



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

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The European Voice of Gynaecological Oncology



Dear LiFE readers,

The last three years were challenging for the whole world. However, we are excited to hear that the World Health Organization has declared the end of the COVID-19 pandemic. It means our temporarily introduced chapter on that topic will no longer need to exist. Every new beginning comes from some other beginning's end.

LiFE 16 includes reviews of the most valuable and carefully selected articles in gynaecological oncology published between March 31, 2022, and September 30, 2022.

We warmly welcome the new editor, Khayal Gasimli (Germany), as well as Radwa Hablase (United Kingdom), LiFE contributor, who just recently joined us. In addition, we thank all ENYGO members who continue using LiFE to update their knowledge in the field. We are also grateful to be supported by ESGO and the *International Journal of Gynecological Cancer*.

The LiFE Team hopes you will find this issue informative and enjoy reading it. Please, remember to share the link to the report with your colleagues and on social media. If you are interested in joining the LiFE team, please email adminoffice@esgo.org.

Yours,

Zoia Razumova LiFE Editor-in-Chief

On behalf of the LiFE Editors Joanna Kacperczyk-Bartnik Stamatios Petousis Khayal Gasimli



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Medical treatment of primary ovarian cancer

Ilker Selçuk

After the significant progression-free survival (PFS) benefit of olaparib in newly diagnosed BRCA-mutated advanced epithelial ovarian cancer, the results of overall survival (OS) data have been published after a median follow-up of 88 months. In all, 260 patients were enrolled in the olaparib group and 130 patients were enrolled in the placebo group. Patients received olaparib or placebo randomly for approximately two years. The median treatment duration was 24.6 months with olaparib and 13.9 months with placebo. During the analysis, the data maturity was 38.1% (from randomisation to analysis). The median OS was not reached in the olaparib group and was 75.2 months in the placebo group (HR = 0.55 (95% CI: 0.40-0.76, p = 0.0004 for OS). During the analysis (after seven years of follow-up), 67.0% of olaparib versus 46.5% of placebo patients were alive. In addition, 45.3% of olaparib versus 20.6% of placebo patients were alive and had not received a first subsequent treatment. In patients who received a subsequent treatment, 31.1% in the olaparib group and 59.8% in the placebo group received a PARP inhibitor. Irrespective of the statistical outcomes, the results are clinically meaningful. More than 40% of the placebo patients received a PARP inhibitor in the subsequent treatment line. That will explain the improved OS rates in the placebo arm and may affect the statistical results of OS. The results indicate an improved OS with the maintenance use of olaparib, and the effect continues after two years of treatment. [1]

The ATHENA-MONO trial investigated the role of rucaparib 600mg orally twice against placebo over an expected duration of 24 months. Newly diagnosed advanced epithelial ovarian cancer patients with RO cytoreduction, irrespective of the timing of surgery and chemotherapy response, were included. BRCA-mutated and non-mutated patients were randomly assigned in a 4:1 ratio (rucaparib: 427, placebo: 111) after first-line chemotherapy. In the homologous recombination deficiency (HRD) group (185 vs 49 patients), the median PFS was 28.7m (95% CI: 23.0% to not reached) vs 11.3m (95% Cl: 9.1-22.1) (p = 0.0004, HR = 0.47, 0.31-0.72), in the intendto-treat (ITT) population 20.2m (15.2-24.7) vs 9.2m (8.3-12.2) (p < 0.0001, HR = 0.52, 0.40-0.68) for the rucaparib and placebo, respectively. Results at 24 months showed that 45.1% of rucaparib patients and 25.4% of placebo patients were progression-free in the ITT population. Rucaparib improved PFS regardless of BRCA and HRD positivity in a broad group of patients, with similar toxicity rates to other PARP inhibitors. [2]

The OS analysis of the ICON-8 trial has revealed no survival benefit of first-line weekly dose-dense chemotherapy in terms of OS and PFS for European women. After a median follow-up of 69m, the median OS was 47.4m (43.1–54.8) for patients receiving 3 weekly carboplatin area under curve (AUC) 5 or 6 with paclitaxel 175mg/m², 54.8m (46.6–61.6) for patients receiving 3 weekly carboplatin AUC 5 or 6 and weekly paclitaxel 80 mg/m² and 53.4m (49.2-59.6) for patients receiving weekly carboplatin AUC 2 with paclitaxel 80mg/m². The hazard ratio for group 2 against group 1 was 0.87 (0.73–1.05, p = 0.092) and 0.91 (0.76–1.09, p = 0.24) for group 3 against group 1. In addition, the updated progression-free survival time calculated as the restricted mean survival time was not different between the groups: 17.5, 20.1, and 20.1 months for each group, respectively. [3]

No	Title	Authors	Journal	Link to abstract
1	Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: The SOL01/GOG 3004 trial	DiSilvestro P et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/36082969/
2	A randomized, phase III trial to evaluate rucaparib monotherapy as maintenan- ce treatment in patients with newly diagnosed ovarian cancer (ATHENA-MONO/ GOG-3020/ENGOT-ov45)	Monk BJ et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/35658487/
3	Weekly dose-dense chemotherapy in first-line epithelial ovarian, fallopian tube, or primary peritoneal cancer treatment (ICON8): overall survival results from an open-label, randomised, controlled, phase 3 trial	Clamp AR et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih. gov/35690073/



Medical treatment of recurrent ovarian cancer

Seda Şahin Aker

The SOLO2/ENGOT-Ov21 study evaluated the safety and efficacy of olaparib according to age in BRCA1/2-mutated patients with recurrent platinum-sensitive relapsed ovarian cancer (PSROC). Two hundred ninety-five patients were randomised in a 2:1 ratio and divided into two groups: < 65 years (n :233) versus \geq 65 (n: 62). Progression-free survival (PFS) was 19.7 months in the younger compared to 17 months in the older group (p = 0.20). Overall survival (OS) is longer in < 65 years (52.4 vs 38.8 months; HR 0.67; 95% CI: 0.48–0.96). The most common adverse events (AEs) were anemia, fatigue, and nausea. Nausea is higher in the younger group (18.7% vs 7.5%, p < 0.05). The diagnosis of AML/ MDS was higher in older patients with 15.0% versus 6.5% (p = 0.10). Time without significant symptoms of toxicity scores showed meaningful duration of good QoL on olaparib for both groups (13.5 for ≥ 65 vs 18.4 months for < 65, p = 0.05). [1]

The APPROVE trial analysed the efficacy and safety of treatment with apatinib (tyrosine kinase inhibitor) in combination with pegylated liposomal doxorubicin (PLD) compared with PLD alone in patients with PSROC. In all, 152 patients were enrolled and randomised in a 1:1 ratio. Median follow-up was 8.7 months. Median PFS was significantly higher in the apatinib + PLD group versus the PLD group (5.8 vs 3.3 months, HR 0.44; p < 0.001). Median OS was 23.0 versus 14.4 months, respectively (HR 0.66; p = 0.10). The most common AEs were decreased leukopenia and neutropenia. A study limitation was the fact that the OS events in the combination group were immature and the QoL data were absent. [2]

The L-MOCA trial reported the efficacy and tolerability of olaparib as maintenance in Asian patients with recurrent PSOC. In all, 225 patients enrolled in the study and 224 patients received olaparib treatment. The median follow-up was 15.5 months and median PFS was 16.1 months. The estimated PFS rates for 6 and 12 months were 76.0% and 57.1%, respectively. According to BRCA status, the median PFS was 21.2 months in mBRCA. 16.1 months in sBRCA, 21.4 months in gBRCA, and 11.0 months in BRCAwt patients, respectively. The median PFS was 18.3 months in HRRm and 13.3 months in HRRwt. The most common AEs were anemia, nausea, and leukopenia. Three patients had serious AEs of MDS or AML. The limitations of this study were its single-arm nature and that, because it only included China and Malaysia, it could not represent the whole Asian population. [3]

Francis et. al. evaluated the impact of olaparib dose reductions on PFS and OS in SOLO2/ENGOT-ov21 PSOC patients. In this study, relative dose intensity (RDI) was calculated and defined as the actual dose divided by the standard dose. One hundred eightyfive patients were divided into three groups according to the 12-week RDI: >98%, >90%-98%, and \leq 90%. AEs occurred in 37% of patients and G3+ AEs occurred in 22%. The median PFS was 14.2 months in >98%, 19.3 months in >90%-98%, and 34.4 months in \leq 90% (p = 0.37). The median OS was 49.7, 49.5, and 54.1 months, respectively (p = 0.84). The median PFS and OS were not statistically different between patients who experienced G3+ AE and those who had not experienced them (PFS: 16.4 vs 19.3 months, p = 0.70; OS were 37.3 vs 51.6 months, p = 0.30). Performance status 1 (OR 2.54), nausea (OR 3.17) and a body weight of 70kg (OR 1.86) were all associated with an increased RDI of 90%. [4]

Finally, Frenel et al. reported the post-hoc analyses of the SOLO2 trial to investigate the efficacy of different chemotherapy regimens after disease progression in patients who received either olaparib maintenance or placebo. One hundred forty-seven patients who received CT as their first subsequent treatment are included in the study. Seventy-eight patients were in the olaparib and 69 patients were in the placebo arm. Platinum-based CT was used in 69.2% (54/78) and 60.8% (42/69) of patients in the olaparib and placebo arms, respectively. The median follow-up was 17.8 months. The median TTSP was significantly longer in patients who were treated with CT and platinum-based CT following progression on placebo than on olaparib (12.1 vs 6.9 months/14.3 vs 7 months; HR 2.17/2.89). The median TTSP did not significantly differ in non-platinum-based CT between the two groups (6.0 vs 8.3 months; HR 1.58). [5]

No	Title	Authors	Journal	Link to abstract
1	Efficacy and safety of olaparib according to age in BRCA1/2-mutated patients with recurrent platinum-sensitive ovarian cancer: Analysis of the phase III SOL02/ENG0T-0v21 study	Trillsch F et al.	Gynecologic Oncology	https://pubmed.ncbi.nlm.nih. gov/35115180/
2	Effect of Apatinib Plus Pegylated Liposomal Doxorubicin vs Pegylated Liposo- mal Doxorubicin Alone on Platinum-Resistant Recurrent Ovarian cancer The APPROVE randomized clinical trial	Wang T et al.	JAMA Oncology	https://pubmed.ncbi.nlm.nih. gov/35771546/
3	Olaparib maintenance monotherapy in asian patients with platinum-sensitive relapsed ovarian cancer: Phase III trial (L-MOCA)	Gao Q et al.	Clin. Cancer Research	https://pubmed.ncbi.nlm.nih. gov/35131903/
4	The impact of olaparib dose reduction and treatment interruption on treatment outcome in the SOL02/ENG0T-ov21 platinum-sensitive recurrent ovarian cancer	Francis KE et al.	Annals of oncology	https://pubmed.ncbi.nlm.nih. gov/35219776/
5	Efficacy of subsequent chemotherapy for patients with BRCA1/2-mutated recurrent epithelial ovarian cancer progressing on olaparib versus placebo maintenance: post-hoc analyses of the SOLO2/ENGOT Ov-21 trial	Frenel JS et al.	Annals of Oncology	https://pubmed.ncbi.nlm.nih. gov/35772665/



Surgical treatment of primary and recurrent ovarian cancer

Ilker Kahramanoglu and Patriciu Achimas-Cadariu

Lago et al. performed a retrospective, multicentre study to define an anastomotic leak prognostic score.In all, 848patients who underwent cytoreductive surgery for primary or recurrent ovarian cancer with colorectal resection and anastomosis were included. The OVA-LEAK formula (https://n9.cl/ ova-leakscore) was used for calculating the risk of leakage following anastomosis. Using a cutoff value of 22.1%, 0.45 sensitivity, 0.80 specificity, 0.09 positive predictive value, and 0.97 negative predictive value were achieved for an anastomotic leaks would be protected by the stoma. The use of an objective predictive model for anastomotic leak improves the selection of patients for ileostomy. [1]

Surgical treatment of recurrent ovarian cancer

In a retrospective, multi-institutional study of 190 patients who had undergone primary and recurrent ovarian cancer surgery, the presence of a BRCA

mutation was significantly correlated with optimal debulking during the first or second/third relapse (82% vs 56%, p = 0.004; 75% vs. 26%, p = 0.005). Overall survival was significantly longer for patients with a BRCA mutation compared with patients without a BRCA mutation (80.6 vs 56.3 months, p = 0.003). Paper limitations include the retrospective design, lack of patient exposure to PARP inhibitors as maintenance, and the fact that up to 27% of patients were still untested for BRCA status. [2]

