LiFE report
Literature for ENYGO

LiFE | Literature for ENYGO

Reviews covering publications from September 30, 2021 – March 31, 2022

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ESGO European Network of Young Gynae Oncologists
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The European Voice of Gynaecological Oncology

Dear LiFE readers,

We are grateful for choosing LiFE 15 as your source of continuous learning. The Report includes reviews of the most important publications in the field of gynaecological oncology published between September 30, 2021, and March 31, 2022. LiFE is an initiative of ENYGO supported by ESGO. Due to collaboration with the *International Journal of Gynecological Cancer* LiFE report is available for the professional community as a journal supplement.

In this issue, we want to give a warm welcome to our new contributors Georgia Margioula-Siarkou (Greece) and Catherine O'Gorman (Ireland), who will also help us to make up-to-date knowledge in the field more accessible. We want to thank exiting senior editors Kristina Lindemann (Norway), Michael J. Halaska (Czech Republic), and Kamil Zalewski (United Kingdom), who were the founders of the current initiative. We truly appreciate your work and will try to continue making the LiFE with the same level of expertise and enthusiasm. We also thank junior editor Anna Maria Schütz (Austria) for her work on past issues of LiFE. Joanna Kacperczyk-Bartnik (Poland) and Stamatios Petousis (Greece), recently junior editors in the team, are now joining us as senior editors.

We thank all ENYGO members for being a part of this great project and sharing each issue's content with their colleagues and on social media. We hope that you will find LiFE 15 informative and enjoy reading it.

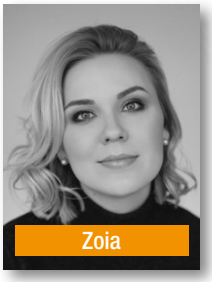
If you are interested in becoming one of the LiFE authors, please email adminoffice@esgo.org.

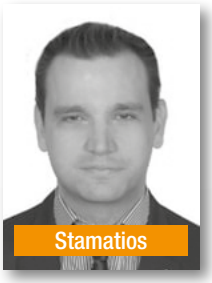
The LiFE editors would also like to take an opportunity to invite you again to the 23rd ESGO Congress, which will be held already October 27–30, 2022, in Berlin (Germany).

Yours,

The LiFE Editors

Zoia Razumova
Joanna Kacperczyk-Bartnik
Kamil Zalewski
Stamatios Petousis





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CONTENTS

Ovarian cancer

Uterine cancer

Cervical cancer

Vulvar and vaginal cancer

Miscellaneous

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LiFE report Literature for ENYGO

Screening of gynaecological cancer

Catarina Pardal

A prospective study analysed the utility of the immunohistochemistry (IHC) test for mismatch repair protein expression in tissue samples together with a brief family history questionnaire (bFHQ) to detect Lynch syndrome (LS) in 200 adult women with endometrial cancer. Genetic testing identified 8 LS cases (prevalence = 4%, 95% CI: 1.84%–7.34%). The IHC test had a sensitivity of 75% or 87.5%, depending on the interpretation of test results (95% CI: 43.2%–94.6% or 56.7%–99.1%, respectively), with a specificity of 79.8% (95% CI: 73.6%–85.1%), and a PPV of 14.0% or 15.9% (95% CI: 5.8%–26.2% or 7.2%–28.4%, respectively), suggesting that this method of interpretation is highly variable. The bFHQ revealed a sensitivity of 62.5% (95% CI: 31.5%–87.6%), a much lower performance than the original bFHQ Canadian Study results (62.5% vs 100% sensitivity). For this screening test the specificity was 56.8% (95% CI: 49.8%–63.7%) and PPV was 5.7% (95% CI: 2.1– 12.0). The authors concluded that the IHC test was not a preferable LS screening method and that the bFHQ did not perform well outside its original scenario. [1]

An observational cohort study aiming to validate a panel of DNA methylation-based markers (CADM1, MAL, FAM19A4, and hsamiR124-2 promoter) as a triage test for women with hr-HPV assessed the biomarkers' performance in formalin-fixed paraffin embedded samples and in cervical scrapes. Analysis of the methylation levels of each gene in tissue samples (MALme, FAM19A4me, and hsamiR124-2me promoters) revealed differences in methylation between the HSIL+ group and the NILM and LSIL groups. In cervical scrapes, FAM19A, MAL and hsa-miR124-2 promoter methylation levels significantly differed between the histological HSIL+ group and the NILM and LSIL groups, and although a reduction in sensitivity was apparent in cervical scrapes, specificity was higher than 70% for all combinations. The authors concluded that results were comparable to those previously reported, confirming the performance of these biomarkers in this population. [2]

A cross-sectional retrospective study including 973 women from 10 countries aimed to evaluate the S5 methylation classifier performance to detect CIN3 and cervical cancer in diverse geographic settings in high-, medium-, and low-income countries. S5 methylation increased proportionally with disease severity and accurately separated women with negative histology from CIN3 or cancer ($p < 0.0001$). At the 0.80 cut-off, S5 showed a sensitivity of 99.81%, and a sensitivity of 95.77% with improved specificity with a cut-off 3.70. The S5 odds ratios of women negative for cervical disease versus CIN3+ were significantly higher than for HPV16/18 genotyping at all cut-offs (all $p < 0.0001$). The authors concluded that the S5 test can accurately detect CIN3 and malignancy irrespective of geographic context and setting and can be used as a screening and triage tool. [3]

Longitudinal outcomes of the Papillomavirus Dumfries and Galloway study (PaVDaG) were evaluated concerning the performance of high-risk human papillomavirus (Hr-HPV) self-sampling testing, 5.5 years after the end of enrolment. The longitudinal sensitivity of Hr-HPV self-sampling to detect CIN2+ and CIN3+ remained high at 88.0% (95% CI: 82.2–92.1) and 93.1% (95% CI: 85.9–97.0), respectively. Risk of CIN2+ and CIN3+ following a Hr-HPV negative self-sample was 0.6% and 0.2%, respectively. The relative sensitivity for CIN3+ and specificity for ≤CIN1 of Hr-HPV testing on self-taken specimens was slightly lower versis clinician-collected samples: 0.95 (95% CI: 0.90–0.99; PMcN = 0.0625) and 0.98 (95% CI: 0.95–1.00; PMcN = < 0.0000), respectively. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Determination of test performance of two contemporary screening tests for Lynch syndrome in endometrial cancer: A clinical trial	Gudgeon JM et al.	Gynecologic Oncology	https://pubmed.ncbi.nlm.nih.gov/34689999/
2	Performance of DNA methylation-based biomarkers in the cervical cancer screening program of northern Portugal: A feasibility study	Salta S et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/34460099/
3	Clinical performance of methylation as a biomarker for cervical carcinoma in situ and cancer diagnosis: A worldwide study	Banila C et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/34562270/
4	Self-sampling as the principal modality for population based cervical screening: Five-year follow-up of the PaVDaG study	Stanczuk GA et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/34850395/

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Medical treatment of primary ovarian cancer

Ilker Selçuk

PARP inhibitors (PARPi)

Olaparib

The posthoc analyses of progression-free survival (PFS) after the median follow-up of 4.8 years for the olaparib group (260 patients) and 5.0 years for the placebo group (131 patients) in the SOLO-1 trial were recently published. The study population constitutes women with a complete or partial response to platinum-based first-line chemotherapy. Median PFS was 56.0m (95% CI: 41.9–not reached) in the olaparib group, whereas it was 13.8m (11.1–18.2) in the placebo group (HR 0.33, 95% CI: 0.25–0.43). The PFS benefit was observed both in patients with a higher (stage IV disease or stage III with residual disease after surgery) and lower (stage III without residual disease after surgery) clinical risk irrespective of BRCA type. In addition, time to second disease progression and death were also improved in the olaparib group (64% vs 41%, HR 0.46, 95% CI: 0.33–0.65). Adverse events were similar to the common PARPi effects. Olaparib treatment was administered up to two years after the platinum-based chemotherapy, and these results demonstrate that the benefits of olaparib maintenance therapy persist after treatment termination, independent of surgical status. [1]

Veliparib

The results of the VELIA trial showed the PFS benefit of veliparib-throughout regimen against chemotherapy alone (median follow-up 28m). In this study, patients were enrolled during the diagnosis and have not been selected with regard to response to platinum-based chemotherapy or BRCA mutations. The exploratory analyses investigated the role of paclitaxel dosing. Comparison of the arms favoured veliparib-throughout against control in both dose-dense (paclitaxel weekly) (PFS 24.2m vs 18.3m, HR 0.67) and every-3-week paclitaxel (PFS 19.3m vs 14.6m, HR 0.69) subgroups. Those results should be interpreted cautiously with the previous studies evaluating the role of dose-dense protocol, JGOG-3016, ICON-8, and GOG-0262. [2]

PARPi plus bevacizumab

In the PAOLA-1/ENGOT-ov25 trial, the patient selection was not performed on basis of surgical outcome. The study by Harter et al. evaluated the subgroups regarding higher-risk (stage III with upfront surgery and residual disease or neoadjuvant chemotherapy; stage IV) and lower-risk (stage III with upfront surgery and no residual disease) in a median follow-up of 22.9m. Olaparib plus bevacizumab provided an improved PFS both in the higher-risk (HR 0.60, 95% CI: 0.49–0.74) and lower-risk patients (HR 0.46, 95% CI: 0.30–0.72). In the homologous recombination deficiency- (HRD-) positive subgroup, olaparib plus bevacizumab favoured a significant PFS benefit both in higher-risk (HR 0.39, 95% CI: 0.28–0.54) and lower-risk patients (HR 0.15, 95% CI: 0.07–0.30). These results suggest that, irrespective of the surgical outcome, maintenance of olaparib to bevacizumab has a great PFS effect in HRD-positive newly diagnosed advanced ovarian cancer patients. [3]

In the lack of randomised prospective studies comparing the survival benefit of PARPi plus bevacizumab against PARPi, Vergote et al. performed a population-adjusted indirect treatment comparison. Individual patient data from the SOLO-1 trial (olaparib, n=254) and from BRCA-mutated patients in the PAOLA-1/ENGOT-ov25 trial (olaparib plus bevacizumab, n=151) were pooled, and key baseline patient characteristics were maintained to be similar. A numerical improvement in PFS was found in the olaparib plus bevacizumab arm against olaparib alone (HR 0.71, 95% CI: 0.45–1.09), 82% versus 73% of patients, respectively, were progression-free at 24 months. Although the 95% CI crossed 1.0 and the analysis was not powered for this comparison, data suggest a potential improvement in PFS with olaparib plus bevacizumab against olaparib alone. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Maintenance olaparib for patients with newly diagnosed advanced ovarian cancer and a BRCA mutation (SOLO1/GOG 3004): 5-year follow-up of a randomised, double-blind, placebo-controlled, phase 3 trial	Banerjee S et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/34715071/
2	Impact of veliparib, paclitaxel dosing regimen, and germline BRCA status on the primary treatment of serous ovarian cancer - an ancillary data analysis of the VELIA trial	Aghajanian C et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34930617/
3	Efficacy of maintenance olaparib plus bevacizumab according to clinical risk in patients with newly diagnosed, advanced ovarian cancer in the phase III PAOLA-1/ENGOT-ov25 trial	Harter P et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34952708/
4	Population-adjusted indirect treatment comparison of the SOLO1 and PAOLA-1/ENGOT-ov25 trials evaluating maintenance olaparib or bevacizumab or the combination of both in newly diagnosed, advanced BRCA-mutated ovarian cancer	Vergote I et al.	Eur J Cancer	https://pubmed.ncbi.nlm.nih.gov/34597975/

Surgical treatment of primary and recurrent ovarian cancer

Ilker Kahramanoglu and Patriciu Achimas-Cadariu

Surgical treatment of primary ovarian cancer

In a single-centre, randomised controlled trial, Cascales Campos et al. analysed whether addition of HIPEC into interval cytoreductive surgery (CRS) had a significant impact in terms of survival, morbidity, and quality of life. The trial enrolled 71 patients: 36 in the CRS group and 35 in the CRS with HIPEC group. Cisplatin 75mg/m2 at 42oC was used as the HIPEC regimen. The duration of HIPEC was 60 minutes. Within a median follow-up of 32 months, the median disease-free survival was 12 months and 18 months in CRS alone and CRS with HIPEC groups, respectively. The median overall survival was 45 months and 52 months in CRS alone and CRS with HIPEC groups, respectively. Perioperative morbidity and quality of life did not differ among two groups. [1]

