Review Article

Precision, prevention and progress: charting two decades of change in gynaecological oncology—a narrative review

Sabina Ioana Nistor[1#^], Ruyu Shao[2#^], Jacopo Conforti[1,3^], Francis Gardner[1], Federico Ferrari[3^], Lamiese Ismail[4^], Xiaoyu Niu[5^], Desheng Yao[2^], Hooman Soleymani majd[1,6^]

[1]Department of Gynaecological Oncology, Churchill Hospital, Oxford University Hospitals National Health Service (NHS) Foundation Trust, Oxford, UK; [2]Department of Gynaecological Oncology, Guangxi Medical University Cancer Hospital, Nanning, China; [3]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy; [4]Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford University Hospitals National Health Service (NHS) Foundation Trust, Oxford, UK; [5]Obstetrics and Gynaecology Department, The West China Second University Hospital of Sichuan University, Chengdu, China; [6]Nuffield Department of Women's and Reproductive Health, University of Oxford, Oxford, UK

Contributions: (I) Conception and design: SI Nistor, R Shao, H Soleymani majd; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: SI Nistor, R Shao, J Conforti; (V) Data analysis and interpretation: SI Nistor, R Shao, H Soleymani majd; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work as co-first authors.

Correspondence to: Hooman Soleymani majd, MD. Department of Gynaecology Oncology, Churchill Hospital, Oxford University Hospitals National Health Service (NHS) Foundation Trust, Old Rd, Headington, Oxford OX3 7LE, UK; Nuffield Department of Women's and Reproductive Health, University of Oxford, Oxford, UK. Email: hooman.soleymanimajd@msd.ox.ac.uk.

Background and Objective: The field of Gynaecological Oncology (GO) has undergone a paradigm shift over recent decades, shaped by advancements in prevention, molecular therapeutics, and surgical innovation. We explore how the management of gynaecological malignancies has transformed in the past 25 years.

Methods: A structured narrative review of landmark publications and guideline updates published between 2000 and 2025 was undertaken. Key developments in the management of cervical, ovarian, endometrial, vulvar, and vaginal cancers were critically analysed, with particular focus on prevention strategies, surgical evolution, and integration of targeted and immune therapies.

Key Content and Findings: In cervical cancer, population-level human papillomavirus (HPV) vaccination has dramatically reduced incidence, while the LACC and SHAPE trials prompted a return to open and less radical surgery, respectively. Sentinel node biopsy is supplanting systematic lymphadenectomy, and combined chemoradiotherapy (CRT) with immunotherapy is improving survival in locally advanced disease. For ovarian cancer, optimal cytoreduction remains key, with TRUST highlighting surgical quality, while heated intraperitoneal chemotherapy (HIPEC) and poly-ADP ribose polymerase (PARP) inhibitors—alone or combined with immunotherapy—extend progression-free survival (PFS). Endometrial cancer management is now driven by molecular classification [The Cancer Genome Atlas (TCGA)/Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE)], with immunotherapy and targeted therapy transforming outcomes. In vulvar and vaginal cancers, GROINSS-V (Groin Sentinel Node Trial in Vulvar Cancer) and related studies underpin de-escalated and minimally invasive nodal surgery, while immunotherapy emerges for advanced disease.

Conclusions: Modern GO is defined by prevention, precision, and personalisation. The contemporary Gynaecological Oncologist now integrates molecular insight, function-preserving surgery, and multidisciplinary collaboration to deliver optimised, patient-centred care.

^ ORCID: Sabina Ioana Nistor, 0009-0000-1228-1602; Ruyu Shao, 0009-0009-0638-9452; Jacopo Conforti, 0009-0004-2831-2134; Federico Ferrari, 0000-0001-7065-2432; Lamiese Ismail, 0000-0002-3106-0730; Xiaoyu Niu, 0000-0002-4058-9564; Desheng Yao, 0000-0002-2124-3138; Hooman Soleymani majd, 0000-0003-3293-5321.

© AME Publishing Company.

Keywords: Precision medicine; cancer prevention; Gynaecological Oncology (GO); targeted therapy; surgery de-escalation

Submitted Jan 01, 2026. Accepted for publication Apr 01, 2026. Published online Apr 28, 2026.
doi: 10.21037/tcr-2025-1-2924
View this article at: https://dx.doi.org/10.21037/tcr-2025-1-2924

Introduction

The field of Gynaecological Oncology (GO) has been reshaped in the past decades. Substantial progress has been seen in preventative strategies such as human papillomavirus (HPV) vaccination, while molecular markers have revolutionised neoadjuvant and adjuvant therapies. Growing evidence supports de-escalation of surgery for vulval, vaginal and cervical cancer, while ultra-radical cytoreductive surgery, involving multivisceral resections, upper abdominal and thoracic surgery remains essential for carefully selected patients with advanced ovarian cancers.

This is a narrative review of the recent landmark publications driving change in GO. We aim to describe how our speciality is changing and what the role of the contemporary GO surgeon would entail. We present this article in accordance with the Narrative Review reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1-2924/rc).

Methods

We conducted a structured narrative review of major advances in the management of cervical, ovarian, uterine, vulval and vaginal malignancies and gestational trophoblastic neoplasia (GTN) published between January 2000 and March 2025. Literature searches were performed in PubMed and Google Scholar.

The search strategy is described in *Table 1*.

Studies were considered "landmark" if they met one or more of the following criteria:

(I) Phase III randomised controlled trials demonstrating clinically meaningful survival or toxicity outcomes;
(II) Prospective multicentre trials establishing new diagnostic or surgical standards;
(III) Studies that directly informed major international guideline updates [e.g., European Society of Gynaecological Oncology (ESGO), International Federation of Gynecology and Obstetrics (FIGO), National Comprehensive Cancer Network (NCCN)];
(IV) Large population-based or international cohort studies influencing clinical practice.

Titles and abstracts were screened by the authors to identify relevant publications.

Approximately 600 records were screened, with 220 full-text articles assessed for eligibility and 98 ultimately included. Given the narrative nature of the review, formal meta-analysis was not performed. However, evidence was prioritised using a predefined hierarchy [guidelines > phase III randomized controlled trials (RCTs) > prospective cohort studies > retrospective analyses]. Findings were synthesised thematically to illustrate major paradigm shifts in prevention, surgical management and systemic therapy across tumour sites

Cervical cancer

The management of cervical cancer has seen major advancements over the past decade, driven by widespread HPV vaccination, a return to open surgery over minimally invasive surgery (MIS) techniques, de-escalation of surgery for early-stage disease, and advances in non-surgical therapies. Large randomized trials—including PATRICIA (bivalent HPV-16/18) (1), FUTURE I & II (quadrivalent HPV-6/11/16/18) (2,3), the Costa Rica vaccine trial (4), and the nonavalent HPV vaccine trial (5)—demonstrate >90% efficacy in preventing CIN2+/CIN3+ from vaccine HPV types in HPV-naïve women, with durable (>10-year) protection and cross-protection. Real-world data from Sweden (6), Scotland (7), Australia (8), and England (9) confirm these benefits, showing up to 88% reductions in invasive cervical cancer and near-elimination of CIN3+ in fully vaccinated cohorts. The UK introduced the bivalent vaccine in 2008 and transitioned to the nonavalent vaccine in 2023 for girls and boys aged 12–13 years. This is expected to be a powerful and long-lasting intervention for cervical cancer prevention.

Surgical practice shifted dramatically after the 2018

© AME Publishing Company.

Table 1 Search strategy

Items	Specification
Date of search	Initial search performed on 01.07.2025
	Search repeated on 31.12.2025
Databases and other sources searched	PubMed, Google Scholar
Search terms used	• Cervical cancer: ("cervical cancer" OR "cervix carcinoma") AND ("radical hysterectomy" OR "sentinel lymph node" OR "chemoradiotherapy" OR "immunotherapy")
	• Ovarian cancer: ("ovarian cancer") AND ("prevention" OR "primary debulking" OR "neoadjuvant chemotherapy" OR "HIPEC" OR "PARP inhibitor" OR "bevacizumab" OR "immunotherapy")
	• Endometrial cancer: ("endometrial cancer") AND ("Lynch syndrome" OR "laparoscopy" OR "molecular classification" OR "sentinel node" OR "immunotherapy" OR "adjuvant therapy")
	• Uterine sarcoma: ("uterine sarcoma") AND ("molecular" OR "surgery" OR "hormonal therapy" OR "chemotherapy" OR "radiotherapy")
	• Vulvar cancer: ("vulvar cancer") AND ("sentinel node biopsy" OR "inguinofemoral lymphadenectomy" OR "surgery" OR "immunotherapy")
	• Vaginal cancer: ("vaginal cancer") AND ("surgery" OR "radiotherapy")
	• Gestational trophoblastic neoplasia: ("gestational trophoblastic neoplasia") AND ("chemotherapy" or "immunotherapy")
Timeframe	01.01.2000–31.12.2025
Inclusion and exclusion criteria	Included: prospective and retrospective cohorts, randomised controlled trials, systematic reviews and meta-analyses, international guidelines adding a valuable contribution to the field of Gynaecological Oncology
	Excluded: publications which have not had an impact on clinical practice and were not thought to be relevant
Selection process	Studies selected by S.I.N. and R.S. independently. Consensus obtained by S.I.N., R.S., H.S.M. Final manuscript was reviewed by all authors

HIPEC, heated intraperitoneal chemotherapy; PARP, poly-ADP ribose polymerase.

LACC trial (10), which showed inferior disease-free survival (DFS) and overall survival (OS) with MIS compared with open radical hysterectomy, with MIS associated with up to a six-fold higher risk of death. This led to rapid guideline changes, with open surgery becoming the recommended approach for early cervical cancer—except FIGO stage IA1 disease without lymphovascular space invasion (LVSI). While the LACC trial demonstrated inferior survival with minimally invasive radical hysterectomy, its interpretation has been debated due to lack of standardisation of surgical technique, potential variability in surgical expertise, and early trial termination, raising the possibility that outcomes may reflect procedural factors rather than a universal limitation of minimally invasive approaches. Ongoing trials—RACC (11), ROCC (12), and LAUNCH-2 (13)—are evaluating whether improved laparoscopic or robotic approaches (e.g. avoiding uterine manipulators or using tumour-containment strategies) may be oncologically safe.

Growing evidence also supports reducing surgical radicality in selected early-stage cases. The ConCerv trial [2021] (14) showed that conservative procedures such as conization or simple hysterectomy with nodal assessment, are safe for very low-risk IA2–IB1 tumors—<2 cm, negative LVSI, clear margins—reporting a 3-year recurrence rate of 3.5%. The LESSER trial [2021] (15) found no early oncological disadvantage with simple *vs.* modified radical hysterectomy. The SHAPE trial [2023] (16), a large phase III RCT, confirmed that simple hysterectomy is non-inferior to radical hysterectomy for low-risk tumors ≤2 cm, with lower urinary tract morbidity and better quality of life. While the SHAPE trial provides high-level evidence supporting surgical de-escalation in early-stage cervical cancer, its findings should be interpreted within the context of several limitations. The study population was highly

© AME Publishing Company.

selected, restricted to patients with tumours ≤2 cm and favourable pathological features, limiting generalisability to higher-risk disease. The non-inferiority design and relatively low event rates raise the possibility that small differences in oncological outcomes may not yet be fully detected, particularly given the still-maturing follow-up. In addition, the widespread use of MIS within the trial introduces complexity in interpretation in the post-LACC era. A recent meta-analysis (17) pooling these and other datasets reported no significant differences in recurrence or survival between simple and radical hysterectomy, but a clear reduction in perioperative and long-term complications with the less radical approach. Collectively, these findings support tailoring surgical radicality to tumour characteristics to preserve function and quality of life without compromising oncological outcomes. Building on the results of the LACC and SHAPE trials, the single-arm prospective multicentre study LASH is investigating whether MIS simple hysterectomy represents an oncologically safe approach in selected patients with low-risk cervical cancer (FIGO 1A2–1B1, size <2 cm) (18).