In a study of 272 patients with platinum-sensitive recurrent epithelial ovarian cancer who were deemed surgical candidates for secondary cytoreduction after a PET-CT scan and diagnostic laparoscopy, 60% had initially received primary debulking surgery and 40% had interval debulking surgery. Secondary cytoreduction was done in 65% of cases, with a complete R0 rate achieved in 87% of cases. The post-recurrence survival was similar between the two groups, with no significant differences, (81 vs 77 months, p = 0.574), demonstrating that current selection models developed for patients that initially had primary debulking surgery can also be applied for patients that initially received interval debulking surgery, in combination with a PET-CT-scan and diagnostic laparoscopy. Limitations of this study include the retrospective design, potential selection bias, and selection for secondary cytoreduction using the Gemelli algorithm. [3]

No	Title	Authors	Journal	Link to abstract
1	OVA-LEAK: Prognostic score for colo-rectal anastomotic leakage in patients undergoing ovarian cancer surgery	Lago V et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/36058743/
2	Impact of BRCA mutation status on tumor dissemination pattern, surgical outcome and patient survival in primary and recurrent high-grade serous ovarian cancer: A multicenter retrospective study by the Ovarian Cancer Therapy-Innovative Models Prolong Survival (OCTIPS) Consortium	Glajzer J et al.	Ann Surg Oncol	https://pubmed.ncbi.nlm.nih. gov/36085390/
3	The impact of secondary cytoreductive surgery in platinum sensitive recurrent ovarian cancer treated with upfront neoadjuvant chemotherapy and interval debulking surgery	Bizzarri N et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35397918/



Borderline ovarian tumours

Anton Ilin

Borderline ovarian tumours (BOTs) are already well investigated. At the same time, the main controversial topic which causes debates among gynaecological oncologists is fertility-sparing treatment (FST). One of the Multicenter Italian Trials in Ovarian cancer (MITO) Group's database analyses performed by Falcone et al. described the feasibility of FST among patients with stage II-III serous BOT with invasive implants. During the follow-up period of 146 months, 11 out of 13 patients (84.6%) experienced a recurrence. Three of five women who attempted to conceive achieved at least one pregnancy and two gave birth to a healthy child. The authors concluded that FST could be carefully applied even for advanced disease because of good reproductive outcomes and without a negative impact on overall survival (all patients were alive with no evidence of disease during the observation period). A strength of this study is that it was conducted among oncological referral centres, members of the main gynaecologic oncology Italian cooperative group. The main weakness of the study is the number of patients—only 13 cases. However, this is explained by its design and remains the largest series of patients undergoing FST for advanced-stage serous BOTs with invasive implants so far. [1]

When planning conservative management, it is important to understand the recurrence risk factors after surgical treatment to provide a patient with objective information. In the retrospective study of 230 early-stage cases, Capozzi et al. described independent predictive factors of BOT recurrence, which are: lesions with maximum diameter > 50mm (p = 0.014), multilocular cysts > 10 loculi (p =0.012), and cysts with > 4 papillae (p = 0.003) PROS: a good number of cases. CONS: the study has limitations because of its retrospective nature and a low number of relapse events. [2]

No	Title	Authors	Journal	Link to abstract
1	Fertility-sparing treatment for serous borderline ovarian tumours with extra-ovarian invasive implants: Analysis from the MIT014 study database	Falcone F et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35232587/
2	Predictive features of borderline ovarian tumor recurrence in patients with childbearing potential undergoing conservative treatment	Capozzi VA et al.	Mol Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/35761896/



Ovarian sex cord stromal and germ cell tumours

Paul Kubelac

Between 1973 and 2018, 240 patients with stage I ovarian sex cord stromal tumours were found via a retrospective review of the SEER database. One group of patients (n = 116) had definitive surgery, while the other group (n = 124) underwent fertility-preserving surgery. The Kaplan-Meier survival analysis revealed no significant differences in overall survival and cancer-specific survival between the two groups (p > 0.05). However, the multivariate

analysis using the Fine-Gray model revealed a 40% lower cancer-specific mortality for patients receiving definitive surgery versus those receiving fertility-sparing surgery (HR 0.599, p = 0.005), suggesting a minimum follow-up of 15 years and careful selection for fertility-sparing surgery. This research is limited by a lack of data on environment, lifestyle, and adjuvant therapy. In addition, chemotherapy protocols and indications are still debatable, and the

inclusion of younger patients in the fertility-sparing surgery group in this retrospective analysis may result in a selection bias. [1]

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No	Title	Authors	Journal	Link to abstract
1	Could fertility-sparing surgery be considered for stage I ovarian sex cord-stromal tumors? A comparison of the Fine-Gray model with Cox model	Sun D et al.	Front Oncol	https://pubmed.ncbi.nlm.nih. gov/36158691/



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

Richard Tóth

Fu et al. investigated the safety and efficacy of navicixizumab in combination with paclitaxel in platinum-resistant ovarian cancer in a phase lb study. The study was an open-label, non-randomised, dose-escalation and dose-expansion study. Navicixizumab is an antiangiogenic agent which binds to vascular endothelial growth factor and delta-like ligand 4 of the NOTCH signalling pathway. For dose escalation, patients received 3mg/kg navicixizumab every second week and paclitaxel on the 0, 7th, 14th days of the 28-day cycle. Additionally, three patients were selected for 4mg/kg dose. However, due to the novel data on the elevated toxicity of doses greater than 3.5mg/kg, examination of the 4mg/kg-dose group (3 people) was discontinued and maximal tolerated dose, the primary endpoint, was not determined. Secondary endpoints were the safety profile of the combination, presence of antidrug antibodies (ADA), and efficacy (objective response rate (ORR), progress-free survival (PFS), and duration of response.

Forty-four patients were selected for the study who had platinum-resistant ovarian cancer larger than 1 cm and had previous therapy with bevacizumab or at least two different chemotherapy regimens. Tumour response was assessed by CT every eight weeks and CA-125 levels every four weeks. The level of ADAs was measured every six weeks. A tumour microenvironment analysis was performed retrospectively, to determine the response according to the level of immune activity.

The median number of doses administered was eight, without dose-limiting toxicities. All patients had adverse events (AEs); 79.5% had grade 3–4 (hypertension [40.9%], neutropenia [6.8%], and thrombocytopenia [4.5%]) while one patient (2.3%) had sudden cardiac death. Treatment-related AEs occurred in 90% of the patients (hypertension, fatigue, and headache). Infusion-related reaction was noticed in two people, both of whom were positive for ADAs. Pulmonary hypertension was observed in eight and gastrointestinal AEs in two cases.

ORR and disease control rates were 43.2% and 77.3%, respectively, and lower in patients pretreated with bevacizumab. Tumour response in 16 of the 19 responders had visible changes in the following CT scan. Eleven had disease progression during immediate previous therapy. Median PFS was 7.2 months, 5.4 months with, and 7.6 months without prior bevacizumab treatment. Biomarker positivity resulted in a 5.3-month PFS advantage. The median duration of response was six months, the ORR was 43%, the median PFS was 77.2 months, and 53% had stable disease at least for four months. The confirmed ORR of 36% for navicixizumab with paclitaxel shows superiority over the ORR of 27% for the AURELIA trial's bevacizumab combination. Considering the promising results, a further phase III study is being planned. [1]

No	Title	Authors	Journal	Link to abstract
1	Phase Ib study of navicixizumab plus paclitaxel in patients with platinum-resis-	Fu S et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.
	tant ovarian, primary peritoneal, or fallopian tube cancer			gov/35439029/



Medical (chemo and radiotherapy) treatment of primary uterine cancer

Radwa Hablase

Egawa-Takata et al., in their phase II trial, compared the feasibility and efficacy of three post-operative first-line adjuvant chemotherapy regimens for advanced endometrial cancer. They concluded that the completion rate of six cycles of epirubicin- paclitaxel-carboplatin regimen was the highest at 94%. The completion rates of the doxorubicin-paclitaxel-carboplatin and the dose-dense paclitaxel and carboplatin regimens were comparable at 61% and 69%. Haematological toxicities and grade 3 and 4 adverse events were among the common causes of withdrawing treatment in the doxorubicin-paclitaxel-carboplatin and the dose dense paclitaxel and carboplatin groups. The two-year progression free survival (PFS) and the overall survival were not statistically significant between the three arms. Limitations of the study were the small number of patients in each arm, the short observation period, and the inclusion of early stages and low-grade disease. [1]

Maio et al., in their updated analysis of the KEY-NOTE-158 trial, demonstrated consistent results with O'Malley et al. of an objective response rate (ORR) to pembrolizumab of 48.5% among patients with advanced, pre-treated, microsatellite instability-high or mismatch repair-deficient endometrial cancer. Responses continued to be durable with a longer follow-up of 47.1 months. [2]

Co-inhibition of angiogenesis and programmed death-1 pathway as second-line treatment for advanced endometrial cancer was evaluated in a phase II trial from China. A combination of sintilimab, anti-programmed death-1 antibody, and anlotinib, a small molecule multi-tyrosine kinase inhibitor affecting angiogenesis, was administered in a threeweek cycle. They demonstrated an ORR of 73.9% measured by immune-related Response Evaluation Criteria in Solid Tumors. The study's second endpoints included a disease control rate of 91.3% and clinical benefit rate of 69.9%. Time to response averaged at 2.8 months. The median follow-up time was 15.4 months, and the probability of patients with PFS>12 months was 57.1%. The predominant histological subtype was endometrioid adenocarcinoma. Notably, The ORR of the subset with mismatch repair-deficient endometrial cancer was 100% and represented 39.1% of the study cohort. Grade 3-4 adverse events occurred in 50% of the cases. In

addition, a trend for higher ORR and longer PFS was noted among patients with mutations in the homologous repair pathway. The study was limited by its small sample size, single-arm design, and the use of formalin-fixed samples for genomic analysis. [3]

Cui et al., in their analysis of 56 heavily treated patients with recurrent and metastatic endometrial cancer, demonstrated an overall ORR of 42.9% of anlotinib alone or in combination with pembrolizumab. The ORR and disease-control rate of anlotinib monotherapy were 40.9% and 72.7%, respectively, compared to 50% and 83.3% for the 12 patients who received the combination with pembrolizumab. There were no cases of complete response, and two-thirds of the patients had poor performance status. The median PFS of all patients was six months, and the median overall survival was 13.3 months. Grade 3 and above adverse events occurred in 35.7% of the patients, of which hypertension was the most common. Study limitations included the retrospective nature, small sample size, lack of tumour grade and biomarker analysis data, and short follow-up time. [4]

No	Title	Authors	Journal	Link to abstract
1	Adjuvant Chemotherapy for Endometrial Cancer (ACE) trial: a randomized phase II study for advanced endometrial carcinoma	Egawa-Takata T et al.	Cancer Sci	https://pubmed.ncbi.nlm.nih. gov/35218673/
2	Pembrolizumab in microsatellite instability high or mismatch repair deficient cancers: updated analysis from the phase II KEYNOTE-158 study	Maio M et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih. gov/35680043/
3	Phase II trial of efficacy, safety, and biomarker analysis of sintilimab plus anlotinib for patients with recurrent or advanced endometrial cancer	Wei W et al.	J Immunother Cancer	https://pubmed.ncbi.nlm.nih. gov/35623659/
4	Anlotinib in recurrent or metastatic endometrial cancer	Cui Q et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. qov/35606048/



Medical (chemo and radiotherapy) treatment of recurrent uterine cancer

Stamatios Petousis

A phase II prospective study was performed to investigate the effectiveness and safety of combination of letrozole and abemaciclib in oestrogen-positive recurrent endometrial cancer (EC). Eight of 30 patients presented complete response. Median PFS was 9.1 month; PFS at 6 months was 55.6%. The authors concluded that the combination letrozole and abemaciclib might be promising to treat recurrent ER-positive endometrial cancer. The fact that no adjustment was made regarding parameters such as grade, prior hormonal therapy, mismatch repair, and progesterone receptor status might be considered as the main study limitations. [1]

Oaknin et al. published an interim analysis of the GARNET study. This is a prospective, phase I, single-arm study in which safety and effectiveness of dostarlimab was examined in advanced or recurrent endometrial cancer. The study included two cohorts, the first one with dMMR/MSI-H disease and the second with proficient/stable (MMRp/MSS) disease. Objective response rate was 43.5% for the first cohort and 14.1% for the second one. The occurrence of grade 3 or worse adverse events was extremely low in both arms, at16.6% and 5.5%, respectively.