Surgical treatment of recurrent ovarian cancer

A systematic review and meta-analysis on secondary cytoreductive surgery (SCS) for recurrent low-grade serous ovarian carcinoma found that SCS without residual disease had a positive impact on PFS (HR 3.51, 95% CI: 1.72–7.14) and OS (HR 0.4, 95% CI: 0.23–0.7). Additionally, SCS as an initial treatment for recurrent disease was associated with improved survival in comparison to chemotherapy. Patients with recurrent LGSC should be evaluated for the role of SCS irrespective of the platinum-free interval. [2]

The final results of the DESKTOP III randomised trial of cytoreductive surgery for relapsed ovarian cancer that included 407 patients were recently published. Patients who had a first relapse after a platinum-free interval of 6 months were eligible if they presented with a positive AGO score (ECOG PS 0, ascites less than 500 mL, and complete resection at initial surgery). Cytoreductive surgery followed by chemotherapy resulted in longer overall survival than chemotherapy alone (53.7 months vs 46.0 months in the no-surgery group, HR 0.75, 95% CI: 0.59–0.96, p=0.02). [3]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Cytoreductive surgery with or without HIPEC after neoadjuvant chemotherapy in ovarian cancer: A phase clinical trial	Cascales Campos PA et al.	Ann Surg Oncol	https://pubmed.ncbi.nlm.nih.gov/34812982/
2	Secondary cytoreductive surgery for recurrent low-grade serous ovarian carcinoma: A systematic review and meta-analysis	Goldberg RM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34756470/
3	Randomized trial of cytoreductive surgery for relapsed ovarian cancer	Harter P et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/34874631/

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Medical treatment of recurrent ovarian cancer

Seda Şahin Aker

The FZOCUS-2 trial reported the efficacy and safety of fuzuloparib versus placebo as a maintenance therapy in patients with high-grade, platinum-sensitive, recurrent OC. In all, 252 patients were randomised in a 2:1 ratio. Median PFS was 12.9 for the study group versus 5.5 months for control group (HR 0.25, 95% CI: 0.17–0.36, p < 0.0001). In the fuzuloparib group, patients with gBRCA 1/2 mutations had a significantly longer median PFS compared with those without BRCA (HR 0.46, 95% CI: 0.29–0.74). The most common AEs described were anaemia and thrombocytopenia. [1]

The NRG-GY004 trial evaluated the efficacy of combination olaparib/cediranib to olaparib alone with platinum-based chemotherapy (CT) in platinum-sensitive relapsed ovarian cancer. The authors enrolled 565 patients. The distribution of CT choice for patients was randomly assigned as following: carboplatin and pegylated liposomal doxorubicin (n = 89), carboplatin and gemcitabine (n = 51), and carboplatin and paclitaxel (n = 47). The median PFS was 10.3, 8.2, and 10.4 months with CT, olaparib, and olaparib/cediranib, respectively. Olaparib/cediranib did not improve PFS compared with platinum-based CT. Regarding patients with gBRCA mutation, the PFS HR of CT was 0.55 for olaparib/cediranib and 0.63 for olaparib, while for those without a gBRCA mutation, the PFS HR of CT were 0.97 and 1.41, respectively. The most common AEs were haematologic in the CT group and non-haematologic AEs (diarrhoea, fatigue, nausea, hypertension) in the olaparib/cediranib group. This was the first study to compare an all oral non-platinum regimen to platinum-based regimen. A study limitation was the fact that the olaparib/cediranib group did not meet the primary endpoint of PFS. [2]

The OPINION study evaluated olaparib maintenance monotherapy in a platinum-sensitive relapsed OC without a gBRCA mutation. In all, 279 patients were enrolled. The median follow up duration for PFS was 19.2 months (0.0–30.4). The median total treatment duration was 9.4 months (0.0–31.9), and median PFS was 9.2 months. The percentage of patients who were progression-free at 12 and 18 months was 38.5% (95% CI: 32.7–44.3) and 24.3% (95% CI: 19.2–29.7). The most common AEs were nausea, fatigue/asthenia. The limitation of this study was the lack of a placebo group. The strength of this study was the large dataset to demonstrate activity of maintenance olaparib in a population without a gBRCAm. [3]

Finally, the GOG 281/LOGS study analysed the efficacy and safety of the trametinib (MEK inhibitor) compared with physician's choice standard of care in women with recurrent low-grade serous carcinoma. In all, 260 patients were enrolled and randomised in a 1:1 ratio. Patients received oral trametinib (2 mg once daily) or one of five CT protocol (paclitaxel, pegylated liposomal doxorubicin, topotecan, oral letrozole, or oral tamoxifen). Median PFS was 13.0 versus 7.2 months in the trametinib and the CT group (HR 0.48, 95% CI: 0.36–0.64, p < 0.0001). Median OS was 37.6 months in the trametinib group and 29.2 months in the CT group, respectively. The HR for death was 0·76 (95% CI: 0.51–1·12, p : 0.056), favouring the trametinib group. This was the first positive randomised trial in LGSOC showing trametinib reducing the risk of disease progression or death. A limitation of the study was the bias of investigators in allowing their patient to cross over to trametinib to prematurely ascertain disease progression. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Fuzuloparib maintenance therapy in patients with platinum-sensitive, recurrent ovarian carcinoma (FZOCUS-2): A multicenter , randomized, double-blind, placebo-controlled, phase III trial	Li N et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/35404684/
2	Olaparib with or without cediranib versus platinum-based CT in recurrent platinum-sensitive ovarian cancer (NRG-GY004): A randomized, open-Label, phase III trial	Liu JF et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/35290101/
3	Olaparib maintenance monotherapy in platinum-sensitive relapsed ovarian cancer patients without a germline BRCA1/BRCA2 mutation: OPINION primary analysis	Poveda A et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35063276/
4	Trametinib versus standard of care in patients with recurrent low-grade serous ovarian cancer (GOG 281/LOGS): an international, randomised, open-label, multicentre, phase 2/3 trial	Gershenson DM et al.	Lancet	https://pubmed.ncbi.nlm.nih.gov/35123694/

Borderline ovarian tumours

Anton Ilin

Since treatment approaches for borderline ovarian tumours (BOT) have started to change, the question of fertility-sparing treatment is one of the most important and debated at the same time. That seems to be reasonable since many patients are of their reproductive age at the time of BOT diagnosis. Raimondo. et al. assessed the impact of hysterectomy on oncological outcomes in this group of patients. After analysis of 2,223 cases, it was found that hysterectomy decreases the risk of recurrence but the overall survival remains much the same. In the hysterectomy group, pooled odds ratios were 0.23 ($p = 0.00001$) for recurrence, 1.26 ($p = 0.77$) for death due to BOT, and 4.23 ($p = 0.11$) for the death of any cause, which supports the uterine preserving strategy. [1]

When performing surgery for ovarian tumours with unclear malignant potential, a frozen section is typically performed to encourage a correct treatment strategy. In our practice, a significant part of intraoperative results sounds "at least borderline" which presents physicians with the dilemma of whether or not to perform a full ovarian cancer staging procedure. Decker et al., in a retrospective cohort study of 223 cases, found that "at least borderline" frozen section report has a chance of 31.7% carcinoma at the final pathology. For decisive BOT, the chance of carcinoma was 7.7%. The authors concluded that full staging during initial surgery might be considered after preoperative consent to prevent a second surgical procedure or chemotherapy in unstaged women. [2]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	The impact of hysterectomy on oncological outcomes in patients with borderline ovarian tumours: A systematic review and meta-analysis	Raimondo D et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35090745/
2	Borderline ovarian tumor frozen section diagnoses with features suspicious of invasive cancer: a retrospective study	Decker K et al.	J Ovarian Res	https://pubmed.ncbi.nlm.nih.gov/34686192/

Treatment of ovarian sex cord stromal and germ cell tumours

Paul Kubelac

The impact of fertility-sparing surgery on sexuality and general quality of life in women with malignant ovarian germ cell and sex cord stromal tumours was examined in a multicentre, observational study that included 355 patients. Following fertility-sparing surgery, patients had a 2.6 greater likelihood of being sexually active than after non-fertility-conserving therapy (p=0.01) and a considerably superior quality of life (p=0.03). The study concluded that where oncologically feasible, all patients should be provided fertility-preserving treatments. [1]

The long-term survival and subsequent effects of 77 participants who were treated for childhood ovarian non-seminomatous germ cell tumours as part of a French trial were recently described. The 5-year relapse-free survival and overall survival was 88.2% and 94.6%, respectively, after more than 13 years of follow-up. All relapses occurred within 24 months, and four mature contralateral teratomas were detected within eight years. All 51 survivors aged >15 years with residual ovarian function at two years had spontaneously entered puberty, and 41% had a minimum of one pregnancy. Four out of 69 patients treated with platinum-based chemotherapy were diagnosed with chronic renal disease, and three patients had substantial ototoxicity. The authors suggested that the etoposide-free VBP schedule might be an option for children with intermediate-risk disease, and that the risk of subsequent mature teratoma must be monitored regularly. [2]

A multicentre retrospective research on surgical therapy for stage I malignant ovarian germ cell tumours followed 86 patients for a median of 4.4 years. In all, 93% of patients were given fertility-preserving surgery. There were no significant variations in recurrence or survival rate between individuals with immature teratoma who received unilateral cystectomy alone or salpingo-oophorectomy. There was no notable change in event-free survival between patients who had surgical staging (83%, 95% CI: 71–98) and those who did not (84%, 95% CI:72–98). The 5-year overall survival rate was 96.6% and the event-free survival rate was 81.8%; nevertheless, the authors caution that these results need further examination in larger cohorts. [3]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	The effect of fertility-sparing surgery on sexuality and global quality of life in women with malignant ovarian germ cell and sex cord stromal tumours: an analysis of the CORSETT database of the AGO study group	Hasenburg A et al.	Arch Gynecol Obstet	https://pubmed.ncbi.nlm.nih.gov/34287678
2	Childhood ovarian nonseminomatous germ cell tumors: A highly curable disease with few long-term treatment-related toxicities-Results of the French TGM95 study	Pavone R et al.	Int J Cancer	https://pubmed.ncbi.nlm.nih.gov/34146403
3	Surgical management and outcomes for stage 1 malignant ovarian germ cell tumours: A UK multicentre retrospective cohort study	Graham R et al.	Eur J Obstet Gynecol Reprod Biol	https://pubmed.ncbi.nlm.nih.gov/35192975

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

Anna-Maria Schütz

Phase I

Liu et al. published a multicentre open-label 3+3 dose-escalation study on safety, tolerability, dose-limiting toxicities (DLTs), maximum tolerated dose (MTD), and recommended Phase II dose (RP2D) of an anti- MUC16 (formerly known as CA-125) monoclonal antibody, called DMUC4064A, in patients with platinum-resistant ovarian cancer (OC). It was administered iv q3w in a 1.0–5.6mg/kg dose escalation. Sixty-five patients received a median of five cycles (1–20). The RP2D was 5.2mg/kg and the MTD was not reached. Dose modifications due to adverse events (AEs) were reported in 45%, with blurred vision leading most frequently to a dose interruption, and blurred vision along with peripheral neuropathy resulting most frequently in dose reductions. Twenty-five percent (16) reported a grade ≥ 3 toxicity. Two patients (3%) experienced DLTs, one having a grade 5 septic shock resulting in the patient's death at a dose level of 5.2mg/kg and another one having grade 3 colitis (and hypokalaemia). Confirmed objective partial response (PR or CR) was reported for 16 patients (25%) starting at ≥3.2mg/kg dose levels and 23 patients (35%) had best responses of PR or CR (confirmed and unconfirmed). Overall, the clinical benefit rate (PR+ stable disease (SD)) was 42% versus 46% in the cohort with high MUC16 immunohistochemistry scores. Median PFS was 3.9 months. The study enrolment was stopped early due to sponsor decision on development of the molecule. In summary, this study showed that MUC16 might be a potential therapeutic target which needs to be further assessed. [1]