Another major area of surgical de-escalation is optimizing lymph-node assessment (*Table 2*). SENTICOL I (19) showed that sentinel lymph-node biopsy (SLNB) is highly accurate in early-stage cervical cancer when bilateral mapping is achieved (76%), with a sensitivity of 92% and a negative predictive value (NPV) of 98%. In the randomised SENTICOL II trial (20), lymphatic morbidity was significantly lower with SLNB than with bilateral pelvic lymph-node dissection (BPLND) (31.4% *vs.* 51.5%, P<0.0046), as were postoperative neurological symptoms (7.8% *vs.* 20.6%, P<0.01). Three international trials—SENTICOL III (21), SENTIX (22), and PHENIX (23)—are evaluating whether BPLND after negative (SENTICOL III, SENTIX, PHENIX arm I) or positive (PHENIX arm II) intraoperative SLNB confers any survival benefit. In SENTIX (22), SLNB with ultra-staging was followed by radical hysterectomy or trachelectomy; frozen section SLNB-positive patients were excluded from the analysis and underwent BPLND. Two-year DFS and OS were 93.3% and 97.9%, with a 6.1% 2-year recurrence rate (non-inferior to the 7% reference rate), and ultra-staging detected ~44% of metastases missed by standard pathology. PHENIX arm I data show 3-year DFS of 96.9% with SLNB alone versus 94.6% with BPLND [hazard ratio (HR) 0.61, 95% confidence interval (CI): 0.33–1.14; P=0.12] (23). SENTICOL III is expected to complete follow-up in 2026 (21).

The management of locally advanced cervical cancer has evolved rapidly toward precision, image-guided and biologically informed treatment (*Table 3*). This progression is clearly illustrated by five landmark trials: retroEMBRACE (24), EMBRACE I (25), EMBRACE II (26), INTERLACE (27) and KEYNOTE-A18 (28). RetroEMBRACE first demonstrated the major clinical impact of image-guided adaptive brachytherapy (IGABT). By analysing outcomes from centres using MRI/CT-based brachytherapy versus conventional point-A techniques, the study reported markedly higher 3-year local control (~91% *vs.* ~76% historical) and roughly 50% lower rates of ≥ grade 3 late toxicity. This established imaging, contouring and dose adaptation as the foundation for modern personalised brachytherapy (24). EMBRACE I, a prospective cohort of >1,400 patients with FIGO IB–IVA and selected IVB disease, confirmed these advantages in a real-world multicentre setting. With CRT plus magnetic resonance imaging (MRI)-based IGABT, 5-year local control reached 92% and 5-year OS ~74%, with low severe late morbidity (genitourinary 7%, gastrointestinal 8–9%, vaginal ~6%). These results firmly defined CRT + MRI-IGABT as the global standard (25). EMBRACE II advances personalisation further by standardising all radiotherapy components—positron emission tomography (PET)/MRI staging, intensity-modulated radiation therapy/image-guided radiation therapy (IMRT/IGRT), nodal simultaneous-integrated boosts and risk-adapted IGABT. Its aim is to improve pelvic and nodal control while minimizing toxicity through harmonized dose constraints. Early analyses show >93% 3-year local control with low severe toxicity; full results are awaited (26). Systemic therapy has also been refined. The phase III INTERLACE trial demonstrated that short-course induction carboplatin-paclitaxel before CRT significantly improved survival, increasing 5-year OS from 72% to 80% and progression-free survival (PFS) from 64% to 73% (OS HR 0.65; P=0.013) (27). Extending treatment individualisation into immuno-oncology, KEYNOTE-A18 showed that adding pembrolizumab to CRT resulted in improved OS, with manageable toxicity. Three-year OS was 82.6% in the chemotherapy-pembrolizumab group *vs.* 74.8% in the placebo-CRT group and HR for death was 0.67 (95% CI: 0.50–0.90; P=0.0040). (OS HR 0.92, 95% CI: 0.62–1.38). This trial established chemo-immunoradiation as a new standard for high-risk locally advanced cervical cancer (28).

Together, these trials chart a clear trajectory: from improved tumour targeting (retroEMBRACE, EMBRACE I) to fully integrated precision radiotherapy (EMBRACE II), and finally to personalised systemic intensification

© AME Publishing Company.

Table 2 Trials investigating SLNB versus systematic BPLND in cervical cancer

Trial/year/recruitment period	Inclusion criteria	Primary outcome	Key results	Conclusion
SENTICOL I (2011; 2005–2007), prospective, multicentre, single-arm	FIGO IA1 (LVSI+) to IB	Accuracy of SLNB *vs.* full lymphadenectomy	Bilateral detection 76%; sensitivity 92%; NPV 98%	SLNB is highly accurate when bilateral mapping is achieved; supports SLNB as a staging method
SENTICOL II (2021; 2009–2012), RCT	FIGO IA2 to IIA1; bilateral SLN detection; randomised to SLNB alone *vs.* SLNB + BPLND	Postoperative morbidity	Lymphatic morbidity: 31.4% (SLNB) *vs.* 51.5% (BPLND); neurological symptoms: 7.8% *vs.* 20.6%. 3-DFS 92% (SLNB) *vs.* 94.4% (BPLND)	SLNB significantly reduces morbidity without early oncologic compromise
SENTICOL III (Ongoing; started 2017; completion expected 2026), RCT	FIGO IA1 (LVSI+) to 2A1; bilateral SLN detection; SLN-negative → no BPLND	3-year DFS and QoL	Results pending	Designed to confirm long-term oncologic safety of omitting BPLND after negative SLNB
SENTIX (2025; ~2016–2020), prospective, multicentre, single-arm	FIGO IA1 (LVSI+) to IB2; SLNB frozen section negative; SLNB with ultra-staging;	2-year DFS	2-year DFS 93.3%; OS 97.9%; recurrence 6.1%; ultra-staging detected ~44% of metastases missed by routine pathology	SLNB with ultra-staging offers excellent survival for early-stage cervical cancer and avoids unnecessary BPLND
PHENIX—Arm I (2025; 2015–2023), RCT	FIGO IA1 (LVSI+) to IIA1; SLN-negative on frozen section; randomised: SLNB alone *vs.* SLNB + BPLND	3-year DFS	3-year DFS: 96.8% (SLNB) *vs.* 94.5% (BPLND), HR 0.61 (95% CI: 0.33–1.14; P=0.12)	SLNB alone is non-inferior to BPLND with respect to DFS and is associated with fewer complications
PHENIX—Arm II (results pending, closed early)	FIGO IA2–IB1; SLN-positive on frozen section; randomised: completion BPLND *vs.* tailored management	3-year DFS	No results available yet	Will evaluate whether SLNB-positive patients require routine BPLND or if less radical approaches are safe

BPLND, bilateral pelvic lymph node dissection; CI, confidence interval; DFS, disease-free survival; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; LVSI, lympho-vascular space invasion; NPV, negative predictive value; OS, overall survival; QoL, quality of life; RCT, randomized controlled trial; SLN, sentinel lymph node; SLNB, sentinel lymph-node biopsy.

(INTERLACE) and immune-enhanced CRT (KEYNOTE-A18). The result is a modern, individualised multimodality approach that delivers superior outcomes while reducing toxicity.

Ovarian cancer

The management of advanced ovarian cancer has long centred on the optimal timing of cytoreductive surgery relative to chemotherapy. Five pivotal randomised trials—Vergote *et al.* (EORTC 55971) (29), CHORUS (30), Onda *et al.* (JCOG0602) (31), SCORPION (32), and TRUST (33)—have defined current practice (*Table 4*). Historically, PDS was considered standard of care. The trial by Vergote *et al.* [2010] (29) was the first large multicentre study to show that neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) was non-inferior to primary debulking surgery (PDS) in FIGO IIIC–IV disease. CHORUS [2015] (30) confirmed this in a UK cohort with a slightly poorer performance status (20% PS 2–3 *vs.* 12% in Vergote *et al.*), reporting similar median OS (23–24 months) but lower early morbidity and mortality in the NACT arm. Together, these two trials established NACT as a safe alternative to upfront surgery, particularly for patients with high tumour burden or reduced fitness. However, the interpretation of these trials has been subject to important

© AME Publishing Company.

Table 3 Trials outlining the management of locally-advanced cervical cancer

Trial name/publication year/ recruitment period	Inclusion criteria	Primary outcome	Key results	Conclusion
RetroEMBRACE (2016; treated 1997–2012), retrospective multicentre cohort	FIGO IB–IVA; treated with EBRT +/– chemotherapy with MRI/CT-IGABT	Local control & survival with IGABT	3-year LC 91% (*vs.* 76% historical), improved OS, ~50% reduction in ≥ G3 morbidity	Demonstrated superiority of image-guided brachytherapy over point-A technique; foundation for EMBRACE prospective trials
EMBRACE I (2021; 2008–2015), prospective cohort	FIGO IB–IVA, selected IVB with para-aortic nodes below L1–L2; treated with CRT + MRI-IGABT	Local control & late morbidity	5-year LC 92%; 5-year OS 74%; low ≥ G3 late toxicity (GU 7%, GI 8–9%, vaginal 6%)	Established CRT + MRI-IGABT as global standard for locally advanced cervical cancer
EMBRACE II (protocol 2018; recruitment ~2016–2024), prospective multicentre cohort	FIGO IB–IVA; treated with CRT + modern MRI-IGABT using IMRT/IGRT, nodal SIB, PET/ MRI staging, and risk-adapted IGABT	Pelvic control, toxicity reduction, validated OAR constraints	Early data show >93% 3-year LC with low severe toxicity; full results pending	Aims to standardise all radiotherapy components in order to improve nodal/ systemic control while maintaining excellent local control
INTERLACE (2024; 2012–2020) Multicentre randomised Phase III trial	FIGO IB2–IVA; randomised to standard CRT *vs.* induction chemotherapy + standard CRT	OS and PFS	5-year OS 80% *vs.* 72% (OS HR 0.65, P=0.013); 5-year PFS 72% *vs.* 64%	First phase III trial showing survival benefit from induction carboplatin-paclitaxel before CRT
KEYNOTE-A18 (2024; 2018–2021), multicentre randomised phase III trial	FIGO IB2–IVA; randomised to 5 cycles pembrolizumab + CRT + 15 cycles pembrolizumab *vs.* placebo + CRT + placebo	OS and PFS	3-year OS 81.8% *vs.* 74.4% (HR 0.73; 95% CI: 0.57–0.94); manageable immune-related toxicity	Establishes pembrolizumab + CRT as new standard for high-risk locally-advanced cervical cancer

CRT, chemoradiotherapy; CT, computed tomography; EBRT, external beam radiotherapy; EBRT, external beam radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; GI, gastrointestinal; GU, genitourinary; HR, hazard ratio; IGABT, image-guided adaptive brachytherapy; IGRT, image-guided radiotherapy; IMRT, intensity modulated radiotherapy; LC, local control; MRI, magnetic resonance imaging; OAR, organ at risk; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; SIB, simultaneous integrated boost.

criticism. In both studies, complete cytoreduction (R0) rates in the primary surgery arms were relatively low compared with those reported from high-volume specialist centres, raising concerns that surgical outcomes may not reflect optimal contemporary practice. In CHORUS, this is further highlighted by the relatively short mean operative time for PDS (approximately 120 minutes), suggesting less extensive surgical effort and potentially lower surgical aggressiveness. Together, these factors have led to the view that the apparent equivalence between strategies may, at least in part, reflect suboptimal surgical performance rather than true oncological parity. As such, these trials are often interpreted as supporting NACT as a safe option in selected patients, rather than demonstrating equivalence to maximal-effort PDS in expert settings.