The authors concluded that dostarlimab indicated remarkable antitumor activity with tolerable rate of adverse events. The prospective character of the study is one of the main advantages. The multicentre character of the study with over 170 different centres could be associated with differences in evaluation or management. [2]

De Jaeghere et al. published the results of the PRIMMO study. This was a phase II study of patients with persistent/recurrent/metastatic cervical or endometrial cancer. In this study, patients received an immunomodulatory five-drug cocktail (IDC) two weeks before radioimmunotherapy, while pembrolizumab was also administered three-weekly from day 15 onwards. The objective response rate was only 12% in endometrial cancer, while median interval-censored PFS was 3.6. Despite the prospective character of the study, the assessed management was proven to be inefficient for patients with advanced or metastatic EC. [3]

Heudel et al. published the results of the VICTORIA study. It was a prospective randomised, phase I/ II trial, in which 73 recurrent or metastatic EC

patients were randomised to oral vistusertib and oral anastrozole or oral anastrozole alone. Final outcomes indicated that adding oral vistusetib significantly improved progression-free survival in the first 8 weeks, overall response rate and PFS, while adverse events rate was reasonable. The good design of the study is its main advantage. [4]

Post et al. published the results of a multicentre, phase II DOMEC trial. The main objective was to study the efficacy and safety of combination therapy with PD-L1 and PARP inhibitors for advanced EC. The authors reported that the combination was well tolerated but did not achieve the 50% six-month progression-free survival. The heterogenous study population might be considered the main study limitation. [5]

No	Title	Authors	Journal	Link to abstract
1	A phase II, two stage study of letrozole and abemaciclib in estrogen receptor-positive recurrent endometrial cancer	Konstantinopoulos PA et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/36174113/
2	Patient-reported outcomes in the GARNET trial in patients with advanced or recurrent mismatch repair-deficient/microsatellite instability-high endometrial cancer treated with dostarlimab	Oaknin A et al.	J Immunother Cancer	https://pubmed.ncbi.nlm.nih. gov/35064011/
3	Pembrolizumab, radiotherapy, and an immunomodulatory five-drug cocktail in pretreated patients with persistent, recurrent, or metastatic cervical or endometrial carcinoma: Results of the phase II PRIMMO study	De Jaeghere EA et al.	Cancer Immunol Immuno- therapy	https://pubmed.ncbi.nlm.nih. gov/35960332/
4	Safety and efficacy of the mTOR Inhibitor, vistusertib, combined with anastrozole in patients with hormone receptor-positive recurrent or metastatic endometrial Cancer: The VICTORIA multicenter, open-label, phase 1/2 randomized clinical trial	Heudel P et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih. gov/35551299/
5	Efficacy and safety of durvalumab with olaparib in metastatic or recurrent endo- metrial cancer (phase II DOMEC trial)	Post CCB et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35287967/



Surgical treatment of primary and recurrent endometrial cancer

Houssein El Hajj and Joanna Kacperczyk-Bartnik

Ovarian preservation

In a multicentre retrospective study, Akgor et al. evaluated the feasibility and outcome of ovarian preservation in patients with FIGO stage I endometrial adenocarcinoma below 40 years of age who underwent hysterectomy. The study enrolled 196 patients, of whom 54 (32%) underwent ovarian preservation surgery, and 115 (68%) underwent bilateral salpingo-oophorectomy. The median follow-up was 59 months, during which no adnexal recurrences were diagnosed. The authors did not observe significant differences in the mean patients' age, overall survival, or recurrence-free survival between the two groups. One of the study's limitations is the lack of information about patients' endometrial cancer molecular profiles. [1]

Use of intrauterine manipulator

In a prospective multicentre study, Siegenthaler et al. evaluated peritoneal cytology during different stages of laparoscopic staging surgeries with manipulator use in patients with endometrial cancer. They compared the results with the oncological outcomes. Ninety-eight (79%) patients had negative peritoneal cytology, while 16 (13%) had positive results before manipulator insertion, and ten (8%) patients with initially negative results had positive peritoneal cytology after manipulator use. The recurrence rate was significantly higher in patients with positive peritoneal cytology, and the worst oncological outcome was observed in the group with positive peritoneal cytology conversion. The study's limitations include a lack of a control group operated without a uterine manipulator and a small sample size of the subgroups. [2]

Conversely, a systematic review and meta-analysis by Scutiero et al. showed that the use of uterine manipulator during minimally invasive surgery for endometrial cancer was not associated with the worse oncological outcome than open abdominal hysterectomies or minimally invasive surgeries without uterine manipulator. However, the results showed that malignant peritoneal cytology results were significantly more frequent in patients undergoing laparoscopic or laparoscopy-assisted vaginal hysterectomy with uterine manipulator use compared to those who experienced total abdominal hysterectomies. One of the study limitations is the lack of information about uterine manipulator types used in the included studies. [3]

Para-aortic lymphadenectomy

A retrospective study by Lai et al. aimed to evaluate recurrence-free survival and overall survival in patients with FIGO stage I–II grade 3 endometrial cancer based on the extent of performed lym-

phadenectomy. One hundred and forty-four (51%) patients had pelvic lymphadenectomy alone and 137 (49%) underwent both pelvic and para-aortic lymphadenectomy. The median follow-up was 45 months. No statistically significant differences regarding benefit in survival nor recurrence were observed. The lack of molecular classification is one of the study's limitations. [4]

Cytoreductive surgery in recurrent endometrial cancer

In a systematic review, Dhanis et al. evaluated the role of cytoreductive surgery in recurrent endometrial cancer. The authors concluded that cytoreductive surgery in recurrent endometrial cancer could be beneficial, especially in the case where complete cytoreduction is achieved following adherence to specific qualification criteria defined as good patient performance status, tumour size less than 6cm, and solitary disease. The review included non-randomized and retrospective studies, which poses one of its limitations. [5]

No	Title	Authors	Journal	Link to abstract
1	OPEC study: An international multicenter study of ovarian preservation in endometrial cancers	Akgor U et al.	Int J Gynaecol Obstet	https://pubmed.ncbi.nlm.nih. gov/35323994/
2	Prospective multicenter trial assessing the impact of positive peritoneal cytology conversion on oncological outcome in patients with endometrial cancer undergoing minimally invasive surgery with the use of an intrauterine manipulator	Siegenthaler F et al.	Ann Surg Oncol	https://www.ncbi.nlm.nih.gov/pmc/ articles/PMC9640429/
3	Influence of uterine manipulator on oncological outcome in minimally invasive surgery of endometrial cancer: A systematic review and meta-analysis	Scutiero G et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih. gov/35725683/
4	Does para-aortic lymphadenectomy improve survival in pathologically dia- gnosed early-stage grade 3 endometrioid and non-endometrioid endometrial cancers? A retrospective cohort study in Korea and Taiwan	Lai YL et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35995599/
5	Cytoreductive surgery in recurrent endometrial cancer: A new paradigm for surgical management?	Dhanis J et al.	Surgical Oncol	https://pubmed.ncbi.nlm.nih. gov/35849994/



Uterine sarcoma

Marcin Bobiński

Chemotherapy

The results of the extremely important LMS-04 trial were published by the French Sarcoma Group. This was a randomised, multicentre, open-label, phase III trial, comparing doxorubicin alone versus doxorubicin with trabectedin followed by trabectedin alone as first-line therapy for metastatic or unresectable leiomyosarcoma. One hundred and fifty patients (67 with uterine leiomyosarcomas and 83 with soft tissue leiomyosarcomas) were randomly assigned to receive either intravenous doxorubicin alone (75mg/ m²) once every three weeks for up to six cycles or of intravenous doxorubicin (60mg/m²) + intravenous trabectedin (1.1mg/m²) once every three weeks up to six cycles followed by maintenance with trabectedin alone. Median progression-free survival was significantly longer with doxorubicin + trabectedin versus doxorubicin alone (12.2 vs 6.2 months, p < 0.0001). Nine (12%) patients in the doxorubicin alone group and 15 (21%) patients in the doxorubicin + trabectedin group had serious adverse events. The authors concluded that doxorubicin + trabectedin in first-line therapy was found to significantly increase progression-free survival compared with doxorubicin alone and could be considered an option for the first-line treatment of metastatic leiomyosarcomas. [1]

Due to rarity and lack of preoperative diagnostic methods the prospective, randomised trials are very seldom in uterine sarcomas. This trial raised wide discussion among experts and has a chance to change practice. However, longer follow-up is required to assess the efficacy of second line treatment.

Radiotherapy

Two papers supporting the benefit from radiotherapy in sarcoma treatment were published. Hao et al. presented a retrospective analysis of 2,897 patients from the Surveillance, Epidemiology, and End Results (SEER) database. It was observed that radiotherapy demonstrated beneficial effect on overall and disease-specific survival. Further subgroup analysis indicated radiotherapy improved overall and disease specific survival among a subset of patients in stage II–IV, particularly with uterine leiomyosarcoma. Tumour grade, tumour size larger than 100mm, and chemotherapy administration were identified as factors increasing the effect of radiotherapy. The authors considered adjuvant radiotherapy underutilised in clinical practice. [2]

Another analysis of the SEER database including 947 stage I uterine sarcoma patients was released by Huang et al. The authors indicated that the role of radiotherapy added benefit to surgery outcome in the prolongation of disease specific survival among the high-risk group. A similar effect was not noted in the low-risk group. [3]

The results of both studies indicate the potential role of radiotherapy in the treatment of uterine sarcomas. The benefit was observed especially in the presence of risk factors. Even though the results seem to be promising, the retrospective design of both studies is the main limitation and does not allow for the results to be translated directly into clinical practice

No	Title	Authors	Journal	Link to abstract
1	Doxorubicin alone versus doxorubicin with trabectedin followed by trabectedin alone as first-line therapy for metastatic or unresectable leiomyosarcoma (LMS-04): a randomised, multicentre, open-label phase 3 trial	Pautier P et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih. gov/35835135/
2	The role of postoperative radiotherapy in patients with uterine sarcomas: A PSM-IPTW analysis based on SEER database	Hao Z et al.	Front Surg	https://pubmed.ncbi.nlm.nih. gov/36017510/
3	Adjuvant radiotherapy shows benefit in selected stage I uterine sarcoma: A risk scoring system based on a population analysis	Huang YX et al.	Cancer Med	https://pubmed.ncbi.nlm.nih. gov/35277934/



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

Zoia Razumova

Cemiplimab is a programmed cell death 1 (PD-1) antibody already used to treat several solid malignancies.

Tewari et al. performed a phase 3 randomised trial in patients with cervical cancer progression after platinum-based chemotherapy (CHT) in the first line, despite the PD-1 status. Patients were randomised (1:1) to cemiplimab (350 mg every three weeks) or the single-agent CHT based on the researcher's selection.

Six hundred eight women were enrolled, and median overall survival was longer in those taking cemiplimab than in the CHT arm (hazard ratio for death, 0.69; 95% confidence interval [CI], 0.56 to 0.84; two-sided P<0.001) in both squamous-cell carcinoma and adenocarcinoma. Progression-free survival was also longer in the cemiplimab arm than in the arm of patients taking CHT of choice in the overall population (hazard ratio for disease progression or death, 0.75; 95% CI, 0.63 to 0.89; two-sided P<0.001). Besides, an objective response in the overall population developed in 16.4% (95% CI, 12.5 to 21.1) of the cases in the cemiplimab arm, compared with 6.3% (95% CI, 3.8 to 9.6) in the CHT arm. Objective response occurred in 18% (95% CI, 11 to 28) of the patients with PD-L1 expression \geq 1% and in 11% (95% CI, 4 to 25) of those with

PD-L1 <1% who received cemiplimab. Grade $3\geq$ side effects developed in 45.0% of the patients treated with cemiplimab and 53.4% of those with just CHT. [1]

PROS: novelty, study design and sample size. CONS: funded by the industry.

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No	Title	Authors	Journal	Link to abstract
1	Survival with cemiplimab in recurrent cervical cancer	Tewari KS et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih. gov/35139273/



Medical treatment of primary and recurrent cervical cancer

Zoia Razumova

The PI3K/Akt/mTOR pathway is often dysregulated in solid cancer, boosting tumour cell growth, survival, and resistance to the treatment.

Phase I

Sapanisertib is an inhibitor of raptor-mTOR and rictor-mTOR with potential antineoplastic activity. Serabelisib is a selective PI3K alpha isoform inhibitor, including PIK3CA mutations. Both sapanisertib and serabelisib have possible antineoplastic activity due to involvement in the PI3K/Akt/mTOR pathway.

Starks et al. investigated the combination of paclitaxel, sapanisertib, and serabelisib in 19 extensively pretreated patients, including 6 with endometrial cancer (EC) (5 endometrioid, 1 papillary serous). This was an open-label, cohort study of sapanisertib 3mg or 4mg, serabelisib 200mg on days 2–4, 9–11, 16–18 and 23–25 with paclitaxel 80mg/m2 on days 1, 8, and 15 every 28 days. Genomic profiling was done before starting the treatment. The results have shown that the combination is safe and tolerated, chiefly in patients with aberrations in PI3K/AKT/mTOR pathway and even those not sensitive to platinum, and had no effect of taxane, everolimus, or temsirolimus. At the same time, sapanisertib 4mg and serabelisib 200mg were not tolerated and were hardly manageable due to hyperglycaemia. The study was stopped because the manufacturer ceased production of the used compounds. A strength of the study was its novelty, though it was potentially limited by the small study sample which did not exclusively include patients with EC; besides, no biomarkers were used in selection. [1]

Phase I/II

Vistusertib is an mTOR inhibitor with a potential anti-cancerogenic effect due to its positive role in apoptosis and negative in cell proliferation, involved in the PI3K/Akt/mTOR signalling pathway.

