing fertility outcomes and preservation strategies. Recent histological studies show a notable reduction in follicle density and increased follicle atresia in ovarian cortex adjacent to epithelial BOTs compared to healthy tissue (20.1% vs 9.2%, p<0.001). Occult malignant lesions were found in about 14.6% of ovarian cortex samples, even when fertility preservation was initially considered feasible. [1] These findings emphasize the complexity of fertility counselling, necessitating thorough histological assessments. Approaches like ovarian cortex cryopreservation and autotransplantation represent promising fertility-preserving options but require ongoing validation due to potential risks of harbouring undetected malignant cells.

Fertility-sparing surgery (FSS) remains crucial in managing BOTs, especially for younger women desiring fertility. Large-scale analyses consistently report higher recurrence rates after FSS compared to radical surgery. In a recent cohort of 507 BOT patients, recurrence was 13.7% following FSS, significantly greater than after radical interventions (p<0.0001). Independent predictors of recurrence include advanced FIGO stages (II–IV), bilateral ovarian involvement, microinvasion (HR=8.6), and micropapillary growth patterns (HR=4.4). Nonetheless, overall survival remains unaffected by higher recurrence rates associated with FSS, confirming its oncological acceptability for carefully selected patients. [2] Proper patient selection, individualized counselling, and diligent postoperative follow-up are essential for optimizing outcomes.

Recent molecular research has significantly advanced understanding of BOT pathogenesis, identifying key markers and pathways suitable for targeted diagnostics and therapeutics. CXCR4, frequently upregulated in BOTs, enhances tumour migration and invasion through activation of PI3K-AKT and MAPK pathways. Similarly, AGR2 is consistently elevated in mucinous and serous BOTs, facilitating proliferation, migration, and angiogenesis via EGFR and ERK1/2-MAPK signalling. [3] These molecular insights provide new opportunities for targeted interventions, including potential pathway inhibitors or antibody therapies, aiming to improve clinical outcomes.

Chronic inflammation is increasingly recognized as an important risk factor in BOT development, particularly serous subtypes. Epidemiological data from a large Swedish study involving 4,782 BOT cases and 45,167 controls strongly link previous pelvic inflammatory disease (PID) to an increased risk of serous BOT (adjusted OR=1.76), demonstrating a clear dose-response relationship (p<0.001). [4] These findings underscore the importance of inflammation as a modifiable factor in BOT aetiology, highlighting the need for preventive strategies and timely PID management to reduce disease incidence. Further research into inflammatory mechanisms may identify additional preventive or therapeutic targets.

These insights emphasize the necessity of personalized patient management in clinical practice. Balancing fertility preservation with oncological safety requires dynamic, evidence-based strategies, integrating detailed pathological, molecular, and clinical data. Effective risk stratification and interdisciplinary collaboration will remain essential for optimizing therapeutic decisions and improving outcomes for BOT patients.

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Fertility potential and safety assessment of residual ovarian cortex in young women diagnosed with epithelial borderline and early-stage malignant ovarian tumors	Cacciottola L, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38492474/
2	Role of fertility-sparing surgery and further prognostic factors in borderline tumors of the ovary	Westermann T, et al.	Int J Gyanecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38627034/
3	Advances in understanding the molecular mechanisms of borderline ovarian tumors	Chen S, et al.	Front Mol Biosci	https://pubmed.ncbi.nlm.nih.gov/39281319/
4	Pelvic inflammatory disease and risk of borderline ovarian tumors: a national population-based case-control study in Sweden	Jonsson S, et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/39319548/

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Ovarian sex cord-stromal and germ cell tumours

Paul Kubelac and Luiz Felipe Lessa Ortiz

A phase II randomized trial compared paclitaxel-carboplatin (PC) with bleomycin, etoposide, and cisplatin (BEP) in 63 chemotherapy-naive patients with ovarian stromal tumours, mostly granulosa cell type (87%), either newly diagnosed (Stage IIA–IV) or recurrent. Patients received six cycles of PC (n=31) or four cycles of BEP (n=32). BEP showed a higher objective response rate (50% vs. 18%) but was associated with greater toxicity (90% vs. 80% severe adverse events). Progression-free survival was comparable (27.7 vs. 19.7 months; p=0.62). PC had a more favourable toxicity profile, with fewer infections, gastrointestinal, hematologic toxicities, and thromboembolisms. Limitations included small sample size and early termination, limiting subgroup analyses by histology or disease stage. [1]

A multi-institutional analysis of 115 ovarian steroid cell tumours, rare neoplasms frequently presenting with androgenic symptoms, reported elevated preoperative androgen levels in 84.2% of patients. Median age was 55 years (range 9–84), and most tumours (96.5%) were stage I. Median tumour size was 3 cm. Key histologic features included cytologic atypia (52%), necrosis (9.6%), haemorrhage (37%), and mitotic index >1/10 HPF (19%). Recurrence occurred in 6.1% at a median of 33 months. Tumour size >4 cm, stage ≥IB, necrosis, and haemorrhage were significantly associated with recurrence. Age >65 had borderline significance (HR=5.4); multivariate analysis confirmed stage ≥IB (HR=27.5) and age >65 (HR=21.8) as independent predictors. AR expression was not evaluated. Malignancy occurred in <10%, lower than previously reported. Despite early-stage predominance, late recurrences up to 15 years were observed. [2]

A single-centre retrospective study evaluated fertility outcomes in 74 reproductive-age women with stage I immature ovarian teratoma (1980–2019) after fertility-sparing surgery (FSS). Patients were stratified by surgical type, approach, and postoperative management (chemotherapy vs. surveillance). Median follow-up was 191.4 months. Most were stage IA (78.7%), and 63% attempted conception. FSS was performed in 83%, with 17% receiving adjuvant chemotherapy (mostly BEP). Recurrence occurred in 17%. Of those attempting conception, 78.7% achieved pregnancy (63 pregnancies), with 80.9% live births and 98% term deliveries. Miscarriage, elective abortion, and ectopic pregnancy rates were 11.1%, 9.5%, and 1.6%, respectively. No significant fertility differences were seen between treatments; only stage IC correlated with reduced fertility (86.5% vs. 50%, p=0.024). Limitations included retrospective design and treatment variability. [3]

A retrospective cohort of 278 patients with malignant ovarian sex cord-stromal tumours (OSCSTs) treated from 2000 to 2019 evaluated the impact of surgical approach. Median age was 42 years (range 8–78) and median follow-up was 73 months. Surgery extent (fertility-sparing vs. non-sparing) did not influence prognosis (five-year disease-free survival [DFS] 91.9% vs. 94.1%; 10-year DFS 86.5% vs. 91.7%). FSS was safe in early stages. Independent predictors of recurrence included age <40, advanced stage (II–III), elevated CA125, and WT-1 positivity. Limitations were retrospective nature and treatment heterogeneity. [4]

A Turkish multicentre study analysed 322 adult granulosa cell tumour (AGCT) cases (1988–2021). Median age was 51; follow-up was 41 months. Most were early-stage (85.1%) and received surgery (88.5% total hysterectomy with BSO, 10.9% fertility-sparing). Lymphadenectomy was done in 65.2%, with 3.3% nodal involvement. Recurrence occurred in 10.6%; mortality was 2.8%. Five-year DFS and disease-specific survival were 86% and 98%, respectively. Risk factors for recurrence included positive peritoneal cytology (HR=6.17), stage II–IV (HR=3.76), and postmenopausal status (HR=2.52). Lymphadenectomy appeared unnecessary. [5]

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No	Title	Authors	Journal	Link to abstract
1	Results of a randomized phase II trial of paclitaxel and carboplatin versus bleomycin, etoposide and cisplatin for newly diagnosed and recurrent Chemo-naive stromal ovarian tumors: an NRG oncology/gynecologic oncology group study14	Brown J, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/39265466
2	The malignant potential of ovarian steroid cell tumors revisited: a multi-institutional clinicopathologic analysis of 115 cases	Fadare O, et al.	Am J Surg Pathol	https://pubmed.ncbi.nlm.nih.gov/38512100
3	Fertility outcomes in stage I ovarian immature teratomas	Marino G, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39222973
4	Effects of different surgical extents on prognosis of patients with malignant ovarian sex cord-stromal tumors: a retrospective cohort study	Li J, et al.	Sci Rep	https://pubmed.ncbi.nlm.nih.gov/39349505
5	Prognostic factors of adult granulosa cell tumors of the ovary: a Turkish retrospective multicenter study	Oktar O, et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38156722

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

Richárd Tóth

In phase I and II studies by Landen, et al., the JAK1/2 inhibitor ruxolitinib was evaluated for its potential to overcome chemotherapy resistance in ovarian cancer (OC). In phase I, the tolerated regimen included dose-dense paclitaxel (70 mg/m²), carboplatin (AUC 5), and ruxolitinib (15 mg twice daily). After three cycles, patients underwent interval debulking surgery, followed by additional chemotherapy/ruxolitinib cycles and maintenance ruxolitinib. In phase II, patients were randomized to chemotherapy with or without ruxolitinib. While well-tolerated, the experimental arm showed higher rates of anaemia, neutropenia, and thromboembolic events. Median progression-free survival (PFS) was 14.6 months with ruxolitinib vs. 11.6 months in the control arm. Overall survival (OS) was not significantly different (HR=0.785; p=0.24). Ruxolitinib demonstrated a manageable safety profile and a trend toward improved PFS in OC treatment. [1]

The OCTOVA trial evaluated olaparib (O) versus weekly paclitaxel (wP) or olaparib plus cediranib (O + C) in recurrent OC. A total of 139 patients were randomized to O (300 mg twice daily), wP (80 mg/m² on days 1, 8, and 15 every 28 days), or O + C (300 mg twice daily/20 mg daily). The primary endpoint was PFS. Most patients (90%) had platinum-resistant disease, with 22% having prior PARP inhibitor exposure and 30% carrying BRCA1/2 mutations. PFS was longer with O + C (5.4 months) than O alone (3.7 months), while wP (3.9 months) showed no advantage over O. Treatment-related adverse events (TRAE) were mostly manageable, with grade 3 diarrhoea and hypertension (4% each) in the O + C arm. These findings support O + C as a potential non-chemotherapy option for recurrent OC. [2]

A phase II trial by Liu, et al. evaluated the efficacy of cediranib/olaparib in relapsed OC and its association with homologous recombination deficiency (HRD). Seventy patients received olaparib (200 mg twice daily) and cediranib (30 mg once daily) continuously. HRD was assessed via HRR gene sequencing and genomic LOH analysis. In platinum-sensitive patients (n=35), the objective response rate (ORR) was 77.1%, with a median PFS of 16.4 months, regardless of HRD status. In platinum-resistant cases (n=35), ORR was 22.9%, with a median PFS of 6.8 months (10.5 months in HRD vs. 5.6 months in HR-proficient cancers). Cediranib/olaparib demonstrated activity in both settings, though HRR mutations were not predictive of response. [3]

The phase II LEAP-005 study assessed lenvatinib plus pembrolizumab in patients with advanced ovarian cancer after three prior treatments. Patients received lenvatinib (20 mg/day) and pembrolizumab (200 mg every three weeks) until progression, toxicity, or 35 cycles. Among 31 patients, 39% had high-grade serous OC, 23% were platinum-sensitive, 55% platinum-resistant, and 23% platinum-refractory. PD-L1 CPS ≥1 was observed in 84%. ORR was 35%, with a median duration of response (DOR) of 9.2 months. ORRs were 35% in PD-L1 CPS ≥1 patients and 50% in CPS <1 patients. Median PFS and OS were 6.2 and 21.3 months, respectively. TRAE occurred in 94% (grade 3-4 in 77%), with one fatality. Lenvatinib plus pembrolizumab demonstrated antitumour activity as a fourth-line treatment, with responses independent of PD-L1 status and a manageable safety profile. [4]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Phase I and randomized phase II study of ruxolitinib with frontline neoadjuvant therapy in advanced ovarian cancer: an NRG Oncology group study	Landen CN, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/38776484/
2	Results of a randomised phase II trial of olaparib, chemotherapy or olaparib and cediranib in patients with platinum-resistant ovarian cancer	Nicum S, et al.	Br J Cancer	https://pubmed.ncbi.nlm.nih.gov/38245661/
3	A phase 2 trial exploring the significance of homologous recombination status in patients with platinum sensitive or platinum resistant relapsed ovarian cancer receiving combination cediranib and Olaparib	Liu JF, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38759516/
4	Lenvatinib plus pembrolizumab for patients with previously treated advanced ovarian cancer: results from the phase 2 multicohort LEAP-005 study	González- Martín A, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38718741/

Medical (chemo and radiotherapy) treatment of primary uterine cancer

Radwa Hablase

Colombo, et al. investigated the efficacy of adding atezolizumab to carboplatin/paclitaxel chemotherapy in patients with advanced or recurrent endometrial cancer who had not received previous chemotherapy for recurrence in a phase III, randomized, double-blind, placebo-controlled study. A total of 551 patients were randomized in a 2:1 ratio to either the atezolizumab arm (n=362) or the placebo arm (n=189).

The primary endpoint, the median progression-free survival (PFS) in the mismatch repair-deficient (dMMR) patients, was not estimable in the atezolizumab group versus 6.9 months in the placebo group (HR=0.36; p=0.0005). In the overall population, the median PFS was 10.1 months in the atezolizumab arm compared to 8.9 months in the placebo group (HR=0.74; p=0.022). The interim median overall survival (OS) was 38.7 months in the atezolizumab group and 30.2 months in the placebo arm (HR=0.82; p=0.048). The incidence of grade 3-4 adverse events was similar between groups.

There was no PFS benefit seen in mismatch repair-proficient (pMMR) patients, which could be attributed to the enrolment of a substantial proportion of the Asian population, suggesting a racial impact on immunotherapy efficacy. The trial's limitations included the lack of tumour molecular classification beyond MMR status, and the trial was not powered to measure efficacy in the pMMR group. The strength of the trial is the longer follow-up duration (28.3 months). [1]

Van Gorp, et al. conducted a phase III, randomized, double-blind trial evaluating the addition of pembrolizumab to adjuvant chemotherapy, with or without radiotherapy, in patients with newly diagnosed high-risk endometrial cancer. This included stage I/II non-endometrioid, endometrioid histology with P53 mutation, and stage III/IV cases following surgery with curative intent. A total of 1,095 patients were randomized to pembrolizumab (n=545) or placebo (n=550). The primary endpoints were disease-free survival (DFS) and OS.