Later trials aimed to refine patient selection. The trial conducted by Onda *et al.* [2020] in Japan (31), did not demonstrate non-inferiority of NACT—potentially influenced by a higher proportion of chemoresistant clear cell carcinomas (8% *vs.* 4% in CHORUS), an upper age limit of 75 years, low complete resection rates with PDS (12%), and a higher rate of subsequent IDS (33% *vs.* 17% in Vergote). These differences may contribute to an improved median overall survival (mOS) in the PDS group. SCORPION [2020] (32) focused on patients with high tumour load, identified by laparoscopic assessment, and achieved markedly higher complete resection rates (46.7% in PDS *vs.* 12% in Onda *et al.* and 17% in CHORUS). Although survival was similar between arms, NACT resulted in significantly higher R0 rates (77% *vs.* 46.7%) and fewer complications (25.9% *vs.* 7.6%), underscoring the importance of accurate surgical triage.

© AME Publishing Company.

Table 4 Randomised controlled trials comparing PCS with NACT in the management of advanced ovarian cancer

Trial/year/recruitment period	Inclusion criteria	Primary outcome	R0 rates	Key results	Conclusion
EORTC 55971 (Vergote *et al.* 2010; 1998–2006)	FIGO IIIC–IV EOC/FT/peritoneal cancer; eligible for either PDS or NACT	mOS	PDS: 19% NACT: 51%	mOS: 29 m (PDS) *vs.* 30 m (NACT), HR 0.98; postoperative (28 days) mortality 2.5% *vs.* 0.7%	NACT is non-inferior to PDS with reduced morbidity and mortality and higher R0 rates
CHORUS (Kehoe *et al.* 2015; 2004–2010)	FIGO stage III–IV ovarian cancer; eligible for either PDS or NACT	mOS	PDS: 17% NACT: 39%	mOS 22.6 m (PDS) *vs.* 24.1 m (NACT), HR 0.87; NACT associated with fewer grade ≥3 complications	Confirms non-inferiority of NACT and reduced perioperative morbidity
SCORPION (Fagotti *et al.* 2020; 2011–2015)	Stage IIIC–IV EOC/FT/peritoneal cancer, high tumour load (laparoscopic predictive index)	mPFS, postoperative complications	PDS: 46.7%; NACT: 77%	mPFS 15 m (PDS) *vs.* 14 m (NACT); mOS 41 m (PDS) *vs.* 43 m (NACT); major postoperative complications 25.9% (PDS) *vs.* 7.6% (NACT); P=0.0001	Confirms non-inferiority of NACT. In heavy tumour load, NACT enables far higher R0 rates with less morbidity
JCOG0602 (Onda *et al.* 2020; 2006–2011)	Stage III–IV EOC/FT/peritoneal cancer; eligible for either PDS or NACT	mOS	PDS: 12%; PDS + IDS 31%; NACT: 64%	mOS 49 m (PDS) *vs.* 44.3 m (NACT); HR 1.05; non-inferiority criteria of NACT not met	Suggests potential advantage for PDS in this population; NACT not proven non-inferior
TRUST (Mahner *et al.* 2025 ASCO abstract; 2014–2020)	FIGO IIIB–IVB EOC/FT/peritoneal cancer; expert high-volume centres only	mOS	PCS 62.9%; NACT 76.6%	mOS 54.3 m (PDS) *vs.* 48.3 m (NACT) (HR 0.89 95% CI: 0.74–1.08; P=0.24, no statistically significant difference; mPFS 22.2 m (PDS) *vs.* 19.7 m (NACT) (HR 0.80, P=0.02)	In expert centres, PDS may provide superior PFS, especially in stage III patients achieving R0
SUNNY (ongoing; protocol 2020; recruitment ~2018–2024)	FIGO IIIC–IV EOC/FT/peritoneal cancer; centres with >50% R0 rates	mOS	Pending	Pending	Designed to evaluate PDS *vs.* NACT in very high-performing surgical centres; expected to clarify impact of surgical excellence

EOC, epithelial ovarian cancer; FIGO, International Federation of Gynecology and Obstetrics; FT, fallopian tube; HR, hazard ratio; m, months; mOS, median overall survival; mPFS, median progression-free survival; NACT, neoadjuvant chemotherapy; PCS, primary cytoreductive surgery; PDS, primary debulking surgery; R0, complete macroscopic resection.

The TRUST trial (33) is unique in its stringent surgical quality assurance. Conducted exclusively in high-volume expert centres with audited surgical outcomes, TRUST demonstrated no mOS difference between PDS and NACT, but a significant median progression-free survival (mPFS) advantage for upfront surgery (22.2 *vs.* 19.7 months, HR 0.80, P=0.02). Importantly, the benefit was most pronounced in stage III disease and in patients achieving complete gross resection, emphasising the prognostic impact of surgical quality. A subgroup analysis of patients with R0 resection demonstrates mPFS and mOS benefit with PDS, however the trial was not powered to assess this.

The SUROVA study, a retrospective, international cohort involving 3,286 patients with FIGO IIB–IVB epithelial ovarian cancer (EOC), found mOS was similar between the PDS *vs.* NACT/IDS groups (67.2 *vs.* 65.0 months; HR 1.002, 95% CI: 0.85–1.18, P=0.98) however post-operative complications (28%) significantly worsened survival (66 *vs.* 46 months; HR 1.5, 95% CI: 1.2–1.9, P<0.001), especially among patients undergoing primary surgery (73 *vs.* 46 months; HR 1.85, 95% CI: 1.43–2.37, P<0.001) (34).

In summary, while earlier trials established NACT as a non-inferior, less morbid option, TRUST underscores that in expert hands, PDS may deliver superior PFS, particularly for non-frail patients with stage 3 disease,

© AME Publishing Company.

while SUROVA warns about the negative impact of post-surgical complications on survival. This shifts the focus from a binary choice between PDS and NACT to nuanced patient selection and ensuring surgical excellence and low complications rates. Results from the Shanghai-led SUNNY trial, comparing mOS following PDS *vs.* NACT/IDS in centres with >50% R0 rates may shed further light on this topic (35).

A recent international retrospective cohort study by Gaba *et al.* [2025], including 2,498 patients with FIGO stage III/IV ovarian cancer found that patients undergoing delayed (>4 cycles NACT) versus interval cytoreduction had poorer mOS, despite achieving R0 at surgery. R0 was more likely (72.2% *vs.* 64.6%) and postoperative morbidity was less in the IDS compared to the DDS group (36).

The role of heated intraperitoneal chemotherapy (HIPEC) following cytoreductive surgery has been evaluated in multiple trials. Intraperitoneal delivery achieves higher local drug concentrations and targets microscopic peritoneal disease, while hyperthermia enhances membrane permeability, impairs DNA repair, inhibits angiogenesis, and promotes apoptosis. The OV-HIPEC-1 trial [2018] demonstrated significant improvements in median PFS (14.2 *vs.* 10.7 months) and OS (45.7 *vs.* 33.9 months) in FIGO stage III patients undergoing IDS with residual disease <2.5 mm, without increased Clavien-Dindo grade 3–4 complications (27% *vs.* 25%) (37). These findings were supported by Antonio *et al.* [2022] in the IDS setting (38). Lim *et al.* [2022] similarly reported a survival benefit confined to the IDS subgroup, with no benefit after PDS (39). Long-term follow-up data from the OV-HIPEC-1 trial confirmed the durability of these survival benefits, reinforcing HIPEC as a valid adjunct in carefully selected patients undergoing IDS (40).

The 2019 LION trial provided evidence to support de-escalation of lymph node surgery in ovarian cancer. The trial included patients with stage IIB–IVB undergoing ovarian cytoreductive surgery, who achieved R0 resection and did not have clinically-enlarged lymph nodes. Despite the presence of microscopic lymph node metastases in 55.7% of the patients in the lymphadenectomy group, the trial demonstrated that systematic pelvic and para-aortic lymphadenectomy did not result in a mOS (65.5 *vs.* 69.2 months) or mPFS (25.5 months in both groups) benefit and was associated with a higher complication rate (12.4% *vs.* 6.5%) and mortality (3.1% *vs.* 0.9%) (41).

In recent years, with improved insight into the molecular basis of ovarian cancer, targeted therapies have increasingly been incorporated into contemporary treatment approaches.

Vascular endothelial growth factor (VEGF) is a key promoter of angiogenesis, which contributes to solid tumour growth and metastasis in ovarian cancer. Bevacizumab, a humanised anti-VEGF monoclonal antibody, acts by inhibits angiogenesis. The GOG218 (42) and ICON 7 (43) trials, including patients with FIGO III/IV disease, showed that the use of bevacizumab during and up to 10 months after carboplatin-paclitaxel chemotherapy prolongs the mPFS by 2–4 months, with a greater survival benefit among those at high risk for disease progression. The main reported adverse side effects were high blood pressure (22.9%) and bowel perforation (2.8%) (42).

Poly-ADP ribose polymerase (PARP) inhibitors (e.g., olaparib) induce synthetic lethality by trapping PARP at single-strand DNA breaks, causing double-strand breaks that cannot be repaired in homologous recombination-deficient tumors, including BRCA1/2-mutant cancers. The SOLO1 trial (44) established the use of olaparib in maintenance therapy for patients with FIGO stage III–IV ovarian cancer with a BRCA1/2 mutation, who had a complete or partial response to platinum-based chemotherapy (without bevacizumab), demonstrating, at a 41-month median follow-up, a 70% lower risk of disease progression or death with olaparib than with placebo.

HRD is not limited to tumors with BRCA mutations and is present in approx. 50% of high-grade serous ovarian tumours. The PAOLA 1 trial (45) showed that, in HRD positive patients with advanced high-grade serous or endometrioid ovarian cancer, irrespective of BRCA status, the addition of olaparib to bevacizumab for maintenance treatment results in a survival benefit. mPFS was 37.2 *vs.* 21.7 in BRCA positive patients. In HRD positive/BRCA negative patients, mPFS was 28.1 *vs.* 16.6, while in HRD negative patients mPFS was 16 months in both arms.

The KEYLYNK-001 trial supports the addition of immunotherapy in the adjuvant and maintenance treatment of patients with BRCA negative, advanced EOC, BRCA negative patients. The combination of pembrolizumab and chemotherapy, followed by maintenance pembrolizumab plus Olaparib with or without bevacizumab, met the PFS endpoint. Further subgroup analyses from this trial are in progress (46).

In summary, the future of ovarian cancer is being shaped by molecular advancements, allowing us to tailor therapies, based on molecular signatures of chemoresistance or sensitivity. Primary surgery in expert centers offers a PFS advantage when complete gross resection is achievable,

© AME Publishing Company.

while NACT/IDS is appropriate for frail patients, or those with a high tumor burden and low probability of achieving R0. The addition of HIPEC at the time of IDS, for patients with FIGO stage III disease who have achieved optimal cytoreduction, has promising results, while its role in upfront surgery remains uncertain.

Endometrial cancer

Endometrial cancer is the most common gynaecological cancer, with a rising incidence in the western world, as a consequence of the obesity pandemic. It is estimated that patients with a body mass index (BMI) >40 kg/m^2 have a 10–15% lifetime risk of developing endometrial cancer. Over 90% of patients with endometrial cancer present with post-menopausal bleeding and most of them (approx. 80%) have disease confined to the uterus (47). Screening for endometrial cancer, traditionally performed by ultrasound (US) scan and hysteroscopy, has been revolutionised by the development of the WID-Easy test, a polymerase chain reaction (PCR) DNA methylation assay from cervicovaginal secretions, first described by Herzog *et al.* in 2022 (48).

Diagnosis

EPI-SURE, a prospective, observational study based at UCLH in London, assessed the real-world performance of WID-Easy, in comparison to US. Women aged ≥45 years with abnormal uterine bleeding attending a tertiary gynaecological diagnostic referral centre were included. Reported sensitivity was the same for US and Wid-EASY (90.9%), while specificity was much higher for Wid-EASY (92.1% *vs.* 79.1%). 88% patient had a negative test and could be removed from the cancer pathway (49). Furthermore, Ken-Amoah *et al.* extended this evidence to a Black African population, showing WID-qEC retained high sensitivity and specificity where ultrasound underperforms, helping to address a critical equity gap in uterine cancer diagnostics (50).