Phase II

The efficacy and safety of tivozanib, a tyrosine kinase inhibitor, was evaluated in a phase II trial in recurrent, platinum-resistant OC. Thirty patients received tivozanib 1.5mg orally daily for 21 days in a 28-day cycle. The median rate of prior regimens was four (range 1–9). Twenty-four patients were evaluable for response with four (16.7%) having a PR and 14 (58.3%) having a SD. Clinical benefit rate (PR + SD) was 75%; the median duration of OR was 5.7 months. Median PFS was 4.1 months and OS 8.6 months. Serious AEs occurred in 13.3% and included small intestinal perforation, obstruction, and stroke. Grade 3–4 AEs were reported in 60%, including hypertension and fatigue. According to these results, tivozanib might have potential as a single-agent treatment strategy in this cohort. [2]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	An open-label phase I dose-escalation study of the safety and pharmacokinetics of DMUC4064A in patients with platinum-resistant ovarian cancer	Liu J et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34627611/
2	Efficacy and safety of tivozanib in recurrent, platinum-resistant ovarian, fallopian tube or primary peritoneal cancer, an NCCN phase II trial	Cowan M et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34419285/

Medical (chemo- and radiotherapy) treatment of primary uterine cancer

Kamil Zalewski

Makker et al., in their phase III randomised 309/KEYNOTE-775 study, demonstrated that lenvatinib (20mg po daily) combined with pembrolizumab (200 mg, iv every 3 weeks) led to significantly longer progression-free survival (PFS) and overall survival (OS) than chemotherapy of physician's choice (doxorubicin or paclitaxel) among patients with pretreated advanced endometrial cancer. Patients enrolled into the study had progression or recurrence of disease after at least one previous line of platinum-based chemotherapy and were stratified according to MMR status. PFS was significant longer with lenvatinib plus pembrolizumab than with chemotherapy (pMMR population: 6.6 vs 3.8 months; all patients: 7.2 vs 3.8 months). OS was also significant longer with lenvatinib plus pembrolizumab than with chemotherapy (pMMR population: 17.4 vs 12.0; all patients: 18.3 vs 11.4 months). Due to adverse events, more than half of the patients receiving lenvatinib plus pembrolizumab required dose reduction. The authors noted the relatively short duration of follow-up (median 12.2 and 10.7 months in both groups respectively) was a potential limitation of the study. Safety and efficacy monitoring is ongoing. [1]

O'Malley et al., based on the results of the phase II study, evaluated the efficacy and safety of pembrolizumab in patients with previously treated advanced (metastatic and/or unresectable) endometrial cancer with tumours that had high levels of microsatellite instability/mismatch repair deficiency. The authors noted the objective response rate per RECIST (v1.1) as the primary endpoint and duration of response, PFS, OS, and safety as secondary endpoints. Forty-eight percent of 90 patients with advanced microsatellite instability–high or mismatch repair–deficient (MSI-H/ dMMR) endometrial cancer had an objective response. Based on the median follow-up of 42.6 months, responses were found to be long-lasting. Three-year PFS and OS were estimated to be 37% and 60%, respectively. A limitation of this study was its non-randomised design. [2]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Lenvatinib plus pembrolizumab for advanced endometrial cancer	Makker V et al.	N Engl J Med.	https://pubmed.ncbi.nlm.nih.gov/35045221/
2	Pembrolizumab in patients with microsatellite instability-high advanced endometrial cancer: results from the KEYNOTE-158 study	O'Malley DM et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/34990208/

Medical (chemo and radiotherapy) treatment of recurrent uterine cancer

Stamatios Petousis

Dai et al. published a meta-analysis whose objective was to study the efficacy of PD-1/PD-L1 inhibitors for endometrial cancer. There was an overall response rate of 29%. However, when performing the subgroup analysis, the pooled ORR was only 4% for pMMR group but was raised to 45% for the deficient MMR group. The overall adverse rate was 65%. The authors concluded that PD-1/PD-L1 inhibitors are rather efficient in the dMMR group, while efficacy is reduced in the pMMR population. [1]

Marth et al. published the protocol of a phase 3, randomised, open-label study of combination therapy of pembrolizumab plus lenvatinib versus only chemotherapy as the first-line treatment of advanced-stage or recurrent endometrial cancer. The primary aim will be to compare the efficacy and safety within the two study groups. Patients will be allocated to receive pembrolizumab iv every three weeks plus lenvatinib orally daily (study group) or paclitaxel plus carboplatin iv every three weeks (control group), based on the mismatch repair status (proficient vs deficient). Only patients with histologically confirmed endometrial cancer of stage III/IV will be included. Sample size has been estimated to be about 875 patients, while the enrolment period is expected to take approximately 24 months. [2]

Liu et al. published the protocol of a phase IIb study of adavosertib, a Wee1 inhibitor, in women with recurrence or persistency of uterine serous carcinoma. The primary aim will be to study the efficacy of the regimen in women with recurrent or persistent disease. Participants will receive the regimen as monotherapy until diagnosis of disease progression or occurrence of unacceptable toxicity. Included patients will be with histologically confirmed recurrent or persistent uterine serous carcinoma, as well as patients with endometrial carcinoma of mixed histology with at least 10% serous component. Sample size is estimated at approximately 120 patients. The completion of study and presentation of results are projected to be at the end of 2022. [3]

Tymon-Rosario et al. have published the results of a multicentre randomised phase II trial regarding trastuzumab tolerability in the treatment of advanced or recurrent uterine serous carcinomas. Patients were randomised to receive combined chemotherapy (carboplatin/paclitaxel) ± trastuzumab with the study group continuing to receive maintenance treatment until recurrence or severe adverse event. Overall, 60 patients were included, with 28 patients in the control group and 32 patients in the study group. The rate of adverse events was 97%; however, only 10.4% were observed to be high-grade. Gastrointestinal adverse events were the most frequent in both arms (15.7%); however, the majority were low-grade. The authors reported that trastuzumab appears to be safe, with acceptable toxicity both in combination with chemotherapy and also as single-agent maintenance in patients with HER2/neu positive USC. [4]

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No	Title	Authors	Journal	Link to abstract
1	PD-1/PD-L1 Inhibitors monotherapy for the treatment of endometrial cancer: Meta-analysis and systematic review	Dai Y et al.	Cancer Invest	https://pubmed.ncbi.nlm.nih.gov/34825855/
2	Phase 3, randomized, open-label study of pembrolizumab plus lenvatinib versus chemotherapy for first-line treatment of advanced or recurrent endometrial cancer: ENGOT-en9/LEAP-001	Marth C, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34799418/
3	ADAGIO: a phase IIb international study of the Wee1 inhibitor adavosertib in women with recurrent or persistent uterine serous carcinoma	Liu J, et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34716177/
4	Trastuzumab tolerability in the treatment of advanced (stage III-IV) or recurrent uterine serous carcinomas that overexpress HER2/neu	Tymon-Rosario J, et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34372971/

Emerging molecular targeted therapies or early preclinical trials in endometrial cancer

Joanna Kacperczyk-Bartnik and Zoia Razumova

A recent study by Oaknin et al. revealed data of advanced endometrial cancer patients recruited in the ongoing GARNET trial examining clinical efficacy and safety outcomes of the anti-PD-1 monoclonal antibody dostarlimab in individuals with solid tumours. In the subgroup of women with mismatch repair deficient/microsatellite instability-high disease (n = 129) the median follow-up was 16.3 months and objective response rate reached 43.5%. In the cohort of patients with mismatch repair proficient/microsatellite stable endometrial cancer (n = 161) the median follow-up lasted 11.5 months and the objective response rate was 14.1%. Most prevalent treatment-related adverse events included fatigue (reported by 17.6% patients) and gastrointestinal symptoms—diarrhoea and nausea (each reported by 13.8% of patients). [1]

In a phase II trial, Lheureux et al. compared the outcome of recurrent endometrial cancer patients treated with nivolumab (checkpoint inhibitor) and cabozantinib (antiangiogenic agent) within the median follow-up of 15.9 months. Women who had not earlier undergone immunotherapy received both agents (Arm A, n = 36) or nivolumab alone (Arm B, n = 18). The progression-free survival among immunotherapy-naïve patients was longer in the combination therapy subgroup (5.3 vs 1.9 months, p = 0.09). Stabilisation of the disease was achieved by 44% of patients in Arm A and 11% in Arm B. The authors concluded that the addition of cabozantinib to nivolumab improved outcomes in patients with recurrent endometrial cancer. [2]

Bellone et al. published results of a phase II trial evaluating the efficacy of pembrolizumab in recurrent endometrial cancer patients with Lynch-like (n = 6) and sporadic high microsatellite instability (n = 18). The objective response rate was higher in patients with Lynch-like than in the group of sporadic endometrial cancers (100% vs 44%, p = 0.02). Similarly, the 3-year progression-free survival (100% vs 30%, p = 0.02) and overall survival (100% vs 43%, p = 0.04) proportions were higher among patients with Lynch-like mutations than in the second group. [3]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) or proficient/stable (MMRp/MSS) endometrial cancer: interim results from GARNET-a phase I, single-arm study	Oaknin A et al.	J Immunother Cancer	https://pubmed.ncbi.nlm.nih.gov/35064011/
2	Translational randomized phase II trial of cabozantinib in combination with nivolumab in advanced, recurrent, or metastatic endometrial cancer	Lheureux S et al.	J Immunother Cancer	https://pubmed.ncbi.nlm.nih.gov/35288469/
3	A phase 2 evaluation of pembrolizumab for recurrent Lynch-like versus sporadic endometrial cancers with microsatellite instability	Bellone S et al.	Cancer	https://pubmed.ncbi.nlm.nih.gov/34875107/

Uterine sarcoma

Marcin Bobiński

Condic et al. published a study validating the scoring system (pLMS) to distinguish between LMS and benign myometrial lesions. The original study by Kohler et al. was previously discussed in the LiFE 11 report. Briefly, the proposed scoring system combines clinical and ultrasonographic characteristics to count the risk of malignancy. The scoring system was validated on a retrospective cohort of LMS patients retrieved from the German NOGGO-REGSA registry (n=177). The authors' results were the opposite to those presented in the original publication. In the validation cohort: "threshold of the pLMS score for 'leiomyosarcoma not probable' (< –3) failed for 7.5% of the patients and the threshold 'indicator for leiomyosarcoma' (>+1) was true for 39.1% of the patients. 53.4% of the patients were attributed to the group 'additional investigations are recommended' (–3 to +1)". Limitations of the study include the fact that the cohort analysed by Kohler et al., proposing the pLMS sore, and the validation cohort from the NOGGO-REGSA registry were not the same. In addition, the characteristics of both populations were different. The paper is a rare example of a validation study and the results indicate that every new tool aiming to solve the difficult clinical problem of preoperative differentiation of myometrial lesions should be treated carefully. [1]

Russo et al. analysed the sonographic characteristics of myometrial lesions, based on a cohort of 70 patients, including mostly benign lesions (32 typical leiomyoma, 29 other variants of leiomyoma, 4 adenomyomas) and a few malignant ones (2 uterine sarcomas, 1 leiomyosarcoma, 1 neuroendocrine tumour, 1 STUMP). The study aim did not propose any method of differentiation between malignant and benign lesions, rather showing the characteristics of typical leiomyomas (circumferential and intralesional vascularity, presence of cystic areas, and border regularity), which might be useful in order to identify patients with typical lesions that do not require further diagnostics such as MRI or biopsy. The main study limitations included the low number of cases, the extremely low number of malignancies in the study group, and the fact that only basic clinical features were evaluated. [2]

The results of the PARAGON trial (a phase II study of anastrozole in rare cohorts of patients with oestrogen receptor/progesterone receptor positive leiomyosarcomas and carcinosarcomas of the uterine corpus) were published. The investigators enrolled 39 patients (32 and 7 with LMS and UCS, respectively); all were treated with anastrozole 1mg/day. Median PFS was 2.8 months, while the median durations of clinical benefit (complete/partial response + stable disease) were 5.8 and 5.6 in the LMS and UCS groups, respectively. The safety was considered as acceptable (about 13% of patients experienced grade 3 toxicity). The results showed that the benefit for LMS and UCS patients from anastrozole treatment is limited but is associated with a low complications rate and has a potential role where there are limited therapeutic options. [3]

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No	Title	Authors	Journal	Link to abstract
1	Clinical value of pre-operative scoring systems to predict leiomyosarcoma: results of a validation study in 177 patients from the NOGGO-REGSA Registry	Condic M et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/35288460/
2	Highly vascularized uterine myomas (uterine smooth muscle tumors) on ultrasound and correlation to histopathology	Russo C et al.	Ultrasound Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/35018681/
3	Phase 2 study of anastrozole in rare cohorts of patients with oestrogen receptor/progesterone receptor positive leiomyosarcomas and carcinosarcomas of the uterine corpus: The PARAGON trial (ANZGOG 0903)	Edmondson RJ et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34625284/