At the interim analysis, no significant difference in DFS was observed in the overall population (HR=1.02; p=0.570). However, in dMMR patients, pembrolizumab improved DFS (HR=0.31; p=0.0002). Grade ≥3 adverse events were reported in 71% of patients in the pembrolizumab arm versus 63% in the placebo arm. The strength of the study is the large sample size and consistency of eligibility criteria. The limitation is the difficulty of cross-study comparisons due to different baseline characteristics. [2]

In the recent safety analysis of the RUBY trial, evaluating the use of dostarlimab plus chemotherapy in primary advanced or recurrent endometrial cancer, Auranen, et al. reported treatment-related adverse events (TRAE) in 97.9% of patients in the dostarlimab group and 98.8% in the placebo group. Immune-related adverse events (irAEs) were more common in the dostarlimab arm (58.5% vs. 37%). The safety profile was consistent with previous reports. [3]

The second interim analysis of the RUBY trial by Powell, et al., assessing the OS with 51% maturity, demonstrated a statistically significant OS benefit of dostarlimab (HR=0.69; p=0.002), which was more pronounced in dMMR patients (HR=0.32; p=0.0002). In pMMR cases, the trend favoured dostarlimab but was not statistically significant (HR=0.79; p=0.0493). [4]

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No	Title	Authors	Journal	Link to abstract
1	Atezolizumab and chemotherapy for advanced or recurrent endometrial cancer (AtTEnd): a randomised, double-blind, placebo-controlled, phase 3 trial	Colombo N, et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/39102832/
2	ENGOT-en11/GOG-3053/KEYNOTE-B21: a randomised, double-blind, phase III study of pembrolizumab or placebo plus adjuvant chemotherapy with or without radiotherapy in patients with newly diagnosed, high-risk endometrial cancer	Van Gorp T, et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/39284383/
3	Safety of dostarlimab in combination with chemotherapy in patients with primary advanced or recurrent endometrial cancer in a phase III, randomized, placebo-controlled trial (ENGOT-EN6-NSGO/GOG-3031/RUBY)	Auranen A, et al.	Ther Adv Med Oncol	https://pubmed.ncbi.nlm.nih.gov/39346117/
4	Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin-paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial	Powell MA, et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/38866180/

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Medical (chemo and radiotherapy) treatment of recurrent uterine cancer

Stamatios Petousis and Aristarchos Almperis

The ENGOT-EN5/GOG-3055/SIENDO phase III trial evaluated selinexor for maintenance therapy in stage IV or recurrent TP53 wild-type endometrial cancer (EC) patients. The long-term follow-up results demonstrated significantly improved median progression-free survival (PFS) (28.4 vs. 5.2 months; HR=0.44). Benefits were observed regardless of mismatch repair (MMR) status in these patients, who achieved partial remission (PR) or complete remission (CR) following chemotherapy. The study's limitations are the small TP53 wild-type subgroup and treatment discontinuation rates in both groups. [1]

Regarding anti-PD1 or anti PD-L1 agents, the AtTEnd phase III trial evaluated atezolizumab plus chemotherapy in 551 patients with advanced/recurrent EC. Atezolizumab significantly improved PFS, particularly in MMR-deficient (dMMR) tumours (HR=0.36; p=0.0005). Median overall survival (OS) favoured atezolizumab but did not cross interim significance. Despite the common adverse events, results support atezolizumab for dMMR carcinomas. Dostarlimab prevails also as another option for this population. The study's limitations include the absence of a primary endpoint for MMR-proficient efficacy, insufficient molecular characterization, and potential racial impact on treatment efficacy. [2]

The RUBY phase III trial evaluated dostarlimab plus carboplatin-paclitaxel versus placebo plus carboplatin-paclitaxel in 494 patients with advanced or recurrent EC. Recently published data of the second interim analysis showed that dostarlimab significantly reduced the risk of death (HR=0.69; p=0.002) in the overall population, with greater benefit in dMMR/MSI-H spatients (HR=0.32; p=0.0002) and an acceptable safety profile. [3]

Kim, et al. conducted a meta-analysis of four trials (2,335 patients), showing that immune checkpoint inhibitors (ICIs) combined with platinum-based chemotherapy significantly improved PFS (HR=0.70) and OS (HR=0.75) compared to chemotherapy alone in advanced/recurrent EC. The importance of personalized treatment strategies is highlighted by the PFS benefit not only in the dMMR patients (HR=0.33; OS: HR=0.37), but in the Caucasian, endometrioid histology, and PD-L1-positive populations as well. The study's limitations include selection bias from not pooling individual data and a small number of RCTs. [4]

Nagao, et al. assessed the duration of response to secondary platinum-based chemotherapy in recurrent EC using pooled data from the SGSG-012/GOTIC-004/Intergroup study. Among 279 participants, 130 (47%) responded to platinum-based chemotherapy, with 31% of these responses exceeding the platinum-free interval and 39% lasting more than 12 months. Notably, 6% of patients had responses lasting more than 36 months, suggesting that readministering platinum-based chemotherapy may yield long-term responses despite the introduction of ICIs. Limitations included outdated patient data and missing MMR gene status. [5]

In radiation therapy, Klopp, et al. demonstrated that radiation alone is effective for low-grade vaginal recurrences and compared to chemoradiation, the randomized trial demonstrated a longer median PFS (not reached vs. 73 months for chemoradiation). While three-year disease-free survival rates were similar (73% for radiation vs. 62% for chemoradiation), chemoradiation increased acute toxicity. [6]

Aiming to assess definitive radiotherapy, Cong, et al. retrospectively reviewed 20 patients with locally recurrent cervical and EC treated with salvage 3D image-based HDR brachytherapy, with or without external beam radiotherapy (EBRT). Results showed a 95% tumour objective RR and three-year disease-free survival and OS rates of 89.4% and 90.9%, respectively, providing effective tumour control and an acceptable toxicity profile. Limitations of this study included its retrospective nature and small sample size. [7]

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1	Long-term follow-up of efficacy and safety of selinexor maintenance treatment in patients with TP53wt advanced or recurrent endometrial cancer: a subgroup analysis of the ENGOT-EN5/GOG-3055/SIENDO study	Makker V, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38834399/
2	Atezolizumab and chemotherapy for advanced or recurrent endometrial cancer (AtTEnd): a randomised, double-blind, placebo-controlled, phase 3 trial	Colombo N, et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/39102832/
3	Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin-paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial	Powell MA, et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/38866180/
4	Efficacy of immune-checkpoint inhibitors combined with cytotoxic chemotherapy in advanced or recurrent endometrial cancer: a systematic review and meta-analysis	Kim JH, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38735144/
5	Re-administration of platinum-based chemotherapy for recurrent endometrial cancer: an ancillary analysis of the SGSG-012/GOTIC-004/Intergroup study	Nagao S, et al.	Int J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/39001945/
6	Radiation therapy with or without cisplatin for local recurrences of endometrial cancer: results from an NRG Oncology/GOG prospective randomized multicenter clinical trial	Klopp AH, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/38662968/
7	Salvage radiotherapy for locally recurrent cervical and endometrial carcinoma: clinical outcomes and toxicities	Cong H, et al.	BMC Cancer	https://pubmed.ncbi.nlm.nih.gov/39030527/

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Surgical treatment of primary and recurrent uterine cancer

Houssein El Hajj and Maria Fanaki

Two retrospective studies assessed the feasibility and safety of vaginal natural orifice transluminal endoscopic surgery (vNOTES) compared to conventional laparoscopy (CL) in early-stage endometrial cancer (EC). [1,2] Mat, et al. concluded both techniques had comparable operative times, haemoglobin level changes, and hospital stays, with lower postoperative pain scores ($p<0.001$) and reduced analgesic use ($p=0.037$) with vNOTES. [1] Comba, et al. reported similar operative times, blood loss, and oncological outcomes for vNOTES and CL, with lower pain scores and shorter hospital stays ($p=0.003$) with vNOTES. [2] A multicentre prospective study by Baekelandt, et al. found a 97% sentinel lymph node (SLN) detection rate with vNOTES, minimal blood loss, and no major complications. [3] The main limitations of these studies include small cohort size, the retrospective design of the first two studies, and the lack of comparison with the standard of care in the third study.

Cuccu, et al. showed no significant differences in five-year disease-free survival (DFS) and overall survival (OS) between SLN and lymph node dissection (LND) in high-intermediate and high-risk EC, while Jaafar, et al. noted better OS for early-stage high-risk EC patients who underwent SLN compared to those who underwent systematic LND ($p=0.047$), as well as a higher rate of patients with positive pelvic lymph nodes (18% vs 14%, $p=0.04$). [4,5] The ALIEN study found that both 2 mL and 4 mL of indocyanine green (ICG) in early-stage EC were effective for bilateral SLN detection, though 4 mL had a slightly higher overall detection rate ($p=0.024$). [6] Obesity and advanced stages negatively impacted detection rates. [6] The main limitation of these studies was their retrospective design. [4-6]

In their multicentre study, Puppo, et al. compared 1,028 early-stage patients treated with minimally invasive surgery (MIS) to those treated with laparotomy, finding no significant difference in recurrence rates (7.4% vs. 7.9%, OR=0.9395), recurrence patterns, or time to recurrence. [7] However, distant metastases were more frequent with laparotomy.

Buderath, et al. evaluated robotic peritoneal mesometrial resection plus targeted compartmental lymphadenectomy (PMMS+TCL) in 135 stage I–IV patients. [8] After a mean follow-up of 27.5 months, the recurrence rate was 8.1%, with 1.5% as isolated locoregional recurrences. Although 50.4% required radiotherapy, only 10.4% received it, indicating peritoneal PMMR+TCL's efficacy in locoregional control and the reduction of adjuvant treatment.

In their randomized trial, Kivekäs, et al. reported that OS was more favourable in the robotic-assisted (RA) group than in the CL group (HR=0.39; $p=0.047$). [9] Similarly, Koek, et al. observed comparable oncologic outcomes between CL and RA in high-intermediate/high-risk EC when compared to laparotomy. [10] Dagher, et al. further confirmed that RA provided similar oncologic outcomes to CL in patients with high-grade EC, with no significant differences in postoperative complications or long-term survival. [11]

Laminam, et al. compared 5,074 patients with stage I–III type II EC who underwent RA with 2,094 patients who underwent CL, finding no significant difference in OS. [12] However, RA was associated with lower conversion rates (2.7% vs. 12%), shorter hospital stays, decreased 90-day mortality (1.3% vs. 2.2%), and a higher number of lymph nodes sampled. These findings were also observed in studies evaluating high body mass index (BMI). [13]

Morton, et al. found no evidence that surgical approach (laparoscopy vs. laparotomy) or mismatch repair status impact survival outcomes in early-stage EC. [14]

Additionally, Vargiu, et al. identified that age of less than 65 years ($p=0.025$), single-site recurrence ($p=0.006$), lymph node ($p=0.004$), and hematogenous relapse ($p=0.021$) were favourable prognostic factors for successful cytoreduction in recurrent EC. [15]

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No	Title	Authors	Journal	Link to abstract
1	Comparison of laparoscopy and vNOTES in early-stage endometrial cancer	Mat E, et al.	J Obstet Gynaecol Res	https://pubmed.ncbi.nlm.nih.gov/39160113/
2	Transvaginal natural orifice transluminal endoscopic surgery (VNOTES) retroperitoneal sentinel lymph node BIOPSY compared with conventional laparoscopy in patients with endometrial cancer	Comba C, et al.	Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/38991626/
3	vNOTES retroperitoneal sentinel lymph node dissection for endometrial cancer staging: first multicenter, prospective case series	Baekelandt J, et al.	Acta Obstet Gynecol Scand	https://pubmed.ncbi.nlm.nih.gov/38623778/
4	Sentinel node mapping in high-intermediate and high-risk endometrial cancer: analysis of 5-year oncologic outcomes	Cuccu I, et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/38428106/
5	Impact of sentinel lymph node mapping on survival in patients with high-risk endometrial cancer in the early stage: a matched cohort study	Jaafar E, et al.	Int J Gynaecol Obstet	https://pubmed.ncbi.nlm.nih.gov/38226675/
6	Assessment of sentinel lymph node mapping with different volumes of indocyanine green in early-stage endometrial cancer: the ALIEN study	Mauro J, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38336372/
7	Surgical access and pattern of recurrence of endometrial cancer: the SUPeR study, a multicenter retrospective observational study	Puppo A, et al.	J Minim Invasive Gynecol	https://pubmed.ncbi.nlm.nih.gov/38301845/
8	Cancer-field surgery for endometrial cancer by robotic peritoneal mesometrial resection and targeted compartmental lymphadenectomy (PMMR+TCL)	Buderath P, et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38945527/
9	Robotic-assisted versus conventional laparoscopic surgery for endometrial cancer: long-term results of a randomized controlled trial	Kivekäs E, et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/39181495/

Surgical treatment of primary and recurrent uterine cancer

Houssein El Hajj and Maria Fanaki

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10	Oncological outcomes after laparotomic, laparoscopic, and robot-assisted laparoscopic staging for early-stage high-intermediate or high-risk endometrial cancer	Koek RCG, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39019491/
11	Oncologic and perioperative outcomes of robot-assisted versus conventional laparoscopy for the treatment of clinically uterine-confined high-grade adenocarcinoma	Dagher C, et al.	Ann Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/39317893/
12	Impact of robotic assistance on minimally invasive surgery for type II endometrial cancer: a National Cancer Database analysis	Lamiman K, et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/39061223/
13	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/
14	Mismatch repair status and surgical approach in apparent early-stage endometrial cancer	Morton R, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38431289/
15	Optimizing patient selection for secondary cytoreductive surgery in recurrent endometrial cancer	Vargiu V, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38876787/

Uterine sarcoma

Marcin Bobiński

The phase III LMS04 trial by the French Sarcoma Group assessed doxorubicin plus trabectedin followed by trabectedin maintenance in metastatic/unresectable leiomyosarcoma. [1] Among 121 chemotherapy-naïve patients, the combination therapy significantly improved median progression-free survival (PFS) (12.2 vs. 6.2 months) and overall survival (OS) (34.4 vs. 19.0 months) compared to doxorubicin alone. However, adverse events were higher in the combination group, with grade 3/4 neutropenia (54% vs. 20%) and febrile neutropenia (19% vs. 8%). Limitations include the small sample size, lack of biomarker-based analysis, and increased toxicity, warranting further trials.

A study by De Wispelaere, et al. investigated PI3K/mTOR pathway activation in uterine leiomyosarcoma (uLMS) and immune evasion. [2] Analysis of 101 LMS samples showed high phosphorylated S6 (pS6^high) levels correlated with reduced lymphocyte infiltration. Patient-derived xenografts treated with PI3K/mTOR inhibitors (sapanisertib, alpelisib) altered the tumour microenvironment, enhancing antigen presentation and repolarizing macrophages. Combining these inhibitors with PD-1 blockade (nivolumab) led to partial/complete tumour responses. However, the study lacks clinical trial data, and its preclinical design limits real-world applicability.

The MYLUNA study developed an ultrasound-based algorithm to classify myometrial lesions (≥3 cm) into low-, intermediate-, and high-risk categories. [3] Among 2,268 women, 95.1% had benign tumours, 2.6% had other malignancies, and 2.3% had mesenchymal uterine malignancies. Key malignancy predictors included age (OR=1.05), tumour size greater than 8 cm (OR=5.92), irregular margins (OR=2.34), and a colour score of 4 (OR=2.73), while acoustic shadowing was protective (OR=0.39). The model had an area under the curve (AUC) of 0.87, but its single-centre design and tertiary care recruitment limit generalizability.

A retrospective study validated the Oman-Canada Scoring System of Myometrial Masses (OCSSMM), an MRI-based tool distinguishing benign from malignant uterine smooth muscle tumours. [4] Among 244 patients (218 leiomyomas, 13 smooth muscle tumour of uncertain malignant potential, 13 leiomyosarcomas), OCSSMM had 92.3% sensitivity, 64.7% specificity, and 98.6% negative predictive value. High-risk MRI features included non-cystic T2 hyperintensity and diffusion restriction. While effective, the study's retrospective design and need for broader validation remain challenges.