Heudel et al. examined the combination of vistusertib and anastrozole in oestrogen and progesterone receptor-positive recurrent or metastatic EC in the

VICTORIA study. Seventy-five patients recruited in 12 French oncological centres were randomised in a 2:1 ratio to vistusertib (125mg x 2 per day, two days per week) plus anastrozole (1mg per day), or just anastrozole. No adverse side effects were present in patients taking vistusertib and anastrozole during the safety run-in period. The overall response rate of patients taking the combination of drugs was 24.5% (95% CI: 13.3%-38.9%) versus 17.4% (95% CI: 5.0%-38.8%) in those taking just anastrozole. The median follow-up was 27.7 months, and median progression-free survival was 5.2 (95% CI: 3.4-8.9) in the combination arm and 1.9 (95% CI: 1.6-8.9) months in the anastrozole arm. Grade ≥ 2 side effects were connected to the intake of vistusertib. This study benefitted from being a multicentre, open-label, phase 1/2 randomised clinical trial, though it was potentially weakened because no molecular analyses were done. [2]

No	Title	Authors	Journal	Link to abstract
1	Phase I dose escalation study of dual PI3K/mTOR inhibition by sapanisertib and serabelisib in combination with paclitaxel in patients with advanced solid tumors	Starks DC et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35843739/
2	Safety and efficacy of the mTOR Inhibitor, vistusertib, combined with anastro- zole in patients with hormone receptor-positive recurrent or metastatic endo- metrial cancer: the VICTORIA multicenter, open-label, phase 1/2 randomized clinical trial	Heudel P et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih. gov/35551299/



Surgical treatment of primary and recurrent cervical cancer

Chrysoula Margioula-Siarkou and Georgia Margioula-Siarkou

The MEMORY study by Leitao Jr et al., a multi-institutional, retrospective cohort study on 1,093 patients with 2009 FIGO stage IA1-IB1 cervical carcinoma, compared survival outcomes between patients treated with minimally invasive (n = 715) and abdominal radical hysterectomy (n = 378). No significant differences were detected between the groups, considering both three-year progression-free survival (PFS) rates, which were 87.9% (95% CI: 84.9-90.4%) and 89% (95% CI: 84.9-92%), respectively (p = 0.6), and three-year overall survival (OS) rates, estimated at 95.8% (95% CI: 93.6-97.2%) and 96.6% (95% CI: 93.8-98.2%), respectively (p = 0.8). Consequently, the authors concluded that a minimally invasive approach is not associated with poorer oncological outcomes, compared to an open surgical approach. [1]

The 4C study by Piedimonte et al., a multicentre retrospective cohort study of 423 patients with FIGO 2018 stage IA1–IA2 (microinvasive) cervical cancer, analysed the differences in five-year recurrence-free survival (RFS) rates after minimally invasive (n = 212), abdominal (n = 148) and combined vaginal-laparoscopic hysterectomy (n = 63). There were no statistically significant differences in five-year RFS rates among the three groups (96.7%, 93.7%, and 90.0%, respectively; p = 0.34), as well as in peri-operative complication rates (p = 0.19), leading the authors to the conclusion that minimally invasive hysterectomy does not appear to compromise oncological safety in patients with microinvasive cervical cancer. [2]

Kim et al. performed a retrospective cohort study to evaluate the association between surgical approach and oncological outcomes on a population of 161 patients with FIGO stage IB1-IB2 usual-type adenocarcinoma and adenosquamous cervical carcinoma, who underwent either minimally invasive (n = 99)or open radical hysterectomy (n = 62). Both OS (p = 0.201) and disease-free survival (DFS) rates (p = 0.184) were not significantly different between the two groups. However, regardless of surgical approach, pathological parametrial invasion was associated with worse DFS rate (adjusted HR 3.41, 95% Cl: 1.25–9.29, p = 0.016). Conclusively, the authors noted that in terms of survival outcomes, open surgical approach is not superior to minimally invasive approach. [3]

Pécout et al. investigated the effect of different surgical routes in laparoscopic para-aortic lymphadenectomy (PAAL) on morbidity and mortality, in a multicentre retrospective study of 448 patients with locally advanced cervical cancers (FIGO IB3-IVA), receiving pretherapeutic nodal staging. Transperitoneal PAAL was performed on 225 patients, while the retroperitoneal route was preferred in 223 patients. No significant differences were reported between the groups, regarding intraoperative (p = 0.28) and postoperative complications (p = 0.44), mortality rate (HR 0.968, 95% CI: 0.591-1.585), RFS and OS rates, but length of hospitalisation was significantly shorter in patients who underwent retroperitoneal PAAL (3.97 vs 4.88 days, p < 0.001). In conclusion, the authors suggested that retroperitoneal route is

a safe option for surgical nodal assessment that could be offered instead of standard transperitoneal PAAL. [4]

The SUCCOR Risk study by Manzour et al. was conducted to identify independent clinicopathological variables associated with risk of relapse in a population of 1,116 patients with stage IB1 cervical cancer treated with radical hysterectomy, as well as to propose a risk predictive index (RPI) for classifying patients depending on risk of recurrence. Conisation before radical hysterectomy was distinguished as the main variable decreasing the rate of relapse (OR 0.31, 95% CI: 0.17-0.60); contrarily, tumour diameter >2cm on preoperative imaging (OR 2.15, 95% CI: 1.33-3.5) and minimally invasive approach (OR 1.61, 95% CI: 1.00-2.57) were associated with increased risk of recurrence. According to these variables and based on RPI, patients were classified as of low, medium, and high risk of relapse, with the five-year DFS rate significantly decreasing as the risk category is increased (p < 0.001).[5]

The CERVANTES study by Cibula et al. is an ongoing international multicentre randomised non-inferiority trial, designed to assess potential differences in DFS between patients with intermediate-risk early-stage cervical cancer (FIGO stage IB1–IIA) treated with radical surgery only and patients also receiving adjuvant external beam radiotherapy \pm brachytherapy \pm concomitant chemotherapy. Primary endpoint results are expected by 2031 [6].

No	Title	Authors	Journal	Link to abstract
1	The MEMORY Study: MulticentEr study of Minimally invasive surgery versus Open Radical hYste- rectomy in the management of early-stage cervical cancer: Survival outcomes	Leitao Jr M et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35879128/
2	Comparison of outcomes between abdominal, minimally invasive and combined vaginal-lapa- roscopic hysterectomy in patients with stage IAI/IA2 cervical cancer: 4C (Canadian Cervical Cancer Collaborative) study	Piedimonte S et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35644731/
3	Open versus minimally invasive radical hysterectomy for early cervical cancer: A two-center retrospective cohort study with pathologic review of usual-type adenocarcinoma and adenosquamous carcinoma	Kim Y et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35970602/
4	Comparison of retroperitoneal and transperitoneal surgical routes in laparoscopic nodal staging for locally advanced cervical cancers (FIGO IB3-IVA)	Pécout M et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih. gov/35643576/
5	SUCCOR Risk: Design and validation of a recurrence prediction index for early-stage cervical cancer	Manzour N et al.	Ann Surg Oncol	https://pubmed.ncbi.nlm.nih. gov/35430668/
6	CERVANTES: an international randomized trial of radical surgery followed by adjuvant (chemo) radiation versus no further treatment in patients with early-stage, intermediate-risk cervical cancer (CEEGOG-CX-05; ENGOT-CX16)	Cibula D et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/36100282/



Radiotherapy in management of primary and recurrent cervical cancer

Joanna Kacperczyk-Bartnik and Erbil Karaman

In a randomised prospective study, Muangwong et al. compared the outcome of patients with cervical cancer who underwent four sessions of in-room brachytherapy (n = 37) or four sessions of out-room brachytherapy (n = 37). Changes in D2cc doses and volume of bladder, rectum and sigmoid were analysed. All patients had computed tomography (CT) performed twice-the first one (CT1) for treatment planning and the second one (CT2) immediately before brachytherapy to assess the exact delivered doses. Between the examinations, the in-room brachytherapy group remained on the CT table, and the out-room brachytherapy group stayed in the waiting room between CT1 and CT2. No differences in D2cc doses and volume changes were observed between the groups regarding the organs at risk (bladder, rectum, and sigmoid). The results of this study could be meaningful for high-volume centres, in which the organisation of in-room brachytherapy is a potential challenge. A drawback of the study was that no information was given on the gross tumour volume doses nor the highrisk clinical target volume doses as it did not assess MRI-guided brachytherapy results. [1]

Kobayashi et al. investigated the results of patients who underwent hyaluronate gel injections in the rectovaginal fossa and vesicouterine fossa during brachytherapy for cervical cancer (n = 52) compared to a control group without hyaluronate gel injections (n = 52). It was observed that in the group with hyaluronate gel injections, patients received a significantly higher median clinical target volume dose than the control group 79.4 Gy (52.6–97.5 Gy) versus 76.0 Gy (63.7–99.5 Gy) (p = 0.017). No differences between

the analysed groups were identified regarding the median bladder and rectal doses. The authors proposed the use of hyaluronate gel injections in the rectovaginal and vesicouterine fossa a method of safe increase of clinical tumour volume dose in patients with cervical cancer. A weakness of the study was its retrospective, single-centre character. [2]

No	Title	Authors	Journal	Link to abstract
1	Brachytherapy dose changes: comparing in-room and out-room image-guided brachytherapy	Muangwong P et al.	J Contemp Brachytherapy	https://pubmed.ncbi.nlm.nih. gov/36199946/
2	Effect of hyaluronate acid Injection on dose-volume parameters in brachytherapy for cervical cancer	Kobayashi R et al.	Adv Radiat Oncol	https://pubmed.ncbi.nlm.nih. gov/35647394/



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

Khayal Gasimli

Phase II

A multicohort basket study investigated the antitumour activity of atezolizumab-monotherapy in 16 different advanced or metastatic solid cancers. Twenty-seven patients with squamous cell or adenocarcinoma cervical cancer (CC) were included in this study until disease progression or unacceptable toxicity. Most patients (70.4%) had previously received two or more lines of chemotherapy. The non-progression rate was 44.4% (\leq 20% at 18 treatment weeks was considered unbeneficial) in patients with CC. At six months, overall response (ORR) and progressive disease rates were registered at 14.8% and 40.7%, respectively. The treatment-related adverse events (TRAEs) were experienced by 55.3% of whole cohorts in the following frequency: fatigue (12.7%), diarrhoea (7.6%), and rash (7.2%). While this was a novel objective, the study was limited by its low recruitment rate (27 patients with CC) and by employing a single target for efficacy in different cancer types. [1]

In a multicentre, single-arm study, Xu et al. explored the efficacy and safety of the second-line combination of sintilimab (anti-PD-1, 200mg IV every 3

weeks) plus anlotinib (tyrosine kinase inhibitor, 10mg PO on days 1-14) in PD-L1 positive (combined positive score >1) metastatic and recurrent CC until disease progression and unacceptable toxicity. Most patients (83.3%) presented a histological picture of a squamous cell cervical cancer. The efficacy analysis showed 73.1% (95% CI: 60.1-88.9) six-month progression-free survival (PFS) rate and 73.8% (95% CI: 59.3–91.7) of 12-month overall survival (OAS). The ORR and DCR were 54.8% and 88.1%, respectively. Solely two (4.7%) patients developed progressive disease. Hypothyroidism (33.3%), elevated aspartate aminotransferase (21.4%), and hypertension (19.0%) were revealed as the most common TRAEs. As a result of TRAEs, treatment was discontinued by three (7.1%) patients. This otherwise strong multicentre study with a novel drug combination was limited by the absence of a control arm. [2]

Japanese colleagues evaluated the efficacy, safety, and pharmacokinetics of tisotumab vedotin (TV) in 17 patients in Japan with recurrent or metastatic CC in a framework of a single-arm, open-label trial (innovaTV 206). The ORR was 29.4%, and the DCR was 70.6%. The median survival rates were 3.1 months (95% CI: 1.2–7.1) for PFS and 11.4 months (95% CI: 6.2–not reached) for OAS. The TRAEs were detected in all patients, particularly anaemia (58.8%), nausea (58.8%), alopecia (47.1%), epistaxis (47.1%), and diarrhoea (35.3%). Solely one patient disrupted the treatment due to a lower gastrointestinal haemorrhage. The efficacy and safety of TV were already evaluated in US and European patients within innovaTV 201 and 204 trials. The Japanese cohorts revealed comparable survival and tolerability result to both previous studies. While the study benefitted from examining a new molecular agent for patients with recurrent or metastatic CC, it was limited by the lack of a control arm and the small sample size. [3]

No	Title	Authors	Journal	Link to abstract
1	Phase II multicohort study of atezolizumab monotherapy in multiple advanced solid cancers	Tabernero J et al.	ESMO Open	https://pubmed.ncbi.nlm.nih. gov/35305400/
2	Efficacy and safety of sintilimab plus anlotinib for PD-L1-positive recurrent or metastatic cervical cancer: A multicenter, single-arm, prospective phase II trial	Xu Q et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/35192397/
3	Tisotumab vedotin in Japanese patients with recurrent/metastatic cervical cancer: Results from the innovaTV 206 study	Yonemori K et al.	Cancer Sci	https://pubmed.ncbi.nlm.nih. gov/35633184/