Surgical treatment of primary and recurrent endometrial cancer

Houssein El Hajj

Zhou et al. identified 1,618 stage IV patients treated with NACT/IDS between 2010 and 2017. Laparoscopy (LS) and laparotomy (LT) were performed in 503 (31.1%) and 1,115 (68.9%), respectively. Univariate and multivariate analysis showed a higher rate of LS-IDS with time (aRR=2.46) in 2017 compared to 2010; they also concluded that non-endometrioid histologies were less likely to undergo LS-IDS: Serous (27.6%, aRR=0.63), clear-cell (26.7%, aRR=0.62), carcinosarcoma (29.5%, aRR=0.74) (p<0.001). After propensity score, there was no difference in median OS (p=0.23) in both groups (24.3 vs 28 months in the LT and LS-IDS respectively); No association was found between LS and OS (HR=0.90). [1]

David et al. compared two cohorts of 30 women treated with CRS or CRS+HIPEC for endometrial carcinomatosis. After a propensity score matching, 96.7% of (CRS+HIPEC) were treated for recurrence, while 83.3% of CRS were treated for primary disease. No significant difference was found concerning PCI (p=0.702), Completeness of cytoreduction (p=0.763), grade III/IV complications (p=0.739), median OS (19.2 months in CRS+HIPEC and 29.7 months in CRS groups, p=0.606), and median PFS (10.7 months in CRS+HIPEC and 13.1 months in CRS groups, p=0.511). After adjustment on the time from diagnosis to surgery, age, and chemotherapy, no difference was found for OS (p=0.207) and PFS (p=0.324). [2]

Argenta et al. compared after a propensity score matching 461 (44.9%) patients treated with LS and 566 (55.1%) patients treated with robotic-assisted LS (RALS) for stage I EC. There was no difference in the rates of adjuvant treatment: 18.2% versus 20.4% in the LS and RA-LS respectively, p=0.7. Patients in the RA-LS had higher BMI (35.9 versus 33.3, p<0.001). RA-LS was associated with poorer RFS (HR:1.41, p=0.004), poorer OS (HR: 1.39, p=0.02), and poorer DSS (HR: 3.51). The median time to first recurrence was shorter in the RA-LS group (16.3 vs 28.7 months, p = 0.07). [3]

In a review, Marchocki et al. evaluated SLN performance in high-grade EC patients. The overall node-positivity rate was 26% per patient and 20% per hemipelvis. The pooled overall SLN detection and bilateral SLN detection rates were 91% and 64%, respectively. The pooled SLN-sensitivity per patient, SLN-sensitivity per hemipelvis, NPV per patient, and NPV per hemipelvis were 92% and 90%, 97%, and 98%, respectively. The pooled FNR per patient and FNR per hemipelvis were 8% and 10%, respectively. In conclusion, SLN accurately detects LN metastases in high-grade EC. [4]

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No	Title	Authors	Journal	Link to abstract
1	Adoption of minimally invasive surgery after neoadjuvant chemotherapy in women with metastatic uterine cancer	Zhou ZN et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34920885/
2	Cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) vs CRS alone for treatment of endometrial cancer with peritoneal metastases: a multi-institutional study from PSOGI and BIG RENAPE groups	David MG et al.	BMC Surg	https://pubmed.ncbi.nlm.nih.gov/34996419/
3	Robot-assisted versus laparoscopic minimally invasive surgery for the treatment of stage I endometrial cancer	Argenta PA et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35314086/
4	Sentinel lymph node biopsy in high-grade endometrial cancer: a systematic review and meta-analysis of performance characteristics	Marchocki Z et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/34058168/

Surgical treatment of primary and recurrent cervical cancer

Chrysoula Margioula-Siarkou and Georgia Margioula-Siarkou

The SUCCOR cone study reported by Chacon et al. analysed the impact of cervical conisation prior to radical hysterectomy on the disease-free and overall survival, in patients with stage IB1 cervical cancer. The authors conducted a multicentre retrospective observational study on a 1:1 matched population of 374 patients (187 with prior conisation and 187 without conisation). The risk of relapse was decreased by 65% for patients who underwent conisation before radical hysterectomy (HR 0.35, 95% CI: 0.16–0.75, p<0.007), while the risk of death was reduced by 75% (HR 0.25, 95% CI: 0.07–0.90, p<0.033), compared to non-conisation patients. Conclusively, the authors suggest that conisation before radical hysterectomy can significantly decrease the risk of relapse and death in patients with early-stage cervical cancer. [1]

The International Radical Trachelectomy Assessment Study reported by Salvo et al. examined the difference in 4.5-year survival outcomes after open versus minimally invasive radical trachelectomy. This international retrospective study included 646 early-stage cervical cancer patients with a preoperative tumour size of ≤2cm who underwent abdominal (n=358) or minimally invasive (n=288) radical trachelectomy with surgical nodal assessment. No significant differences were detected between the two groups, regarding both the 4.5-year disease-free survival (log-rank p=0.37) and the 4.5-year overall survival (log-rank p=0.49), leading the authors to the conclusion that open surgical approach is not superior to the minimally invasive approach in terms of the survival outcome. [2]

Devaja et al. performed a prospective clinical trial to evaluate the efficacy and safety of sentinel lymph node (SLN) biopsy for nodal assessment in patients with early-stage cervical carcinoma. The study enrolled 103 patients with FIGO 2009 stage IA1–IB1 cervical cancer who opted for double-technique (use of methylene blue dye and Tc-99m nanocolloid tracer) SLN biopsy, instead of systematic pelvic lymphadenectomy combined with SLN detection. At least one SLN was identified in all patients by at least one of the two mapping techniques, with a bilateral detection rate of 83%, while 6,7% of the patients were confirmed to have nodal involvement according to histopathology report. The specificity and negative predictive value of a negative SLN were both estimated at 100%. During the follow-up period (medial 53 months, range 8–120), no nodal recurrences were reported. The authors concluded that SLN biopsy is a safe alternative method for assessment of nodal status in selected cases of early-stage cervical cancer. [3]

Chen et al. investigated the effect of para-aortic lymphadenectomy on the survival outcomes, in a retrospective comparative study of 8,802 patients with stage IB1–IIA2 cervical cancer, who either were treated with abdominal radical hysterectomy combined with pelvic lymph node dissection (PLND) (n=8445) or received the same procedure with additional para-aortic lymphadenectomy (PALND) (n=357). In total, positive pelvic and para-aortic lymph nodes were detected in 18.38% and 10.36 % of the patients, respectively. The rate of simultaneous pelvic – para-aortic lymph node metastases was 30%; on the contrary, an isolated para-aortic nodal metastasis was detected in 0.42% of the patients. Regarding the 5-year disease-free survival and the 5-year overall survival, no significant differences were reported between the patients who received PALND and the patients who received only PLND, even after a 1:4 propensity score matching analysis between the two groups. In conclusion, the authors propose that PALND should be reserved for selected cervical cancer patients with pelvic nodal metastasis, since it does not seem to significantly improve 5-year survival outcomes. [4]

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No	Title	Authors	Journal	Link to abstract
1	SUCCOR cone study: conization before radical hysterectomy	Chacon E et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/35039455/
2	Open vs minimally invasive radical trachelectomy in early-stage cervical cancer: International Radical Trachelectomy Assessment Study	Salvo G et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/34461074/
3	Sentinel lymph node biopsy alone in the management of early cervical carcinoma	Devaja O et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/32546643/
4	Comparison of survival outcomes with or without Para-aortic lymphadenectomy in surgical patients with stage IB1-IIA2 cervical cancer in China from 2004 to 2016	Chen C et al.	BMC Cancer	https://pubmed.ncbi.nlm.nih.gov/34627169/

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

Radiotherapy of primary and recurrent cervical cancer

Erbil Karaman

Peters et al. performed the risk analysis for nodal failure in patients from the EMBRACE I study. The study included 152 pelvic (NF) and 104 paraaortic (PAO) nodal failure patients among 1,338 cases treated with definitive chemoradiotherapy and brachytherapy for locally advanced cervical cancer (LACC). The main risk factors for NF were node involvement and tumour diameter as well as local recurrence. Any PAO node involvement in the absence or presence of pelvic nodes and any common iliac nodes (without PAO involvement) were found to be stronger risk factors for nodal failure than nodes in the pelvis alone. [1]

Corbeau et al. published the protocol of The PROTECT trial, the first prospective phase II clinical trial to compare intensity-modulated proton therapy (IMPT) with intensity-modulated radiation therapy/volumetric-modulated arc therapy (IMRT/VMAT) for women with LACC treated with definitive chemoradiotherapy. In this nonrandomised multicentre study, the authors evaluated the effects of dose-volume factors and therapy-associated morbidity for cases with LACC managed with chemoradiotherapy. During the first of the study's two phases, 15 women will be included in the IMRT/VMAT therapy group. In the second phase of the study, 15 cases will be included in the IMPT arm. The first aim of this study is to evaluate whether IMPT can remarkably decrease the Dmean to the pelvic skeletons and the mean V15Gy to the intestines with comparison to that of IMRT/VMAT with photons. The secondary aim is the comparison of IMPT with standard treatment of IMRT/VMAT in regards with dosimetric factors, practical results, health-associated quality of life, reliability, and tolerability. The trial is planned to terminate within 2.5 years. [2]

Macchia et al. conducted a multicentre retrospective study (MITO-RT2/RAD study) to evaluate the efficacy and reliability of stereotactic body radiotherapy in a total of 83 patients with oligometastatic/persistent/recurrent cervical cancer. A total of 125 lesions underwent treatment by this method at 15 different centres that were included in the study's analysis. The most common metastatic site was lymph nodes (55.2%), followed by parenchyma lesions (44.8%). There was a statistically significantly higher overall survival rate in the complete response group than partial or stable or progressive disease (68.9% vs 44.3%, $p = 0.015$). There was a low toxicity profile (15 patients had mild toxicity and four cases had late toxicity) which showed the wider use of stereotactic body radiation in these patients. This study confirmed the efficacy of this radiation therapy in oligometastatic cervical cancer. [3]

Hande et al. reported a meta-analysis that evaluated the efficacy of point-A and volume-based brachytherapy in patients with stage I-IVA cervical cancer. This meta-analysis included 24 studies with 5,488 patients. The point-A versus volume-based treatments was found to have no statistically significant difference regarding to the 3-year OS (72% vs 79%, $p = 0.12$). The two groups showed no difference in terms of toxicities, including gastrointestinal or genitourinary ones. However, the volume-based brachytherapy with 3D planning was found to be superior to the point-A group regarding the three-year DFS and three-year LC. This study reported the best evidence with regards to a change to the 3D planning even in the absence of randomised studies. [4]

Vaginal stenosis (VS) in women managed for LACC with chemoradiotherapy and image-guided adaptive brachytherapy was investigated in an EMBRACE-I sub-study by Westerveld et al. A total of 301 cases were evaluated with a median 49 months of follow-up. Increased doses to PIBS, PIBS+2 cm, and RV-RP points were related with higher risk for VS. Older age, shorter VRL, vaginal tumour at first admission, and use of a tandem-ovoid applicator were the other risk factors observed for VS. [5]

Williamson et al. reported the final outcomes of the INTERTECC phase II/III trial. The main objective was to evaluate the effect of positron emission tomography (PET)-based bone marrow-sparing (BMS) image-guided intensity modulated radiation therapy (IG-IMRT) on efficacy and toxicity for cases with LACC. The patients were divided into two groups in an international phase II/III study with either the PET-BMS-IMRT group or the standard IMRT group, with concurrent cisplatin (40 mg/m2 weekly) followed by brachytherapy. The PFS and OS at five years for all cases were 73.6% and 84% respectively. When analysing the cisplatin cycles, OS, PFS, or types of failure among groups for the whole cohort, there were no differences. However, the grade ≥ 3 neutropenia was remarkably decreased in the PET-BMS-IMRT group compared to IMRT for randomised patients (19% vs 54%, x2p = 0.048) and in the combined cohort (13% vs 35%, x2p = 0.01). The study concluded that there was no evidence that PET-BMS-IMRT affected chemotherapy management or long-term results, and low-level evidence of a relationship between pre-treatment absolute lymphocyte count and OS. [6]