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No	Title	Authors	Journal	Link to abstract
1	Doxorubicin-trabectedin with trabectedin maintenance in leiomyosarcoma	Pautier P, et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/39231341/
2	PI3K/mTOR inhibition induces tumour microenvironment remodelling and sensitises pS6high uterine leiomyosarcoma to PD-1 blockade	De Wispelaere, et al.	Clin Transl Med	https://pubmed.ncbi.nlm.nih.gov/38711203/
3	A clinical ultrasound algorithm to identify uterine sarcoma and smooth muscle tumors of uncertain malignant potential in patients with myometrial lesions: the myometrial lesion ultrasound and MRI study	Ciccarone F, et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/39084498/
4	Validating the diagnostic accuracy of an MRI-based scoring system for differentiating benign uterine leiomyomas from leiomyosarcoma	Al Khuri, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38658016/

Emerging molecular targeted therapies or early preclinical trials in uterine tumours

Jakub Dobroch and Jagannath Mishra

Westermann, et al. reported the results of PAZEC, a Dutch phase II study on the efficacy of the multi-tyrosine kinase inhibitor pazopanib. Sixty participants diagnosed with progression or recurrence of endometrial cancer (EC) were prescribed pazopanib 800 mg daily. The primary endpoint of three-month progression free survival (PFS) was achieved by 63.3% of patients. Median overall survival (OS) was 7.5 months. A considerable rate (21%) of severe gastrointestinal toxicity was observed, including perforation or haemorrhage. It has been concluded that a correlation of previously received treatment (first-line chemotherapy or radiotherapy) and presence of severe pazopanib toxicity should be further investigated. [1]

The efficacy of combined treatment with the anti-PD-1 agent camrelizumab and the VEGFR2 inhibitor apatinib was assessed in a phase II trial conducted by Tian, et al. Camrelizumab was prescribed 200 mg every two weeks intravenously and apatinib 250 mg daily by mouth. The study consisted of 36 patients with recurrent EC. The majority of patients were tested for mismatch-repair deficiency (MMRd) and PD-L1 expression; however, formed subgroups were not large (2 MMRd, 7 PD-L1+ patients). The objective response rate (ORR) was achieved in 44.4% of participants. Median PFS was 6.2 months. The most commonly occurring side effects included hepatotoxicity expressed by elevation of liver enzyme concentration and were considered manageable. [2]

The phase II NRG-GY012 study investigated efficacy of the poly-ADP-rybose polymerase inhibitor (PARPi) olaparib, either in monotherapy or in combination with the antiangiogenic agent cediranib in EC. Eligible patients with recurrent EC were randomized into three study arms — olaparib alone (300 mg twice daily), combined therapy (olaparib 200 mg twice daily, cediranib 30 mg once daily), or the reference arm (cediranib 30 mg). No significant differences between groups were observed in terms of PFS, with a marked trend of improved result in the combined treatment arm (5.5 months vs. 3.8 months for cediranib and 2.0 months for olaparib). Similarly, OS analysis revealed relatively better prognosis in patients receiving combined therapy. The most common serious adverse event was hypertension, which occurred in most patients prescribed cediranib. Rimel, et al. highlighted the necessity of further research on PARPi in EC, with consideration of tumour molecular profile, especially homologous recombination deficiency (HRD) status and p53 mutations. [3]

A noteworthy update on MITO END-3 trial results has been published. Pignata, et al. examined the efficacy of the PD-L1 inhibitor avelumab in different molecular subgroups according to the Cancer Genome Atlas. Molecular analysis by next-generation sequencing (NGS) was performed in most of the participants (n=109), who were diagnosed with advanced or recurrent EC. Patients were divided into subgroups based on microsatellite instability (MSI) status, p53 mutation, or POLE mutation (only 1 patient). Additionally, a significant number of participants was diagnosed with PIK3CA, ARID1A, or PTEN mutation. The prescription of avelumab as a maintenance regimen was particularly beneficial for the MSI-high subgroup, with a significant increase in PFS. A poor effect was described in p53-mutated cases. Tumours expressing ARID1A and PTEN mutations positively responded to treatment with avelumab. [4]

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No	Title	Authors	Journal	Link to abstract
1	PAZEC: a Dutch Gynaecological Oncology Group open-label, multicenter, phase II study of pazopanib in metastatic and locally advanced hormone-resistant endometrial cancer	Westermann A, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38184318/
2	Camrelizumab plus apatinib in patients with advanced or recurrent endometrial cancer after failure of at least one prior systemic therapy (CAP 04): a single-arm phase II trial	Tian W, et al.	BMC Med	https://pubmed.ncbi.nlm.nih.gov/39183277/
3	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/
4	MITO END-3: efficacy of avelumab immunotherapy according to molecular profiling in first-line endometrial cancer therapy	Pignata S, et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih.gov/38704093/

Medical treatment of primary and recurrent cervical cancer

Wilfried Loic Tatsipie

The KEYNOTE-A18 clinical trial (ENGOT-cx11/GOG-3047) evaluated the addition of pembrolizumab, a PD-1 inhibitor, to chemoradiotherapy (CRT) in patients with locally advanced cervical cancer. The study involved 1,060 patients (stages IB2 to IVA). The results showed that the addition of pembrolizumab reduced the risk of progression or death by 30% compared with CRT alone (HR=0.70). At two years, 68% of patients treated with pembrolizumab were progression-free, compared with 57% in the placebo group. Overall survival at 24 months was 87% in the pembrolizumab group and 81% in the placebo group. The authors concluded that the addition of pembrolizumab improved clinical outcomes, with a favourable trend in terms of survival. [1]

At recurrence, the SKYSCRAPER-04 trial evaluated the efficacy of the combination of tiragolumab (anti-TIGIT) and atezolizumab (anti-PD-L1) as a second- or third-line treatment for persistent/recurrent PD-L1-positive cervical cancer. Results showed a response rate of 19.0% for the combination of tiragolumab plus atezolizumab in 126 patients, compared with 15.6% for atezolizumab alone in 45 patients. Progression-free survival was 2.8 months with the combination, compared with 1.9 months with atezolizumab alone. These results suggest a modest benefit from immunotherapy in this setting. [2]

In addition, the COMPASSION-13 study demonstrated the safety and efficacy of cadonilimab, a bispecific antibody targeting PD-1 and CTLA-4 combined with standard therapy for recurrent and/or metastatic cervical cancer. Patients in three cohorts received cadonilimab with chemotherapy (cohort A-15: cadonilimab (15 mg/kg every 3 weeks) plus chemotherapy; cohort A-10: cadonilimab (10 mg/kg every 3 weeks) plus chemotherapy; cohort B-10: cadonilimab (10 mg/kg every 3 weeks) plus chemotherapy and bevacizumab). The results showed promising tumour response rates: 66.7% in cohort A-15, 68.8% in cohort A-10, and 92.3% in cohort B-10. However, treatment-related adverse events were common, with 73.3% of patients experiencing severe side effects. Despite these risks, the combination therapy demonstrated encouraging efficacy and warrants further exploration. [3]

The CheckMate 358 study evaluated the efficacy of nivolumab and the combination of nivolumab and ipilimumab in patients with recurrent or metastatic cervical cancer. Patients were treated with nivolumab 240 mg every two weeks or were randomised into one of two regimens: nivolumab 3 mg/kg every two weeks plus ipilimumab 1 mg/kg every six weeks (NIVO3 plus IPI1) or nivolumab 1 mg/kg every three weeks plus ipilimumab 3 mg/kg every three weeks for four cycles, followed by nivolumab 240 mg every two weeks (NIVO1 plus IPI3). In total, 176 patients were treated. The results showed objective response rates of 26% for nivolumab alone, 31% for NIVO3 plus IPI1, and 38% for NIVO1 plus IPI3. Serious side effects were more frequent with the combined treatments, and one patient died of treatment-related colitis in the NIVO1 plus IPI3 arm. These results suggest that both treatments are promising, but further randomised trials are needed to confirm their efficacy. [4]

Finally, another phase II clinical trial evaluated bintrafusp alfa, a bifunctional therapy, in patients with recurrent or metastatic cervical cancer that has progressed after platinum-based chemotherapy. Patients received bintrafusp alfa 1,200 mg intravenously once every two weeks. A total of 146 patients were enrolled. Results showed a confirmed objective response rate of 21.9%, with 59.4% of responders having a durable response of six months or more. The most common adverse events were anaemia, rash, and hypothyroidism. The study met its primary objective, suggesting that bintrafusp alfa could be a promising therapeutic option for this group of patients. [5]

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1	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/
2	A non-comparative, randomized, phase II trial of atezolizumab or atezolizumab plus tiragolumab for programmed death-ligand 1-positive recurrent cervical cancer (SKYSCRAPER-04	Salani R, et al	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38858106/
3	Cadonilimab combined with chemotherapy with or without bevacizumab as first-line treatment in recurrent or metastatic cervical cancer (COMPASSION-13): a phase 2 study	Lou H, et al,	Clin Cancer Res	https://pubmed.ncbi.nlm.nih.gov/38372727/
4	Nivolumab with or without ipilimumab in patients with recurrent or metastatic cervical cancer (CheckMate 358): a phase 1-2, open-label, multicohort trial	Oaknin A, et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/38608691/
5	Bintrafusp alfa for recurrent or metastatic cervical cancer after platinum failure: a nonrandomized controlled trial	Birrer M, et al	JAMA Oncol	https://pubmed.ncbi.nlm.nih.gov/39052242/

Radiotherapy in management of primary and recurrent cervical cancer

Erbil Karaman and Nadia Veiga

Cho, et al. reported a multicentre, non-randomized prospective trial assessing the safety of hypofractionated pelvic intensity-modulated radiotherapy (IMRT) combined with concurrent chemotherapy in postoperative high-risk cervical cancer (CC) patients. Enrolling 84 patients between June 2017 and February 2023, the study aimed to assess acute toxicities during treatment with 40 Gy in 16 fractions. In 79 analysed patients, the incidence of grade 3 or higher toxicities was low, with only 2.5% of patients affected. After a median follow-up of 43 (21.1-59.0) months, the three-year disease-free survival was 79.3%, and overall survival was 98%. The authors concluded that this regimen was well-tolerated and safe, recommending further studies with a comparison arm and oncologic outcomes. [1]

Han, et al. published a population-based study using the SEER database analysing the impact of brachytherapy on mortality in 24,205 patients with locally advanced stage IB2-IVA CC, treated between 2000 and 2020. Among those who received external beam radiotherapy (EBRT) and chemotherapy, 64% also received brachytherapy. In the propensity-score matched cohort (n=5,566), results showed that brachytherapy was associated with significantly lower cancer-specific mortality (HR=0.70, 95% CI 0.64-0.76; p<.001) and all-cause mortality (HR=0.72, 95% CI 0.67-0.78; p<.001). The study is limited by the absence of information regarding the reason for not administering brachytherapy. Despite these benefits, the study highlighted persistent disparities in brachytherapy utilization. The authors recommended its more widespread use, particularly for locally advanced CC. [2]

Isohashi, et al. conducted a retrospective multicentre study in Japan to evaluate the role of high-dose-rate (HDR) brachytherapy in the reirradiation of recurrent gynaecologic cancers. The study included 165 patients from nine centres, of whom 142 were treated with curative intent from 2000 to 2018. Among 140 patients with CC, the three-year overall survival, progression-free survival, and local control rates were 53% (95% CI 42-63%), 44% (95% CI 35-53%), and 61% (95% CI 50-70%), respectively. Multivariate analysis identified an interval of less than one year between initial treatment and reirradiation as a significant risk factor for poor outcomes. The study concluded that HDR brachytherapy can be effective for recurrent CC, particularly when the reirradiation interval is longer, although late grade ≥3 toxicities were noted in 30% of patients. [3]

Gagrani, et al. aimed to compare the acute treatment-related gastrointestinal and genitourinary toxicities between two HDR brachytherapy regimens in patients with FIGO stage IIB and stage IIIC1 cervical cancer. This was a prospective study, conducted in India, involving 66 patients randomized to either 7 Gy × 3 fractions or 6 Gy × 4 fractions after concurrent chemoradiation with an EBRT dose of 46 to 50 Gy. Results reported non-statistically significant differences between the two groups regarding acute gastrointestinal or urinary toxicity, with the 7 Gy × 3 fractions regimen being preferable due to a lower hospital burden. The study is limited by the small sample size, the high lost to follow-up rate, and the short follow-up time. [4]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Postoperative hypofractionated intensity-modulated radiotherapy with concurrent chemotherapy in cervical cancer: the POHIM-CCRT nonrandomized controlled trial	Cho WK, et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih.gov/38662364/
2	Updated trends in the utilization of brachytherapy in cervical cancer in the United States: a surveillance, epidemiology, and end-results study	Han K, et al.	Int J Radiat Oncol Biol Phys	https://pubmed.ncbi.nlm.nih.gov/37951548/
3	Reirradiation for recurrent gynecologic cancer using high-dose-rate brachytherapy in Japan: a multicenter survey on practice patterns and outcomes	Isohashi F, et al.	Radiother Oncol	https://pubmed.ncbi.nlm.nih.gov/38583719/
4	A comparative study between two different dose fractionation schedules of cobalt-60-based HDR intracavitary brachytherapy in carcinoma cervix stages IIB-IIIC1	Gagrani V, et al.	J Cancer Res Ther	https://pubmed.ncbi.nlm.nih.gov/38261446/

Surgical treatment of primary and recurrent cervical cancer

Chrysoula Margioula-Siarkou and Georgia Margioula-Siarkou

Ramirez, et al. published the final analysis of the LACC trial, designed to compare survival outcomes between patients with cervical cancer (CC) up to FIGO 2009 IB2 stage who underwent open (n=312) or minimally invasive (MIS) (n=319) radical hysterectomy. Both 4.5-year disease-free survival (DFS) (HR=3.91, 95% CI 2.02-7.58; p<.0001) and 4.5-year overall survival (OS) (HR=2.71, 95% CI 1.32-5.59; p<.007) were significantly lower for MIS. There was an increased rate of 4.5-year locoregional recurrence (HR=4.70, 95% CI 1.95-11.37; p<.001) for MIS. Main limitations of the trial were the inability to reach final intended enrolment due to safety concerns and to generalize outcomes for low-risk, early-stage CC patients. The authors concluded that because MIS leads to worse survival outcomes, the open abdominal approach remains the standard of care. [1]

The PROSACC study by Persson, et al., a single-centre prospective non-randomized study that enrolled 181 patients with FIGO 2009 stage IA2-IIA1 CC treated with robotic radical hysterectomy/trachelectomy, was conducted to assess the sensitivity of sentinel lymph node (SLN) algorithm in identifying pelvic nodal metastases using indocyanine green. All metastatic LN were correctly identified, resulting in 100% sensitivity (95% CI 88.4%-100%) and 100% negative predictive value (95% CI 97.6%-100%). Regarding study limitations, the participation of only one centre may impact generalizability of results. In conclusion, following a standardized SLN surgical algorithm enables accurate identification of pelvic nodal metastases in early-stage CC. [2]

The ETERNITY project by Bogani, et al., a multi-centre retrospective study, aimed to evaluate the oncological outcomes of 123 patients with CC up to FIGO 2009 stage IB1 after fertility-sparing surgery (conization or trachelectomy) and LN assessment via sentinel node mapping (SNM) (n=32), SNM plus backup lymphadenectomy (LND) (n=31), or pelvic LND (n=60). No statistically significant differences in terms of DFS (p=0.332, log-rank test) and OS (p=0.769, log-rank test) were reported among the three groups, leading the authors to conclude that SLN is oncologically safe in patients with early-stage CC requesting fertility preservation. The most notable limitations of the study are its retrospective design, the small sample size, and the lack of independent validation for each participating centre. [3]

Nica, et al. published a retrospective multicentre cohort study with a population of 197 patients with FIGO 2009 IA1-IB2 CC, which compared oncological outcomes between patients undergoing MIS nodal assessment and either robotic (RRT) (n=56) or vaginal (VRT) (n=141) radical trachelectomy. Recurrence-free survival was 97% in both groups at a median follow-up of 57 months. PFS was not significantly different (HR=2.1, 95% CI 0.3-7.1; p=0.5). The most outstanding study limitations are the relatively small sample size, retrospective design and subsequent attrition, and especially selection bias, as patients in VRT had more high-risk characteristics. In conclusion, among early-stage CC patients eligible for fertility-sparing trachelectomy, the choice of surgical approach does not appear to influence recurrence outcomes. [4]

Kohler, et al. performed a retrospective cohort study of 471 patients with FIGO 2009 stages IA1 with lymphovascular space involvement to IB1 CC who underwent vaginal radical trachelectomy and surgical nodal staging, aiming to evaluate and report long-term oncological and fertility outcomes. Among 270 patients desiring pregnancy, 196 (73%) had successful pregnancies, with a high prematurity rate of 46% (n=94), attributed mainly to cervical volume loss. Regarding survival outcomes after a median follow-up of 159 months, OS, DFS, and cancer-specific survival were 97.5%, 96.2%, and 97.9% respectively. Considerable limitations of the study are its retrospective design, the lack of information on preoperative radiologic assessment, initial depth of stromal invasion, and inadequate reporting of peri- and post-operative morbidity. [5]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	LACC trial: final analysis on overall survival comparing open versus minimally invasive radical hysterectomy for early-stage cervical cancer	Ramirez PT, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/38810208/
2	A prospective study evaluating an optimized sentinel node algorithm in early stage cervical cancer: the PROSACC-study	Persson J, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38788515/
3	Sentinel node mapping, sentinel node mapping plus back-up lymphadenectomy, and lymphadenectomy in early-stage cervical cancer scheduled for fertility-sparing approach: the ETERNITY project	Bogani G, et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/38901291/
4	Robotic versus vaginal radical trachelectomy for reproductive-aged patients with early-stage cervical carcinoma: a multi-center cohort study	Nica A, et al,	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38377763/
5	Radical vaginal trachelectomy: long-term oncologic and fertility outcomes in patients with early cervical cancer	Kohler C, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38599782/