Laparoscopy versus laparotomy

The safety of laparoscopic surgery in early-stage uterine cancer has been established by the LAP2 (51) and LACE (52) trials. The LAP2 trial in 2012 included 2550 patients with FIGO stage I–IIA uterine carcinoma or sarcoma, allocated 2:1 to laparoscopy [1,696] *vs.* laparotomy [920] for hysterectomy, bilateral salpingo-oophorectomy and bilateral systematic pelvic lymph node dissection. The difference in recurrence rates at 3 years was 1.14% (11.4% *vs.* 10.2%, not significant), but laparoscopy was associated with a shorter stay and superior short-term safety (51). The 2017 LACE trial, a multi-centre RCT, included 760 patients with FIGO stage I endometrioid endometrial adenocarcinoma: 407 allocated to total laparoscopic hysterectomy, while 353 had total abdominal hysterectomy. The DFS at 4.5 years was equivalent between the laparoscopy and laparotomy groups (52). Neither of these two RCTs were powered to assess recurrence rates/DFS for high-grade tumours involving the cervix. Following the publication of LACC trial for cervical cancer, the management of high-grade endometrial tumours involving the cervix (FIGO stage II) may perhaps need to be reassessed.

Lymph node surgery

Two RCTs, Benedetti Panici *et al.* [2008] (53) and ASTEC (54) in 2009, demonstrated that lymph node surgery does not have a therapeutic value but it's role is to assess the extent of disease (staging) and to provide information for adjuvant treatment decisions, as patients with positive lymph nodes benefit from chemotherapy. Two prospective non-randomised trials, FIRES (USA, 2017) (55) and SHREC (Sweden, 2019) (56) proved that SLNB, performed robotically with indocyanine green (ICG), is equivalent to systematic pelvic lymphadenectomy (PLND) and infra-renal para-aortic lymphadenectomy (IRPALND) in staging EC. After SLNB, a PLND+/– IRPALND were performed in both trials. The FIRES trial, including 385 patients with FIGO stage I endometrial cancer of all histologies and grades, reported a sensitivity of 97.2% (95% CI: 85–100%) and a NPV of 99.6% (95% CI: 97.9–100%). The rate of bilateral mapping rate was only 52%, which was thought to be related to limited surgical experience with sentinel node mapping in some centres. In 15% of cases, the sentinel node was located in the para-aortic area (55). As only 28% of the FIRES patients had high-grade tumours, a new prospective trial, SHREC, was designed to assess the diagnostic accuracy of SLNB in patients with FIGO stage I–II, high-risk EC. SHREC reported a sensitivity of 100% (95% CI: 92–100%) and NPV of 100% (95% CI: 98–100%). In case of non-display in any pathway after 10 minutes, an ipsilateral reinjection was performed at 3 or 9 o'clock. The bilateral mapping rate was 82% before and 95% after reinjection. Nodes macroscopically-suspicious were excised and sent separately from the SLNB. Only 1%

© AME Publishing Company.

of patients had isolated para-aortic metastases (56). Sozzi *et al.* [2020], in the SENTIFAIL retrospective study, identified the following factors as predictors of SLNB failure: the presence of LVSI, non-endometrioid histology and enlarged lymph nodes at surgery (57). Finally, Nagar *et al.* [2021] published a Cochrane review looking at the diagnostic accuracy of SLNB. Thirty-three studies, including a total of 2,237 women were included. The pooled sensitivity of SLNB was 91.8% (95% CI: 86.5–95.1%) (58).

Management of uterine serous carcinoma

The management of uterine serous carcinoma is the subject of a longstanding debate, with many authors supporting, based on retrospective data, a PDS *vs.* NACT approach, similar to ovarian high-grade serous carcinoma. In a retrospective cohort, Bristow *et al.* [2001] found that, at 24 months, 57.1% of optimally cytoreduced patients were still alive, compared with just 6.7% of patients left with suboptimal disease. The strongest predictor of OS for patients with stage IV uterine papillary serous carcinoma was the amount of residual disease following surgery (59).

Mantovani *et al.* [2025] published a meta-analysis of 16 retrospective studies with 285 patients, comparing survival outcomes following PDS *vs.* IDS for patients with stage 4 EC with peritoneal carcinosis, found a mPFS of 18 *vs.* 12 months (P=0.028), and a mOS of 30.9 *vs.* 28.7 months (P=0.40), supporting PDS, when R0 can be achieved (60).

The new FIGO staging and molecular classification

The Cancer Genome Atlas (TCGA) was a landmark, large-scale project launched in 2006 (61), producing multidimensional maps of cancer genomics for 33 cancer types, showing how mutations, gene expression, and epigenetic changes drive tumor biology. It provided molecular classifications with implications for treatment and cross-cancer analyses of major biological themes. It set the foundation of precision oncology and transformed the treatment of a number of cancers including endometrial, ovarian, breast, bladder, lung, glioblastoma (62). In 2013, the TCGA project first proposed a reclassification of EC into four molecular subtypes, based on comprehensive genomic analyses: POLE ultramutated, microsatellite instability hypermutated (MSI-H), copy-number low, and copy-number high (63).

However, methodologies used in the TGCA study were costly and complex. Talhouk *et al.* introduced the Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) in 2017 (64), reproducing the TCGA classification with assays that could be used in routine clinical practice. Sequential immunohistochemistry (IHC) testing for MMR proteins and p53, along with POLE mutation analysis, were used to classify tumors into four molecular subtypes similar to, but not identical with TCGA: MMR-deficient (MMR-d), POLE ultramutated, p53 abnormal (p53abn), and p53 wild-type (p53wt). POLE has the best prognosis, and p53abn has the worst. This TCGA surrogate approach has been verified by the molecular portion of PORTEC 3.

The 2023 FIGO update for EC shifts staging from a purely anatomical model to an integrated system that combines histological aggressiveness, lymphovascular involvement, size and type of nodal metastases (micro- *vs.* macro-metastases), and—critically—molecular classification (e.g., POLE mutations, p53 status) to refine prognostic stratification (65).

The 2025 ESGO-ESTRO-ESP guidelines defined prognostic groups and treatment options for EC, based on the 2023 molecular classification (66).

Evolving adjuvant therapy

Postoperative adjuvant treatment for EC includes radiotherapy, chemotherapy and, increasingly, immunotherapy and targeted agents. Radiotherapy is delivered as external-beam radiotherapy (EBRT), vaginal brachytherapy (VBT), or both. PORTEC-1 [2000] was the first major trial of adjuvant radiotherapy in EC and enrolled women with intermediate-risk stage I disease (grade 1 with >50% myometrial invasion; grade 2 with any invasion; grade 3 with <50% invasion). Pelvic radiotherapy reduced locoregional recurrence (LRR) (4% *vs.* 14%) but did not improve 5-year OS (81% *vs.* 85%) and increased toxicity. Approximately 75% of recurrences in the control arm were vaginal (67). PORTEC-2, conducted in stage I–IIA high-intermediate-risk EC, showed that VBT and EBRT achieved similar vaginal-recurrence rates (5-year rates 1.8% *vs.* 1.6%), but VBT resulted in far fewer gastrointestinal toxicities (12.6% *vs.* 53.8%), establishing VBT as the preferred option for this group (68). PORTEC-3 compared CRT with EBRT alone in high-risk EC (grade 3 stage I with deep invasion and/or LVSI, stage II–III endometrioid tumours, or stage I–III serous/clear-cell cancers). Combined treatment improved 5-year PFS (75.5% *vs.* 68.6%, P=0.022) but not OS (81.8% *vs.*

© AME Publishing Company.

76.7%, P=0.11), with the greatest benefit seen in stage III disease, at the cost of higher toxicity (69). PORTEC-4A, a phase III trial, evaluated molecularly guided adjuvant therapy in high-intermediate-risk endometrioid EC. Patients were assigned treatment by molecular subgroup (POLE-mutated, MMR-deficient, p53-abnormal, NSMP). In the molecular arm, favourable-risk tumours (POLE-mut, MMRd, and NSMP without CTNNB1 exon 3 mutation) received no adjuvant radiotherapy; intermediate-risk tumours (NSMP with CTNNB1 exon 3 mutation) received VBT, and unfavourable-risk tumours (p53-abnormal) received EBRT. Five-year vaginal recurrence was 4.5% (95% CI: 2.23–6.76%) in the molecular arm versus 1.6% (95% CI: 0.00–3.32%) with standard treatment (HR 2.71; 95% CI: 0.79–9.34). Overall, 46% of patients with favourable molecular profiles avoided radiotherapy without compromising locoregional control, while escalation for p53-abnormal tumours improved outcomes, supporting molecular classification to individualize adjuvant therapy and reduce overtreatment (70) (*Table 5*).

Immune checkpoint inhibitors combined with chemotherapy have recently transformed the management of advanced or recurrent EC, with greater benefit in mismatch-repair-deficient (dMMR) than mismatch-repair-proficient (pMMR) tumours (*Table 6*). dMMR cancers account for ~25% of EC and are usually endometrioid, whereas pMMR tumours are more heterogeneous and include carcinosarcomas. In NRG-GY018/KEYNOTE-868, the addition of pembrolizumab to first-line carboplatin-paclitaxel followed by pembrolizumab maintenance significantly improved PFS, with HRs of 0.54 in pMMR (95% CI: 0.41–0.71; P<0.001) and 0.30 in dMMR tumours (95% CI: 0.19–0.48; P<0.001), establishing pembrolizumab-based therapy as a new standard regardless of MMR status (71). Similarly, the RUBY/ENGOT-EN6/GOG-3031 trial demonstrated benefit with Dostarlimab: in the dMMR/MSI-H cohort, 24-month PFS was 61.4% versus 15.7% (HR 0.28; P<0.0001) and OS 83.3% versus 58.7% (HR 0.30; 95% CI: 0.13–0.70); in the pMMR/microsatelite stable (MSS) cohort, 24-month PFS was 28.4% versus 18.8% (HR 0.76; 95% CI: 0.59–0.98) and OS 67.7% versus 55.1% (HR 0.73; 95% CI: 0.52–1.02). These findings show statistically-significant benefit in dMMR disease and a favourable trend in pMMR tumours (72). The DUO-E (ENGOT-EN10/GOG-3041) trial evaluated whether adding the PARP inhibitor Olaparib to immunotherapy improves outcomes in advanced or recurrent endometrial cancer, particularly in pMMR disease. Patients were randomised 1:1:1 to chemotherapy alone (carboplatin-paclitaxel), chemotherapy plus durvalumab with durvalumab maintenance (D), or chemotherapy plus durvalumab followed by maintenance durvalumab-olaparib (D+O). Both experimental arms significantly improved PFS versus chemotherapy, with HRs of 0.71 (95% CI: 0.57–0.89; P=0.003) for D and 0.55 (95% CI: 0.43–0.69; P<0.0001) for D+O. Benefit was observed in both dMMR (HR 0.42 and 0.41) and pMMR tumours (HR 0.77 and 0.57, respectively) (73). NIVEC is an ongoing single-arm phase II trial evaluating neoadjuvant nivolumab in resectable dMMR/MSI-H endometrial cancer (stage I–IIIC2) to reduce or potentially obviate the need for surgery. Patients receive induction programmed cell death protein 1 (PD-1) blockade prior to planned operative management. Interim phase I data presented at the 2025 SGO Annual Meeting demonstrated an 80% complete response rate among 15 patients, with seven avoiding surgery and no recurrences reported during early follow-up (74).

Targeted therapy also plays an emerging role. In human epidermal growth factor receptor 2 (HER2)-positive uterine serous carcinoma, a randomised phase II trial (NCT01367002) showed that adding trastuzumab to carboplatin-paclitaxel significantly improved PFS (12.9 *vs.* 8.0 months; HR 0.46; P=0.005), with the largest effect in stage III–IV primary treatment patients (17.7 *vs.* 9.3 months), and improved OS (29.6 *vs.* 24.4 months; HR 0.58; P=0.046) (75). Finally, the RAINBO programme comprises four molecularly driven adjuvant trials—p53abn-RED (olaparib after chemoradiation), MMRd-GREEN (durvalumab + RT), NSMP-ORANGE (RT + progestin de-escalation), and POLEmut-BLUE (minimal or no adjuvant therapy)—collectively enrolling ~1,600 women, with results expected by 2028 to refine personalised treatment and reduce toxicity (76).