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1	Risk factors for nodal failure after radiochemotherapy and image guided brachytherapy in locally advanced cervical cancer: An EMBRACE analysis	Peters M et al.	Radiotherapy and oncology	https://pubmed.ncbi.nlm.nih.gov/34480958/
2	PROTECT: prospective phase-II-trial evaluating adaptive proton therapy for cervical cancer to reduce the impact on morbidity and the immune system	Corbeau A et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/34680328/
3	Stereotactic body radiotherapy in oligometastatic cervical cancer (MITO-RT2/RAD study): a collaboration of MITO, AIRO GYN, and MaNGO groups	Macchia G et al.	International Journal of Gynecological Cancer	https://pubmed.ncbi.nlm.nih.gov/35193941/
4	Point-A vs. volume-based brachytherapy for the treatment of cervix cancer: A meta-analysis	Hande V et al.	Radiotherapy and oncology	https://pubmed.ncbi.nlm.nih.gov/35259419/
5	Dose-effect relationship between vaginal dose points and vaginal stenosis in cervical cancer: An EMBRACE-I sub-study	Westerveld H et al.	Radiotherapy and oncology	https://pubmed.ncbi.nlm.nih.gov/35063582/
6	Positron emission tomography-guided bone marrow-sparing radiation therapy for locoregionally advanced cervix cancer: Final results from the INTERTECC phase II/III trial	Williamson CW et al.	International journal of radiation oncology, biology, physics	https://pubmed.ncbi.nlm.nih.gov/34419564/

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

Khayal Gasimli

Phase II

The objective response rate (ORR) and safety of balstilimab, an anti-PD-1 checkpoint inhibitor, were investigated in a multicentre phase II study in patients with metastatic or recurrent cervical cancer after prior platinum-based chemotherapy. The PD-L1 status and the histological subtypes of the carcinoma were not respected in patient selection. Thus, only 61.5% of the patients had a PD-L1 positive tumour (CPS ≥1%), and 62.7% had squamous cell carcinoma. The drug applied 3mg/kg IV q2w regimen by good tolerability and response until 24 months. An independent review committee performed ORR and safety assessment using RECIST (V1.1) criteria and National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CT-CAE-V 4.03). A disease control rate was achieved in 49.3% of cases with a median duration of response (DOR) of 15.4 months. The ORR was 15%, and the best response was observed in patients with positive PD-L1 status (20.0% vs 7.9%). During therapy, most patients complained of asthenia (23.0%) and diarrhoea (12.4%). The most common immune-related adverse events (AE) were hypothyroidism (6.8%) and hyperthyroidism (3.7%). [1]

Another phase II study explored the anti-tumour activity of balstilimab in combination with the next checkpoint inhibitor, zalifrelimab (CTLA-4; anticytotoxic T-lymphocyte-associated antigen-4). [2]. The characteristics of the study patients were similar to the above study of monotherapy. [1] The application of zalifrelimab was 1mg/kg IV every 6 weeks. The median follow-up and DOR were 21 months. This combination therapy showed a better ORR of 25.6%. Even in this study, patients with PD-L1 positive tumours benefited more than negative ones (32.8% vs 9.1%). Overall, the AE profile of the combination therapy was comparably tolerable with monotherapy but with more grade 3 (20% vs 11.8%) events such as increased ALT (2.6%), diarrhoea (1.9%), etc. [1,2].

Phase III

The multicentre randomised study from Tewari et al. examined the therapeutic effect and safety of cemiplimab (anti-PD-1 checkpoint inhibitor) in patients with progressive disease of cervical cancer after receiving the treatment before platinum-based chemotherapy. The patients in the experimental arm received cemiplimab 350mg IV q3w for up to 96 weeks and the control arm received investigator's choice chemotherapy (pemetrexed, gemcitabine, topotecan, irinotecan, and vinorelbine) according to their local guidelines. The included patients mostly had squamous-cell carcinoma (77.8%). The PD-L1 was expressed in 162 samples of the 254 possible cases ≥1%. The overall survival was significantly better in the cemiplimab arm than the chemotherapy arm (12.0 vs 8.5 months). The efficacy assessment showed a 16.4% ORR for the cemiplimab arm with a median DOR of 16.4 months and 6.3% ORR for chemotherapy arm with a median DOR of 6.9 months. Serious AE of grade 3 and higher were 23.0% in cemiplimab arm and 22.1% in chemotherapy arm. There are no specific AE of cemiplimab leading to death reported by the treating investigator. [3]

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No	Title	Authors	Journal	Link to abstract
1	Phase II study of the safety and efficacy of the anti-PD-1 antibody balstilimab in patients with recurrent and/or metastatic cervical cancer	O'Malley DM et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34452745/
2	Dual PD-1 and CTLA-4 Checkpoint Blockade Using Balstilimab and Zalifrelimab Combination as Second-Line Treatment for Advanced Cervical Cancer: An Open-Label Phase II Study	O'Malley DM et al.	J Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/34932394/
3	Survival with Cemiplimab in Recurrent Cervical Cancer	Tewari KS et al.	N Engl J Med	https://pubmed.ncbi.nlm.nih.gov/35139273/

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

María de los Reyes Oliver and Rubén M. Betoret

After the long-awaited results of the GROINSS-V-II study last year, establishing feasibility and security of inguinofemoral radiotherapy (RT) in sentinel lymph node (SLN) micrometastases as an alternative to inguinofemoral lymphadenectomy (IFL), clinicians worldwide are eager to confirm the widespread of this therapeutical strategy in clinical practice. While this happens, the retrospective cohort study of Brunette et al., based on 5,604 vulvar squamous cell cancer (VSCC) patients, clearly confirms the shift from IFL to SLN detection in pT1b or pT2(<4cm) tumours in the 2006– 2018 period. IFL decreased from 64.1% to 48.8%, while SLN detection increased from 5.7% to 23.3%, without significant changes in 5-year cumulative cancer-specific mortality (15.2% in the SLN group vs 16.9% in the IFL group ; p=0.217 in the propensity score weighted model). [1]

Following with RT as a preeminent tool in the treatment of VSCC, the retrospective subanalysis of Woelber et al. documented 1,618 VSCC stage>1B patients, 360 of whom were included on the basis of nodal involvement (pN+), known RT treatment and known radiation fields. In all, 83.1% were pT1b/pT2 tumours and, in 76.7% of them, R0 resection was achieved. Three groups were analysed, depending on adjuvant treatment received: 43.6% did not receive adjuvant RT ; 15.8% received adjuvant RT to groins/pelvis only, and 40.5% had adjuvant RT to groins/pelvis and vulva. During median follow-up of 17.2 months, recurrence occurred in 25.5%, 22.8%, and 15.8%, respectively, being the risk-reducing effect of local RT to the vulva independent of resection margin status. Fifty-percent disease-free survival time was 20.7 months in the HPV+ group and 17.8 months in HPV- patients, indicating a stronger impact of adjuvant RT to the vulva in this subgroup. [2]

HPV-associated VSCC is increasing, particularly in low- and middle-income countries, where the burden of coincident HIV infection magnifies the risk of developing this still rare malignancy. The work of MacDuffie et al. focusing on treatment patterns and survival outcomes on a prospective cohort of 120 VSCC patients in Botswana, brings some light to the topic. The median age was 42 years. In all, 89% of patients were HIV+ and only 79% received treatment, being 20.8% surgery, 67.5% RT, and 24.2% chemotherapy, alone or in combination. For the HIV+ patients, 54.2% were early stage (FIGO I/II), as were 46.2% of HIV- patients. In the median follow-up of 24.7 months, the overall survival was 74%, worse than that of women in high-income countries, with improved survival of those who received surgery, and poor survival in patients with advanced stage. Survival was not associated with HIV status. [3]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Population-level trends and outcomes of sentinel lymph node biopsy in vulvar cancer surgery in the United States	Brunette LL et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35031190/
2	Adjuvant radiotherapy and local recurrence in vulvar cancer- a subset analysis of the AGO-CaRE-1 study	Woelber L et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34794839/
3	Vulvar cancer in Botswana in women with and without HIV infection: patterns of treatment and survival outcomes	MacDuffie E et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34493586/

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Follow-up after gynaecological malignancies

Sunaina Wadhwa

From January 2009 to March 2019, Sarwar et al. studied 900 patients with stage I–IVa endometrial cancer of all histological subtypes. With a focus on salvageable relapses, the aim of this study was to assess the outcomes of endometrial cancer patients after categorisation into risk groups. Data on the patient and tumour features, the course of treatment, any relapses, deaths, and the most recent follow-up dates were collected. Relapse-free and overall survival rates were calculated, and the ESMO-ESGO 2020 risk stratification was assigned. The follow-up period lasted 35 months, with a median age of 66 years (range: 28–96). Relapse occurred in 16.7% (n = 144) of patients, with 1.3% (n = 12) from the low-risk group, 3.5% (n = 35) from the intermediate risk group, 2.2% (n = 20) from the high-intermediate risk group, and 8.7% (n = 77) from the high-risk group. Salvageable relapses were less frequent at 2% (n = 18), of which 33% (n = 6) were from the low-risk group, 22% (n = 4) from the intermediate risk group, 11% (n = 2) from the high-intermediate risk group, and 33% (n = 6) from the high-risk group. Salvageable relapses were infrequent; therefore, comprehensive hospital-based follow-up is not warranted. In accordance with the recommendations of the British Gynaecological Cancer Society, patient-initiated follow-up is therefore recommended for all risk groups. [1]

To investigate the rate of asymptomatic recurrence of stage I endometrioid endometrial cancer and assess the role of routine hospital follow-up after treatment, Nikolopoulos M et al. retrospectively reviewed 299 patients and concluded that routine clinical examinations have a low yield in finding recurrence. Larger studies are required to support stratified follow-up, which will include telephone and patient-initiated follow-up. [2]

In a retrospective study involving 98 patients with early endometrial cancer, Johnson and Choy came to the conclusion that patient-initiated follow-up and post-surgical treatment of early endometrial cancer are safe and can be used holistically to enhance cardiovascular health. Ninety-one percent of patients suggested this type of model for follow-up in the same circumstances. [3]

In a retrospective analysis, Feinberg et al. evaluated the value of in-person physical examinations for patients involved in a routine surveillance programme in identifying ovarian cancer recurrence. In all, 147 patients with ovarian cancer recurrence during initial clinical remission were included. To assess variations in detection techniques as well as in patient and disease variables, descriptive statistics and bivariate analyses were performed. Recurrences were detected in 46 patients (31%), 81 (55%) by radiographic scan, 17 (12%) by the emergence of new symptoms, and 3 (2%) by biopsies performed during non-oncological surgery. At the time of recurrence, 111 individuals (75%) had multiple positive results. Forty-eight (33%) of the 147 patients reported symptoms; 21 (14%) had physical exam findings, 106 (72%) had increased tumour markers, and 141 (96%) showed changes on imaging. Physical examination alone did not reveal any recurrences. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Stratified follow-up for endometrial cancer: a move to more personalized cancer care	Sarwar A et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34795021/
2	Stage one endometrioid endometrial adenocarcinoma: is there a role of traditional hospital follow-up in the detection of cancer recurrence in women after treatment?	Nikolopoulos M et al.	Obstet Gynecol Sci	https://pubmed.ncbi.nlm.nih.gov/34517692/
3	Patient-initiated follow-up of early endometrial cancer: a potential to improve post-treatment cardiovascular risk?	Johnson RL et al.	Arch Gynecol Obstet	https://pubmed.ncbi.nlm.nih.gov/34363114/
4	Ovarian cancer recurrence detection may not require in-person physical examination: an MSK team ovary study	Feinberg J et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34969828/

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Prevention and management of surgical complications

Anastasia Prodromidou

The retrospective study by Ye et al. evaluated patients who had bowel resection as part of cytoreductive surgery (CRS) due to ovarian cancer (OC) and revealed a 9.2% severe morbidity rate. The reported overall complication rate was 23%. The most commonly reported severe complication was pleural effusion that required drainage (3.5%) while wound dehiscence that required delayed surgical repair reached a rate of 1.8%. The incidence of anastomotic leakage (AL) was 4.2% for the overall population (8 in anastomosis and 1 in the ostomy group). Further analysis of 119 patients who had anastomosis after rectosigmoid resection showed that in end-to-end anastomosis six LA occurred, compared to none in the end-to side. [1]

According to a meta-analysis on the effect of protective ostomies in the reduction of AL during CRS in patients with OC, no difference was detected in postoperative rates of AL among patients who had ostomies and those who had anastomosis after bowel resection (2.719 patients, OR 1.01, 95% CI: 0.6–1.7, p=0.98). This was also observed in subgroup analysis of patients who had rectosigmoid resection with or without other bowel resection (1,416 patients, OR 1.49, 95% CI: 0.91–2.42, p=0.11). The statistical heterogeneity for AL was low (I2=18%, p=0.260). Urgent reoperations were also not different among the two groups (1,452 patients, OR 0.72, 95% CI: 0.35–1.46, p=0.36). [2]