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

Khayal Gasimli and Beāte Sārta

COMPASSION-13, a phase II trial, evaluated cadonilimab (a bispecific PD-1 and CTLA-4 antibody) combined with standard therapy for first-line treatment of recurrent/metastatic cervical cancer (CC). Patients were divided into three cohorts: A-15 (15 mg/kg Q3W + chemotherapy); A-10 (10 mg/kg Q3W + chemotherapy); and B-10 (10 mg/kg Q3W + chemotherapy and bevacizumab). All 45 patients experienced treatment-related adverse events (TRAEs), with grade ≥3 TRAEs in 73.3%, commonly anaemia, neutropenia, and leukopenia. Cadonilimab-related grade ≥3 TRAEs occurred in 55.6% overall and 50.0% in cohort B-10. Objective response rates (ORRs) were 66.7% in A-15, 68.8% in A-10, 92.3% in B-10, and 79.3% in A-10/B-10 combined. Cadonilimab showed promising antitumor activity, with a manageable safety profile and no new safety concerns. Despite limitations like a small sample size and non-randomized design, cadonilimab appears to be a viable first-line treatment option. [1]

CheckMate 358, a phase I-II trial by Oaknin, et al., evaluated nivolumab (anti-PD-1) with or without ipilimumab (anti-CTLA-4) in recurrent/metastatic CC. Patients received nivolumab monotherapy (240 mg Q2W) or were randomized to nivolumab 3 mg/kg Q2W plus ipilimumab 1 mg/kg Q6W (NIVO3+IPI1) or nivolumab 1 mg/kg Q3W plus ipilimumab 3 mg/kg Q3W for four cycles, followed by nivolumab 240 mg Q2W (NIVO1+IPI3). ORR was 26% for nivolumab, 31% for NIVO3+IPI1, 40% for randomized NIVO1+IPI3, and 38% for pooled NIVO1+IPI3. Common grade 3-4 TRAEs included diarrhoea, lipase elevation, vomiting, and anaemia. Dual therapy (nivolumab + ipilimumab) improved overall survival (OS) and response rates compared to nivolumab alone but showed higher TRAEs and discontinuations in the NIVO1+IPI3 group. Results indicate durable antitumor activity and promising two-year progression-free survival (PFS) and OS, though the study lacked power to confirm survival improvements. [2]

The phase II CLAP study by Lan, et al. examined camrelizumab (PD-1 inhibitor) plus apatinib (VEGFR2 inhibitor) in advanced CC. Median duration of response (DOR) was 16.6 months, 12-month PFS was 40.7%, and median OS was 20.3 months. Factors like age greater than 50 years, PD-L1 CPS ≥1, high tumour mutational burden, and PIK3CA mutations correlated with improved PFS and OS. Of eight patients retreated with immune checkpoint inhibitors (ICIs), 25% showed partial responses and 62.5% had stable disease, with four surviving beyond 45 months. No new safety concerns were identified. [3]

The phase II SKYSCRAPER-04 trial by Salani, et al. assessed atezolizumab (anti-PD-L1) with or without tiragolumab (anti-TIGIT) in PD-L1-positive CC after one to two chemotherapy lines. Patients were randomized 3:1 to atezolizumab 1,200 mg with/without tiragolumab 600 mg once every three weeks. ORR was 19.0% with the combination (p=0.0787 vs. historical control) and 15.6% with atezolizumab alone. No significant differences were observed in PFS or OS. Disease progression was the primary reason for treatment discontinuation (72–73%). Both therapies were well-tolerated, showing low adverse event rates. The combination showed a numerically higher response but lacked statistical significance. [4]

A phase II trial evaluated toripalimab (240 mg Q3W) with platinum-based chemoradiotherapy in untreated locally advanced CC (2018 FIGO stage IB3–IVA). The ORR was 87.8%, with trends of longer PFS in patients with high PD-L1 expression and low tumour mutation burden. Median PFS and OS were not reached. Grade ≥3 adverse events occurred in 20.7% of patients. The combination demonstrated promising efficacy and manageable safety. [5]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Cadonilimab combined with chemotherapy with or without bevacizumab as first-line treatment in recurrent or metastatic cervical cancer (COMPASSION-13): a phase 2 study	Lou H, et al.	Clin Cancer Res	https://pubmed.ncbi.nlm.nih.gov/38372727/
2	Nivolumab with or without ipilimumab in patients with recurrent or metastatic cervical cancer (CheckMate 358): a phase 1-2, open-label, multicohort trial	Oaknin A, et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/38608691/
3	Long-term survival outcomes and immune checkpoint inhibitor retreatment in patients with advanced cervical cancer treated with camrelizumab plus apatinib in the phase II CLAP study	Lan C, et al.	Cancer Commun (Lond)	https://pubmed.ncbi.nlm.nih.gov/38741375/
4	A non-comparative, randomized, phase II trial of atezolizumab or atezolizumab plus tiragolumab for programmed death-ligand 1-positive recurrent cervical cancer (SKYSCRAPER-04)	Salani R, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38858106/
5	A new treatment approach of toripalimab in combination with concurrent platinum-based chemoradiotherapy for locally advanced cervical cancer: a phase II clinical trial	Chen J, et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/39340335/

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

María de los Reyes Oliver and Rubén M. Betoret

A meta-analysis conducted by Li, et al. of 12 retrospective studies with a total of 3,967 patients showed that human papilloma virus (HPV)-dependent vulvar cancer (VC) has a better overall survival rate after radiotherapy (HR=0.71, 95% CI 0.54-0.93; p=0.01) and a significant improvement in disease-free survival and progression-free survival (PFS). Complete remission rate and local control rates were higher, and relapse had a reduced incidence (HR=0.21, 95% CI 0.10-0.42; p<0.001) when compared to HPV-independent VC, although the mechanisms underlying this high sensitivity to radiotherapy remain unclear. [1]

Horowitz, et al. conducted a single-arm phase II trial in 57 patients with locally advanced VC (77% with stage II or III disease and up to 23% with stage IV disease) ineligible for radical surgery, to assess the efficacy of weekly cisplatin and gemcitabine in combination with intensity-modulated radiation therapy (IMRT). After a mean of six cycles, 73% achieved a complete pathological response on subsequent biopsies, and the PFS rate at 12 and 24 months was 74% and 70%, respectively. Unfortunately, and in line with the findings suggested in Li, et al., HPV status was unknown in 61% of the patients (only 34% of whom were HPV+/p16+), so no conclusions can be drawn regarding this interesting issue. [2]

Di Donato, et al. assessed the use of a V-Y fasciocutaneous reconstructive flap after radical vulvar surgery for VC and reported a significant reduction in the incidence of postoperative wound infection and dehiscence, especially in larger tumours greater than 4 cm, in a multicentre, retrospective, controlled study involving 361 patients (52% of whom underwent reconstructive flap after radical excision). [3]

As lymph node status is the most important prognostic factor in VC (and the role of surgical assessment of lymph node status versus definitive groin radiation for locally advanced stage >4 cm surgically unresectable VC is controversial), Given, et al. conducted a retrospective study of 112 patients (67 of whom received primary groin node radiation and 45 of whom underwent prior groin node resection). A significantly higher complete clinical response (CCR) rate of 80% was reported in the surgical groin resection group compared to 58.2% CCR in the primary radiation therapy group. Surgical groin resection was significantly associated with lower groin recurrence (HR=0.2, 95% CI 0.05-0.92; p=0.04), and the three-year groin recurrence-free survival was 94.4% in the surgical resection group compared to 79.2% in the primary radiation therapy group (p=0.02). [4]

In a single-centre, prospective, interventional non-inferiority study, Valle, et al. showed the accuracy of superparamagnetic iron oxide (SPIO) in the detection of sentinel lymph nodes (SLNs) for early-stage VC compared with the standard Tc99 radioisotope procedure. A total of 18 patients who met the GROINSS-V criteria were included, and 41 SLNs were retrieved, with a 92.7% concordance between tracers and a 100% detection rate per groin for SPIO. The authors highlight the advantage of not requiring nuclear medicine, thus simplifying the surgical workflow with this novel tracer. [5]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Review effects of radiation treatment on HPV-related vulvar cancer: a meta-analysis and systematic review	Li W, et al.	Front Oncol	https://pubmed.ncbi.nlm.nih.gov/39324004/
2	Phase II trial of cisplatine, gemcitabine, and intensity-moduated radiation therapy for locally advanced vulvar squamous cell carcinoma: NRG Oncology/GOG Study 279	Horowitz NS, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/38574312/
3	Role of V-Y flap reconstruction in vulvar cancer patients: multicenter retrospective study	Di Donato, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39002981/
4	Management of inguinal lymph nodes in locally advanced, surgically unresectable, squamous cell carcinoma of the vulva	Swift BE, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38723339/
5	Superparamagnetic iron oxide (SPIO) for sentinel lymph node detection in vulvar cancer	Del Valle D, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38776632/

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Organisation of gynaecological oncology services

Esra Bilir

Ovarian cancer (OC) presents a significant challenge in low- and middle-income countries (LMICs), where disparities in healthcare access further complicate patient outcomes. These encompass restricted access to healthcare, a shortage of surgical expertise, limited availability of genetic and tumour testing, prolonged approval timelines for new treatments, high treatment costs, difficulties in accessing clinical trials, health disparities, and the impact of military conflicts. To overcome these barriers, strategies are needed to accelerate drug approvals and lower treatment costs, including expenses related to genetic testing, molecular tumour analysis, surgery, and antineoplastic therapy. A crucial factor in reducing disparities is the exchange of data and experiences among professionals, patients, organizations, and societies. Regarding the treatment costs, the authors concluded approval of high-cost medications in LMICs does not guarantee access, as public health institutions often do not provide them. Availability often relies on private insurance, which varies widely across countries and is not directly proportional to gross domestic product. [1]

A review evaluated endometrial cancer (EC) care, with a focus on racial disparities. The authors found that African American women (AAW) and white American women experienced a 39% and 2% increase in incidence and a 26% and 17% rise in mortality, respectively. Disparities were further highlighted by higher rates of poor prognostic factors, comorbidities, lower income, and undertreatment among AAW. No actionable genetic markers or effective policies were identified. [2]

A study showed 600 GoFundMe campaigns for EC, cervical cancer (CC), and OC patients in the U.S. These reveal financial toxicity, with insufficient insurance. A multifaceted approach is needed to reduce costs and improve support systems. [3]

Hereditary breast and OC syndrome increases the lifetime risk of developing breast (80%) or ovarian (40%) cancer where genetic testing is vital. Medicolegal issues include failure to recommend testing, misinterpretation of results, improper integration into clinical practice, lack of informed consent, and failure to refer patients to specialised genetic counselling. Insurance concerns include genetic discrimination, where insurers may limit options, increase costs, or affect employment opportunities, also inadequate reimbursement for risk-reducing surgeries. A unified international regulatory framework is necessary to balance insurers' economic interests with individuals' rights to privacy, non-discrimination, and access to care. [4]

In response to lack of trained specialists for screening, diagnosis, and treatment of CC occur in LMICs, International Society of Gynecologic Cancer (IGCS) launched the Global Gynecologic Oncology Fellowship and a training programme for CC. The IGCS Preinvasive Certificate Program enhances skills and knowledge for healthcare providers in all settings. [5]

The Russian invasion of Ukraine in 2022 displaced over 6 million people, including women with urgent gynaecologic oncological needs. The European Network of Young Gynae Oncologists (ENYGO) led a study to evaluate healthcare responses for Ukrainian gynaecologic oncology patients across Europe during the first six months of the conflict including 400 displaced patients received care in 38 European centres. [6]. Common needs included surgery (54%), chemotherapy (40%), and specialist consultations (32%). Key challenges were language barrier (44%), lack of medical documentation (40%), inconsistent treatment protocols, and inadequate psychological support (36%). [6] It highlights the need for international collaboration, improved access to medical histories, and enhanced psychological support during humanitarian crises. [6]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Real world challenges and disparities in the systemic treatment of ovarian cancer	Nogueira-Rodrigues A, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38442493/
2	Racial disparities in endometrial cancer: Where are we after 26 years?	Hicks ML, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38382150/
3	Unmet financial needs among patients crowdfunding to support gynecologic cancer care	O'Connor RM, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38833852/
4	Medicolegal and insurance issues regarding BRCA1 and BRCA2 gene tests in high income countries	Oliva R, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38642925/
5	The International Gynecologic Cancer Society Preinvasive Certificate Program: building a skilled workforce for the detection and treatment of cervical pre-cancer	Haney K, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38346845/
6	Health care organization for gynecologic oncology patients fleeing Ukraine: insights from the European Network of Young Gyne Oncologists survey during the first six months of the military conflict	Kacperczyk-Bartnika J, et al.	Int Journal Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/40032541/

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Screening and prevention of gynaecological cancers

Amrita Gaurav and Priyanka Singh

The Women's Health Initiative (WHI) 20-year follow-up by Chlebowski et al. (2024) found conjugated equine estrogen (CEE) alone increased ovarian cancer incidence (HR=2.04, p=.014) and mortality (p=.006), while CEE plus medroxyprogesterone acetate (MPA) showed no significant effect (HR=1.14, p=.44). By contrast, CEE plus MPA significantly reduced endometrial cancer incidence (106 cases [0.073%] vs. 140 [0.10%]; HR=0.72, p=.01). These findings highlight the need for personalized hormone therapy, weighing ovarian cancer risks against endometrial protection, with further research needed on underlying mechanisms.[1]

Baisely, et. al compared vaccine-induced HPV-specific antibody responses 24 months after a single dose of HPV vaccine in the Dose Reduction Immunobridging and Safety Study (DoRIS), a randomised trial of single- dose (including 2 and 9-valent vaccines) regimens in 930 girls (9 to 14 years), with those after one dose of the same vaccine in the KEN SHE trial, which included 2,275 sexually active women aged 15 to 20 years. DoRIS trial enrolled 930 participants (155 per group); 154 participants in single dose 2-valent vaccine group and 152 in single dose 9-valent group. KEN SHE trial enrolled 302 participants in the immunobridging substudy in single dose 2-valent vaccine group and 303 in single-dose 9-valent group. The Kenya single-dose HPV-vaccine efficacy (KEN SHE) and DoRIS trials demonstrated >97% efficacy against persistent HPV16/18 infections at 36 months. Baisely et al. compared antibody responses in girls (9–14 years, DoRIS) to sexually active women (15–20 years, KEN SHE), finding non-inferiority for 2-valent (GMC ratios: 0.90 HPV16, 1.02 HPV18) and 9-valent vaccines (1.44 HPV16, 1.47 HPV18). The authors projected that results from these two randomised trials provide the strongest available evidence favouring single-dose vaccination in young girls in low resource settings. [2]

Lehtinen et al.'s 15-year Finnish cancer registry follow-up of quadrivalent (FUTURE II) and bivalent (PATRICIA, HPV-012) HPV vaccine trials reported 68.4% and 64.5% efficacy against CIN3+, respectively. Despite robust protection, the study wasn't powered for non-inferiority between vaccines, and generalizability to global populations is limited, necessitating larger comparative trials.[3]

The Cervical Cancer Screening and Treatment Algorithms (CESTAP) pilot in South Africa evaluated HPV-based screening with or without visual inspection after acetic acid (VIA) triage in 350 women (30–54 years). VIA triage showed low sensitivity (3/17 VIA-negative with CIN2+), suggesting limited benefit. HPV-based screening was feasible, but larger studies, particularly for women living with HIV, are needed to refine protocols in resource-limited settings.[4]

Vahteristo et al.'s Finnish trial randomized 236,000 women to HPV or cytology screening, finding a 60% reduction in vaginal and 25% in vulvar cancer incidence (IRR=0.67, MRR=0.67) over 15 years in the HPV arm. While HPV screening shows broader preventive potential, not all vaginal/vulvar cancers are HPV-related, warranting research into preventive mechanisms.[5]