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

María de los Reyes Oliver and Rubén M. Betoret

Contralateral groin treatment

In a manuscript including data from 366 patients from two prospective multicentre studies, Van der Kolk et al. examined whether surgical treatment of the contralateral groin can be omitted in women with early-stage vulvar squamous cell carcinoma and a unilateral metastatic sentinel lymph node . Results showed that the risk of contralateral lymph node metastases in this group of patients is low and unilateral inguinofemoral lymphadenectomy or unilateral inguinofemoral radiotherapy are safe therapeutic options. However, individualised management based on tumour localisation and size are advised. [1]

Superficial vs deep lymph node dissection

In a retrospective cohort study, Mattson et al. evaluated the outcome of 233 patients with suspected early-stage vulvar squamous cell carcinoma depending on the performed lymph node dissection type: superficial (n = 102) or deep (n = 133). No significant differences in the recurrence or survival rates were observed between the groups. Patients with deep lymph node dissection developed significantly more frequent complications, including lymphoedema, readmission, and infection. Potential bias of the study is associated with missing data, differences in institutional classification, and treatment patterns. [2]

Vulvar reconstruction

A retrospective study by Parpex et al. aimed to analyse the outcome of 254 patients undergoing vulvar reconstruction in eight FRANCOGYN centres between 1998 and 2017. Survival without local recurrence at two years was similar for patients with (n = 49) and without (n = 204) vulvar reconstruction (82.1% vs 84.8%, respectively, p = 0.26). Study limitations are associated with its retrospective design. [3]

Radiotherapy

A retrospective analysis of data from the National Cancer Database was performed by Ni et al. to assess the survival benefit from adjuvant radiotherapy in 2,396 patients with node-positive vulvar cancer aged 65–90. Results showed that adjuvant radiotherapy was beneficial for patients 65–84 years but not for patients 85 or older. Potential bias resulting from missing data, patient selection, and variations in management are the limitations of this study. [4]

Immunotherapy

The phase II KEYNOTE-158 study by Shapira-Frommer et al. evaluated the results of pembrolizumab monotherapy in 101 patients with advanced vulvar cancer. It was observed that pembrolizumab monotherapy was associated with durable responses in a subset of patients with vulvar squamous cell carcinoma regardless of tumor PD-L1 status. Pembrolizumab monotherapy was also well tolerated. Study limitations are associated with small size of some subgroups. [5]

Survival

Mayo et al. developed normograms predicting survival rates of patients with vulvar squamous cell carcinoma based on the Surveillance, Epidemiology, and End Results (SEER) database [6]. Presented normograms were characterised by excellent predictive ability for overall survival and cancer-specific death. Study limitations included the lack of complete clinical information and lack of data on tumour markers. [6]

No	Title	Authors	Journal	Link to abstract
1	Unilateral inguinofemoral lymphadenectomy in patients with early-stage vulvar squamous cell carcinoma and a unilateral metastatic sentinel lymph node is safe	Van der Kolk WL et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/36085090/
2	Superficial versus deep inguinal nodal dissection for vulvar cancer staging	Mattson J et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35781163/
3	Impact of vulvar reconstruction on the accuracy of a nomogram for predicting local recurrence after surgery for vulvar cancer	Parpex G et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35177278/
4	The role of adjuvant radiation therapy in older patients with node-positive vulvar cancer: A national cancer database analysis	Ni L et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/36150913/
5	Efficacy and safety of pembrolizumab for patients with previously treated advanced vulvar squamous cell carcinoma: Results from the phase 2 KEYNO-TE-158 study	Shapira-Frommer R et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35361487/
6	Prognostic nomograms to predict overall survival and cause specific death in vulvar squamous cell carcinoma	Mayo Y et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35428690/



Screening of gynaecological cancer

Catarina Pardal

The NTCC2 study aimed to evaluate the E6/E7 mRNA test as a screening tool for cervical dysplasia, testing the performance and referral rates to colposcopy compared to the HPV DNA-based test. A total of 41,127 women participating in routine HPV DNA-based screening were recruited, and all HPV positives were tested for E6/E7 mRNA, cytology, and p16/Ki67. A consecutive sample of 1108 HPV DNA negatives was tested for E6/E7 mRNA for test specificity. The E6/E7 mRNA test sensitivity for CIN3+ was 96.9% (95% CI: 91.3%-99.1%), 3% inferior compared with HPV DNA sensitivity but with a 22% reduction of positivity and a lower referral to colposcopy (6% vs 7.7%). Specificity for <CIN2 was 94.5% (95% CI: 93.9%-94.9%). Estimated total positivity of E6/E7 mRNA was 6.0% in the whole screening population, with a PPV for CIN3+ of 4.2%. Adopting cytology or p16/Ki67 triage for E6/ E7 mRNA-positive women, colposcopy referral, and PPV were 1.7% and 11.2% for cytology and 2% and 11.7% for p16/Ki67. The HPV E6/E7 mRNA assay, used as a primary screening test, showed similar sensitivity for CIN3+ but a lower positivity rate than HPV DNA testing. The study's main limitation is that the sensibility test may be overestimated since it was calculated among HPV DNA positives. [1]

The HPV FOCAL RCT compared HPV DNA-based testing at extended-intervals (every 48 months) to cytology (every 24 months) by calculating the cumulative incidence of CIN2+ 48 months after screening. To address the concern that some CIN2+ lesions would be missed in the transition from cytology to HPV DNA-based test at extended intervals, the authors examined which precancers would have been missed by HPV DNA-based or cytology-based screening at trial exit. In the cytology arm, 25/8,296 women screened would have CIN2+ missed lesions (0.301%) compared to 3/8078 (0.037%) in the HPV DNA-based arm. The study concludes that HPV DNA-based testing at extended intervals will miss fewer precancers than cytology and enables better safety for subsequent CIN2+ detection in screening programs. [2]

Women's cancer risk Identification—PCR test for Endometrial Cancer (WID-qEC test) is a three-marker DNA methylation-based test (ZSCAN12 and GYPCin genes) and was developed for endometrial cancer triage. By assessing DNA methylation in 1,288 cervicovaginal specimens, the authors developed and validated the test in different settings (symptomatic, asymptomatic, and high-risk Lynch

syndrome) and with different collection methods (cervical smear, self collection, and vaginal swab). In symptomatic patients, the WID-qEC test revealed sensitivities of 97.2% (95% CI: 90.2-99.7), 90.1% (83.6-94.6), and 100% (63.1-100) and specificities of 75.8% (63.6-85.5), 86.7% (79.3-92.2), and 89.1% (77.8-95.9), regarding the three collection methods, respectively. The WID-qEC was able to identify endometrial cancer cases up to three years of advance, with higher sensibility (90.9% [95% CI: 70.8–98.9]) in samples predating diagnosis by up to one year. The WID-gEC offered similar sensitivity but significantly increased specificity compared with transvaginal ultrasound and, therefore, the possibility of fewer specialist referrals and invasive tests. The main study limitation is its small sample size in premenopausal women and non-white ethnicities. [3]

No	Title	Authors	Journal	Link to abstract
1	Performance of HPV E6/E7 mRNA assay as primary screening test: Results from the NTCC2 trial	Rossi et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih. gov/35579975/
2	Human papillomavirus-based screening at extended intervals missed fewer cervi- cal precancers than cytology in the HPV For Cervical Cancer (HPV FOCAL) trial	Gottschlich et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih. gov/35460070/
3	A Simple Cervicovaginal Epigenetic Test for Screening and Rapid Triage of Women With Suspected Endometrial Cancer: Validation in Several Cohort and Case/Control Sets	Herzog et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/36001862/



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

Joanna Kacperczyk-Bartnik

Diagnosis

A prospective multicentre study by Shoenen et al. aimed to evaluate the centralised expert pathology assessment of gestational trophoblastic diseases. Samples from 867 patients collected between July 2012 and December 2020 were analysed. Referral pathologist diagnosis differed from the initial diagnosis in 35% of cases. Complete moles were confirmed in about 95% of files, but incomplete mole diagnosis was accurate in only 61% of cases. In addition, 42% of gestational trophoblastic neoplasia diagnoses required alteration, which included downstaging (65%), upstaging (33%), or was irrelevant for the treatment in 2% of cases. This prospective, multicentre registry study had a strong design but the voluntary basis of the registry could lead to an unknown number of missed cases. [1].

Treatment

A randomised control trial by Ji et al. compared the outcome of patients with primary gestational trophoblastic neoplasia treated with floxuridine, actinomycin D, etoposide, and vincristine (FAEV) regimen (n = 46) or etoposide, methotrexate, actinomycin D / cyclophosphamide, vincristine (EMA/CO) regimen (n = 43). The authors reported comparable efficacy and toxicity results in both groups. One of the study's limitations could be its sample size. [2]

Fertility

In a systematic review and meta-analysis, Madi et al. analysed perinatal outcomes of the first pregnancy after chemotherapy treatment due to gestational trophoblastic neoplasia. Comparison to the general population showed the similar occurrences of spontaneous abortion, foetal malformation, prematurity, and stillbirth. Chemotherapy did not increase the risk of unfavourable outcomes, except for the higher prevalence of spontaneous abortion in pregnancies occurring sooner than six months after treatment. While it is valuable to look at a global picture of the topic by including studies from Europe, Asia, South America, and North America, the inclusion of retrospective observational and cross-sectional studies is associated with a high risk of bias. [3]

No	Title	Authors	Journal	Link to abstract
1	Importance of pathological review of gestational trophoblastic diseases: results of the Belgian Gestational Trophoblastic Diseases Registry	Shoenen S et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35487585/
2	Efficacies of FAEV and EMA/CO regimens as primary treatment for gestational trophoblastic neoplasia	Ji M et al.	Br J Cancer	https://pubmed.ncbi.nlm.nih. gov/35459802 /
3	Perinatal outcomes of first pregnancy after chemotherapy for gestational trophoblastic neopla- sia: a systematic review of observational studies and meta-analysis	Madi JM et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih. gov/34634262/



Cancer in pregnancy

Michael J. Halaska

Amant et al. evaluated the outcome of breast cancer patients treated with chemotherapy during pregnancy compared to non-pregnant patients. Using the international registries Network of Cancer, Infertility and Pregnancy (INCIP) and the German Breast Group (GBG) they identified 662 pregnant patients and matched them with 2,081 non-pregnant patients. With a median follow-up of 66 months, both disease-free survival (DFS) and overall survival (OS) were similar (DFS: HR 1.02, 95% CI: 0.82-1.27, p = 0.83; OS: HR 1.08, 95% CI: 0.81–1.45, p = 0.59). A strength of the study was its large set of pregnant patients. Drawbacks to the study included that there were statistically significant differences in both groups in favour of non-pregnant patients (lower stage, lower grade, less triple negative patients), which could influence the survival outcomes. [1].

Enomoto et al. evaluated 203 cases of cervical cancer patients diagnosed during pregnancy, 163 diagnosed after the 22nd week of pregnancy and 40 patients before. A high rate of termination and

iatrogenic premature delivery was found. A comparison of different treatment modalities (follow-up, surgery, and chemotherapy) did not reveal any survival differences in IB1 tumours. A strength of the study was its large data set while weaknesses were that the old FIGO classification 2008 was used, and very little data on the tumour size, type of surgery, or chemotherapy were available. [2]

A German data set of three cases of vulvar cancer treated during pregnancy was described by Winarno et al. Surgery, including SLN was used during pregnancy. While this study brings three new cases to the only 36 cases reported so far, no conclusions could be made. [3]

Khazzaka et al. performed a literature search for placental and foetal metastasis in patients with cancer diagnosed during pregnancy. They found 76 cases, of which the most frequent were melanoma and lung cancer. Both findings indicated a poor prognosis (maternal survival of 1 (95% CI: 0.7–1.3) months post-partum and one-year infant survival

rate of 51.1%). The most frequent sites of lesions in neonates were lungs, scalp, and liver. While this is a valuable update to the literature on a rare condition with survival analysis, a weakness of the study was that a different level of detail was available from case reports. [4]

The National Health Registry of Denmark was used by Greiber et al. to identify mortality and morbidity in newborns exposed to maternal cancer in utero and, moreover, a subgroup of infants prenatally exposed to chemotherapy in utero. Six hundred ninety infants exposed to maternal cancer in utero were identified without significant findings (similar mortality, congenital malformations, psychiatric disorders). A subgroup of 42 infants exposed to chemotherapy from 2002–2018 also did not exhibit any increased morbidity. The large registry-based data set was a strength of the study, though fewer details are available for subgroup analysis in registry-based papers. [5]