Uterine sarcoma

Uterine sarcomas comprise a heterogeneous group of rare mesenchymal malignancies, including leiomyosarcoma, low-grade and high-grade endometrial stromal sarcoma, and undifferentiated uterine sarcoma, each characterised by distinct molecular alterations and clinical behaviour. Advances in genomic profiling have refined diagnostic classification, identifying recurrent gene fusions such as JAZF1-SUZ12 in low-grade stromal sarcoma and YWHAE rearrangements in high-grade disease, as well as frequent TP53 and RB1 pathway alterations in leiomyosarcoma (77).

© AME Publishing Company.

Table 5 The PORTEC trials investigating adjuvant treatment in the management of endometrial cancer

Trial [year]; recruitment period	Inclusion criteria	Primary outcome(s)	Key results	Conclusions
PORTEC-1 [2000]; 1990–1997	FIGO I; intermediate-risk	LRR, OS	5-year LRR: 4% (RT) *vs.* 14% (no RT) 5-year OS: 81% (RT) *vs.* 85% (no RT)	EBRT reduces recurrence but no OS benefit; many intermediate-risk patients can avoid EBRT
PORTEC-2 [2010]; 2002–2006	FIGO I–IIA; high-intermediate-risk (age/grade/invasion) excluding serous/clear-cell	Vaginal recurrence (VBT *vs.* EBRT non-inferiority)	5-year vaginal recurrence: 1.8% (VBT) *vs.* 1.6% (EBRT); OS/DFS similar; VBT much less toxic	VBT is non-inferior and preferred due to low toxicity
PORTEC-3 [2018]; 2006–2013	FIGO I high-risk: G3, deep invasion or LVSI; FIGO II–III endometrioid; FIGO I–III serous/clear cell	OS and FFS (CRT *vs.* EBRT)	5-year OS: 81.8% (CRT) *vs.* 76.7% (RT); HR 0.76; P=0.11. 5-year PFS: 75.5% (CRT) *vs.* 68.6% (RT); HR 0.71; P=0.022	CRT does not significantly improve OS, but does improve PFS, especially in stage III/serous cancers
PORTEC-4A [2026]; 2016–2021	FIGO I high-intermediate-risk endometrioid endometrial cancer. Molecular-guided arm treatment allocations: (I) POLE-mutated → no adjuvant RT; (II) MMR-deficient → no adjuvant RT; (III) NSMP without CTNNB1 exon 3 mutation → no adjuvant RT; (IV) NSMP with CTNNB1 exon 3 mutation → VBT; (V) p53-abnormal → EBRT	Vaginal recurrence	5-year vaginal recurrence 4.5% (95% CI: 2.23–6.76%) in the molecular profile group and 1.6% (0.00–3.32%) in the standard group (HR 2.71 95% CI: 0.79–9.34, P non-inferiority 0.005). 46% of women with a favourable molecular profile avoided radiotherapy without compromising locoregional control	Molecular classification enables personalised adjuvant therapy, reducing overtreatment and directing escalation for high-risk biology

CI, confidence interval; CRT, chemoradiotherapy; DFS, disease-free survival; EBRT, external-beam radiotherapy; FFS, failure-free survival; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; LRR, locoregional recurrence; LVSI, lympho-vascular space invasion; MMR, mismatch repair; NSMP, no specific molecular profile; OS, overall survival; RT, radiotherapy; VBT, vaginal brachytherapy.

Surgical resection remains the cornerstone of treatment, typically involving total hysterectomy with or without bilateral salpingo-oophorectomy, while routine lymphadenectomy is not recommended given low nodal involvement rates. However, the role of adjuvant therapy remains controversial. Randomised data evaluating adjuvant chemotherapy or radiotherapy have generally failed to demonstrate consistent survival benefit, contributing to ongoing variation in international practice (78). Hormonal therapy has emerged as an important strategy in hormone receptor-positive stromal sarcomas, while targeted therapies and immune checkpoint inhibitors are being explored in advanced leiomyosarcoma. Overall, modern management reflects increasing molecular stratification and the continued challenge of balancing aggressive disease biology against limited high-quality evidence in rare tumours.

Vulval cancer

Surgical management of vulval cancer has evolved substantially over recent decades, with an increasing focus on preserving vulval and groin anatomy and function while maintaining oncological safety. A key advance has been the adoption of SLNB in appropriately selected patients, allowing many to avoid full inguinofemoral lymphadenectomy (IFL), which carries lymphoedema rates approaching 50%, and thereby markedly reducing treatment-related morbidity. The GROINSS-V (Groin Sentinel Node Trial in Vulvar Cancer) series of prospective multicentre studies were designed around this objective (*Table* 7). Results from the 2008 GROINSS-V I trial demonstrated that omitting IFL in patients with negative SLNB confirmed by pathological ultra-staging, was associated with low groin recurrence rates (2-year 2.3%, 5-year 2.5%), and high disease-specific survival rates (3-year 97%, 10-year 91%) (79). Building on the safety data established by GROINSS-V I, GOG-173 was a prospective, multicentre validation study designed to rigorously assess the diagnostic accuracy of SLNB in early-stage vulval SCC. Women with unifocal tumours ≤6 cm and clinically negative

© AME Publishing Company.

Table 6 Comparison of major immunotherapy trials in the management of advanced or recurrent endometrial cancer

Trial details	Inclusion criteria	Primary outcomes	Results	Conclusion
NRG-GY018/ KEYNOTE-868 (pembrolizumab); 2023; phase III (n=816)	FIGO III–IVA, IVB, or recurrent EC (excluding carcinosarcoma); separate dMMR and pMMR cohorts; prior adjuvant chemo allowed if ≥12 months earlier	PFS in dMMR and pMMR populations	Pembrolizumab + carboplatin/ paclitaxel significantly improved PFS: HR 0.30 (dMMR) and HR 0.54 (pMMR); median PFS in pMMR: 13.1 *vs.* 8.7 months	Pembrolizumab + CT improves PFS across MMR subtypes and is a new standard first-line option for advanced/recurrent EC
RUBY (dostarlimab); 2023; phase III (n=494)	FIGO III–IV or first recurrent EC, systemic-therapy-naïve in advanced setting or ≥6 months post-adjuvant; includes serous/ clear-cell histologies and carcinosarcoma	24 months PFS and OS (overall and by MMR status)	dMMR/MSI-H cohort: PFS was 61.4% *vs.* 15.7% with chemotherapy alone (HR 0.28; P<0.0001) and 24-month OS was 83.3% *vs.* 58.7% (HR 0.30; 95% CI: 0.13–0.70). pMMR/MSS cohort: PFS was 28.4% *vs.* 18.8% (HR 0.76; 95% CI: 0.59–0.98) and 24-month OS was 67.7% *vs.* 55.1% (HR 0.73; 95% CI: 0.52–1.02).	Dostarlimab + CT markedly improves PFS and OS, especially in dMMR/MSI-H EC
DUO-E (durvalumab ± olaparib); 2024; phase III (n=718)	Newly diagnosed stage III–IV or recurrent EC (all epithelial histologies except sarcoma); chemo-naïve in advanced setting or relapse ≥12 months post-adjuvant	PFS (durvalumab + CT *vs.* control; durvalumab + olaparib + CT *vs.* control)	Both experimental arms met PFS endpoint: HR 0.71 (durvalumab) and HR 0.55 (durvalumab + olaparib); interim OS favoured durvalumab + olaparib (HR 0.59)	Durvalumab + CT, with or without olaparib maintenance, provides significant PFS benefit; supports immunotherapy + CT ± PARPi as a first-line standard
NIVEC (nivolumab); 2025; phase II (n≈40)	Resectable stage I–III dMMR/MSI-H EC; no prior immune-checkpoint inhibitor; ECOG 0–1; neoadjuvant design	Clinical or pathological CR rate post-nivolumab; secondary = ORR, PFS, OS, safety	Early phase II results: ~80% clinical CR, many omitted surgery; no early recurrences; toxicity manageable	Neoadjuvant nivolumab shows striking activity in dMMR/MSI-H EC and may allow organ-sparing treatment if durable responses are confirmed

CI, confidence interval; CR, complete response; CT, chemotherapy; dMMR, mismatch-repair-deficient; EC, endometrial cancer; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; MSI-H, microsatellite instability-high; MSS, microsatelite stable; ORR, objective response rate; OS, overall survival; PARPi, poly-ADP ribose polymerase inhibitors; PFS, progression-free survival; pMMR, mismatch-repair-proficient.

groins underwent SLN mapping using technetium and/ or blue dye, followed by mandatory IFL for comparison. The trial demonstrated high sensitivity (92%) and a low false-negative rate (2–3%), particularly with dual-tracer mapping, confirming the technical reliability of SLNB (80). Together with GROINSS-V I, these results firmly established SLNB as a safe and accurate alternative to IFL in appropriately selected patients. The GROINSS-V II trial assessed whether inguinofemoral radiotherapy (50 Gy) could replace IFL in patients with early-stage unifocal vulvar SCC (<4 cm) and a positive sentinel node. Among 1,535 patients, 322 (21%) had nodal involvement. The trial was amended early due to high groin-recurrence rates in patients with sentinel-node macrometastases (>2 mm). After amendment, radiotherapy for micrometastases (≤2 mm) resulted in a low 2-year isolated groin-recurrence rate (1.6%), whereas radiotherapy alone for macrometastases led to substantially higher recurrence (22%) compared with IFL (6.9%). The study concluded that radiotherapy is a safe, lower-morbidity alternative to IFL for micrometastases, while IFL remains required for macrometastases (81). Building on GROINSS-V II, which demonstrated inadequate control of sentinel-node macrometastases with 50 Gy radiotherapy, the ongoing GROINSS-V III (NRG-GY024) trial is evaluating whether dose-escalated groin radiotherapy (56 Gy) with weekly

© AME Publishing Company.

Table 7 Trials investigating groin nodes management in vulval cancer

Trial [year]; recruitment period	Primary outcome	Key results	Conclusions
GROINSS-V [2008]; 2000–2006	Isolated groin-recurrence rate with omission of IFL in SLNB-negative patients	In SLNB-negative patients: isolated groin recurrence 2–3%; 10-year disease-specific survival ~91%	SLNB-negative patients with early unifocal vulvar SCC <4 cm can safely avoid IFL
GOG-173 [2012]; 1999–2009	Diagnostic accuracy of SLNB *vs.* full IFL	Sensitivity 92%; false-negative rate 2–3% (best with dual tracers)	Validated the accuracy of SLN biopsy, supporting its use as an alternative to full IFL in selected early-stage disease
GROINSS-V II [2021]; 2005–2016	2-year isolated groin-recurrence rate using RT (50 Gy) instead of IFL for SLN-positive patients	Micrometastases (≤2 mm): RT recurrence ~1.6%. Macrometastases (>2 mm): RT recurrence ~22% *vs.* 6.9% with IFL	RT is safe for SLN micrometastases but not for macrometastases; IFL remains standard for >2 mm disease
GROINSS-V III (ongoing); 2021–	2-year groin-recurrence rate using dose-escalated chemoradiation instead of IFL in SLN macrometastases	Ongoing; planned intervention is escalated groin RT to 56 Gy + weekly cisplatin	Evaluates whether intensified chemoradiation can safely replace IFL in higher-risk patients (macrometastases/ ECE/multiple micrometastases)

ECE, extracapsular extension; FIGO, International Federation of Gynecology and Obstetrics; IFL, inguinofemoral lymphadenectomy; RT, radiotherapy; SCC, squamous cell carcinoma; SLN, sentinel lymph node; SLNB, sentinel lymph node biopsy.

cisplatin can replace IFL in patients with early-stage vulvar SCC and high-risk nodal features (>2 mm macrometastases, extracapsular extension, or multiple micrometastases). Eligible patients have unifocal tumors <4 cm, clinically node-negative groins, and adequate performance status. The trial is actively recruiting, with results anticipated around 2029 (82).