Zaman et al.'s interim analysis of the Cecolin bivalent HPV vaccine trial in Bangladesh and Ghana showed two-dose Cecolin (0, 6-month schedule) was non-inferior to Gardasil, with comparable single-dose immunogenicity up to 6 months. Despite promising results for low-resource settings, the open-label design and early analysis limit conclusions about long-term efficacy. [6]

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No	Title	Authors	Journal	Link to abstract
1	Menopausal hormone therapy and ovarian and endometrial cancers: long-term follow-up of the Women's Health Initiative randomized trials	Chlebowski RT, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/39173088/
2	Comparing one dose of HPV vaccine in girls aged 9-14 years in Tanzania (DoRIS) with one dose in young women aged 15-20 years in Kenya (KEN SHE): an immunobridging analysis of randomised controlled trials	Baisley K, et al.	Lancet Glob Health	https://pubmed.ncbi.nlm.nih.gov/38365419/
3	Head-to-head comparison of two human papillomavirus vaccines for efficacy against cervical intraepithelial neoplasia grade 3 and adenocarcinoma in situ-population-based follow-up of two cluster-randomized trials	Lehtinen M, et al.	Front Cell Infect Microbiol	https://pubmed.ncbi.nlm.nih.gov/39315334/
4	Cervical cancer screening and treatment algorithms using human papillomavirus testing: lessons learnt from a South African pilot randomized controlled trial	Sebitloane HM, et al.	Cancer Epidemiol Biomarkers Prev	https://pubmed.ncbi.nlm.nih.gov/37955560/
5	Lower incidence of vaginal cancer after cervical human papillomavirus screening: long-term follow-up of Finnish randomized screening trial	Vahteristo M, et al.	Prev Med	https://pubmed.ncbi.nlm.nih.gov/38849059/
6	Safety and immunogenicity of Innovax bivalent human papillomavirus vaccine in girls 9-14 years of age: Interim analysis from a phase 3 clinical trial	Zaman K, et al.	Vaccine	https://pubmed.ncbi.nlm.nih.gov/38431444/

Treatment of pre-invasive gynaecological malignancies

Elko Gliozheni

A study by Ferrari, et al. compared cold knife and carbon dioxide (CO2) laser conization for treating pre-invasive cervical lesions in 1,270 women. CO2 conization was more common (96.5%) and achieved significantly lower positive margin rates (4.3% vs. 13.3%; p=0.015). Both techniques showed equivalent oncological outcomes for incidental cervical cancer. Among patients managed non-radically, adverse obstetric outcomes were rare, and no recurrences were noted after a median 53-month follow-up. Strengths include long-term data and practical insights, but the study's retrospective design and sample imbalance limit its generalizability. CO2 conization appears superior for margin clearance, though prospective studies are needed to confirm these findings. [1]

The TOPIC-2 trial conducted by van de Sande, et al. evaluated the efficacy of topical imiquimod versus large loop excision of the transformation zone (LLETZ) for treating residual or recurrent cervical intraepithelial neoplasia (rrCIN) in 35 women in a randomized, controlled non-inferiority trial. Imiquimod showed significantly lower success rates for reducing cytology abnormalities (33% vs. 100%; $p < 0.001$) and clearing high-risk HPV (22% vs. 88%; $p < 0.001$) compared to LLETZ. The trial was halted early due to the futility of imiquimod, with most patients requiring additional surgical treatment. LLETZ consistently prevented the need for further interventions during two years of follow-up. While innovative, imiquimod proved less effective and had more side effects, affirming LLETZ as the superior treatment for rrCIN. [2]

A systematic review and meta-analysis by Hamar, et al. evaluated the efficacy and safety of topical imiquimod for treating cervical intraepithelial neoplasia (CIN) and HPV-positive patients. Based on analysis of data from eight studies including 672 patients, imiquimod showed a pooled regression rate (RR) of 61% for CIN2-3 and a 60% HPV clearance rate, though it was less effective than conization (RR=0.62, 95% CI 0.42-0.92). Side effects were mostly mild to moderate. Despite its inferiority to surgical methods, imiquimod demonstrated potential as a non-invasive treatment option for high-grade CIN, offering a safer alternative for patients seeking to preserve fertility. The study suggests incorporating imiquimod into treatment guidelines, highlighting its value in selected cases while recognizing its limitations compared to conization. [3]

A prospective study by Liu, et al. evaluated the efficacy and safety of HiPorfin photodynamic therapy (PDT) in treating high-grade squamous intraepithelial lesions (HSIL) in 41 reproductive-aged women. Complete response rates were 100% for CIN2 and 84.2% for CIN3 after 12 months, with a 92.7% HPV eradication rate. Cytology normalization reached 100% at 12 months, with no serious adverse effects reported. The treatment preserved fertility, making it a promising, organ-saving alternative for young women with CIN2-3. While results are encouraging, larger studies are needed to validate its long-term efficacy and safety. HiPorfin-PDT demonstrates significant potential as a non-invasive option for HSIL management, particularly for patients prioritizing reproductive health. The main limitations of the study include its small sample size, single-centre design, short follow-up period, lack of a control group, and absence of data on long-term outcomes and fertility impacts. [4]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Cold knife versus carbon dioxide for the treatment of preinvasive cervical lesion	Ferrari F, et al.	Medicina (Kaunas)	https://pubmed.ncbi.nlm.nih.gov/39064486 /
2	Topical imiquimod treatment of residual or recurrent cervical intraepithelial neoplasia lesions (TOPIC-2): a randomised controlled trial	van de Sande AJM, et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/38556619/
3	Imiquimod Is effective in reducing cervical intraepithelial neoplasia: a systematic review and meta-analysis	Hamar B, et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/38672691/
4	Photodynamic therapy with HiPorfin for cervical squamous intraepithelial lesion at childbearing age	Liu Y, et al.	Photodiagnosis Photodyn Ther	https://pubmed.ncbi.nlm.nih.gov/38401818/

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Epidemiology

Christian Braun

Ovarian Cancer

The impact of BRCA status on survival was examined in a multicentre retrospective study by Marchetti, et al., which analysed 191 patients with FIGO stage I–II high-grade serous ovarian cancer (HGSOC) from 2011 to 2019. While BRCA mutations (BRCAmut) were not associated with significant differences in progression-free survival (PFS) (BRCAmut: 86 months vs. BRCA wild type [BRCAwt]: 110 months; HR=0.71, 95% CI 0.42-1.17; p = 0.18), they improved overall survival (OS). The five-year OS was 100% for BRCAmut and 91.8% for BRCAwt, with median OS not reached in either group (HR=0.28, 95% CI 0.08-1.03; p = 0.05). [1]

Olaoye et al. conducted a retrospective study of 163 patients with primary mucinous ovarian carcinoma between 2005 and 2023. The study found that infiltrative invasion, as classified by the World Health Organization, was more common in women aged ≤45 years (RR=1.38, 95% CI 0.78-2.46) and South Asian women (RR=1.25, 95% CI 0.60-2.58). South Asian women had a worse OS compared to white women (5-year OS: 59% vs. 83%; HR=2.07, 95% CI 0.86-4.36), while the median OS was not reached. [2]

Endometrial Cancer

Concurrent endometrial cancer (EC) was diagnosed in 47.2% of 460 patients with atypical endometrial hyperplasia (AEH) in a multicentre retrospective study by Rosati et al. Among 268 patients who underwent sentinel lymph node (SLN) detection, lymph node metastases were found in 7.6%, mostly micrometastases (75%). SLN biopsy was prognostically and therapeutically beneficial in 60.8% of cases. [3]

De Vitis, et al. conducted a retrospective multicentre study (2013–2020) of 1,570 patients. In a subset of 274 patients with low-grade (G1–G2) endometrioid EC without myometrial invasion, no macro-/micrometastases were observed, and only one ITC was found, suggesting that ultrastaging may not be necessary in this subgroup of patients. [4]

In the multicentre retrospective SENECA study, Chacon, et al. analysed 2,139 stage I–II EC patients (2021 and 2022). SLN metastases were detected in 9.6% of cases, with higher rates observed in p53abn (12.5%) and mismatch repair deficiency (MMRd) (12.4%) subtypes compared to no specific molecular profile (NSMP) (7.8%) and POLE-mutated (POLEmut) EC (6.3%) (p=0.004). SLN metastases were significantly associated with p53abn (OR=1.69, 95% CI 1.11-2.56; p=0.014) and MMRd (OR=1.67, 95% CI 1.21-2.31; p=0.002). [5]

In a retrospective multicentre study of 164 stage IV EC patients, Uijterwaal, et al. analysed molecular classification (p53abn 61.6%, NSMP 21.3%, MMRd 12.8%, POLEmut 3%) and found no significant impact on PFS (p=0.056) or OS (p=0.12). However, oestrogen receptor (ER)-positive tumours were associated with improved OS (31 vs. 16 months, p=0.013) and PFS (27 vs. 9 months, p=0.005) compared to ER-negative tumours, although this was not confirmed in multivariate analysis. [6]

Cervical Cancer

Bizzarri, et al. analysed 1,083 early-stage cervical cancer patients (2007–2016) in the international multicentre retrospective SCCAN study. The addition of SLN biopsy to pelvic lymphadenectomy significantly improved five-year DFS (96.0%, 95% CI 93.5-98.5) compared to pelvic lymphadenectomy alone (92.0%, 95% CI 90.0-94.0; p=0.024). However, no significant difference in OS was observed. [7]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Clinical characteristics and survival outcome of early-stage, high-grade, serous tubo-ovarian carcinoma according to BRCA mutational status	Marchetti C, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38788514/
2	Investigating age and ethnicity as novel high-risk phenotypes in mucinous ovarian cancer: retrospective study in a multi-ethnic population	Olaoye T, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38862154/
3	Concurrent endometrial cancer in atypical endometrial hyperplasia and the role of sentinel lymph nodes: clinical insights from a multicenter experience	Rosati A, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38431287/
4	Incidence of sentinel lymph node metastases in apparent early-stage endometrial cancer: a multicenter observational study	De Vitis LA, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38514100/
5	SENECA study: staging endometrial cancer based on molecular classification	Chacon E, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39153831/
6	Prognostic value of molecular classification in stage IV endometrial cancer	Uijterwaal MH, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38658021/
7	Survival associated with the use of sentinel lymph node in addition to lymphadenectomy in early-stage cervical cancer treated with surgery alone: a sub-analysis of the Surveillance in Cervical Cancer (SCCAN) collaborative study	Bizzarri N, et al.	Eur J Cancer	https://pubmed.ncbi.nlm.nih.gov/39270379/

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Diagnostic methods in gynaecological oncology

Andrea Rosati

Advances in imaging and diagnostic tools have significantly enhanced the detection, staging, and prognostication of gynaecological malignancies. Recent systematic reviews and meta-analyses have assessed the diagnostic performance of various modalities, including MRI-based radiomics, PET/CT, contrast-enhanced ultrasound (CEUS), transvaginal sonography (TVS), and MRI volumetric assessments, offering valuable insights into their clinical applications.

Huang, et al. conducted a systematic review and meta-analysis of 45 MRI-based radiomics studies on endometrial cancer (EC) involving more than 3,000 patients. Radiomics models were evaluated for their ability to distinguish benign from malignant endometrial lesions, classify type I versus type II EC, and predict deep myometrial invasion, lymph node metastasis, and histological grade. The diagnostic odds ratio (DOR) was 23.81 (95% CI 8.48-66.83) for differential diagnosis and 18.23 (95% CI 13.68-24.29) for risk prediction. Despite demonstrating promising diagnostic accuracy, the mean radiomics quality score (RQS) was 13.77 which was 38.2% of the ideal score of 36. This highlights methodological limitations, emphasizing the need for standardized, high-quality studies before clinical adoption. [1]

In advanced ovarian cancer, Wilson, et al analysed 15 studies (918 patients) comparing contrast-enhanced CT and PET/CT for staging. Sensitivity and specificity per patient were 82% (67–91%) and 72% (59–82%) for CT and 87% (75–94%) and 90% (82–95%) for PET/CT, respectively. PET/CT demonstrated significantly higher specificity ($p<0.01$), supporting its role as a supplementary tool for detecting abdominal metastases, which may influence future guideline revisions. [2]

Yi, et al. investigated contrast-enhanced ultrasound (CEUS) combined with Ovarian-Adnexal Reporting and Data System (O-RADS) for characterizing adnexal masses in five studies (598 patients). This combination achieved a sensitivity of 0.95 (95% CI 0.91-0.98), specificity of 0.86 (95% CI 0.79-0.91), DOR of 111.30 (95% CI 65.32-189.65), and area under the curve (AUC) of 0.97. Compared to O-RADS alone (sensitivity 0.96, specificity 0.55, DOR 27.31, AUC 0.93), the addition of CEUS improved specificity and diagnostic performance, highlighting its potential to refine risk stratification in adnexal masses. [3]

In locally advanced cervical cancer (LACC), Kang, et al. conducted a subgroup analysis of a phase II prospective trial (86 patients) assessing MRI-based tumour parameters before and during concurrent chemoradiotherapy (CCRT) and brachytherapy. Restaging tumour size (rTS >2.55 cm) was an independent prognostic factor for overall survival (OS; HR=5.47; p=0.035) and progression-free survival (PFS; HR=3.83; p=0.025). Initial tumour volume (iTV >55.99 cc), restaging tumour volume (rTV >6.25 cc), and tumour downstaging correlated with OS and PFS in univariate analysis, but only rTS remained significant in multivariate analysis, reinforcing the prognostic value of MRI volumetric assessments in LACC management. [4]

Borges, et al. examined the diagnostic accuracy of transvaginal sonography (TVS) for pelvic lymph-node metastases in 967 patients across eight studies on cervical, ovarian, and endometrial cancer. TVS demonstrated a high specificity of 98% (95% CI 93-99%) but low sensitivity of 41% (95% CI 26-58%), with a DOR of 32 months (95% CI 14-72). While TVS may be an alternative to CT and MRI in resource-limited settings, its low sensitivity limits routine clinical use. [5]

These findings underscore the importance of integrating advanced imaging modalities into clinical practice to enhance diagnostic accuracy, optimize patient management, and improve oncological outcomes in gynaecological malignancies.