No	Title	Authors	Journal	Link to abstract
1	Outcome of breast cancer patients treated with chemotherapy during pregnan- cy compared with non-pregnant controls	Amant F et al.	Eur J Cancer	https://pubmed.ncbi.nlm.nih. gov/35594612/
2	Trends in pregnancy-associated cervical cancer in Japan between 2012 and 2017: a multicenter survey	Enomoto S et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih. gov/35804845/
3	Vulvar cancer during pregnancy and/or breastfeeding: a report of five cases from a single center study at the University Hospital of Düsseldorf	Winarno AS et al.	BMC Pregnancy Childbirth	https://pubmed.ncbi.nlm.nih. gov/35291960/
4	Systematic review of fetal and placental metastases among pregnant patients with cancer	Khazzaka A et al.	Cancer Treat Rev	https://pubmed.ncbi.nlm.nih. gov/35182890/
5	Long-Term Morbidity and Mortality in Children After in Utero Exposure to Maternal Cancer	Greiber IK et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/35797496/



Hereditary gynaecological cancer

Ariel Glickman

Kim et al. performed a prospective international cohort study (85 centres, 17 countries) including 4,340 women who carried a BRCA 1 or BRCA 2 mutation. They followed them up for an average of 8.1 years (range, 0.1-23.6). The patients self-reported height and weight at age 18 and updated this information biennially from inclusion. They detected 121 incident cases of ovarian cancer (OC). The authors found that women that gained more than 20kg of weight after age 18 showed a two-fold increased risk of ovarian cancer, compared with those who maintained a stable weight (HR 2.00, 95% CI: 1.13-3.54, p = 0.02). Moreover, BRCA1 mutation carriers with a BMI of 26.5kg/m² or greater presented an increased risk of OC, compared with those with a BMI less than 20.8kg/m² (Q4 vs Q1 HR 2.13, 95% CI: 1.04–4.36, p = 0.04). This study highlights the importance of a healthy body weight in women at high risk for OC. [1]

In 2021, The European Society of Medical Oncology published a consensus on the use of BRCA and homologous recombination repair (HRR) deficiency testing for recently diagnosed patients with advanced OC. Beyond implications for other family members, this is clinically relevant because half of the women with high-grade serous ovarian carcinomas show HRR deficiency, which makes them candidates for poly-ADP ribose polymerase inhibitors (PARPi) therapy, implying a better prognosis. A modified Delphi process was used to establish consensus statements based on a systematic literature search. Vergote et al. stated that all patients with OC should be offered germline and/or tumour BRCA1/2 testing at the time of primary diagnosis or recurrence. Tumour testing should be carried out in all invasive epithelial cancer patients, particularly in those with high-grade non-mucinous disease. Besides, they agreed that HRR deficiency testing should be carried out before the end of first-line chemotherapy, if possible, together with BRCA testing. According to their revision, the experts found that there is not enough evidence to endorse testing for other HRR mutations besides BRCA1/2, although it could be beneficial for clinical research. Regarding mutations in mismatch repair (MMR) genes, germline testing is advised in patients with a family history suggesting Lynch syndrome. This consensus provides a strong clinical tool to claim the universalisation of genetic testing among women diagnosed with OC in Europe. [2]

Bokkers et al. evaluated the impact of implementing mainstream genetic testing (i.e., offered by non-

genetic healthcare professionals such as gynaecologic oncologists and nurse specialists) for newly diagnosed epithelial OC patients in the Netherlands. This study was part of a multicentre, prospective, observational study on the acceptability and feasibility of the implementation of mainstream genetic testing pathway for patients with OC. Between 03/2016 and 09/2017, before the implementation of the mainstream genetic testing, they had identified 183 patients newly diagnosed with OC: 102 (56%) were offered genetic testing within six months after diagnosis. After the implementation of the mainstream strategy, between 04/2018 and 12/2019 they found that 70% of newly diagnosed women (114 of 162) were tested. The genetics-related healthcare costs after implementing mainstream testing were 31% lower than before (€3,511.29 versus €2,418.41 per patient). The authors concluded that mainstream genetic testing should be routine care for patients with epithelial OC. [3]

No	Title	Authors	Journal	Link to abstract
1	Weight fain and the risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers	Kim SJ et al.	Cancer Epidemiol Biomarkers Prev	https://pubmed.ncbi.nlm.nih. gov/34426412/
2	European experts consensus: BRCA/homologous recombination deficiency testing in first-line ovarian cancer	Vergote I et al.	Ann Oncol	https://pubmed.ncbi.nlm.nih. gov/34861371/
3	Mainstream germline genetic testing for patients with epithelial ovarian cancer leads to higher testing rates and a reduction in genetics-related healthcare costs from a healthcare payer perspective	Bokkers K et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/36031452/



Epidemiology in Gynaecological Oncology: systematic reviews and meta-analyses

Catherine O'Gorman

Uterine cancer

The prognostic implications of tumour size in endometrial cancer were investigated by Jin et al through a meta-analysis of the relevant literature. The authors report tumour size of >20mm to be associated with increased risk of myometrial invasion of >50% (OR 5.59), lymphovascular invasion (OR 3.35), and lymph node metastases (OR 4.11), reduced overall survival (HR 2.13). In patients with FIGO stage I-II, tumour size>20mm was associated with increased risk of lymph node metastases (OR 3.69), recurrence (OR 3.15). [1]

In a systematic review and meta-analysis, Xiao et al demonstrated that patients with early-stage EEC who had microsatellite instability were shown to have reduced overall survival (OS) (HR 1.47) and disease-free survival (HR 4.17). Understanding of these prognostic factors may aid in prognostication and adjuvant therapy planning. [2]

Ovarian cancer

The prevalence of mismatch repair deficiency (MMRd), and therefore potential benefit in targeted immunotherapy, in ovarian cancers was investigated through systematic review and meta-analysis of the literature by Atwal et al. The authors report a significant minority of ovarian carcinomas to be MMR deficient at 16%. MMR deficiency is seen in all histopathological subtypes, but commonly associated with endometrioid carcinomas. A germline pathological MMR variant was noted in 47% of cases of MMRd ovarian carcinomas. [3]

Vulvar cancer

Perineural invasion as a prognostic indicator in vulvar cancer was shown to be valuable by both Pergialiotis et al and Santoro et al. The meta-analysis by Pergialiotis et al showed that perineural invasion was a prognostic indicator for both recurrence and death (HR 1.28 progression free survival, HR 2.40 for overall survival). The systematic review and meta-analysis by Santoro et al support these findings, with perineural invasion associated with reduced progression free survival (HR 1.76) and overall survival (HR 2.69). [4, 5]

No	Title	Authors	Journal	Link to abstract
1	Association of tumor size with myometrial invasion, lymphovascular space invasion, lymph node metastasis, and recurrence in endometrial cancer: A Meta-Analysis of 40 studies with 53,276 patients	Jin X et al.	Front Oncol	https://pubmed.ncbi.nlm.nih. gov/35719999/
2	Microsatellite instability as a marker of prognosis: a systematic review and meta-analysis of endometrioid endometrial cancer survival data	Xiao JP et al.	Arch Gynecol Obstet	https://pubmed.ncbi.nlm.nih. gov/35665848/
3	The prevalence of mismatch repair deficiency in ovarian cancer: A systematic review and meta-analysis	Atwal A et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih. gov/35792468/
4	Perineural invasion as a predictive biomarker of groin metastases and survival outcomes in vulvar cancer: A meta-analysis	Pergialiotis V et al.	Cancer Invest	https://pubmed.ncbi.nlm.nih. gov/35467488/
5	Prognostic role of perineural invasion in vulvar squamous cell carcinoma: A systematic review and meta-analysis	Santoro A et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih. gov/35811178/



Pathology of gynaecological cancers

Nicolas Samartzis and Dimitrios Rafail Kalaitzopoulos

Vulvar cancer

Matsuo et al. validated the revised vulvar cancer staging system from 2021. Altogether they included 889 women with stage III–IV vulvar cancer in the analysis. The stage changed in 229 (25.8%) patients: it upstaged in 17.7% and downstaged in 8.1%. Women with stage IVA according to the new classification had a significantly worse survival rate. Comparable survival rates were found in patients with IIIA and IIIB stage and with IVA and IVB stage. One of the study limitations was lack of preoperative information, i.e., nodal involvement in radiology results. [1]

Cervical cancer

An analysis of the Danish Gynaecological Cancer Database, including the restaging of 4,461 cervical cancer cases from 2009 FIGO to 2018 FIGO, showed that FIGO 2018 classification provides an improved discrimination for stage I and IV, while grouping all patients with pelvic or paraaortic lymph nodes as IIIc creates group with heterogeneous survival rates. The study limitation was there is no central review of the pathological results. [2]

Endometrial cancer

Siegenthaler et al. examined the recurrence pattern of 594 molecularly classified endometrial carcinomas. The authors identified 101 patients with recurrence, including 2 POLE-mutated, 33 mismatch repair deficient, 30 abnormal p53, and 36 no specific molecular profile. In total 30.7% had locoregional, 29.7% presented abdominal, and 39.6% developed distant recurrence. MMRd tumours had more locoregional recurrence cases (n = 15/33), and p53abn cancers were associated with higher occurrence of abdominal recurrence (n = 13/30). The retrospective design was the limitation of this study. [3]

Ovarian cancer

Borghese et al. retrospectively studied 61 patients with primary fallopian tube carcinoma at three gynaecological centres. The authors demonstrated that 96.7% were high-grade serous and that 82.4% of small tumours of up to 15mm had FIGO stage of IIA or greater. At least 40% of the patients with stage IVB survived more than 36 months. The five-year overall survival rate was 75.5%. The main limitation of this study was the sample size. [4] A research group systematically investigated the 86 most frequently amplified super-enhancer genes in ovarian cancer using the CRISPR technique. The authors found two dominant members (SE60 and SE14) that promote proliferation and metastasis. Using chromatin interaction maps, their target gene could be explored, providing further insights for the identification of new therapeutical agents and biomarkers. [5]

Diverse

Lewis et al. published a retrospective study about the association of endosalpingiosis, the existence of ectopic epithelium of the fallopian tube, with the occurrence of gynaecologic malignancies. About 40% of women with endosalpingiosis had a concurrent malignancy and this group had also a lower overall survival in comparison to women with endometriosis-associated malignancy. The study's limitations resulted from its retrospective design. [6]

No	Title	Authors	Journal	Link to abstract
1	Validation of the 2021 FIGO staging schema for advanced vulvar cancer	Matsuo K et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/34996835/
2	Prognostic value of the 2018 FIGO staging system for cervical cancer	Mohamud A et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35346512/
3	Time to first recurrence, pattern of recurrence, and survival after recurrence in endometrial cancer according to the molecular classification	Siegenthaler F et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35277281/
4	Retrospective study of histopathological and prognostic characteristics of primary fallopian tube carcinomas: twenty-year experience (SOCRATE)	Borghese M et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35868656/
5	A multi-omic dissection of super-enhancer driven oncogenic gene expression programs in ovarian cancer	Kelly MR et al.	Nat Commun	https://pubmed.ncbi.nlm.nih. gov/35869079/
6	The association of endosalpingiosis with gynecologic malignancy	Lewis GK et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35909004/



Treatment of pre-invasive gynaecological malignancies

Elko Gliozheni

Feng et al. conducted a systematic review and meta-analysis evaluating the relationship between positive margin and residual or recurrence after excision of cervical intraepithelial neoplasia (CIN). The analysis included 11 studies enrolling patients after CIN resection with or without residual disease or recurrence. The differences in exposure factors between the two groups were compared. Alternatively, the patients were grouped by exposure factor, and the differences in residual and recurrence rates under different grouping conditions were compared. The observed outcome was the presence of postoperative residual disease or recurrence. Altogether 774 patients with positive margins and 2,291 patients with negative margins were included. The rate of residual or recurrence after excision of CIN was significantly higher in patients with positive margins (OR = 3.99) and in patients with positive endocervical margins (OR = 2.59) than in patients with negative margins and negative endocervical margins, respectively. There was no significant difference between positive and negative ectocervical margins. Thus, they concluded that positive endocervical margins, but not external cervical

margins, are risk factors for residual/recurrence of CIN after resection. [1]

This is a well-designed meta-analysis, representing level I evidence leading to a clinically important observation. It is worth mentioning that this study included eight low- and three high-risk bias studies.

Kim et al. performed a retrospective study aiming to determine whether endocervical glandular involvement (GI) affects the clinical prognosis of patients with CIN 3 who underwent the loop electrosurgical excision procedure (LEEP). They included 250 patients of whom 58.5% were GI-negative, and 41.5% were GI-positive. Margin involvement was significantly lower in the GI-negative group compared to the GI-positive group (45.4 vs 58.7%). Additional surgical procedures such as repeat conisation or hysterectomy were significantly more performed in GI-positive patients (40.9% vs 23.1%). They found that the mean depth of the GI was significantly greater in patients that had GI confirmed via cervical biopsy before conisation than patients that had GI confirmed via conisation (10.9mm vs 7.6mm). Also, the margins were more frequently involved in the

patients who had GI confirmed via conisation. No significant difference was found in the recurrence rates of CIN between the GI-negative and GI-positive groups. These findings led them to conclude that despite no significant difference in residual disease and CIN recurrence between the groups, additional surgical treatments were more frequently performed in GI-positive patients. Therefore, repeat surgery based on GI positivity should be carefully considered to avoid overtreatment and surgical complications. [2]

The limitation of the study is the retrospective single centre study design.