In SLNB for vulvar cancer, the choice of tracer is crucial for surgical success and minimizing complications. All GROINSS-V studies and GOG-173 used a dual-tracer sentinel-node mapping technique, combining a technetium-99m radiocolloid with a blue dye (Patent Blue or isosulfan blue). In 2020, a randomized control trial demonstrated that SLN detection using ICG with near-infrared (ICG-NIR) fluorescence imaging achieved a significantly higher detection rate compared to blue dye (92.5% *vs.* 65.3%), suggesting that ICG-NIR significantly enhances nodal visualization and may reduce dye-related adverse effects (83). A subsequent systematic review reported SLN detection rates ranging from 90% to 100% with ICG + NIR fluorescence, outperforming traditional approaches such as 99mTc + blue dye (84). A 2025 retrospective study including 225 patients further validated the effectiveness of ICG ± 99mTc in SLN mapping, reinforcing the reliability and promising potential of ICG as a tracer in vulvar cancer surgery (85).

The 2021 FIGO classification for vulval cancer introduced major updates to improve prognostic accuracy and guide clinical management. Early-stage disease was simplified, with stage IA defined solely by ≤1 mm depth of invasion, and stage III restructured to reflect the number and size of nodal metastases and the presence of extracapsular extension. Pelvic nodes were classified as stage IVB, while fixed or ulcerated groin nodes became stage IVA. These refinements better align staging with sentinel-node practice and support more tailored treatment, recognising that metastatic burden and extra-capsular extension carry worse outcomes and may justify more aggressive locoregional therapy (86).

HPV-associated and p53-abnormal (HPV-independent) vulvar SCC are biologically distinct diseases, with HPV-positive tumours generally carrying a lower risk of local recurrence and p53-abnormal tumours behaving more aggressively. The ongoing STRIVE trial, open for recruitment in 2024 with results expected in 2030, applies this biological distinction by stratifying patients according to HPV and p53 status to guide the required width of surgical excision. It enrolls women undergoing primary surgery for vulval SCC and assigns them to molecular subgroups to compare 3-year local-recurrence rates under tailored excision strategies. Key outcomes include local control, margin status, and the feasibility of reducing re-excision in low-risk groups while intensifying treatment only for high-risk disease (87).

© AME Publishing Company.

In the 2022 phase II basket trial KEYNOTE-158, 101 patients with advanced vulval SCC with previous treatment failure, received Pembrolizumab every 3 weeks for up to two years; the objective response rate was 10.9% (95% CI: 5.6–18.7%) overall, with a median duration of response of 20.4 months, median PFS of 2.1 months and median OS of 6.2 months. Responses occurred irrespective of tumour PD-L1 status and the treatment was generally well tolerated (grade ≥3 treatment-related adverse events 11.9%). This shows the promise of immunoradiotherapy in the setting of unresectable disease (88). The APOLLO study, with accrual started July 2023 and completion expected July 2026, is a multicentre, single-arm phase II proof-of-concept trial evaluating neoadjuvant Pembrolizumab in patients with primary, resectable vulval SCC FIGO I–III, whose largest lesion is ≥10 mm. The trial aims to assess tumour shrinkage (RECIST 1.1), immune activation, pathologic complete response at surgery, feasibility and safety, with the hope of reducing surgical radicality and adjuvant therapy in responsive patients (89).

Vaginal cancer

Primary vaginal cancer remains a rare malignancy, accounting for approximately 1–2% of gynaecological cancers, and consequently its management has evolved largely through prospective radiotherapy cohorts, population-based analyses and consensus guideline development rather than disease-specific phase III randomised trials. Contemporary treatment has shifted towards definitive CRT for most stage II–IV tumours, incorporating modern techniques such as intensity-modulated radiotherapy and IGABT, which allow improved tumour coverage and reduced toxicity to surrounding pelvic organs. Early multi-institutional radiotherapy series established the feasibility and efficacy of definitive radiation approaches in vaginal carcinoma, demonstrating meaningful pelvic control rates with combined EBRT and brachytherapy (90). Subsequent advances in MRI-based brachytherapy planning further refined treatment delivery, with studies showing improved local control and reduced severe late morbidity compared with historical point-based techniques (91). Population-level analyses using Surveillance, Epidemiology, and End Results (SEER) datasets have clarified prognostic factors and supported the increasing use of radiotherapy ± chemotherapy as a primary modality, particularly in patients with locally advanced disease (92). Surgical management has become more selective, with local excision reserved for carefully chosen early-stage lesions and radical procedures such as pelvic exenteration concentrated in specialist centres. Sentinel lymph-node mapping is under investigation in small prospective series but has not yet achieved widespread adoption. More recently, recognition of the biological heterogeneity of vaginal squamous cell carcinoma, including HPV-associated and HPV-independent pathways, has stimulated interest in systemic and biomarker-driven therapies. Although evidence remains limited, immune checkpoint inhibitors have demonstrated activity in heavily pretreated patients with rare gynaecological squamous cancers within basket trials such as KEYNOTE-158, supporting their consideration in recurrent or metastatic disease with limited therapeutic options (93). Overall, modern management of vaginal cancer reflects broader trends in GO toward multidisciplinary care, technological refinement in radiotherapy, and cautious treatment individualisation despite the ongoing limitations of a predominantly non-randomised evidence base.

GTN

GTN represents one of the most dramatic success stories in modern oncology, with cure rates exceeding 90–95% even in metastatic disease owing to exquisite chemosensitivity and structured international treatment algorithms. Risk stratification using the FIGO/World Health Organization (WHO) scoring system has enabled treatment individualisation, allowing single-agent chemotherapy such as methotrexate or actinomycin-D for low-risk disease while reserving multi-agent regimens for high-risk patients (94). Centralisation of care to specialist trophoblastic centres has further improved survival and reduced treatment-related morbidity. Contemporary management increasingly emphasises fertility preservation, with most women achieving subsequent successful pregnancies following treatment. Surgical intervention is now selectively employed, typically for chemotherapy-resistant foci or life-threatening haemorrhage. More recently, advances in tumour immunobiology have identified high programmed cell death ligand 1 (PD-L1) expression in trophoblastic tumours, prompting investigation of immune checkpoint inhibitors. Early prospective and retrospective series have demonstrated meaningful response rates to agents such as pembrolizumab or avelumab in chemotherapy-resistant GTN, suggesting a potential paradigm shift for heavily pretreated patients (95,96).

© AME Publishing Company.

These developments highlight GTN as a model for risk-adapted therapy, fertility-sparing care and the integration of immunotherapy into rare gynaecological malignancies.

Discussion

Cervical cancer management is undergoing a decisive shift from uniformly radical surgery towards prevention, precision and de-escalation. Population-level data now confirm that prophylactic HPV vaccination delivers >90% protection against CIN2+/CIN3+ from vaccine types and up to 88% reductions in invasive cancer in fully vaccinated cohorts, suggesting that incident disease burden will fall dramatically in coming decades. In parallel, LACC and subsequent data have re-established open radical hysterectomy as the standard for most early-stage tumours, while trials such as ConCerv, LESSER and SHAPE support downgrading from radical to simple hysterectomy in carefully selected low-risk IA2–IB1 lesions without compromising oncological outcomes. SLNB, validated by SENTICOL and SENTIX, further reduces treatment morbidity, and for locally advanced disease, INTERLACE and KEYNOTE-A18 show that adding induction chemotherapy and pembrolizumab to chemoradiation can meaningfully improve survival.

In advanced ovarian cancer, the debate has shifted from "primary surgery versus chemotherapy" to "who benefits most from which sequence, in which centre". Vergote *et al.*/EORTC 55971 and CHORUS established NACT with IDS as a non-inferior, less morbid alternative to PDS, particularly for frail patients or those with high tumour burden. However, Onda *et al.* and SCORPION highlighted the impact of histology, R0 rates, disease distribution and pre-operative triage on outcomes, while TRUST, conducted in rigorously audited high-volume centres, suggested a PFS advantage for PDS when R0 is achievable. At the same time, LION has supported de-escalation of systematic lymphadenectomy, OV-HIPEC and related trials have revived interest in intraperitoneal strategies at interval surgery, while PARP inhibitors, Bevacizumab and emerging chemo-immunotherapy combinations are pushing ovarian cancer firmly into the era of biomarker-driven, multi-modal care.

Endometrial cancer highlights the rapid clinical impact of molecular classification. Surgical safety has been transformed by high-quality laparoscopic data (LAP2, LACE), and sentinel-node mapping with ICG has largely replaced systematic lymphadenectomy for staging in many centres. TCGA and ProMisE have shifted thinking away from a purely anatomical model toward four distinct molecular risk groups, now incorporated into the 2023 FIGO staging update and the 2025 ESGO–ESTRO-ESP guidelines. PORTEC-1 to 4A trace a clear trajectory from "treat all" pelvic radiotherapy to increasingly personalised adjuvant strategies in which a substantial subset can safely avoid radiotherapy, while others receive escalated chemoradiation. Concurrently, phase III trials such as NRG-GY018, RUBY and DUO-E show that PD-1 blockade (with or without PARP inhibition) delivers particularly striking benefit in dMMR disease but also clinically meaningful improvements in pMMR tumours. HER2-targeted therapy and the RAINBO platform further extend precision approaches to serous and other high-risk subtypes.

In vulval cancer, the dominant theme is radical morbidity reduction anchored in robust prospective data. The GROINSS-V and GOG-173 programmes have transformed groin management, showing that SLNB with ultrastaging can safely replace routine IFL in node-negative early disease, and that radiotherapy is an appropriate substitute for surgery in patients with only micrometastatic nodal involvement. GROINSS-V III will test whether dose-escalated chemoradiation can extend this principle to macrometastatic nodes. Parallel advances in mapping technology, particularly indocyanine-green fluorescence, improve sentinel-node detection while reducing dye-related toxicity. Updated FIGO staging now better reflects nodal burden and extracapsular spread, and trials such as STRIVE, which stratify excision by HPV and p53 status, signal a move toward biologically guided surgical margins. For unresectable or recurrent disease, checkpoint inhibition (KEYNOTE-158) and neoadjuvant immunotherapy studies like APOLLO suggest that even rare tumours will share in the broader immuno-oncology revolution.

Prevention has become a central pillar of contemporary GO, driven by advances in genetic risk assessment and risk-reducing interventions. Germline BRCA1 and BRCA2 mutations confer substantial lifetime ovarian cancer risks (approximately 40–60% and 15–25%, respectively), and risk-reducing bilateral salpingo-oophorectomy reduces incidence by up to 80–90% while improving OS (97). Opportunistic salpingectomy is increasingly adopted as a population-level strategy, reflecting evidence that many high-grade serous carcinomas arise from the distal fallopian tube. In Lynch syndrome, risk-reducing hysterectomy with bilateral salpingo-oophorectomy significantly decreases both

© AME Publishing Company.

endometrial and ovarian cancer risk and is recommended after completion of childbearing (98). Alongside this, molecular tumour testing, cascade genetic screening and personalised surveillance programmes are enabling earlier diagnosis and targeted prevention. Collectively, these developments mark a shift from treatment-focused care toward proactive risk modification.

In parallel, there is a growing emphasis on patient-reported outcome measures (PROMs), functional recovery and survivorship. MIS in endometrial cancer (LAP2, LACE) is associated with faster recovery and improved early quality of life without compromising survival. In cervical cancer, the SHAPE trial demonstrated reduced bladder, urinary and sexual dysfunction with less radical surgery, supporting de-escalation on both oncological and functional grounds. Sentinel lymph-node approaches across cervical, endometrial and vulvar cancers similarly reduce lymphoedema and neurological morbidity. However, PROM reporting remains inconsistent—particularly in ovarian cancer and rare tumours—highlighting the need for routine integration of validated quality-of-life metrics in future trials.