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Application of magnetic resonance imaging radiomics in endometrial cancer: a systematic review and meta-analysis	Huang M-L, et al.	Radiol Med	https://pubmed.ncbi.nlm.nih.gov/38349417/
2	Diagnostic accuracy of contrast-enhanced CT versus PET/CT for advanced ovarian cancer staging: a comparative systematic review and meta-analysis	Wilson MP, et al.	Abdom Radiol (NY)	https://pubmed.ncbi.nlm.nih.gov/38523146/
3	Diagnostic performance of contrast-enhanced ultrasound (CEUS) combined with Ovarian-Adnexal Reporting and Data System (O-RADS) ultrasound risk stratification for adnexal masses: a systematic review and meta-analysis	Yi Y-Y, et al	Clin Radiol	https://pubmed.ncbi.nlm.nih.gov/38942707/
4	MRI-based volumetric tumor parameters before and during chemoradiation predict tumor recurrence and patient survival in locally advanced cervical cancer: a subgroup analysis of a phase II prospective trial	Kang HB, et al	Int J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/38530569/
5	Role of ultrasound in detection of lymph-node metastasis in gynecological cancer: systematic review and meta-analysis	Borges AC, et al.	Ultrasound Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/38452144/

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Pathology of gynaecological cancers

Nicolas Samartzis and Dimitrios Rafail Kalaitzopoulos

Ovarian cancer

Hu, et al. conducted single-cell RNA sequencing on 45 tumour samples from 18 patients with gastric cancer and ovarian metastases. Their findings showed that fibroblasts in ovarian metastases express high levels of oestrogen receptors and midkine, a mediator of the sex hormone signalling axis. Furthermore, they demonstrated that oestrogen promotes the migration and invasion of gastric cancer cells. These results support previous research suggesting that premenopausal women are at greater risk of developing ovarian metastases from gastric cancer compared to metastases from other organs. However, the study's small cohort size limits the generalizability of the findings. Furthermore, the exact mechanism by which oestrogen stimulation of ovarian fibroblasts induces midkine upregulation in gastric cancer cells remains unclear. Nonetheless, the study provides valuable insights into the microenvironment of ovarian metastases, contributing to a better understanding of metastases from distant organs to the ovaries. [1]

Cervical cancer

By analysing 3,929 HPV-positive cervical cell samples from U.S. screening participants, Pinheiro, et al. identified hotspot mutations in 10.2% of precancerous cervical lesions and 25.7% of invasive cervical cancer. These mutations, which vary by HPV type, were detectable up to six years before diagnosis. and can be detected up to six years before diagnosis. The study's strength lies in its large sample size, which enhances statistical power. However, a limitation was the lack of germline DNA profiles, as the samples were collected from residual cells of routine cervical cancer screening. Germline mutations were ruled out using publicly available polymorphism databases, but approach may not be comprehensive. Despite this limitation, the findings highlight the potential of hotspot mutation analysis in precancerous cervical lesions for assessing malignant risk, providing a promising tool for early intervention. [2]

Vulvar cancer

Voss, et al. evaluated DNA methylation and p53 immunohistochemistry (IHC) as biomarkers for identifying high-risk lichen sclerosus (LS) lesions progressing to vulvar squamous cell cancer (VSCC). A three-gene methylation panel (ZNF582, SST, and miR124-2) tested positive in 70% of LS cases that progressed to VSCC, compared to 17% of non-progressing LS cases (p=0.002). Additionally, mutant p53 IHC status strongly correlated with cancer progression (42% vs 3%, p=0.001). The study underscores the prognostic value of combining methylation testing and p53 IHC for the accurate identification of HPV-independent vulvar intraepithelial neoplasia (VIN), particularly in p53 wild-type cases. However, the retrospective design and limited clinical information, such as treatment details, are notable weaknesses. Selection bias also limits generalizability, as patients with clinically diagnosed LS without histological confirmation were excluded. Despite these limitations, the results emphasize the utility of DNA methylation and p53 IHC as biomarkers for predicting cancer risk in LS patients. [3]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	The estrogen response in fibroblasts promotes ovarian metastases of gastric cancer	Hu S, et al.	Nat Commun	https://pubmed.ncbi.nlm.nih.gov/39349474/
2	Somatic mutations in 3929 HPV positive cervical cells associated with infection outcome and HPV type	Pinheiro M, et al.	Nat Commun	https://pubmed.ncbi.nlm.nih.gov/39266536/
3	DNA methylation and p53 immunohistochemistry as prognostic biomarkers for vulvar lichen sclerosus	Voss FO, et al.	Mod Pathol	https://pubmed.ncbi.nlm.nih.gov/38925253/

Hereditary gynaecological cancer

Tibor A. Zwimpfer

Hereditary gynaecological cancers, which are primarily driven by genetic mutations, have become a major focus of oncology research, with significant implications for risk assessment, prevention, and treatment. Recent studies have deepened our understanding of the genetic basis and clinical outcomes of these cancers, providing a roadmap for more personalised and effective care.

A study by Stankovic, et al. highlighted the intricate genetic links between ovarian ageing, cancer risk, and mutation rates. By examining whole exome sequencing data from 454,787 individuals in the UK Biobank, the researchers uncovered several specific genetic loci (ZNF518A, SAMHD1, PNPLA8, ETAA1, and PALB2) that drive ovarian ageing and increase susceptibility to ovarian cancer. De novo mutation rates in these pathways further emphasise the shared mechanisms between reproductive ageing and oncogenesis. These findings provide a rationale for integrating ovarian ageing markers into hereditary cancer risk models, paving the way for improved early detection strategies. [1]

Building on the theme of genetic interplay, Saner, et al. revealed a promising link between tumour genetics and immunological responses in tubo-ovarian high-grade serous carcinoma (HGSC). The concomitant loss of RB1 and mutation of BRCA genes was associated with increased immune infiltration and activation, leading to improved long-term survival. This synergy suggests that genetic defects in hereditary cancer syndromes may also enhance tumour immunogenicity, providing a rationale for prioritising immune-based therapies in this population. These findings highlight the potential of using genetic profiles to refine treatment strategies, particularly in patients with hereditary predisposition. [2]

Treatment modalities for hereditary gynaecological cancers remain a critical area of investigation. A 10-year survival analysis by Kim, et al. provided robust evidence in favour of primary cytoreductive surgery (PCS) over neoadjuvant chemotherapy for BRCA-mutated advanced HGSC. Patients who underwent PCS demonstrated superior overall and recurrence-free survival, reinforcing the importance of PCS in patients with BRCA-mutated tumours. This study highlights the need for individualised treatment planning based on hereditary mutation status to maximise survival benefits. [3]

Beyond ovarian cancer, hereditary syndromes such as Lynch syndrome and BRCA mutations also influence the risk of other gynaecological malignancies. Fummey, et al. examined data from the UK Biobank to quantify cancer risks in Lynch syndrome variant carriers. The study confirmed an increased risk of endometrial cancer, particularly in carriers of pathogenic variants in MLH1, MSH2 and MSH6. These findings highlight the need for tailored surveillance and preventive interventions in this high-risk population. [4] Similarly, Kotsopoulos, et al. investigated the incidence of endometrial cancer in patients with germline BRCA variants (gBRCAv) and found only a modestly increased risk; however, women with prior tamoxifen exposure had a significantly increased risk. The results suggest that risk-reducing strategies such as prophylactic surgery or increased surveillance may benefit patients with gBRCAv, particularly those with tamoxifen exposure. [5]

These studies collectively underscore the complexity and heterogeneity of hereditary gynaecological cancers. They highlight the critical role of genetic research in refining risk prediction, tailoring treatment, and improving prevention. By translating these findings into clinical practice, we are moving closer to a future where the burden of hereditary gynaecological cancers can be reduced through personalised care and precision oncology.

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Genetic links between ovarian ageing, cancer risk and de novo mutation rates	Stankovic S, et al.	Nature	https://pubmed.ncbi.nlm.nih.gov/39261734/
2	Concurrent RB1 loss and BRCA deficiency predicts enhanced immunologic response and long-term survival in tubo-ovarian high-grade serous carcinoma	Saner FAM, et al.	Clin Cancer Res	https://pubmed.ncbi.nlm.nih.gov/38837893/
3	Primary cytoreductive surgery compared with neoadjuvant chemotherapy in patients with BRCA mutated advanced high grade serous ovarian cancer: 10 year survival analysis	Kim SR, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38548312/
4	Estimating cancer risk in carriers of Lynch syndrome variants in UK Biobank	Fummey E, et al.	J Med Genet	https://pubmed.ncbi.nlm.nih.gov/39004446/
5	Incidence of endometrial cancer in BRCA mutation carriers	Kotsopoulos J, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/39173195/

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Gestational trophoblastic disease

Andraž Dovnik

A meta-analysis of five studies included 3,629 patients (1,395 of whom had lung metastases) with gestational trophoblastic neoplasia (GTN). The prognosis of GTN was compared according to the presence of lung metastases. The analysis showed that lung metastases were associated with increased risk of first-line chemoresistance (pooled RR=1.40), recurrence (pooled RR=3.03), and disease-specific death (pooled RR=22.11) and should therefore be considered as a high-risk factor in GTN. The main limitation of this meta-analysis is that only five studies were included and the definition of GTN varied among the studies. Furthermore, the definitions of chemoresistance and relapse were different among the studies. Finally, all included studies were retrospective in design with common missing information and recall bias. On the other hand, this was the first analysis to specifically address the impact of lung metastases on treatment responses and survival of patients with GTN. [1]

A systematic review of 42 studies with 8,249 participants evaluated the role of contraceptive methods after gestational trophoblastic disease on beta-human chorionic gonadotropin (hCG) remission, the risk of unintended incident pregnancy, and post-molar GTN. The authors concluded that hormonal and non-hormonal contraceptive methods are safe after gestational trophoblastic disease. This review included two randomized controlled trials which found no differences among different hormonal and barrier contraceptive methods in terms of risk of post-molar GTN, beta-hCG values, and incident pregnancies. However, most of the studies included in this review were cohort studies and case reports; consequently, a meta-analysis was not completed. The majority of included studies were outdated and did not report the adherence to contraceptive methods, with one-half not reporting the time of contraceptive initiation. Finally, none of these studies analysed the interactions between contraceptive methods and cancer-specific treatment. [2]

A meta-analysis of five studies with 983 participants evaluated the effect of second curettage in reducing the number of chemotherapy cycles in the treatment of post-molar GTN. The results revealed an advantage of second curettage over conventional chemotherapy in avoiding unnecessary chemotherapy and in reducing the number of cycles of chemotherapy. These results could only be applied to patients with post-molar GTN who have abnormal levels of hCG after initial evacuation of molar pregnancy. The number of included studies was low; three of these studies were retrospective and none of these studies reported uniform indications for second curettage. However, this was the first meta-analysis to address the role of second curettage in decreasing the number of chemotherapy cycles. [3]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Effect of lung metastasis on the treatment and prognosis of patients with gestational trophoblastic neoplasia: a systematic review and meta-analysis	Zhang T, et al.	Acta Obstet Gynecol Scand	https://pubmed.ncbi.nlm.nih.gov/38282348/
2	Contraceptive use following gestational trophoblastic disease: a systematic review	Hagey JM, et al.	Contraception	https://pubmed.ncbi.nlm.nih.gov/38763274/
3	Second curettage versus conventional chemotherapy in avoiding unnecessary chemotherapy and reducing the number of chemotherapy courses for patients with gestational trophoblastic neoplasia: a systematic review and meta-analysis	Zhao P, et al.	Int J Gynaecol Obstet	https://pubmed.ncbi.nlm.nih.gov/37753799/

Cancer in pregnancy

Filip Karuga

Betts, et al. examined fertility after cancer in 65,804 adolescents and young adults (AYAs) aged 15-39 years, focusing on racial/ethnic differences. Using Texas Cancer Registry data linked to birth certificates (1995-2016), the authors assessed the cumulative incidence of live births after cancer and compared it across racial/ethnic groups. The results showed that non-Hispanic Black AYAs had the lowest 10-year cumulative incidence of live birth (10.2%), compared with Asian/Pacific Islander (15.9%), Hispanic (14.7%), and non-Hispanic white AYAs (15.2%). Black AYAs were less likely to have a live birth after cancer, particularly those with gynaecological cancer, lymphoma, and thyroid cancer. [1]

Zhang, et al. performed a meta-analysis of whether exposure to the human papillomavirus (HPV) vaccine during pregnancy or the periconceptional period increases the risk of adverse pregnancy outcomes. A meta-analysis of 11 studies published before August 2023 found no association between quadrivalent HPV and adverse pregnancy outcomes such as spontaneous abortion, stillbirth, or birth defects. However, exposure to bivalent HPV or non-valent HPV only around the time of conception appeared to be associated with an increased risk of spontaneous abortion (RR=1.59, 95% CI 1.04-2.45 and RR=2.04, 95% CI 1.28-3.24, respectively). The results suggest that while the risk of adverse outcomes cannot be completely excluded, further research is needed to confirm these findings. The main limitation is that most of the retrospective studies had varying degrees of involvement from HPV vaccine manufacturers. [2]

Nathoo, et al. investigated the association between AYA breast cancer (BC) and adverse pregnancy outcomes, as well as the impact of fertility treatment. The researchers analysed data from Ontario, Canada (2006-2018), with a control group of 1,189,506 mothers, and a study group of 474 . It was found that being an AYA with a history of BC was associated with an increased risk of both planned and unplanned caesarean delivery (aRR=1.26, 95% CI 1.14-1.39), but not with preterm birth, small for gestational age birth, or pre-eclampsia. Fertility treatment did not significantly alter the risk of caesarean delivery. The findings suggest that a history of AYA BC is not associated with other adverse pregnancy outcomes and does not warrant delaying pregnancy after diagnosis. The main limitations of the study are the small number of exposed women and the lack of data on BC subtype and staging. [3]

Gougis, et al. evaluated the risk of adverse pregnancy and foetal and neonatal outcomes associated with immune checkpoint inhibitors (ICIs) (n=91; anti-PD1: 63.7%; anti-PD1 plus anti-CTLA4: 16.5%; anti-CTLA4: 14.3%; anti-PD-L1: 4.4%; other: 1.1%) compared with other anticancer agents (n=3,467). Analysing data from the VigiBase pharmacovigilance database, the study found that exposure to ICIs during pregnancy was not associated with a higher incidence of 45 adverse outcomes compared to other treatments. However, preterm delivery was significantly more common with the anti-PD1 plus anti-CTLA4 combination (80.0% vs. 23.0%; ROR=13.87; 95% CI 3.90-49.28; p<.001). Three potential immune-related adverse events were reported, including spontaneous abortion, neonatal respiratory distress, and congenital hypothyroidism. The findings suggest that while ICIs are not generally associated with increased risks, their use in pregnancy, especially the anti-PD1 plus anti-CTLA4 combination, should be avoided if possible. This study has limitations mainly due to inconsistencies in the data collection methods used in pharmacovigilance. [4]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Racialized inequities in live birth after cancer: a population-based study of 63,000 female adolescents and young adults with cancer	Betts AC, et al.	Cancer	https://pubmed.ncbi.nlm.nih.gov/38696087/
2	Does HPV vaccination during periconceptional or gestational period increase the risk of adverse pregnancy outcomes? an updated systematic review and meta-analysis based on timing of vaccination	Zhang J, et al.	Acta Obstet Gynecol Scand	https://pubmed.ncbi.nlm.nih.gov/39106178/
3	Pregnancy outcomes in survivors of adolescent and young adult breast cancer: a population-based cohort study	Nathoo A, et al.	J Obstet Gynaecol Can	https://pubmed.ncbi.nlm.nih.gov/39154661/
4	Immune checkpoint inhibitor use during pregnancy and outcomes in pregnant individuals and newborns	Gougis P, et al.	JAMA Netw Open	https://pubmed.ncbi.nlm.nih.gov/38630478/

Fertility-sparing treatment for gynaecological cancers

Charalampos Theofanakis and Sinor Soltanizadeh

Cervical cancer: A retrospective study by Kohler, et al. analysed 471 patients who underwent radical vaginal trachelectomy between 1995 and 2021. Sentinel lymph node staging was performed in 151 patients (32%) with a median of seven (range 2-14) nodes, while 320 patients (68%) received systematic lymphadenectomy with a median of 19 (range 10-59) nodes. In total, 205 live births were recorded. Pre-term delivery occurred in 94 pregnancies (46%). After a median follow-up of 159 months, recurrences were detected in 16 patients (3.4%), of which 43% occurred more than five years after surgery. The authors presented that radical vaginal trachelectomy is oncologically safe, while associated with a high chance for childbearing. [1] A retrospective study by Jorgensen, et al. assessed fertility-sparing surgery and life expectancy based on tumour size among patients with cervical cancer measuring ≤4 cm and the probability of adjuvant radiotherapy. A total of 11,946 patients met the inclusion criteria. After propensity-score matching, 897 patients who underwent fertility-sparing surgery were matched 1:1 with those who underwent standard surgery. The probability of receiving adjuvant radiation increased with tumour size, ranging from 5.6% for a 1-cm tumour to 37% for a 4-cm tumour. The authors concluded that, within five years of diagnosis, young patients with stage I cancer measuring ≤4 cm had similar survival outcomes after either fertility-sparing surgery or standard surgery. [2]

Endometrial cancer: A retrospective analysis by Jang, et al. evaluated 178 patients who received fertility-sparing treatment for stage IA and grade 1 endometrioid endometrial cancer (EC). Medroxyprogesterone (MPA) and levonorgestrel-releasing intrauterine devices (LNG-IUD) were used concurrently. Among 178 patients with endometrioid EC who received FST, 142 (79.8 %) achieved complete response (CR). The median time to achieve CR and the median FST duration were 10 and 14 months, respectively. During the median follow-up period of 44 months, 59.9% (85/142) of patients had recurrence, with a median relapse-free survival (RFS) of 14 months after CR. The authors concluded that older age and non-pregnancy status may be risk factors for recurrence after CR. [3] A retrospective study by Chen, et al. evaluated the oncological and reproductive outcomes of fertility-preserving retreatment in 61 progestin-resistant EC and atypical endometrial hyperplasia (AEH) patients. Patients underwent treatment with gonadotropin-releasing hormone agonist (GnRHa) solely or a combination of GnRHa with LNG-IUD or aromatase inhibitor (AI). Maintenance treatments included LNG-IUD, cyclical oral contraceptives, or low-dose cyclic progestin until attempting conception. Fifty-five (90.2%) patients achieved CR, including 90.9% of AEH patients and 89.7% of EC patients. The median retreatment time was six months. The authors concluded that GnRHa-based fertility-sparing treatment exhibited promising oncological and reproductive outcomes for progestin-resistant patients. [4]