No	Title	Authors	Journal	Link to abstract
1	Relationship between positive margin and residual/recurrence after excision of cervical intraepithelial neoplasia: a systematic review and meta-analysis	Feng H et al.	Transl Cancer Res	https://www.ncbi.nlm.nih.gov/pmc/ articles/PMC9273651/
2	Clinical outcomes associated with endocervical glandular involvement in patients with cervical intraepithelial neoplasia III	Kim N et al.	J Clin Med	https://www.ncbi.nlm.nih.gov/pmc/ articles/PMC9181062/



Treatment of elderly patients with gynaecological cancers

Alex Mutombo

Zhao et al. studied the prognosis of ovarian cancer after cytoreductive surgery and adjuvant chemotherapy in 324 patients aged 60 years and over according to chronological age and treatment characteristics. Their results indicated that patient age was not a detrimental factor and thereafter elderly patients could be treated by surgery and adjuvant chemotherapy. [1]

Park et al. examined non-cancer factors associated with adjuvant radiation therapy (RT) receipt in 25,654 women aged \geq 66 years who underwent a hysterectomy for early-stage EC between 2004– 2017. The data were retrieved from the Surveillance Epidemiology and End Results cancer registry program. Comparisons were made between patients treated in the northeastern United States and those treated in other regions of the USA. Adjuvant RT was less administered in other regions (PR 0.75, 95% CI: 0.71–0.79). Adjuvant RT was more administered to patients that underwent lymph node assessment(PR 1.43, 95% CI: 1.34–1.51). [2]

Matanes et al. retrospectively assessed the surgical and oncological outcomes in 278 women aged 65-years that underwent staging with sentinel lymph node (SLN) biopsy and pelvic lymphadenectomy for intermediate to high-risk endometrial cancer. The patients were divided into three groups: the SLN sampling alone group, the SLN sampling with lymphadenectomy, and the lymphadenectomy alone group. The authors observed a shorter operative time in the first group (199 min, range 75-393) compared with the other groups (231 min, range 125-403 and 229 min, range 151-440, respectively) (p < 0.001). There was no significant difference in two-year overall survival and progression-free survival between the three groups (p = 0.45, p =0.51, respectively). [3]

In a cohort study of 152 women aged 60+ with endometrial cancer (EC) and 111 with ovarian cancer (OC), Anic et al. determined the impact of perioperative red blood cell transfusion, anemia of cancer, and frailty status on progression-free survival (PFS) and overall survival (OS). The five- year progression-free survival and overall survival were significantly shorter among women with EC who received a transfusion (79.8% vs 26.0%, p < 0.001 and 82.6% vs 25.7%, p < 0.001, respectively). However, the latter did not hamper the prognosis in women with OC for which the preoperative global health status was determined to be the most significant factor. [4]

No	Title	Authors	Journal	Link to abstract
1	Differences in treatment modalities and prognosis of elderly patients with ovarian cancer: A two-center propensity score-matched study	Zhao Y et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih. gov/35954319/
2	Patient characteristics and health system factors associated with adjuvant radiation therapy receipt in older women with early-stage endometrial cancer	Park J et al.	J Geriatr Oncol	https://pubmed.ncbi.nlm.nih. gov/36088216/
3	Surgical and oncological outcomes of sentinel lymph node sampling in elderly patients with intermediate to high-risk endometrial carcinoma	Matanes E et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35680137/
4	Impact of perioperative red blood cell transfusion, anemia of cancer and global health status on the prognosis of elderly patients with endometrial and ovarian cancer	Anic K et al.	Front Oncol	https://pubmed.ncbi.nlm.nih. gov/36185177/



Fertility-sparing treatment in gynaecological malignancies

Charalampos Theofanakis

Endometrial cancer

A systematic review by Ronsini et al. assessed the possibility of conservative treatment for patients with grade 2, stage IA endometrial cancer. The study included 103 patients who were treated with a combination of LNG-IUD + megestrol acetate (MA) or medroxyprogesterone (MPA), gonadotrophin-releasing hormone (GnRH) + MPA/MA, hysteroscopic resectoscope (HR), and dilation and curettage (D&C). Results showed evidence of 70% to 85% complete response after second-round therapy prolongation to 12 months. The authors concluded that fertility-sparing could be employed for patients with early-stage disease. [1] Lago et al., conducted a multicentre, observational, retrospective study that showed that the levonorgestrel intrauterine device (LNG-IUD) was the most common fertility-sparing treatment (53.4%), followed by megestrol acetate (20.5%), and medroxyprogesterone acetate (16.4%). Four patients relapsed after surgery (5.5%), which was associated with final FIGO stage III (p = 0.036), myometrial invasion > 50% (p = 0.018) and final tumour grade 2-3 (p = 0.018). Reproductive techniques were used in 78.4% of cases. The authors stated that LNG-IUD was associated with higher response rates and pregnancy could be achieved with assisted reproduction. [2]

Cervical cancer

Viveros-Carreño et al. assessed the oncologic and fertility outcomes of patients with FIGO stage IB3 cervical cancer, after neoadjuvant chemotherapy

and conisation, simple or radical trachelectomy. This systematic review included 40 patients and a complete response occurred in 56% of patients. Of six patients who tried to conceive, four (67%) achieved at least one pregnancy and three of the five pregnancies (60%) were pre-term deliveries. The authors concluded that this technique, in patients with tumours > 4cm, should only be used as an experimental intervention. [3]

Gil-Ibañez et al. conducted a retrospective study to assess the importance of tumour size on the oncological outcomes of fertility-sparing surgery. The study included 111 patients: 82 (73.9%) with tumours up to 2cm and 29 (26.1%) with tumours 2–4cm. The three-year progression-free survival (PFS) was 95.7% (95% CI: 87.3–98.6) and 76.9% (95% CI: 55.2–89.0, p = 0.011). The authors stated that tumour size \geq 2cm is the main negative prognostic factor in patients who underwent FSS in Spain. [4]

Ovarian cancer

Hou et al. conducted a SEER database study to evaluate the risk and prognostic factors in women with ovarian cancer who have had fertility-sparing surgery. In FIGO stage I EOC, the prognosis in patients with stage IA/IB-grade 3 or stage IC was worse than stage IA/IB-grade 1, or stage IA/ IB-grade 2. However, chemotherapy improved the survival of patients with stage IA/IB-grade 3 (5-year CSS 78.1% vs 94.6%, p = 0.024) or stage IC (5year CSS 75.1% vs 86.7%, p = 0.170). This study

provided population-based estimates of risk factors and prognoses in patients with OC and with FSS. [5] Swift et al. conducted a retrospective cohort study to evaluate oncologic outcomes in patients with stage I endometrioid ovarian cancer, treated with fertility-sparing compared with conventional surgery and to assess reproductive outcomes. The study included 31 patients, 11 of whom underwent fertility-sparing surgery, and 20 conventional surgery. The five-year recurrence-free survival was 90.9% for the fertility-sparing group and 84.0% for the conventional surgery group (p = 0.65). The 5-year overall survival was 100% for patients in the fertility-sparing group and 92.6% for patients treated with conventional surgery (p = 0.49). Of the five patients who conceived, there were three spontaneous abortions and five live births. The authors concluded that the conservative approach is safe for young women with stage I, low-grade endometrioid ovarian cancer. [6]

No	Title	Authors	Journal	Link to abstract
1	Oncological outcomes in fertility-sparing treatment in stage IA-G2 endometrial cancer	Ronsini C et al.	Front Oncol	https://pubmed.ncbi.nlm.nih. gov/36185260/
2	Fertility sparing treatment in patients with endometrial cancer (FERT-ENC): a multicentric retrospective study from the Spanish Investigational Network Gynecologic Oncology Group (SPAIN-GOG)	Lago V et al.	Arch Gynecol Obstet	https://pubmed.ncbi.nlm.nih. gov/35122158/
3	Fertility-sparing surgery after neo-adjuvant chemotherapy in women with cervical cancer larger than 4 cm: a systematic review	Viveros-Carreño D et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35210296/
4	Tumor Size and Oncological Outcomes in Patients with Early Cervical Cancer Treated by Fertility Preservation Surgery: A Multicenter Retrospective Cohort Study	Gil-Ibañez B et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih. gov/35565238/
5	Women with ovarian cancer and with fertility preservation: A survival analysis using the Surveillance, Epidemiology, and End Results Database and construction of nomograms to predict cancer-specific survival	Hou YM et al.	Front Oncol	https://pubmed.ncbi.nlm.nih. gov/35480098/
6	Oncologic and pregnancy outcomes after fertility-sparing surgery for stage I, low-grade endometrioid ovarian cancer	Swift BE et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35768155/



Prevention and management of surgical complications

Anastasia Prodromidou

In a retrospective study, Wang et al. evaluated the effect of preoperative mechanical and oral antibiotic bowel preparation (MOABP) on postoperative complications in patients who had bowel resection as part of cytoreductive surgery (CRS) due to ovarian cancer (OC). Adjusted and unadjusted logistic regression analysis revealed that patients in the MOABP group (n = 81/215) presented significantly decreased odds for deep/organ infections and readmissions at 30 days, compared to those who did not receive preoperative bowel preparation (n = 134/2150). Nevertheless, patients from the MOABP group had elevated odds of suffering from cardiac and gastrointestinal complications as well as intensive care unit admission. No difference was detected in reoperation rates, \geq 3 grade complications, superficial surgical site infections, venous thromboembolism, and pulmonary complications among the two groups. [1]

A study by Huepenbecker at al. supports early catheter removal in patients who underwent radical hysterectomy (open or minimally invasive) for early-stage cervical cancer (stage IA1–IIA). More specifically, patients were divided into three groups: group 1 included patients that had urinary catheter removal 1–5 days postoperatively (n = 29/234), in

group 2 (n = 141/234) catheter was removed at 6–10 days, while in group 3 (n = 64/234) the catheter was removed 11–15 days after surgery. Despite the fact that no difference was detected in voiding dysfunction rates among the three groups, the group with the earlier removal (group 1) presented a significantly shorter time to urinary functional recovery (4 days vs 8 days vs 13 days, p < 0.01). No difference was observed in urinary tract infections, length of hospital stay, or readmission rates at 60 days for genitourinary complications postoperatively. [2]

Kengsakul et al. performed a prospective study that assessed the risk factors for suffering complications grade \geq Illa according to the Clavien-Dindo classification (CDC) in 300 patients who underwent CRS due to advanced OC. Multivariate analysis showed increased age (p = 0.0036), cardiovascular co-morbidities (p < 0.001), diaphragmatic surgery (p < 0.001), intraoperative urinary tract (p = 0.017) and upper abdominal visceral injury (p = 0.012) were all independent factors associated with increased risk for CDC complications grade \geq Illa. Similarly, occurrence of a grade \geq Illa complication was significantly associated with an increased risk of delaying chemotherapy initiation for > 42 days after surgery. [3] Yu et al. proposed a protocol regarding the use of goal-directed intraoperative fluids in patients who had major surgery for gynecologic oncology indications. In particular, the study group consisted of patients that received intraoperative fluids and vasoactive agents based on the monitoring of stroke volume and mean arterial pressure. The analysis of the outcomes revealed significantly reduced postoperative complications and surgical site infections in the study group compared to standard intraoperative fluid management (p = 0.032 and p = 0.037, respectively). [4]

No	Title	Authors	Journal	Link to abstract
1	Mechanical and oral antibiotic bowel preparation in ovarian cancer debulking: Are we lowering or just trading surgical complications?	Wang et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35589434/
2	Impact of timing of urinary catheter removal on voiding dysfunction after radical hysterectomy for early cervical cancer	Huepenbecker et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35803608/
3	Factors Predicting 30-Day Grade Illa–V Clavien–Dindo Classification Compli- cations and Delayed Chemotherapy Initiation after Cytoreductive Surgery for Advanced-Stage Ovarian Cancer: A Prospective Cohort Study	Kengsakul et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih. gov/36077721/
4	Goal-Directed Intraoperative Fluid Therapy Benefits Patients Undergoing Major Gynecologic Oncology Surgery: A Controlled Before-and-After Study	Yu et al.	Front Oncol	https://pubmed.ncbi.nlm.nih. gov/35463383/