Parrish et al. performed an evaluation of the pharmacotherapeutic prophylaxis for surgical-site infections (SSI), venous thromboembolism (VTE), and post-operative nausea and vomiting (PONV) among patients who had elective colorectal and gynaecologic oncology surgeries from a database of one ERAS site. For SSI prevention, the most prevalent practice included skin preparation with chlorhexidine and single-dose combination of intravenous cefazolin and metronidazole 16–30min before incision. The most common VTE prophylaxis that was prescribed was subcutaneous tinzaparin 4,500 units starting 12 hours after the incision and daily for at least seven days post-discharge in combination with compression stockings. PONV was significantly associated with prolonged length of stay (LOS) while the amount of morphine used had a negative impact on both PONV and LOS. [3]

Ho et al. performed a secondary analysis of a randomised-controlled trial on the postoperative dietary intake and nutrition of 118 gynaecologic oncology patients undergoing elective surgery. The patients were classified into two groups: the early dietary intake achievement (EDIA; 46/118 patients) and the delay dietary intake achievement (DDIA; 72/118 patients). Early dietary intake was related to both shorter length of hospital stay and optimal preservation of body composition. In particular, patients in the EDIA group presented significantly improved outcomes in postoperative weight loss (p=0.002), muscle mass (p=0.018) and handgrip strength (p=0.01) compared to the DDIA group. Preoperative whey protein-infused carbohydrate loading, PONV, age, and time to clear fluid toleration were found to be independent predictors of postoperative intake. The authors highlighted the importance of adopting a dietician-led nutrition and individualisation of the patients' supportive care to hasten their recovery. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	The surgical outcomes and perioperative complications of bowel resection as part of debulking surgery of advanced ovarian cancer patients	Ye S et al.	BMC Surg	https://pubmed.ncbi.nlm.nih.gov/35246104/
2	Protective ostomies in ovarian cancer surgery: a systematic review and meta-analysis	Santana BN et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35245000/
3	Pharmacotherapeutic prophylaxis and post-operative outcomes within an Enhanced Recovery After Surgery (ERAS®) program: A randomized retrospective cohort study	Parrish RH 2nd et al.	Ann Med Surg (Lond)	https://pubmed.ncbi.nlm.nih.gov/35003725/
4	Postoperative dietary intake achievement: A secondary analysis of a randomized controlled trial	Ho CY et al.	Nutrients	https://pubmed.ncbi.nlm.nih.gov/35011097/

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Fertility-sparing treatment in gynaecological malignancies

Charalampos Theofanakis

Endometrial cancer

A meta-analysis by Prodromidou et al. evaluated the addition of metformin to progesterone use in women with endometrial cancer, regarding the prevention of breast cancer and its effect on obesity. This meta-analysis included six studies. On the matter of the pre-surgical treatment with metformin versus placebo, the study revealed no difference. Regarding fertility-sparing management with megestrol acetate and metformin in comparison with monotherapy with 160mg daily MA, the study also revealed no difference. Concerning breast cancer survivors under tamoxifen, metformin was associated with significantly reduced median endometrial thickness after 52 weeks of evaluation compared to the placebo group (2.3mm vs 3.0mm, p=0.05). The authors highlighted a protective effect of metformin in breast cancer survivors under tamoxifen. [1]

Furthermore, a systematic review by Chae-Kim et al. assessed disease relapse after progestin and metformin versus progestin therapy alone in patients with endometrial hyperplasia or cancer. In total, 621 women were included from six studies. Relapse rates were lower for progestin and metformin than for progestin therapy alone, while remission rates were also not significantly different. The authors stated that progestin and metformin therapy is associated with lower relapse rates and similar remission, clinical pregnancy, and live birth rates. [2]

Cervical cancer

A retrospective study by Ekdahl et al. evaluated long-term outcomes after robotic-assisted radical trachelectomy in 149 women. Median tumor size was 9mm (range 3–20mm), 111 women (75%) had FIGO 2009 stage IB1 cancer and 4.8% were node-positive. At a median follow-up of 58 months, 12 of all the women (7.2%) and nine of 149 women (6%) who underwent completed RRT with fertility preservation had recurred and two had died. Seventy of 88 women (80%) who attempted to conceive succeeded, resulting in 81 pregnancies that progressed beyond the first trimester and 76 live births of which 54 (70%) were delivered at term and 65 (86%) delivered after gestational week 32. The authors concluded that recurrence rate is comparable to larger individual studies of minimally invasive or vaginal radical trachelectomy with similar risk profile and follow-up. [3]

Ovarian cancer

A retrospective study by Kasaven et al. aimed to determine the oncological outcomes following fertility-sparing surgery (FSS) for the management of Borderline Ovarian Tumours (BOTs). In the FSS group, the recurrence rate of BOTs was 25.6% (23/90). In the non-FSS group, all recurrences of disease presented as LGSC, with a rate of 7.7% (6/78), following a median of 47.5 months (IQR 47.8). Recurrence of BOT was not significantly associated with the type of FSS performed. The authors stated that non-FSS is associated with negative oncological outcomes compared to FSS. [4]

Furthermore, a retrospective study by Ikeda et al. assessed the effect of adjuvant chemotherapy in 101 young patients' survival, with stage I EOC that underwent FSS. Recurrence was noted in 11 (17.2%) women in the chemotherapy arm and six (16.2%) patients in the observation arm. The 5-year overall and recurrence-free survival (OS/RFS) rates of chemotherapy and observation arms were 86.3/80.8 and 90.2/79.8%, respectively. The study concluded that, even after adjusting for clinicopathologic covariates, performing adjuvant chemotherapy may not improve the oncological outcome in young patients who have undergone FSS. [5]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	The evolving role of targeted metformin administration for the prevention and treatment of endometrial cancer: A systematic review and meta- analysis of randomized controlled trials	Prodromidou A et al.	J Gynecol Obstet Hum Reprod	https://pubmed.ncbi.nlm.nih.gov/33992830/
2	Outcomes of women treated with progestin and metformin for atypical endometrial hyperplasia and early endometrial cancer: a systematic review and meta-analysis	Chae-Kim J et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34785524/
3	Long term oncologic and reproductive outcomes after robot-assisted radical trachelectomy for early-stage cervical cancer. An international multicenter study	Ekdahl L et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34980514/
4	Fertility sparing surgery and borderline ovarian tumours	Kasaven LS et al.	Cancers	https://pubmed.ncbi.nlm.nih.gov/35326636/
5	Is adjuvant chemotherapy necessary for young women with early-stage epithelial ovarian cancer who have undergone fertility-sparing surgery?: a multicenter retrospective analysis	Ikeda Y et al.	BMC Women's Health	https://pubmed.ncbi.nlm.nih.gov/35313889/

Cancer in pregnancy

Michael J. Halaska

Lee et al. evaluated different ultrasonographic scoring systems for ovarian mass diagnosis in patients during pregnancy. The IOTA ADNEX, Sassone, and Lerner systems were examined on a population of 236 patients who underwent surgical treatment for ovarian mass during pregnancy—223 women (94.5%) with a benign ovarian mass and 13 women (5.5%) with a malignant ovarian mass. In all three scoring systems, the highest area under the ROC curve (AUROC) was observed in the Sassone scoring system (0.831), followed by Lerner (0.710) and IOTA ADNEX (0.709); $p < 0.05$. [1]

Non-invasive prenatal testing (NIPT) has been reported several times in a diagnosis of malignancy during pregnancy. Dow et al. described 6 cases of such diagnoses resulting in finding colorectal cancer, breast cancer, melanoma, and Hodgkin lymphoma. This paper tried to set guidelines for interpretation of abnormal NIPT results in order to improve the diagnostic possibilities of this test. [2]

Breast cancer is one of the most prevalent cancer diagnoses found during pregnancy. Suelmann et al. evaluated the influence of gestational age/lactation at diagnosis on histopathologic features of the tumour using a set of 744 patients. When diagnosed during the first trimester, the tumours were less often ER negative (41.9%) compared to the diagnosis during the second and third trimesters (57.4%, $p = 0.036$). During the postpartum period, ER-negative tumours were even more common (63%) in lactating patients, while they constituted of only 49% of tumours in non-lactating women. For human EGF receptor 2, no differences were found. The results are interesting for the knowledge of cancer pathogenesis of pregnancy-associated breast cancer (PABC). [3]

New compounds of systemic therapy concerning checkpoint inhibitors for melanoma (nivolumab/ipilimumab) have been studied by Andrikopoulou et al. Seven cases of pregnancies during which treatment was administered were analysed. In 71.4% of cases, a complication was reported, including intrauterine growth restriction (three cases), HELLP syndrome (one case), placental insufficiency (one case), and low foetal heart rate (one case). The authors concluded that administration of such treatment is not currently recommended during pregnancy. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Ultrasonographic evaluation of ovarian mass for predicting malignancy in pregnant women	Lee SJ et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34561098/
2	Cancer diagnoses following abnormal noninvasive prenatal testing: A case series, literature review, and proposed management model	Dow E et al.	JCO Precis Oncol	https://pubmed.ncbi.nlm.nih.gov/34994626/
3	Pregnancy-associated breast cancer: the influence of gestational age	Suelmann B et al.	Endocr Relat Cancer	https://pubmed.ncbi.nlm.nih.gov/34935632/

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Treatment of pre-invasive gynaecological malignancies

Elko Gliozheni

A comparison of conservative treatment of CIN with imiquimod versus standard excisional technique using LEEP was done by Cokan et al. in an RCT. They randomised patients aged 18–40 with histological HSIL to treatment with imiquimod or LEEP. The primary outcome was defined as the absence of HSIL after either treatment modality. In the imiquimod group, the treatment was successful in 51.9% of the cases, while in the LEEP group the treatment was successful in 92.3% of the cases. They concluded that in patients with HSIL, LEEP remains the gold standard of treatment even though in a subgroup analysis of patients with CIN2p16+, the success rate was comparable but due to the prevalence of side effects, the treatment compliance with imiquimod use may present a clinically important issue. [1]

An investigation on the safety and efficacy of a novel method for treatment of HSIL was done by Zhao et al. in an observational study. In the first group, 16 patients were treated with Nr-CWS once every two days six times. In the second, 184 patients were treated once every two days for 12 times. LEEP was performed once the patients with persistent HR-HPV infection and/or abnormal TCT after the second and last follow-up. The remission rate of cervical HSIL was 100.0% and 87.8% in the first and second groups, respectively, while the control group's remission rate was 25%. The HPV clearance rate was 87.5% and 70.2% in the first and second groups, respectively, and 32.4% in the control group. They reported no serious adverse reaction during treatment and follow-up. Although the sample size was small, Nr-CWS seems an effective and safe drug for treatment of cervical HSIL. [2]

Mac Eochagain et al. assessed through a meta-analysis the serotype-specific efficacy of prophylactic HPV vaccination against HPV16/18 persistent infection and CIN among seropositive, DNA-negative women enrolled in RCTs of HPV L1-based vaccines. From a total of eight studies, with 9,569 participants who met all eligibility criteria, the relative risk of six months persistent infection, 12 months persistent infection, CIN1+, and CIN2+ was significantly reduced in the vaccinated compared to the unvaccinated group. Thus, they concluded that the findings suggest high serotype-specific efficacy for HPV vaccination, including 87% efficacy against HPV16/18 cervical dysplasia. [3]

Beavis et al. aimed to evaluate the complication rate and effectiveness of plasma versus laser ablation in the treatment of vulvovaginal HSIL lesions in a retrospective cohort study. Forty-two women were included, of which 50% underwent plasma and 50% underwent carbon dioxide laser ablation. Complication rates did not differ by treatment: 9.5% for laser ablation versus 4.8% for plasma ablation and over a median follow-up time of 29.3 months recurrence rates were similar: 28.6% in the laser ablation group versus 33.3% in the plasma ablation group. They concluded that plasma energy ablation of vulvovaginal HSIL has similar complication rates and recurrence risk to carbon dioxide laser ablation. This technique could be considered as an alternative to laser ablation while having fewer hazards of operation and regulatory complications. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Comparison of conservative treatment of cervical intraepithelial lesions with imiquimod with standard excisional technique using LLETZ: A randomized controlled trial	Cokan A et al.	J Clin Med	https://pubmed.ncbi.nlm.nih.gov/34945073/
2	The safety and efficacy of a novel method for treatment of HSIL	Zhao J et al.	Arch Gynecol Obstet	https://pubmed.ncbi.nlm.nih.gov/33813597/
3	HPV vaccination among seropositive, DNA negative cohorts: a systematic review & meta-analysis	Mac Eochagain C et al.	J Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35128855/
4	Treatment of vulvar and vaginal dysplasia: plasma energy ablation versus carbon dioxide laser ablation	Beavis A et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34610972/