While several of the studies discussed have driven major changes in clinical practice, it is important to interpret their findings within the context of their limitations. Many landmark trials reflect highly selected patient populations and outcomes achieved in expert centres, which may not be directly generalisable to all clinical settings. In ovarian cancer, for example, differences in surgical quality and complete resection rates across trials have influenced interpretation of the relative benefits of primary versus interval cytoreduction. Similarly, in cervical cancer, the LACC trial raised important concerns regarding MIS, although questions remain regarding the influence of surgical technique and case selection. De-escalation trials such as SHAPE provide high-level evidence in carefully defined low-risk groups, but their findings should not be extrapolated beyond these populations. In addition, emerging therapies, particularly immunotherapy and targeted combinations, are often supported by relatively short follow-up and evolving endpoints. Taken together, these considerations highlight the importance of applying trial data within appropriate clinical context rather than assuming uniform applicability across all patient groups.

Importantly, not all advances are equally implementable in routine practice. Widely adopted interventions include HPV vaccination, sentinel lymph-node mapping in selected early-stage disease, and molecular risk stratification. In contrast, complex procedures such as ultra-radical ovarian cytoreduction, HIPEC and IGABT are largely confined to high-volume specialist centres. Emerging strategies—including neoadjuvant immunotherapy and biologically tailored surgery—remain investigational or selectively applied, pending maturation of survival data and wider resource availability. Recognising this gradient of feasibility is essential to ensure equitable translation of innovation into clinical care.

A critical enabler of many contemporary advances in GO is the centralisation of complex care within high-volume specialist centres and the development of coordinated regional networks. Outcomes in advanced ovarian cancer are closely linked to surgical volume, multidisciplinary expertise and the ability to achieve complete cytoreduction with low morbidity. Similar principles apply to technically demanding treatments such as IGABT, pelvic exenteration and management of rare tumours. Consequently, modern care increasingly follows hub-and-spoke models, whereby patients are managed locally where appropriate but referred to tertiary centres for complex interventions or clinical trials. Effective networks rely on structured referral pathways, shared multidisciplinary decision-making, harmonised treatment protocols and bidirectional communication to support perioperative care and survivorship closer to home. Such models aim to balance equitable access with concentration of expertise and are likely to define the future of high-quality GO.

Limitations of our study include selection bias and lack formal meta-analytic synthesis.

Conclusions

Taken together, these developments redefine the role of the Gynaecological Oncologist. Across cervical, ovarian, endometrial and vulval cancers, the contemporary surgeon must be as comfortable interpreting molecular reports, trial data and immunotherapy indications as performing ultra-radical cytoreduction or meticulously conservative procedures. The trajectory is clear: prevention and early detection where possible; de-escalation of surgery when safe; concentration of ultra-radical procedures in expert centres; and integration of radiotherapy, systemic therapy and immune- or targeted agents according to molecularly defined risk. The next decade will likely see further convergence of these themes, with multidisciplinary, biomarker-driven, surgically excellent care replacing historical “one-size-fits-all” approaches across the spectrum

© AME Publishing Company.

of gynaecological malignancies.

Acknowledgments

The abstract for this study was previously presented as an electronic poster at the European Society of Gynaecological Oncology (ESGO) Congress, Copenhagen, February 2026.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1-2924/rc

Peer Review File: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1-2924/prf

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1-2924/coif). H.S.M. serves as an unpaid Associate Editor-in-Chief of *Translational Cancer Research* from January 2025 to December 2026. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Lehtinen M, Paavonen J, Wheeler CM, et al. Overall efficacy of HPV-16/18 AS04-adjuvanted vaccine against grade 3 or greater cervical intraepithelial neoplasia: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. Lancet Oncol 2012;13:89-99.
2. Garland SM, Hernandez-Avila M, Wheeler CM, et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. N Engl J Med 2007;356:1928-43.
3. Kjaer SK, Nygård M, Dillner J, et al. A 12-Year Follow-up on the Long-Term Effectiveness of the Quadrivalent Human Papillomavirus Vaccine in 4 Nordic Countries. Clin Infect Dis 2018;66:339-45.
4. Kreimer AR, Rodriguez AC, Hildesheim A, et al. Proof-of-principle evaluation of the efficacy of fewer than three doses of a bivalent HPV16/18 vaccine. J Natl Cancer Inst 2011;103:1444-51.
5. Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. N Engl J Med 2015;372:711-23.
6. Lei J, Ploner A, Elfström KM, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med 2020;383:1340-8.
7. Palmer T, Wallace L, Pollock KG, et al. Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study. BMJ 2019;365:l1161.
8. Hall MT, Simms KT, Lew JB, et al. Projected future impact of HPV vaccination and primary HPV screening on cervical cancer rates from 2017-2035: Example from Australia. Lancet Public Health 2019;4:e522-e532.
9. Falcaro M, Castañon A, Ndlela B, et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. Lancet 2021;398:2084-92.
10. Ramirez PT, Frumovitz M, Pareja R, et al. Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer. N Engl J Med 2018;379:1895-904.
11. Persson J, Salehi S, Bollino M, et al. Robot-assisted vs open radical hysterectomy for early-stage cervical cancer: the RACC randomized clinical trial. Lancet Oncol 2023;24:380-90.
12. Leitao MM Jr, Bixel KL, Chase DM, et al. ROCC/GOG-3043: a randomized controlled trial of robotic versus open surgery for early-stage cervical cancer. Int J Gynecol Cancer 2025;35:101760.
13. Wu X, Qiu L, Lou W, et al. A multicenter non-inferior randomized controlled study comparing the efficacy of laparoscopic versus abdominal radical hysterectomy for cervical cancer (stages IB1, IB2, and IIA1): study protocol of the LAUNCH 2 trial. Trials 2022;23:269.
14. Schmeler KM, Pareja R, Lopez Blanco A, et al. ConCerv:

a prospective trial of conservative surgery for low-risk early-stage cervical cancer. Int J Gynecol Cancer 2021;31:1317-25.
15. Carneiro VB, Herrmann F, Zanagnolo V, et al. LESs Surgical Radicality for EaRly stage Cervical cancer (LESSER): a proof-of-concept randomized phase II non-inferiority trial of simple hysterectomy vs modified radical hysterectomy in early-stage cervical cancer. Gynecol Oncol 2021;162:25-32.
16. Plante M, Kwon JS, Ferguson S, et al. Simple versus Radical Hysterectomy in Women with Low-Risk Cervical Cancer. N Engl J Med 2024;390:819-29.
17. Taliento C, Scutiero G, Arcieri M, et al. Simple hysterectomy versus radical hysterectomy in early-stage cervical cancer: A systematic review and meta-analysis. Eur J Surg Oncol 2024;50:108252.
18. Bizzarri N, Querleu D, Ramirez PT, et al. Minimally invasive simple hysterectomy in low-risk cervical cancer: a single-arm trial with stopping rules (ENGOT-cx23/MITO/LASH trial). Int J Gynecol Cancer 2025;35:101818.
19. Lécuru F, Mathevet P, Querleu D, et al. Bilateral negative sentinel nodes accurately predict absence of lymph node metastasis in early cervical cancer: results of the SENTICOL study. J Clin Oncol 2011;29:1686-91.
20. Mathevet P, Lécuru F, Uzan C, et al. Sentinel lymph node biopsy and morbidity outcomes in early cervical cancer: Results of a multicentre randomised trial (SENTICOL-2). Eur J Cancer 2021;148:307-15.
21. Lecuru FR, McCormack M, Hillemanns P, et al. SENTICOL III: an international validation study of sentinel node biopsy in early cervical cancer. A GINECO, ENGOT, GCIG and multicenter study. Int J Gynecol Cancer 2019;29:829-34.
22. Cibula D, Kocian R, Plaikner A, et al. Sentinel lymph node mapping and intraoperative assessment in a prospective, international, multicentre, observational trial of patients with cervical cancer: The SENTIX trial. Eur J Cancer 2020;137:69-80.
23. Tu H, Huang H, Li Y, et al. Sentinel-Lymph-Node Biopsy Alone or with Lymphadenectomy in Cervical Cancer. N Engl J Med 2025;393:1463-74.
24. Sturdza A, Pötter R, Fokdal LU, et al. Image guided brachytherapy in locally advanced cervical cancer: Improved pelvic control and survival in RetroEMBRACE, a multicenter cohort study. Radiother Oncol 2016;120:428-33.
25. Pötter R, Tanderup K, Schmid MP, et al. MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicentre prospective cohort study. Lancet Oncol 2021;22:538-47.
26. Pötter R, Tanderup K, Kirisits C, et al. The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies. Clin Transl Radiat Oncol 2018;9:48-60.
27. McCormack M, Eminowicz G, Gallardo D, et al. Induction chemotherapy followed by standard chemoradiotherapy versus standard chemoradiotherapy alone in patients with locally advanced cervical cancer (GCIG INTERLACE): an international, multicentre, randomised phase 3 trial. Lancet 2024;404:1525-35.
28. Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2024;404:1321-32.
29. Vergote I, Tropé CG, Amant F, et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med 2010;363:943-53.
30. Kehoe S, Hook J, Nankivell M, et al. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. Lancet 2015;386:249-57.
31. Onda T, Satoh T, Ogawa G, et al. Comparison of survival between primary debulking surgery and neoadjuvant chemotherapy for stage III/IV ovarian, tubal and peritoneal cancers in phase III randomised trial. European Journal of Cancer 2020;130,114-25.
32. Fagotti A, Ferrandina MG, Vizzielli G, et al. Randomized trial of primary debulking surgery versus neoadjuvant chemotherapy for advanced epithelial ovarian cancer (SCORPION-NCT01461850). Int J Gynecol Cancer 2020;30:1657-64.
33. Mahner S, Heitz F, Salehi S, et al. TRUST: Trial of radical upfront surgical therapy in advanced ovarian cancer (ENGOT ov33/AGO-OVAR OP7). J Clin Oncol 2025;43:LBA5500.
34. Chiva L, Ordas P, Mishra J, et al. SUROVA study: global real-world treatment strategies and mortality risk prediction in advanced ovarian cancer. Int J Gynecol Cancer 2025;35:102688.
35. Jiang R, Zhu J, Kim JW, et al. Study of upfront surgery

© AME Publishing Company.