Nutrition and perioperative care

Begoña Díaz de la Noval

Mah et al. analysed the usefulness of the modified Frailty Index-5 (mFI-5) in gynaecologic oncology cancer patients over the age of 70 undergoing surgery (by laparotomy). Two-hundred and fifty-nine patients were included; 20.5% were categorised as frail. Frailty, as assessed with the mFI-5, predicted postoperative morbidity (30-day Clavien-Dindo grade III-V complications, OR 24.49, 95% CI: 9.72-70.67, p < 0.0001), and non-completion of chemotherapy (OR 8.42, 95% CI: 2.46–32.79, p = 0.001), independently of age and surgical complexity. The logistic regression model supported a strong predictive ability of the mFI-5: 0.92 (95% CI: 0.86-0.97, p < 0.0001) for Clavien III–V complications, and 0.87 for non-completion of chemotherapy (95% CI: 0.8-0.95, p = 0.02). The heterogeneity of tools to assess frailty and a small single-institution cohort are considered limitations. Although mFI-5 has validity in clinical practice, it may not determine which underlying factors should be targeted to improve outcomes. [1]

Sasamoto et al. analysed the association between the inflammatory component of the diet and the impact on the survival of patients with ovarian cancer. The 1,003 patients included were from the US prospective cohort Nurses' Health Study (NHS) and NHS II. A high postdiagnosis empirical dietary inflammatory pattern (EDIP) was associated with an increased risk of ovarian cancer-specific mortality and all-cause mortality; regardless of the type of diet before diagnosis. The study's external validation is limited by a closed sample group without the possibility of obtaining data by histology given the low statistical power for stratified analysis. [2]

The PROFAST trial (NCT02172638) group published the cost analysis of the enhanced recovery after surgery protocol (ERAS) for high-complexity advanced ovarian cancer (AOC) surgery. The application of the ERAS protocol implied an economic benefit compared to conventional management (from €78 to €2709 per patient), being even higher considering the low readmission rate. Limitations are mentioned due to the number of patients included (n = 99), which, even though it is a study from a single centre, includes highly complex oncological surgery with improved conventional management. [3]

Díaz-Feijoo et al. presented the study protocol of the SOPHIE trial (NCT04862325). A randomised case-control multicentre trial on applying for a multimodal prehabilitation program in patients with AOC undergoing cytoreductive surgery. They hypothesised that trimodal prehabilitation programs (supervised exercise training, nutritional counselling, and psychological support) might reduce post-operative complications and improve first-month recovery better than the standard of care (ERAS). A sample size of 146 patients has been estimated for recruitment from January 2021 to December 2024. [4]

No	Title	Authors	Journal	Link to abstract
1	The five-factor modified frailty index predicts adverse postoperative and chemotherapy outcomes in gynecologic oncology	Mah SJ et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35606168/
2	Pre-diagnosis and post-diagnosis dietary patterns and survival in women with ovarian cancer	Sasamoto N et al.	Br J Cancer	https://pubmed.ncbi.nlm.nih. gov/35760897/
3	Cost analysis of the enhanced recovery after surgery protocol applied in advanced ovarian cancer- A secondary outcome of the PROFAST trial	Sánchez-Iglesias JL et al.	Eur J Surg Oncol	https://pubmed.ncbi.nlm.nih. gov/35922279/
4	A multimodal prehabilitation program for the reduction of post-operative com- plications after surgery in advanced ovarian cancer under an ERAS pathway	Díaz-Feijoo B et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35793862/



Follow-up after gynaecological malignancies

Sunaina Wadhwa

Zola et al. performed a randomised controlled trial, the TOTEM study, to determine if an intense (INT) versus a minimalist (MIN) follow-up strategy increases overall survival (OS) in patients with endometrial cancer (EC). It was conducted in 42 Italian and French hospitals in patients who had a surgical resection for EC and were in remission. Between November 2008 and July 2018, 1,871 patients were randomly assigned (1:1), and 1,847 (98.7%) were included in the final analysis (60% low risk). The five-year OS was 90.6% in the INT and 91.9% in the MIN arms after a median follow-up of 69 months (HR 1.13, 95% CI: 0.86-1.50, p = 0.380). No differences in OS were found in subgroup analyses that considered age, cancer treatment, the risk of relapse, or the degree of adherence of the centre to the scheduled follow-up. In the INT arm, the likelihood of detecting a relapse was higher (HR 1.17; 95% CI: 0.92-1.48; p = 0.194). An INT follow-up in patients treated due to EC does not influence

OS, even if there is high risk. The evidence that is currently available indicates that the MIN regimens employed in this trial do not require routine addition of vaginal cytology, laboratory, or imaging. The advantages of the study were its multicentre design and large sample size, with extended follow-up and enrolled patients that represented the real-life population. However, weaknesses were that the accrual period had to be extended because the contributions of the study's participating centres were inconsistent and were delayed. A certain amount of underrepresentation of non-endometroid histology over these ten years and misclassification of the relapse risk cannot be completely ruled out, particularly in the case of low-risk patients who have mutated p53. But this risk factor was unknown when the study was first initiated. [1]

A retrospective cohort study by de Assiss et al. compared adherence to follow-up after complete mole treatment using telemonitoring (92 women) with

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standard in-person ambulatory visits (206 women). The authors did not observe differences regarding the possibility of hormonal levels inspection or loss to follow-up depending on appointment type. An increase in complete follow-up was achieved in the case of shortening the follow-up period to 90 days after the first hCG level within the norm. While a strength of this study was its a novel objective in this disease type, the study was limited by a lack of analysis, including the distance between patients' residences and the centre. [2

No	Titla	Authore	lournal	Link to abstract
NU	Inte	Autions	Journal	
1	Effectiveness of intensive versus minimalist follow-up regimen on survival in patients with endometrial cancer (TOTEM study): a randomized, pragmatic, parallel Group, multicenter trial	Zola P et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/35858170/
2	Telemedicine in post-molar follow-up: is it a useful tool?	de Assis RT et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih. gov/35314462/



Quality of life in gynaecological cancers/Palliative care

Nadja Taumberger and Engin Çelik

Leung et al. investigated acute genitourinary and bowel toxicity as well as quality of life (QOL) in patients undergoing stereotactic hypofractionated adjuvant pelvic radiation due to uterine cancer. They conducted a phase I/II nonrandomised controlled, multicentre trial and enrolled patients with uterine cancer stages I through III after surgical treatment.

Acute toxic effects on bowel or urinary tract were assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) and QOL was assessed using validated questionnaires such as the EORTC QLQ-C30 and QLQ-EN24 scale. Sixty-one patients were enrolled with a median age of 66 years. Median follow-up was nine months. Treatment-related adverse events were well tolerated in the acute phase of treatment; symptoms increased during treatment but improved at follow-up. The results suggest that stereotactic hypofractionated radiation was well-tolerated in the acute phase of treatment. More randomised controlled trials comparing conventional fractionation to hypofractionated radiation are necessary to evaluate the safety and efficacy of this technique. [1]

Kim et.al assessed the health-related quality of life (HRQOL) in relation to hyperthermic intraperitoneal chemotherapy (HIPEC) in ovarian cancer patients following primary or interval cytoreductive surgery. They enrolled 184 patients in this single-blinded randomised controlled phase III trial and randomly assigned them to receive either cytoreductive surgery with or without HIPEC. QOL was assessed using validated questionnaires as a secondary endpoint at baseline and at predefined time-points after surgery up to 12 months after randomisation. No statistically significant difference was found between the two groups showing impairment of QOL when implementing HIPEC during primary or interval cytoreductive surgery. [2]

EMPOWER- Cervical 1/GOG-3016/ENGOT-cx9; R2810-ONC-1676; NCT03257267 was a randomised phase III, active-controlled trial which included a total of 608 patients with cervical cancer who had progression of disease after receiving first-line platinum-based chemotherapy. They were randomly assigned to either 350mg cemiplimab in a three-week interval or the investigator's choice of a single-agent chemotherapy. Primary end point was defined as overall survival (OS), but further secondary end points such as patient-reported QOL, progression-free survival, and safety were assessed. The results showed that treatment with cemiplimab resulted in a statistically significant benefit in QOL and physical functioning in this treatment group. Furthermore, results showed significantly improved overall survival. [3]

Donovan HS. et al. examined nurse-guided (nurse WRITE), self-directed (SD WRITE), and enhanced usual care (EUC) in enhancing symptom burden and quality of life. The WRITE symptoms website was developed at the University of Pittsburgh. In all, 497 women with recurrent or persisted ovarian, fallopian, or primary peritoneal cancer with 3+ symptoms filled baseline surveys. Participants were randomly assigned into three groups (Nurse-WRITE = 166, SD-WRITE = 166, EUC = 165). Participants were revaluated at eight and 12 weeks. Symptom burden and QOL improved over time significantly for all groups. Symptom controllability significantly increased in the Nurse-WRITE and SD-WRITE groups from baseline to eight weeks and baseline to 12 weeks, respectively, whereas the EUC group had no significant changes over time. [4]

No	Title	Authors	Journal	Link to abstract
1	Quality-of-life outcomes and toxic effects among patients with cancers of the uterus treated with stereotactic pelvic adjuvant radiation therapy the SPARTA-CUS phase 1/2 nonrandomized controlled trial	Leung et al.	JAMA Oncol	https://pubmed.ncbi.nlm.nih. gov/35420695/
2	Quality of life outcomes from the randomized trial of hyperthermic intraperito- neal chemotherapy following cytoreductive surgery for primary ovarian cancer (KOV-HIPEC-01)	Kim et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/35712968/
3	EMPOWER CERVICAL-1: Effects of cemiplimab versus chemotherapy on patient-reported quality of life, functioning and symptoms among women with recurrent cervical cancer	Oaknin et al.	Eur J Cancer	https://pubmed.ncbi.nlm.nih. gov/35922251/
4	Effects of the WRITE symptoms interventions on symptoms and quality of life among patients with recurrent ovarian cancers: An NRG Oncology/GOG study (GOG-0259)	Donovan HS et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih. gov/35130043/



COVID-19 and Gynaecological cancers

Jakub Dobroch

A single-centre study conducted by Ozturk et al. included 800 procedures analysed in 2020. The results presented the differences in types of the scheduled surgeries before and after pandemic-related restrictions were introduced. The most remarkable conclusion stated that the rate of benign post-operative histopathology reports significantly decreased after March 2020. That is coherent with widely acknowledged recommendations of medical societies considering suspension of elective surgeries. Average number of cancer surgeries performed through each month of 2020 remained the same without regard to COVID restrictions. The authors claim that with an application of appropriate safety precautions there was no necessity to reduce qualification for cancer surgery within the pandemic period. [1]

The COVIDSurg-Gynecologic Oncology collaboration group prepared a comprehensive summary of gynaecologic cancer surgical management worldwide during the pandemic. Out of 3,973 patients from 52 countries, about 20% experienced a modification of their treatment due to COVID-related issues. Cancellation of a surgery which would be routinely conducted in pre-pandemic period concerned 7.9% of analysed cases. A higher proportion of dismissed procedures was registered in low- and middle-income countries (23.0%) and areas with more rigorous lockdown (11.0%). Surgeries of patients with advanced (FIGO III or IV) disease were also more often cancelled (11.5%). In the ovarian cancer group, over 11% of patients experienced a significant delay (> 8 weeks from tumour board council) in scheduling a surgery. This was related to more frequent occurrence of adverse outcomes, including disease progression and death. Among all the patients who underwent a surgery, only 0.6% acquired a COVID-19 infection in postoperative period. Authors concluded that a delay in the treatment generally resulted in poorer outcomes. Establishing specific guidelines and safety strategies reduced the incidence of unfavourable events. [2]

Finally, a retrospective study conducted by Glaser et al. analysed 348 cases of gynaecologic cancer patients from seven centres in United States who contracted a SARS-COV-2 infection. Every fourth patient (n = 88) experienced a delay in the prescribed treatment, which was mainly a rescheduled chemotherapy (n = 53) and, less frequently, surgery (n = 32). Hospitalisation was necessary in 101 patients, which included 12 who needed respiratory support in an intensive care setting. The most commonly occurring symptoms were cough, dyspnoea, fever, and fatigue. Eighty-eight patients presented no symptoms of COVID-19. Patients with a poorer general condition, suffering from cardiac, pulmonary, or metabolic comorbidities were more likely to be admitted to the hospital due to an infection. Racial disparities were also recognized, as non-white race was considered a risk factor of admission. The authors highlighted the necessity of introduction of vaccinations in a gynaecologic cancer patient group. They concluded that this cohort had a particularly high risk of hospitalisation, delay of treatment, and death. [3]

No	Title	Authors	Journal	Link to abstract
1	Single centre experience of 800 gynaecologic oncology cases in 2020: influence of pandemy on cancer surgeries	Ozturk UK et al.	J Obstet Gynaecol	https://pubmed.ncbi.nlm.nih. gov/35476608/
2	Outcomes of gynecologic cancer surgery during the COVID-19 pandemic: an international, multicenter, prospective CovidSurg-Gynecologic Oncology Cancer study	Fotopoulou C et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih. gov/35779589/
3	Clinical outcomes in patients with COVID-19 and gynecologic cancer: A society of gynecologic oncology COVID-19 and gynecologic cancer registry study	Glaser GE et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih. gov/36154761/



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