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Pathology of gynaecological cancers

Nicolas Samartzis and Dimitrios Rafail Kalaitzopoulos

Endometrial cancer

After including patients from PORTEC-3, Horeweg et al. investigated the role of B-cells and tertiary lymphoid structures (TLS) in endometrial cancer using single cell RNA-sequencing. L1CAM overexpression in TLS shows strong favourable prognostic impact, independent of clinicopathological and molecular factors. [1]

Wang et al. examined 182 endometrial carcinoma biopsies and then re-evaluated the PTEN IHC pattern in comparison to next-generation sequencing in identifying PTEN abnormality. They found five PTEN IHC patterns (absent, subclonal loss, equivocal, reduced, and retained). A sensitivity of 75.4% (95% CI: 62.7–85.5%), specificity of 84.6% (95% CI: 76.2%–90.9%), and accuracy of 81.2% (95% CI: 74.4%–86.9%) was observed in absence of PTEN IHC. [2]

A meta-analysis conducted by Travaglino et al. aimed to assess the prognostic value of MMRd and p53wt subtypes of clear cell endometrial cancer. Six studies with 136 cases were included. Five-year OS was 95.7% in the MMRd group compared to 40.6% in the p53abn group. No significant differences in prognosis between cases with p53wt and p53abn were found. The author concluded that MMRd clear cell endometrial cancer could be considered prognostically similar to MMRd endometrioid carcinomas and p53wt seems not to differ from p53abn clear cell cancer, suggesting a similar management. [3]

Takahashi et al. used molecular profiling of endometrial carcinomas in Japanese patients with poor prognosis to identify pathways that may be of therapeutical value. They demonstrated that somatic mutations of the Rho GTPase activating protein 35 (ARHGAP35) are accumulated in POLE and MSI subgroups. ARHGAP35 is associated with the promoter region of the glucocorticoid receptor gene and was previously reported in endometriosis and normal endometrium, but the link to chromosomal instability has not yet been established. [4]

Ovarian cancer

Launonen et al. conducted a study aiming to discover how BRCA 1/2 mutations shape the cellular phenotypes and spatial interactions of the tumour microenvironment in high-grade serous ovarian cancer. Spatial proteomic data from multiplex immunofluorescence with 21 markers in 124,623 single cells from 31 tumours with BRCA1/2 mutation (BRCA1/2mut), and from 13 tumours without alterations in HR genes showed that the microenvironment of BRCA1/2 mutated tumours is associated with increased immunosurveillance and the proliferative tumour-cell subpopulation have a prognostic role. [5]

The overall survival and progression-free survival in serous and endometrioid ovarian cancer were investigated in a multicentre retrospective study from the French Epidemiological Strategy and Medical Economics OC database. Patients having an endometrioid ovarian cancer were younger, less often diagnosed at an advanced stage, with lower-grade tumours, had more frequently dMMR/MSI-high and more personal or familial cases of Lynch syndrome. A multivariate analysis showed, independently of age, ECOG-PS, FIGO and grade, a significantly better 5-year OS rate (81% vs 55%) and 5-year PS rate (55% vs 16%) for endometrioid compared to serous ovarian cancer. [6]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Tertiary lymphoid structures critical for prognosis in endometrial cancer patients	Horeweg N et al.	Nat Commun	https://pubmed.ncbi.nlm.nih.gov/35296668/
2	Immunohistochemistry and next-generation sequencing are complementary tests in identifying PTEN abnormality in endometrial carcinoma biopsies	Wang et al.	Int J Gynecol Pathol	https://pubmed.ncbi.nlm.nih.gov/33720084/
3	Clear cell endometrial carcinomas with mismatch repair deficiency have a favorable prognosis: A systematic review and meta-analysis	Travaglino et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34266691/
4	Activation of oxidative phosphorylation in TP53-inactive endometrial carcinomas with a poor prognosis	Takahashi et al.	Int J Gynecologic Cancer	https://pubmed.ncbi.nlm.nih.gov/34725206/
5	Single-cell tumor-immune microenvironment of BRCA1/2 mutated high-grade serous ovarian cancer	Launonen et al.	Nat Commun	https://pubmed.ncbi.nlm.nih.gov/35149709/
6	Clinicopathological characterization of a real-world multicenter cohort of endometrioid ovarian carcinoma: Analysis of the French national ESME-Unicancer database	De Nonneville et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34294414/

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

Joanna Kacperczyk-Bartnik

Treatment

Cheng et al. performed a single-centre, single-arm, open-label, phase II trial examining the effectiveness of treatment with camrelizumab and apatinib in 20 women with chemorefractory or relapsed gestational trophoblastic neoplasia. Complete response to camrelizumab plus apatinib was achieved in 10 (50%) patients and partial response was observed in one (5%) patient. Ten women were treated with subsequent multidrug chemotherapy regimens resulting in complete response in seven of them. Death due to disease progression occurred in two patients. Study results could contribute to an alternative salvage therapeutic option less cytotoxic than chemotherapy regimens. [1]

Follow-up

In a multicentre observational study by Descargues et al., the authors determined the risk of gestational trophoblastic neoplasia in 7,761 after human chorionic gonadotropin normalisation following molar gestation. Development of gestational trophoblastic neoplasia was observed in 20 women—0.26% of the studied group. The highest risk of malignant transformation was identified in women with twin molar pregnancy (2 out of 95 patients, 2.1%). Histologically proven diagnosis of partial mole was associated with 0% risk of malignancy (0 in 2,592 cases). Eighteen out of 5,045 (0.36%) patients with complete mole developed malignancy. The authors propose extension of quarterly human chorionic gonadotropin measurements for patients with risk factors for late malignancy transformation and the history of complete molar or twin molar pregnancy. [2]

Psychology

In a prospective observational multicentre study, Blok et al. evaluated the psychological impact of gestational trophoblastic disease (GTD) in 60 patients immediately after the diagnosis. In 88% of patients, the psychological effect of GTD could be considered an adaptation problem after a traumatic event. Anxiety was present in 47% of the study group. Depressive symptoms were diagnosed in 27% of patients, and distress occurred in 70% of the studied women. The obtained results showed a higher rate of psychological problems than the general population and patients who experienced miscarriage. Psychological support is advised in this group. [3]

Fertility

Cai et al. analysed the clinical outcomes of IVF/ICSI treatments between 2016 and 2020 in a population with secondary infertility and the history of gestational trophoblastic disease (n = 48) compared to controls (n = 8415) without GTD. There were no significant differences regarding the implantation rate nor the incidence of ovarian hyperstimulation syndrome. Patients with GTD history had a lower number of live-births (34.1% vs 66.7%), a higher number of abandoned embryos, a lower number of good-quality embryos, and abnormal immunohistochemical results associated with endometrial receptivity compared to the control group. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Camrelizumab plus apatinib in patients with high-risk chemorefractory or relapsed gestational trophoblastic neoplasia (CAP 01): a single-arm, open-label, phase 2 trial	Cheng H et al.	Lancet Oncol	https://pubmed.ncbi.nlm.nih.gov/34624252/
2	Gestational trophoblastic neoplasia after human chorionic gonadotropin normalization in a retrospective cohort of 7761 patients in France	Descargues P et al.	Am J Obstet Gynecol	https://pubmed.ncbi.nlm.nih.gov/34019886/
3	The psychological impact of gestational trophoblastic disease: a prospective observational multicentre cohort study	Blok LJ et al.	BJOG	https://pubmed.ncbi.nlm.nih.gov/34314567/
4	Association between gestational trophoblastic disease (GTD) history and clinical outcomes in in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycles	Cai X et al.	Reprod Biol Endocrinol	https://pubmed.ncbi.nlm.nih.gov/35120557/

Nutrition and perioperative care

Begoña Díaz de la Noval

Said et al. published a retrospective analysis on the impact of splenectomy in oncologic outcomes of FIGO stage IIIC and IV epithelial ovarian cancer (EOC) patients (n=3978). The research compared the survival of advanced EOC assessed to splenectomy (n=99) or not (n=3812). Patients were registered in the Netherlands Cancer Registry between 1 January 2008 and 31 December 2015. Results show that patients splenectomised had less favourable perioperative outcomes, as increased blood loss and blood transfusion, surgical infection, reintervention, and length of stay at hospital, but no difference in survival. The median progression-free survival was 16 and 18 months for the non-splenectomy and splenectomy patients (p=0.043), respectively; with an overall survival of 36 months for both groups (p=0.306). Thus, splenectomy could be justified to achieve complete cytoreduction in advanced-stage EOC patients. However, the study included a small number of patients in the group of splenectomy and some data weren´t available or reported, so external validation is limited. [1]

Cianci et al. published a single-centre clinical trial on the role of intraoperative thoracostomy tube placement after diaphragmatic resection (DR) in advanced-stage ovarian cancer (DRAGON-trial). Eighty-eight patients were randomised to intra-operative thoracostomy tube placement (TP) or not (NTP). The chest tube was used a prevention measure for postoperative complications (respiratory symptoms and pleural effusion) after DR. No statistically significant differences were detected for intra- and post-operative complications (p=0.291, p=0.127), hospital stay (p=0.511) and time to start chemotherapy (p=0.483). The extension of DR had no influence on outcomes. [2]

The BENITA study evaluated the safety and acceptance of a combined exercise and nutrition intervention during and after first-line chemotherapy in advanced ovarian cancer. Primary, acceptance rate was 25%. Fifteen patients were randomised to intervention (a 12-month exercise and nutrition programme) or control group (usual care). Eleven patients completed the study. No adverse events were reported, so it was assumed that patients with ovarian cancer may benefit from an individualised exercise and nutrition intervention. However, a large multicentre RCT is needed in order to investigate the effectiveness of the intervention on health-related quality of life, cancer-related fatigue, and survival. [3]

The Cochrane Library published an updated review on perioperative enhanced recovery (ERAS) programmes for women with major surgery for gynaecological cancers. Only randomised controlled trials were selected, but the reliability of methodological quality had a high bias. ERAS programmes may reduce the length of postoperative hospital stay (low-certainty evidence), have no difference in postoperative complications (low-certainty evidence), reduce the readmission rate within 30 days of operation (low-certainty evidence), and increase the time to first defaecation (low-certainty evidence). The evidence on mortality within 30 days of discharge, economic outcomes, and patient satisfaction was unreliable. Further well-conducted studies are required to validate the certainty of these findings. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Oncologic outcomes after splenectomy during initial cytoreductive surgery in advanced epithelial ovarian cancer: a nationwide population-based cohort study	Said SA et al.	Acta Obstet Gynecol Scand	https://pubmed.ncbi.nlm.nih.gov/34719790/
2	Surgical outcomes of diaphragmatic resection during cytoreductive surgery for advanced gynecological ovarian neoplasia: A randomized single center clinical trial - DRAGON	Cianci S et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34844774/
3	Randomised controlled trial testing the feasibility of an exercise and nutrition intervention for patients with ovarian cancer during and after first-line chemotherapy (BENITA-study)	Maurer T et al.	BMJ Open	https://pubmed.ncbi.nlm.nih.gov/35197344/
4	Perioperative enhanced recovery programmes for women with gynaecological cancers	Chau JPC et al.	Cochrane Database Syst Rev	https://pubmed.ncbi.nlm.nih.gov/35289396/

Quality of life in gynaecological cancers/Palliative care

Engin Çelik

Noll et al., in a recently published "corner of the world" article, mentioned that, based on recent estimations, ovarian cancer will increase by 40% in the near future. Low and medium human development indexed countries will have greatest load, while as most of these countries do not have cancer registry, accurate strategies can not be designed. The World Ovarian Cancer Coalition and the International Gynecologic Cancer Society are creating a survey to collect information from 300 hospitals in 30 countries to resolve this problem. [1]

Davidson et al. have performed a multi-faceted intervention to increase the rate of outpatient goals of care (GOC) conversations in women with gynaecologic cancers who are at high-risk of death. They reported that, in an overall sample of 220 patients, timely documentation increased from 30.2% to 88.7% ($p < 0.001$). In the post-pilot period (2019–2020), gynaecologic cancer patients had a higher rate of GOC documentation (81% vs 9%, $p < 0.001$), a lower rate of receiving chemotherapy during the last 14 days of life (2% vs 5%, $p = 0.051$), and no difference in end-of-life admissions (29% vs 31%, p = NS). Therefore, they concluded that implementation of systematic outpatient identification of high-risk gynaecologic oncology patients is feasible, sustainable, and increases the timely conduct of GOC conversations. [2]

Lee et al. evaluated symptoms and health-related effect of chemotherapy in recurrent ovarian cancer patients. Platinum resistant/refractory recurrent ovarian cancer (PRR-ROC) (n = 546) and potentially platinum sensitive with ≥3 lines of chemotherapy (PPS-ROC ≥3) recurrent ovarian cancer patients were included in the study.