Ovarian cancer: A retrospective study by Song, et al. investigated survival outcomes of fertility-sparing surgery in patients below 50 years with a diagnosis of stage I epithelial ovarian cancer. A total of 3,027 patients met the study criteria, of which 534 (17.6%) underwent fertility-sparing surgery, while the remaining 2,493 (82.4%) underwent non-sparing staging surgery. During a median follow-up of 5.4 years and 6.3 years, respectively, for the fertility-sparing and non-sparing groups, there was no statistical difference between survival rates after adjusting for clinical and pathological factors (HR=0.87, 95% CI 0.57-1.35). The results support fertility-sparing procedures; however, the authors noted selection bias, risk of misclassification, and unmeasured confounders as possible limitations to the study. [5]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Radical vaginal trachelectomy: long-term oncologic and fertility outcomes in patients with early cervical cancer	Kohler C, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38599782/
2	Fertility-sparing surgery vs standard surgery for early-stage cervical cancer: difference in 5-year life expectancy by tumor size	Jorgensen KA, et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/38365097/
3	Risk factors for the recurrence in patients with early endometrioid endometrial cancer achieving complete remission for fertility-sparing hormonal treatment	Jang EB, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/39332276/
4	Fertility-sparing re-treatment for endometrial cancer and atypical endometrial hyperplasia patients with progestin-resistance: a retrospective analysis of 61 cases	Chen J, et al.	World J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/38918837/
5	Fertility-sparing surgery for stage I epithelial ovarian cancer	Song BB, et al.	Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/38781594/

Treatment of elderly patients with gynaecological cancers

David Viveros-Carreño

A post hoc analysis of the phase III PRIMA/ENGOT-OV26/GOG-3012 study assessed the impact of age on the efficacy and safety of niraparib first-line maintenance therapy in patients with newly diagnosed advanced ovarian cancer (AOC). Among 733 randomized patients, 289 (39.4%) were ≥65 years old (190 received niraparib, 99 placebo). Median progression-free survival (PFS) was comparable between those <65 years (13.9 vs. 8.2 months; HR=0.61 [0.47-0.81]) and ≥65 years (13.7 vs. 8.1 months; HR=0.53 [0.39-0.74]). Adverse events leading to dose discontinuation in the niraparib arm were higher in patients ≥65 years (18.4%) compared to those <65 years (7.8%). Using an individualized starting dose reduced grade ≥3 thrombocytopenia compared to a fixed starting dose (≥65 years: 57.0% vs. 26.1%). These findings support the use of first-line niraparib maintenance therapy for newly diagnosed AOC, irrespective of patient age. [1]

A retrospective, single-centre study evaluated the association between BRCA status and oncologic outcomes in elderly patients with AOC. A total of 1,652 patients with known BRCA status were included. Older women (>65 years) were less frequently BRCA-mutated (22.4% vs. 40.8%; p=0.0001) and less likely to undergo upfront debulking surgery (28.8% vs. 52%; p=0.0001). Median disease-free survival (DFS) was shorter in older patients (18.4 vs. 22.9 months; p<0.0001). Among the elderly, the prognostic benefit of BRCA mutation persisted, with median DFS of 27.2 vs. 16.5 months (p<0.001) for BRCA-mutated and wild-type patients, respectively. The authors concluded that the poorer prognosis in elderly patients results from a combination of medical comorbidities, under-treatment, and adverse tumour biology. [2]

A retrospective cohort study evaluated oncologic outcomes in patients >70 years with AOC treated at two centres, comparing three-weekly carboplatin-paclitaxel (3wCP) versus three-weekly carboplatin (3wC). A total of 107 patients were included; 77 received 3wCP and 30 received 3wC. Patients treated with 3wC were older (84 vs. 75 years; p<0.001), had more comorbidities (median Charlson Comorbidity Index 4 vs. 3; p<0.001), and had worse performance status (47% vs. 17% with performance status ≥2; p=0.015). Univariate analysis showed improved PFS (HR=0.55, 95% CI 0.33-0.90; p=0.017) and overall survival (HR=0.44, 95% CI 0.27-0.73; p=0.001) with 3wCP compared to 3wC, but these differences were not significant in multivariate analysis. Non-haematological adverse events occurred in 85% of 3wCP and 60% of 3wC patients. The authors concluded that 3wCP is a feasible, first-line treatment option in elderly AOC patients. [3]

A single-centre retrospective study assessed chemotherapy completion and reasons for discontinuation in patients with epithelial ovarian cancer, comparing those ≥70 and <70 years. A total of 757 patients were included (108 <70 years; 649 ≥70 years). Chemotherapy completion was significantly lower in older patients (84.3% vs. 92.6%; p=0.007). When excluding discontinuation due to disease progression, completion rates were similar (93.5% vs. 95.7%; p=0.456). After adjusting for confounders, age was not significantly associated with early discontinuation (OR=1.20; 95% CI 0.54-2.66), while comorbidities and surgical approach were identified as independent predictors. The authors concluded that age alone does not determine chemotherapy completion; comorbidity and disease status play a critical role. [4]

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No	Title	Authors	Journal	Link to abstract
1	Efficacy and safety of niraparib in patients aged 65 years and older with advanced ovarian cancer: results from the PRIMA/ENGOT-OV26/GOG-3012 trial	Valabrega G, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38833992/
2	Distribution and prognostic role of BRCA status in elderly ovarian cancer patients	Tortorella L, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38262239/
3	A multicenter retrospective study to assess feasibility, safety and efficacy of first-line carboplatin-paclitaxel versus carboplatin monotherapy in a frail, elderly epithelial ovarian cancer population	Merry E, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39231541/
4	Examining the impact of age on chemotherapy completion in epithelial ovarian, fallopian tube and primary peritoneal cancer: a retrospective cohort study in Thailand	Assavapokee N, et al.	BMJ Open	https://pubmed.ncbi.nlm.nih.gov/39025817/

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Nutrition and perioperative care

Kristina Zdanyte and Sarita Kumari

Fumagalli, et al. retrospectively analysed patients with ovarian cancer undergoing primary cytoreductive surgery at Mayo Clinic (n=627) between 2003 and 2018 and found albumin <3.5 g/dL, Prognostic Nutritional Index (PNI) <45, neutrophil-to-lymphocyte ratio (NLR) >6, and platelet-to-lymphocyte ratio (PLR) ≥200 to be associated with 90-day mortality (all p<0.05), albumin being the easiest predictor to attain. [1]

Wang et al. conducted a retrospective analysis of creatinine in 84,786 patients undergoing surgery from the National Surgical Quality Improvement Program between 2014 and 2021. Both markedly (≤0.44 mg/dL) and mildly low creatinine (0.45–0.64 mg/dL) were associated with a higher likelihood of major complications (OR=1.715, 95% CI 1.299–2.264 and OR=1.093, 95% CI 1.001–1.193, respectively) and infections (OR=1.575, 95% CI 1.118–2.218 and OR=1.165, 95% CI 1.048–1.296, respectively) compared to normal creatinine levels. Markedly low creatinine was associated with a higher likelihood of cardiovascular and pulmonary complications (OR=2.301, 95% CI=1.300–4.071), readmissions (OR=1.403, 95% CI=1.045–1.884) and mortality (OR=2.718, 95% CI=1.050–7.031). [2]

Pergialiotis, et al. aimed to prospectively evaluate malnutrition impact on the post-operative process. There was a significant difference in the Prognostic Nutritional Index (PNI) between patients who developed infections and who did not (p=0.027), as well as between malnourished patients and those with normal nutritional status (p=0.043). It was concluded that PNI and post-operative white blood cell count provided the best information gain. [3]

Chalif, et al. retrospectively analysed 277 patients undergoing cytoreductive surgery with large bowel resection, of whom 49% (n=137) received standard intra-operative antibiotics and 50.5% (n=140) extended post-operative antibiotics. No difference was observed in development of surgical site infection (10.9% vs. 12.9%, respectively; p=0.62). Although the results did not reach statistical significance, prolonged antibiotic administration should be avoided unless clinically indicated. [4]

Li, et al. prospectively studied the impact of short-term multimodal prehabilitation on functional capacity during perioperative period and concluded a significant difference in six-minute walk distance and psychological status on the day before and 30th day after surgery (p<0.001) in intervention group (n=49) compared to control group (n=48). In addition, the quality of recovery in intervention group was significantly higher (p<0.001). [5]

Choi, et al. conducted an analysis of the secondary endpoint (effect of subcutaneous drain insertion on wound dehiscence and infection) in midline laparotomies from the randomised KGOG 4001 study and found no significant difference among 162 patients and both groups (treatment, n=79; control, n=83). Routine usage of subcutaneous drains should be avoided. [6]

The Memorial Sloan Kettering Cancer Center developed a tool to estimate the risk of peri-operative blood transfusion in primary debulking surgery, i.e., blood transfusion over an ovarian cancer debulking surgery (BLOODS score). After retrospective analysis, BLOODS score was significantly directly proportional to the American Society of Anaesthesiologists scores (3 and 4; OR=1.34, 95% CI 1.09-1.63), presence of bulky upper abdominal disease (OR=2.86, 95% CI 2.32-3.54), carcinomatosis (OR=2.45, 95% CI 1.93-3.11), CA125 level (OR=2.43, 95% CI 1.98-2.99), and platelets level (OR=1.59, 95% CI 1.45-1.74). The score could be helpful in surgical planning. [7]

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No	Title	Authors	Journal	Link to abstract
1	Evaluating nutrition in advanced ovarian cancer: which biomarker works best?	Fumagalli D, et al.	Gynecol Oncol.	https://pubmed.ncbi.nlm.nih.gov/38943693/
2	Low serum creatinine levels are associated with major post- operative complications in patients undergoing surgery with gynecologic oncologists	Wang CC, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38627036/
3	Prognostic Nutritional Index as a predictive biomarker of post-operative infectious morbidity in gynaecological cancer patients: a prospective cohort study	Pergialiotis V, et al.	Nutr Cancer	https://pubmed.ncbi.nlm.nih.gov/38369888/
4	Extended-duration antibiotics are not associated with a reduction in surgical site infection in patients with ovarian cancer undergoing cytoreductive surgery with large bowel resection	Chalif J, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38691986/
5	The impact of short-term multimodal prehabilitation on functional capacity in patients with gynecologic malignancies during the perioperative period: a prospective study	Li X, et al.	Eur J Oncol Nurs	https://pubmed.ncbi.nlm.nih.gov/38636115/
6	Effects of subcutaneous drain on wound dehiscence and infection in gynaecological midline laparotomy: secondary analysis of a Korean Gynecologic Oncology Group study (KGOG 4001)	Choi CH, et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/38901293/
7	A pre-operative scoring model to estimate the risk of blood transfusion over an ovarian cancer debulking surgery (BLOODS score): a Memorial Sloan Kettering Cancer Center Team Ovary study	Kahn RM, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38950927/

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Prevention and management of surgical complications

Alexandra Stoia and Anastasia Prodromidou

A retrospective cohort study by Norbeck, et al. examined the impact of patient blood management (PBM) strategies on recovery outcomes for surgical patients with advanced ovarian cancer. The proportion of patients receiving transfusions decreased significantly (83% to 52% p<0.001). There was no significant difference in severe complications (Clavien-Dindo grade ≥3a) between groups. The length of hospital stay decreased from 8.5 to 7.5 days. [1]

The study by Wang, et al. investigated the relationship between low pre-operative serum creatinine levels and postoperative outcomes in 84,786 patients undergoing gynaecologic oncology surgery. Both markedly low (≤0.44mg/dL) and mildly low (0.45–0.64mg/dL) levels were associated with higher risk of major complications and infections. Markedly low creatinine was also linked to increased risks of cardiovascular and pulmonary complications, readmissions, and mortality. However, only the first 30 post-operative days were analysed. [2]

Casarin, et al. evaluated the impact of sentinel lymph node (SLN) mapping on lower extremity lymphedema in 239 patients with early-stage endometrial cancer (EC) who underwent laparoscopic staging. The prevalence of lymphedema was significantly lower in the SLN group compared to the systematic lymphadenectomy group (21.4% vs. 44.6%; p=0.003), while the risk of lymphedema in the lymphadenectomy group was threefold higher. [3]

A systematic review and meta-analysis by Chen, et al. examined the necessity of pharmacologic thromboprophylaxis for patients undergoing minimally invasive surgery (MIS) for EC. Among the 3.931 patients, the 30-day postoperative venous thromboembolism (VTE) rate was 0.51% for pharmacologic prophylaxis and 0.70% for mechanical prophylaxis. While the latter appears sufficient for most patients undergoing MIS, high-risk patients might require pharmacologic or extended prophylaxis. [4]

The retrospective study by Levin, et al. analysed 3,611 patients undergoing radical hysterectomy (RH) for cervical cancer. MIS decreased from 75.3% in 2017 to 11.4% in 2022 (p<.001). Despite the significant decrease in MIS after the Laparoscopic Approach to Cervical Cancer trial, the prevalence of major complications was comparable before and after the trial (7.4% vs. 5.8%; p=0.26). Major complication rates were also similar in the laparotomy and minimally invasive groups (p=0.89). A lack of standard definition of type of complications was noted as a limitation. [5]

Wagar, et al. observed no difference in the incidence of 30-day postoperative VTE in 1,672 patients with vulvar cancer who had vulvectomy with or without lymphadenectomy by any method. Operative time and hospital stay were significantly associated with elevated risk of VTE (p=0.033 and p=0.001, respectively). However, given the low total incidence of VTE, the findings of the study do not justify the implementation of extended pharmacologic prophylaxis for vulvar cancer surgical patients. [6]

The GOTIC-VTE trial conducted by Takahashi, et al. was a prospective, multicentre study evaluating the effect of perioperative anticoagulant therapy in prevention of symptomatic postoperative pulmonary embolism (PE) in 82 gynaecologic oncology patients with asymptomatic VTE preoperatively. None of the patients was postoperatively diagnosed with PE within the first 28 days, while bleeding incidence was 2.4%. However, the lack of drug standardization across centres and the discrepancies in asymptomatic VTE detection are significant limitations. [7]

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No	Title	Authors	Journal	Link to abstract
1	Safe to save blood in ovarian cancer surgery: time to change transfusion habits	Norbeck A, et al.	Acta Oncol	https://pubmed.ncbi.nlm.nih.gov/39319937/
2	Low serum creatinine levels are associated with major post-operative complications in patients undergoing surgery with gynecologic oncologists	Wang CC, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38627036/
3	Laparoscopic treatment of early-stage endometrial cancer: benefits of sentinel lymph node mapping and impact on lower extremity lymphedema	Casarin J, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39313300/
4	Is pharmacologic venous thromboprophylaxis necessary for patients undergoing minimally invasive surgery for endometrial cancer? a systematic review and meta-analysis	Chen H, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38901080/
5	Approach to radical hysterectomy for cervical cancer after the Laparoscopic Approach to Cervical Cancer trial and associated complications: a National Surgical Quality Improvement Program study	Levin G, et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/39151769/
6	Incidence of postoperative venous thromboembolism in patients with vulvar carcinoma undergoing vulvectomy with or without lymphadenectomy	Wagar MK, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38795507/
7	Prevention of symptomatic pulmonary embolism for gynecologic malignancies with preoperative asymptomatic venous thromboembolism: GOTIC-VTE trial	Takahashi Y, et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38178702/

Palliative care in gynaecological oncology

Andrej Cokan

Fujiwara, et al. presented the International Gynecologic Cancer Society (IGCS) consensus statement on palliative care (PC), emphasizing its integration into gynaecologic cancer management. The statement highlights key principles, including fair access to PC, the importance of education and training, and the need for global collaboration. It also introduces the IGCS PC Pledge, encouraging communication, patient-centred approaches, and advocacy for quality-of=life measures. This framework aims to enhance care and address disparities in PC access worldwide. [1]

Martinsson, et al. analysed data from the Swedish Register of PC to examine the link between parenteral hydration and symptoms in cancer patients during their final week of life. Among 147,448 patients, hydration was more frequent in younger individuals, men, and those with haematological malignancies or ovarian cancer, particularly in hospitals. Breathlessness was significantly associated with hydration (adjusted OR=1.56), while respiratory secretions and confusion were not. Limitations include the lack of distinction between parenteral hydration and enteral feeding in the data, lack of adjustment for disease-related symptoms, and variability in clinician-reported symptom severity. [2]

Pozzar, et al. assessed the feasibility and acceptability of BOLSTER, a nurse-led telehealth intervention for patients with peritoneal carcinomatosis and their caregivers. In this pilot randomized controlled trial (RCT) with 65 participants, 91% of patients and all caregivers reported high satisfaction. BOLSTER improved quality of life, self-efficacy, and advance care planning, demonstrating its potential to enhance symptom management and care coordination, warranting further evaluation in a larger trial. Limitations include a small, predominantly white, college-educated sample, potential selection bias, and high attrition. [3]

Wall, et al. conducted a secondary analysis of data from a pilot RCT of BOLSTER to explore decision-making for palliative procedures in patients with peritoneal carcinomatosis and their caregivers. The study identified challenges such as illness uncertainty, communication gaps, and the need for clearer guidance on the impact of procedures on daily life. Misalignment between patient goals and procedural outcomes was also highlighted. Limitations include the use of non-targeted interview data, a homogenous sample, single-centre design, and lack of insights from patients who declined procedures. [4]

Sun, et al. analysed national inpatient data on malignant bowel obstruction (MBO) due to peritoneal carcinomatosis, comparing nonoperative, procedural, and surgical management. Surgical and procedural interventions were linked to longer hospital stays, higher costs, and greater post-discharge care needs. Mortality was slightly higher in intervention groups. Findings highlight the need for personalized MBO management. Limitations include reliance on ICD coding, lack of cancer staging and functional status data, and inability to track readmissions or post-discharge outcomes. [5]

Wilke, et al. conducted a retrospective study on outcomes of palliative colostomy for large bowel obstruction (LBO) in 78 patients with advanced gynaecologic cancers. The median overall survival was 4.5 months, with 27% of patients not surviving beyond 60 days of surgery. Poor performance status and platinum resistance were linked to worse outcomes. Findings highlight the importance of thoughtful decision-making and personalized care in managing LBOs, ensuring interventions align with patient goals and prognosis. Limitations include single-centre, retrospective design and lack of patient-reported outcomes. [6]

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No	Title	Authors	Journal	Link to abstract
1	The International Gynecologic Cancer Society consensus statement on palliative care	Fujiwara K, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38909991/
2	Parenteral hydration in dying patients with cancer: a national registry study	Martinsson L, et al.	J Pain Symptom Manage	https://pubmed.ncbi.nlm.nih.gov/38342476/
3	Feasibility and acceptability of a nurse-led telehealth intervention (BOLSTER) to support patients with peritoneal carcinomatosis and their caregivers: a pilot randomized clinical trial.	Pozzar RA, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38851039/
4	Improving the palliative-procedure decision-making process for patients with peritoneal carcinomatosis: a secondary analysis	Wall JA, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38954989/
5	Palliative intervention for malignant bowel obstruction comes at a cost: a national inpatient study (first published online May 23, 2024)	Sun BJ, et al.	Am Surg	https://pubmed.ncbi.nlm.nih.gov/38782409/
6	A colostomy for large bowel obstruction at the end of life: What do patients gain from palliative surgery?	Wilke RN, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38945019/

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Rehabilitation and social reintegration in gynaecological oncology

Dmitry Utkin and Cristina Celada-Castro

Recent advances in the care of patients with gynaecological cancer highlight the importance of multidisciplinary approaches to address functional, psychosocial, and physical well-being.

A prospective randomized phase III trial (SHAPE, NCT01658930) by Ferguson, et al. investigated the secondary outcomes of sexual health and quality of life (QOL) in patients with gynaecological cancer. It compared simple with radical hysterectomy for oncological outcomes in low-risk cervical cancer. Data were analysed from 700 patients diagnosed with cervical cancer, divided into two groups of 350 women each who underwent simple hysterectomy with lymphadenectomy or radical hysterectomy with lymphadenectomy between December 2012 and March 2023. The Female Sexual Function Index (FSFI) and the Revised Female Sexual Disorder Scale, and QOL using the European Organization for Research and Treatment of Cancer Core 30 and the Cervical Cancer-Specific Module (QLQ-CX24) questionnaires, were used to assess sexual health at 36 months postoperatively. Results showed that the simple hysterectomy group had better FSFI scales for desire and arousal ($p \leq .001$) and pain and lubrication ($p \leq .018$) compared with radical hysterectomy. In addition, sexual-vaginal function ($p \leq .022$) and sexual activity ($p = .024$) were significantly better in the simple hysterectomy group. Global health status was significantly better in the simple hysterectomy group at 36 months ($p = .025$). A potential limitation is the lack of data on treatment-induced menopausal status and hormone replacement therapy, including systemic and local oestrogen use, although ovarian preservation is standard for patients under 50. This study's strengths include balanced surgical groups and high participation rates. [1]

Sebio-Garcia, et al. conducted a prospective study to assess the impact of multimodal prehabilitation on functional capacity in patients with advanced ovarian cancer undergoing cytoreductive surgery. The prehabilitation program, which integrated physical exercise, nutritional support, and psychological counselling, resulted in significant improvements in functional capacity. Specifically, patients in the prehabilitation group showed an increase of 33.1 metres (95% CI 10.5-55.5) in the six-minute walk test and an additional 3.3 repetitions (95% CI 1.8-4.8) in the 30-second sit-to-stand test. Furthermore, participants reported substantial reductions in anxiety, depression, and overall scores on the Hospital Anxiety and Depression Scale. These findings underscore the value of incorporating multimodal prehabilitation into the perioperative care of patients undergoing complex oncological surgery, highlighting its role in optimizing both physical and psychological outcomes. [2]

A retrospective study by McCracken, et al. evaluated the sustainability of same-day discharge (SDD) rates and outcomes following a quality improvement program in minimally invasive gynaecological oncology surgery. Initially, SDD rates increased from 30% to 75% during active intervention and remained high at 72% one-year post-implementation. Comparing 100 patients' post-intervention (2021) with 102 patients during the intervention period (2020), SDD rates were consistent (72% vs. 75%; $p=0.69$), with no significant differences in complications, readmissions, or emergency visits. Significant improvements included fewer 30-day clinic visits (18% vs. 5%; $p=0.007$) and reduced unnecessary bowel preparation (35% vs. 14%; $p<0.001$). Key factors associated with overnight admissions were second-case scheduling (OR=0.06) and postoperative narcotic use (OR=0.12). The program demonstrated sustainable SDD rates while maintaining safety and improving efficiency. Based on the principles of enhanced recovery, the initiative demonstrated cost-effectiveness, safety, and a cultural change in perioperative care. This model offers scalability to other centres, improving patient outcomes and optimizing healthcare resources. [3]

These studies collectively emphasize the value of integrative and tailored approaches in optimizing outcomes for patients with gynaecological cancers, from prehabilitation to addressing unmet needs and incorporating specialized interventions.

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No	Title	Authors	Journal	Link to abstract
1	Sexual health and quality of life in patients with low-risk early-stage cervical cancer: results from GCIG/CCTG CX.5/SHAPE trial comparing simple versus radical hysterectomy	Ferguson SE, et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/39353164/
2	Multimodal prehabilitation improves functional capacity in patients with advanced ovarian cancer undergoing cytoreductive surgery	Sebio-Garcia R, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39375165/
3	Sustainability of an enhanced recovery pathway after minimally invasive gynecologic oncology surgery	McCracken A, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/38531541/

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Follow-up after gynaecological malignancies

Sunaina Wadhwa and Mathilde Del

Ezendam, et al. conducted the ENSURE (Endometrial Cancer Survivors' Follow-up Care) trial, a non-inferiority, randomised controlled multicentric study of 316 women across 42 hospitals in the Netherlands. The intervention group received reduced follow-up care (four visits over three years), while the control group followed usual care (eight to 11 visits over three years). The study outcomes were overall satisfaction with care and PSQSIII score over a three-year follow-up period. The satisfaction scores were similar in both groups (similar mean 82; SD=15). At six, 12, and 36 months, satisfaction was higher in the reduced follow-up group (93%, 94%, and 90%) than in the usual follow-up group (79%, 79%, and 82%; p<0.001). Women with low-risk, early-stage endometrial cancer reported being as satisfied with reduced follow-up as with usual care, despite fewer clinical visits. The trial highlights the feasibility of reduced follow-up, supporting a person-centred approach tailored to individual needs. Strengths of the study include the randomised design, adequate sample size, inclusion of several relevant outcomes, a limited attrition rate, and extensive analyses and generalizability of the results. Limitations of the study include the absence of survival data and the failure to blind patients and/or healthcare professionals to which counselling may have an impact, especially with anxious patients. [1]

Gynaecological cancer survivors face significant challenges after discharge from hospital treatment. Although quality of life is improved by support and rehabilitation, survivors feel that these interventions are insufficient. Breistig, et al. employed a phenomenological hermeneutic approach in a single-centre study to describe the experiences of survivors and their demands for follow-up. Twenty women's individual interviews were transcribed, with the Lindseth and Norberg approach used for analysis. Four themes emerged: “a brutal transition to life after cancer,” “fear of recurrence overshadowing existence,” “a need for professional support,” and “information is not given unless asked for.” Survivors emphasised the need for proactive, routine communication and cancer-specific information to reduce existential suffering. A systematic, person-centred follow-up programme is essential to continuing care after treatment. Although this innovative design-based method offers insights, its generalisability is limited by its small sample size and single-centre nature. [2]

Finding molecular markers to facilitate early recurrence diagnosis is key to the future of gynaecological cancer screening. Casas-Arozamena, et al. conducted a comprehensive study to assess the role of circulating cell-free DNA (cfDNA) and tumour-derived cfDNA (ctDNA) in the identification of endometrial cancer relapse. Samples were collected from 198 patients during surgery and follow-up. It was observed that high cfDNA levels and detectable ctDNA at baseline were associated with poor disease-free survival (p<0.0001; HR=9.25) and disease-specific survival (p<0.0001; HR=11.20). cfDNA/ctDNA analyses detected recurrence before clinical signs emerged. Including cfDNA analysis in follow-up strategies could personalise monitoring, reducing unnecessary visits and improving intervention timing. However, this single-centre study requires validation in larger, multicentre trials to confirm its clinical utility. [3]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Effect of reduced follow-up care on patient satisfaction with care among patients with endometrial cancer: the ENSURE randomized controlled trial	Ezendam NPM, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38970844/
2	Gynecological cancer survivors' experiences and desire for follow-up after recent treatment: a phenomenological hermeneutic study	Breistig S, et al.	Cancer Nurs	https://pubmed.ncbi.nlm.nih.gov/37272739/
3	Role of cfDNA and ctDNA to improve the risk stratification and the disease follow-up in patients with endometrial cancer: towards the clinical application	Casas-Arozamena C, et al.	J Exp Clin Cancer Res	https://pubmed.ncbi.nlm.nih.gov/39304963/

ENYGO ESGO European Network of Young Gynae Oncologists | LiFE report Literature for ENYGO

Quality of life in gynaecological oncology

Elena Rodríguez González

The PRIMA/ENGOT-OV26/GOG-3012 trial enrolled patients with newly diagnosed advanced ovarian cancer who responded to first-line platinum-based chemotherapy. They were randomized to niraparib or placebo as maintenance therapy. It was observed that patients treated with niraparib experienced significantly longer progression-free survival (PFS) than those treated with placebo. The study's secondary endpoint was health-related quality of life (HRQoL). Scores for abdominal and gastrointestinal symptoms, nausea, vomiting, appetite loss, and constipation were higher in niraparib-treated patients; except for constipation, these differences resolved over time. There was no worsening in baseline fatigue, insomnia, abdominal pain, or headache reported by patients. In conclusion, patients treated with niraparib first-line maintenance therapy reported no worsening in overall HRQoL, except for some largely transient increases in gastrointestinal symptoms. [1]

A cross-sectional, population-based study was conducted to evaluate the HRQoL of women surviving a borderline ovarian tumour in comparison with early-stage ovarian cancer survivors treated surgically alone and with a matched cancer-free population. In most HRQoL domains, borderline ovarian tumour survivors were not significantly different from early-stage ovarian cancer survivors and the cancer-free population. The only exceptions were lower levels of insomnia in borderline ovarian tumour patients compared with early-stage ovarian cancer patients and higher levels of dyspnoea in borderline ovarian tumour patients compared with cancer-free people. In conclusion, it was observed that the HRQoL of borderline ovarian tumour survivors generally lies between that of early-stage ovarian cancer survivors and the cancer-free population. [2]

A prospective longitudinal multicentre study was conducted to investigate the HRQoL, sexual function, psychological health, reproductive concerns, and fertility outcomes of women of reproductive age undergoing fertility-sparing surgery for the treatment of ovarian cancer or borderline ovarian tumours. The majority had a strong desire to become biological mothers, which remained or increased over time. HRQoL, psychological-health, and sexual function improved over time, and the proportion of women with sexual dysfunction decreased. At one-year follow-up, 50% of nulliparous women had scores indicating sexual dysfunction compared to 0% of the women who had given birth either before or after surgery. [3]

In the ENGOT-EN6-NSGO/GOG3031/RUBY trial, the use of dostarlimab plus carboplatin–paclitaxel showed, in patients with primary advanced or recurrent endometrial carcinoma, a significant increase in PFS in comparison with placebo plus carboplatin–paclitaxel. The study's secondary endpoint was to evaluate patient-reported outcomes in the mismatch repair-deficient/microsatellite instability-high population. Those receiving dostarlimab plus carboplatin–paclitaxel demonstrated improvements in several QoL domains compared to those receiving placebo plus carboplatin–paclitaxel. These improvements in PFS and overall survival (OS) without worsening in QoL support use of dostarlimab plus carboplatin–paclitaxel as the standard of care in this context. [4]

A cohort study was performed to evaluate the effects of radical hysterectomy, due to cervical cancer, in urinary symptoms and sexual function, as well as the disorder-related impact on QoL. Women who underwent radical hysterectomy due to cervical cancer presented higher percentages of urinary symptoms, higher risk of sexual dysfunction, and worse general and specific QoL scores compared to women who underwent hysterectomy for benign gynaecological conditions. [5]

Relevant articles retrieved March 31, 2024 – September 30, 2024

No	Title	Authors	Journal	Link to abstract
1	Health-related quality of life in patients with newly diagnosed advanced ovarian cancer treated with niraparib vs placebo: results from the phase 3 randomized PRIMA/ENGOT-OV26/GOG-3012 trial	Pothuri B, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/38325276/
2	Quality of life among borderline ovarian tumor survivors: a comparison with survivors of early-stage ovarian cancer and a cancer-free population: a cross-sectional population-based PROFILES study	van der Eerden B, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/39096588/
3	Health-related quality of life, sexual function, psychological health, reproductive concerns and fertility outcome in young women treated with fertility-sparing surgery for ovarian tumors: a prospective longitudinal multicentre study	Johansen G, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/39084159/
4	Patient- reported outcomes in the subpopulation of patients with mismatch repair-deficient/microsatellite instability-high primary advanced or recurrent endometrial cancer treated with dostarlimab plus chemotherapy compared with chemotherapy alone in the ENGOT-EN6-NSGO/GOG3031/RUBY trial	Valabrega G, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/39322611/
5	Urinary symptoms and sexual function after hysterectomy secondary to cervical cancer: a prospective, cohort study	Firmeza MA, et al.	Eur J Obstet Gynecol Reprod Biol	https://pubmed.ncbi.nlm.nih.gov/38461785/

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We are also most grateful to Tereza Cicáková (ENYGO Manager) for her administrative support, Tomáš Grünwald for design and layout, and Jonathan Wolfe for proofreading.