The measure of ovarian cancer symptoms and treatment (MOST) and European Organisation for Research and Treatment of Cancer (EORTC) quality life questionnaire (QLQ-C30) were completed by patients at baseline and before each cycle of chemotherapy. According to MOST indexes, 54% of patients have abdominal symptoms and 40% of were improved after chemotherapy with a median time to improve range from four to 7 weeks. Progression-free survival was longer, while abdominal discomfort was resolved after chemotherapy (median 7.2 vs 2.5 months, $p < 0.0001$). [3]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Building opportunities to improve quality of life for women with ovarian cancer in low- and middle-income countries: the Every Woman Study	Noll F et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/35314459/
2	Promoting timely goals of care conversations between gynecologic cancer patients at high-risk of death and their providers	Davidson BA et al.	Gynecologic Oncology	https://pubmed.ncbi.nlm.nih.gov/34922770/
3	Symptom burden and quality of life with chemotherapy for recurrent ovarian cancer: the Gynecologic Cancer InterGroup-Symptom Benefit Study	Lee YC et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/35086926/

Treatment of elderly patients with gynaecological cancers

Alex Mutombo

In a retrospective study evaluating the prognostic impact of global health status assessment tools in elderly patients with endometrial cancer on survival, Anic et al. found that only the G8 Score retained independent significance as a prognostic factor for disease-specific survival (DSS) (HR:4.58, 95% CI: 1.35–15.51) and overall survival (OS) (HR: 2.89, 95% CI: 1.31–6.39). In this study, 92 patients (61.3%) were classified as G8-non-frail with a significantly increased DSS and OS rate compared to the 58 G8-frail patients (DSS: 93.8% vs 60.8%, $p < 0.001$ and OS:88.2% vs 49.7%; $p < 0.001$, respectively). [1]

In a position paper, a consortium of French oncology societies has proposed multi-disciplinary care planning of ovarian cancer in older patients. According to them, the treatment pathway should be based on four successive decisional nodes (diagnosis, resectability assessment, operability assessment, adjuvant, and maintenance treatment decision) implying multidisciplinarity and adaptation of the treatment plan according to the patient's geriatric covariates and motivation for treatment. [2]

Ekmann-Gade et al. in Denmark evaluated clinical trends for 7,522 younger and older epithelial ovarian cancer patients, focusing on incidence, treatment, and survival changes. In 2014–2018, 36% and 24% had primary debulking surgery for younger and older patients, respectively, compared to 72% and 62% in 2005–2009. Two-year cancer-specific survival increased from 75% (2005–2009) to 84% (2014–2018) for younger patients and from 53% to 66% for older patients. After adjusting for potential confounders, age >/= 70 was associated with a 1.4-fold increased risk of cancer-specific death (95% CI: 1.2–1.5) [3]

The Belgian and Luxembourg Gynaecological Oncology Group conducted a multicentre, non-interventional prospective study to evaluate the safety and effectiveness of treatment with bevacizumab in combination with frontline carboplatin and paclitaxel chemotherapy. As reported in the paper by Vergote et al., the most frequently reported adverse events for bevacizumab were hypertension (55%), epistaxis (32%), and proteinuria (21%). The Kaplan-Meier estimate of progression-free survival was 14.5 months. Elderly patients aged 70 years and older should not be excluded from treatment for advanced ovarian cancer based on age alone. [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	The preoperative G8 geriatric screening tool independently predicts survival in older patients with endometrial cancer: results of a retrospective single-institution cohort study	Anic K et al.	J Cancer Res Clin Oncol	https://pubmed.ncbi.nlm.nih.gov/35212815/
2	Multi-Disciplinary Care Planning of Ovarian Cancer in Older Patients: General Statement-A Position Paper from SOFOG-GINECO-FRANCOGYN-SFPO	Bengrine L et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/35267603/
3	Incidence, treatment, and survival trends in older versus younger women with epithelial ovarian cancer from 2005 to 2018: A nationwide Danish study	Ekmann-Gade AW et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34716025/
4	Prospective non-interventional BELOVA/BGOG-ov16 study on safety of frontline bevacizumab in elderly patients with FIGO stage IV ovarian cancer: a study of the Belgian and Luxembourg Gynaecological Oncology Group	Vergote I et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/35063943/

COVID-19 and Gynaecological cancers

Jakub Dobroch

A wide-ranging Dutch study conducted by Algera et al. examined the topic of gynaecologic oncological radical surgeries count and delay in the pandemic. One of the major observed results was a significant decrease (-17.2%) in the number of yearly performed cervical cancer surgeries compared to pre-COVID period. There was also a trend of more frequent neoadjuvant chemotherapy prescription noticed when considering advanced cases of gynaecological malignancies. The registered complications rate in gyn-onc surgery remained at a similar level regardless of epidemiological situation. [1]

Extended results from an observational study presented in LiFE Report 13 was provided by researchers from New York. An updated analysis included 193 patients that had been diagnosed with gynaecological cancer and COVID-19. The mortality associated with SARS-CoV-2 infection in this group was observed to be 17.6%. A risk of a severe course of COVID-19 and hospital admission was associated with age over 65 years, poor clinical condition at diagnosis, and presence of comorbidities. Prior prescription of cytotoxic treatment was neither connected with a more frequent hospitalisation nor with an increased mortality. [2]

Federico et al. published a noteworthy paper considering vulvar cancer and SARS-CoV-2 infection epidemiology. Out of 191 patients diagnosed with cancer, 7 presented as COVID-19 positive. Despite the small number of patients in the aforementioned group, the results provided information about a strongly negative impact of COVID-19 complications in vulvar cancer management. Only three patients experienced no further obstacles due to an infection. Two patients had their treatment postponed and then abandoned because of primary disease progression. Other two patients died due to respiratory complications in the postoperative period. [3]

A study concerning the psychological state of patients during lockdown was conducted in France. There were 205 patients included with diagnosed gynaecological malignancies, also including breast cancer. Seven of them were diagnosed as SARS-CoV-2 positive and two died due to complications. The results revealed a significant rate of treatment postponement (35.1% of analysed cases) or cancellation (5.4%). Patients whose therapy was affected by the pandemic restrictions were more likely to be diagnosed with anxiety disorders. Furthermore, patients' overall health status and signs of anxiety, based on standardised questionnaires, were significantly improved after the abandonment of lockdown. [4]

Palaia et al. performed a prospective study whose objective was to study the efficacy and safety of a two-dose Pfizer/BioNTech vaccination in gynaecologic oncology patients. In the whole group of 44 ovarian, endometrial, and cervical cancer patients, no severe adverse effects were observed. A lower title of anti-SARS-CoV-2 IgG antibodies was recognized in the study group compared with healthy women. BMI over 30 and age over 50 years were significantly associated with reduced response based on - or 3-month IgG titles. In conclusion, the authors underlined the significant role of vaccine boost in patients with diagnosed gynaecological cancer. [5]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	Impact of the COVID-19-pandemic on patients with gynecological malignancies undergoing surgery: A Dutch population-based study using data from the 'Dutch Gynaecological Oncology Audit'	Algera MD et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/35221132/
2	COVID-19 outcomes of patients with gynecologic cancer in New York City: An updated analysis from the initial surge of the pandemic.	Lara OD et al.	Gynecol Oncol	https://pubmed.ncbi.nlm.nih.gov/34922769/
3	Clinical impact of SARS-CoV-2 infection among patients with vulvar cancer: the Gemelli Vul.Can multidisciplinary team	Federico A et al.	Int J Gynecol Cancer	https://pubmed.ncbi.nlm.nih.gov/34903559/
4	The psychological impact of therapeutic changes during the COVID-19-lockdown for gynaecological and breast cancer patients	Lamblin G et al.	Gynecol Obstet Hum Reprod	https://pubmed.ncbi.nlm.nih.gov/35007776/
5	Pfizer-BioNTech COVID-19 vaccine in gynecologic oncology patients: A prospective cohort study	Palaia I et al.	Vaccines (Basel)	https://pubmed.ncbi.nlm.nih.gov/35062673/

Epidemiology in Gynaecological Oncology: systematic reviews and meta-analyses

Catherine O'Gorman

Ovarian Cancer

Breastfeeding as an ovarian cancer risk-reducing strategy for BRCA1 and 2 mutation carriers was evaluated in a systematic review and meta-analysis by Eoh et al. The authors found that breastfeeding carries a protective effect for ovarian cancer. For BRCA1 mutation carriers who breastfed, the risk was reduced by 23% (OR 0.767, 95% CI: 0.688–0.856) without significant change if breastfeeding was continued to more than one year (OR 0.787, 95% CI: 0.682–0.907). However, for BRCA2 mutation carriers, there was no significant risk-reduction demonstrated until breastfeeding was continued to more than one year (OR 0.567, 95% CI: 0.400–0.802). [1]

Evidence has been conflicting around the risk of ovarian cancer possibly associated with the use of talcum powder, with heterogeneity in exposure levels included. Woolen et al. performed a systematic review and meta-analysis on the risk associated with frequent use (≥2 per week) of talc. The risk of ovarian cancer was found to be increased with frequent use of talc (OR 1.47, 95% CI: 1.31–1.65). [2]

Considering higher short-term ovarian cancer survival rates in BRCA-mutation carriers, Nashon et al. investigated the long-term survival rates compared to BRCA wild-type carriers with a systematic review and meta-analysis. The data of over 4,500 patients from 13 studies were analysed (1,131 BRCA-m and 3434 BRCA-wt) and the primary outcome was the conditional probability of surviving an additional five years among patients already surviving five years after diagnosis. Survival was found to be improved at five years in the presence of BRCA mutations [Risk Difference (RD) 14.9%, p=0.0002, risk ratio (RR)=1.36, p=0.001] but conditional survival for BRCA 1/2mutation carriers at 10 years was not improved (RR 0.97, p=0.78). Neither BRCA mutation subtype held any significant survival advantage at 10 years (BRCA1 RR 0.98, p=0.81; BRCA2 0.80, p=0.48). [3]

Vulvar

Differentiated vulvar intraepithelial neoplasia (dVIN) is a rare premalignant lesion of HPV-independent squamous cell carcinoma (SCC) of the vulva. Studies included in a systematic review by Voss et al. demonstrated that dVIN carries an absolute risk of Vulval SCC that ranges from 33%–86%, with a median interval from dVIN diagnosis to VSCC diagnosis of 9–23 months. The risk of recurrence of VSCC ranged from 32%–94% with a median recurrence interval of 13–32 months. Recurrence of VSCC was significantly more likely in those with positive surgical margins for dVIN (61% vs 42% after 10 years, p=0.002). [4]

Relevant articles retrieved September 30, 2021 – March 31, 2022

No	Title	Authors	Journal	Link to abstract
1	The preventive effect of breastfeeding against ovarian cancer in BRCA1 and BRCA2 mutation carriers: A systematic review and meta-analysis	Eoh KJ et al.	Gynecologic Oncology	https://pubmed.ncbi.nlm.nih.gov/34304906/
2	Association between the frequent use of perineal talcum powder products and ovarian cancer: a systematic review and meta-analysis	Woolen SA et al.	Journal of General Internal Medicine	https://pubmed.ncbi.nlm.nih.gov/35112281/
3	Five -year survival decreases over time in patients with BRCA-mutated ovarian cancer: a systemic review and meta-analysis	Nahshon C et al.	International Journal of Gynecological Cancer	https://pubmed.ncbi.nlm.nih.gov/32522775/
4	The vulvar cancer risk in differentiated vulvar intraepithelial neoplasia: A systematic review	Voss FO et al.	Cancers (Basel)	https://pubmed.ncbi.nlm.nih.gov/34944788/

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