versus neoadjuvant chemotherapy followed by interval debulking surgery for patients with stage IIIC and IV ovarian cancer, SGOG SUNNY (SOC-2) trial concept. J Gynecol Oncol 2020;31:e86.
36. Gaba F, Blyuss O, Ash K, et al. Survival after interval and delayed cytoreduction surgery in advanced ovarian cancer: a Global Gynaecological Oncology Surgical Outcomes Collaborative-Led Study (GO SOAR2). Int J Gynecol Cancer 2025;35:101650.
37. van Driel WJ, Koole SN, Sikorska K, et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer. N Engl J Med 2018;378:230-40.
38. Antonio CCP, Alida GG, Elena GG, et al. Cytoreductive Surgery With or Without HIPEC After Neoadjuvant Chemotherapy in Ovarian Cancer: A Phase 3 Clinical Trial. Ann Surg Oncol 2022;29:2617-25.
39. Lim MC, Chang SJ, Park B, et al. Survival After Hyperthermic Intraperitoneal Chemotherapy and Primary or Interval Cytoreductive Surgery in Ovarian Cancer: A Randomized Clinical Trial. JAMA Surg 2022;157:374-83.
40. Ghirardi V, Fagotti A, Scambia G. Hyperthermic intraperitoneal chemotherapy for ovarian cancer: long-term findings from the OVHIPEC-1 trial. Lancet Oncol 2023;24:1057-9.
41. Harter P, Sehouli J, Lorusso D, et al. A Randomized Trial of Lymphadenectomy in Patients with Advanced Ovarian Neoplasms. N Engl J Med 2019;380:822-32.
42. Burger RA, Brady MF, Bookman MA, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med 2011;365:2473-83.
43. Perren TJ, Swart AM, Pfisterer J, et al. A phase 3 trial of bevacizumab in ovarian cancer. N Engl J Med 2011;365:2484-96.
44. Moore K, Colombo N, Scambia G, et al. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med 2018;379:2495-505.
45. Ray-Coquard I, Pautier P, Pignata S, et al. Olaparib plus Bevacizumab as First-Line Maintenance in Ovarian Cancer. N Engl J Med 2019;381:2416-28.
46. Vergote I, Cibula D, Powell M et al. Chemotherapy With Or Without Pembrolizumab Followed By Maintenance With Olaparib Or Placebo For First-Line Treatment Of Advanced BRCA Non-Mutated Epithelial Ovarian Cancer: Results From The Randomized Phase 3 ENGOT-OV43/GOG-3036/KEYLYNK-001 Study. International Journal of Gynecological Cancer 2025;35.
47. Creasman WT, Morrow CP, Bundy BN, et al. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Cancer 1987;60:2035-41.
48. Herzog C, Marín F, Jones A, et al. A Simple Cervicovaginal Epigenetic Test for Screening and Rapid Triage of Women With Suspected Endometrial Cancer: Validation in Several Cohort and Case/Control Sets. J Clin Oncol 2022;40:3828-38.
49. Evans I, Reisel D, Jones A, et al. Performance of the WID-qEC test versus sonography to detect uterine cancers in women with abnormal uterine bleeding (EPI-SURE): a prospective, consecutive observational cohort study in the UK. Lancet Oncol 2023;24:1375-86.
50. Ken-Amoah S, Redl E, Domson BKS, et al. Performance of the WID-qEC test to detect uterine cancers in black women with abnormal uterine bleeding: A prospective observational cohort study in Ghana. Int J Cancer 2025;156:1055-64.
51. Walker JL, Piedmonte MR, Spirtos NM, et al. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group LAP2 Study. J Clin Oncol 2012;30:695-700.
52. Janda M, Gebski V, Forder P, et al. Total laparoscopic versus open surgery for stage 1 endometrial cancer: the LACE randomized controlled trial. Contemp Clin Trials 2006;27:353-63.
53. Benedetti Panici P, Basile S, Maneschi F, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst 2008;100:1707-16.
54. ; Kitchener H, Swart AM, et al. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 2009;373:125-36.
55. Rossi EC, Kowalski LD, Scalici J, et al. A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study. Lancet Oncol 2017;18:384-92.
56. Persson J, Salehi S, Bollino M, et al. Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer (SHREC-trial)-the final step towards a paradigm shift in surgical staging. Eur J Cancer 2019;116:77-85.
57. Sozzi G, Fanfani F, Berretta R, et al. Laparoscopic sentinel node mapping with intracervical indocyanine green injection for endometrial cancer: the SENTIFAIL study - a multicentric analysis of predictors of failed mapping. Int J Gynecol Cancer 2020;30:1713-8.
58. Nagar H, Wietek N, Goodall RJ, et al. Sentinel node biopsy for diagnosis of lymph node involvement in

© AME Publishing Company.

endometrial cancer. Cochrane Database Syst Rev 2021;6:CD013021.
59. Bristow RE, Duska LR, Montz FJ. The role of cytoreductive surgery in the management of stage IV uterine papillary serous carcinoma. Gynecol Oncol 2001;81:92-9.
60. Mantovani G, Coada CA, Di Costanzo S, et al. Primary or Interval Debulking Surgery for Advanced Endometrial Cancer with Carcinosis: A Systematic Review and Individual Patient Data Meta-Analysis of Survival Outcomes. Cancers (Basel) 2025;17:1026.
61. National Cancer Institute. The Cancer Genome Atlas (TCGA) program history [Internet]. Bethesda (MD): National Cancer Institute; [cited 2025 Dec 31]. Available online: https://www.cancer.gov/ccg/research/genome-sequencing/tcga/history
62. Cooper LA, Demicco EG, Saltz JH, et al. PanCancer insights from The Cancer Genome Atlas: the pathologist's perspective. J Pathol 2018;244:512-24.
63. Cancer Genome Atlas Research Network; Kandoth C, Schultz N, et al. Integrated genomic characterization of endometrial carcinoma. Nature 2013;497:67-73.
64. Talhouk A, McConechy MK, Leung S, et al. Confirmation of ProMisE: A simple, genomics-based clinical classifier for endometrial cancer. Cancer 2017;123:802-13.
65. Berek JS, Matias-Guiu X, Creutzberg C, et al. FIGO staging of endometrial cancer: 2023. Int J Gynaecol Obstet 2023;162:383-94.
66. Concin N, Matias-Guiu X, Cibula D, et al. ESGO-ESTRO-ESP guidelines for the management of patients with endometrial carcinoma: update 2025. Lancet Oncol 2025;26:e423-35.
67. Creutzberg CL, van Putten WL, Koper PC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. Lancet 2000;355:1404-11.
68. Nout RA, Smit VT, Putter H, et al. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. Lancet 2010;375:816-23.
69. de Boer SM, Powell ME, Mileshkin L, et al. Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial. Lancet Oncol 2018;19:295-309.
70. van den Heerik ASVM, Horeweg N, Haverkort MAD, et al. Molecular profile-based adjuvant treatment for women with high-intermediate risk endometrial cancer (PORTEC-4a): results of a randomised, open-label, phase 3, multicentre, non-inferiority trial. Lancet Oncol 2026;27:23-35.
71. Eskander RN, Sill MW, Beffa L, et al. Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer. N Engl J Med 2023;388:2159-70.
72. Mirza MR, Chase DM, Slomovitz BM, et al. Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. N Engl J Med 2023;388:2145-58.
73. Westin SN, Moore K, Chon HS, et al. Durvalumab Plus Carboplatin/Paclitaxel Followed by Maintenance Durvalumab With or Without Olaparib as First-Line Treatment for Advanced Endometrial Cancer: The Phase III DUO-E Trial. J Clin Oncol 2024;42:283-99.
74. Rohaan MW, Stahlie EHA, Franke V, et al. Neoadjuvant nivolumab + T-VEC combination therapy for resectable early stage or metastatic (IIIB-IVM1a) melanoma with injectable disease: study protocol of the NIVEC trial. BMC Cancer 2022;22:851.
75. Fader AN, Roque DM, Siegel E, et al. Randomized Phase II Trial of Carboplatin-Paclitaxel Compared with Carboplatin-Paclitaxel-Trastuzumab in Advanced (Stage III-IV) or Recurrent Uterine Serous Carcinomas that Overexpress Her2/Neu (NCT01367002): Updated Overall Survival Analysis. Clin Cancer Res 2020;26:3928-35.
76. Refining adjuvant treatment in endometrial cancer based on molecular features: the RAINBO clinical trial program. Int J Gynecol Cancer 2023;33:109-17.
77. WHO Classification of Tumours Editorial Board. Female genital tumours. 5th ed. Lyon (France): International Agency for Research on Cancer; 2020.
78. Hensley ML, Enserro D, Hatcher H, et al. Adjuvant gemcitabine plus docetaxel followed by doxorubicin versus observation for high-grade uterine leiomyosarcoma: a phase III NRG Oncology/Gynecologic Oncology Group study. J Clin Oncol 2018;36:3324–30.
79. Oonk MH, van Hemel BM, Hollema H, et al. Size of sentinel-node metastasis and chances of non-sentinel-node involvement and survival in early stage vulvar cancer: results from GROINSS-V, a multicentre observational study. Lancet Oncol 2010;11:646-52.
80. Levenback CF, Tian C, Coleman RL, et al. Sentinel node (SN) biopsy in patients with vulvar cancer. J Clin Oncol 2009;27:abstr 5505.
81. Oonk MHM, Slomovitz B, Baldwin P, et al. Radiotherapy

© AME Publishing Company.

instead of inguinofemoral lymphadenectomy in vulvar cancer patients with a metastatic sentinel node: results of GROINSS-V II. Int J Gynecol Cancer 2019;29:A14.
82. Gien LT, Slomovitz B, Van der Zee A, et al. Phase II activity trial of high-dose radiation and chemosensitization in patients with macrometastatic lymph node spread after sentinel node biopsy in vulvar cancer: GROningen INternational Study on Sentinel nodes in Vulvar cancer III (GROINSS-V III/NRG-GY024). Int J Gynecol Cancer 2023;33:619-22.
83. Deken MM, van Doorn HC, Verver D, et al. Near-infrared fluorescence imaging compared to standard sentinel lymph node detection with blue dye in patients with vulvar cancer - a randomized controlled trial. Gynecol Oncol 2020;159:672-80.
84. Koual M, Benoit L, Nguyen-Xuan HT, et al. Diagnostic value of indocyanine green fluorescence guided sentinel lymph node biopsy in vulvar cancer: A systematic review. Gynecol Oncol 2021;161:436-41.
85. Cornel KMC, Mehta MP, Swift BE, et al. The use of indocyanine green (ICG) for sentinel lymph node detection in vulvar cancer. Gynecol Oncol 2025;196:146-51.
86. Olawaiye AB, Cotler J, Cuello MA, et al. FIGO staging for carcinoma of the vulva: 2021 revision. Int J Gynaecol Obstet 2021;155:43-7.
87. Jamieson A, McAlpine JN, Hoang L, et al. Stratification of vulvar squamous cell carcinoma (VSCC) by … [abstract]. J Clin Oncol 2025;43:TPS5637.
88. Shapira-Frommer R, Mileshkin L, Manzyuk L, et al. Efficacy and safety of pembrolizumab for patients with previously treated advanced vulvar squamous cell carcinoma: Results from the phase 2 KEYNOTE-158 study. Gynecol Oncol 2022;166:211-8.
89. van Poelgeest MIE, Kortekaas KE, van Doorn HC, et al. APOLLO: neo-adjuvant pembrolizumab for primary vulvar squamous cell carcinoma-a multicenter, single-arm, phase II, clinical proof-of-concept study. Int J Gynecol Cancer 2025;35:101831.
90. Frank SJ, Jhingran A, Levenback C, et al. Definitive radiation therapy for squamous cell carcinoma of the vagina. Int J Radiat Oncol Biol Phys 2005;62:138-47.
91. Dimopoulos JC, Schmid MP, Fidarova E, et al. Treatment of locally advanced vaginal cancer with radiochemotherapy and magnetic resonance image-guided adaptive brachytherapy: dose-volume parameters and first clinical results. Int J Radiat Oncol Biol Phys 2012;82:1880-8.
92. Rajagopalan MS, Xu KM, Lin JF, et al. Adoption and impact of concurrent chemoradiation therapy for vaginal cancer: a National Cancer Data Base (NCDB) study. Gynecol Oncol 2014;135:495-502.
93. Marabelle A, Le DT, Ascierto PA, et al. Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study. J Clin Oncol 2020;38:1-10.
94. Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. Lancet 2010;376:717-29.
95. You B, Bolze PA, Lotz JP, et al. Avelumab in Patients With Gestational Trophoblastic Tumors With Resistance to Single-Agent Chemotherapy: Cohort A of the TROPHIMMUN Phase II Trial. J Clin Oncol 2020;38:3129-37.
96. Ghorani E, Kaur B, Fisher RA, et al. Pembrolizumab is effective for drug-resistant gestational trophoblastic neoplasia. Lancet 2017;390:2343-5.
97. Rebbeck TR, Kauff ND, Domchek SM. Meta-analysis of risk reduction estimates associated with risk-reducing salpingo-oophorectomy in BRCA1 or BRCA2 mutation carriers. J Natl Cancer Inst 2009;101:80-7.
98. Schmeler KM, Lynch HT, Chen LM, et al. Prophylactic surgery to reduce the risk of gynecologic cancers in the Lynch syndrome. N Engl J Med 2006;354:261-9.

Cite this article as: Nistor SI, Shao R, Conforti J, Gardner F, Ferrari F, Ismail L, Niu X, Yao D, Soleymani majd H. Precision, prevention and progress: charting two decades of change in gynaecological oncology—a narrative review. Transl Cancer Res 2026;15(4):343. doi: 10.21037/tcr-2025-1-2924

© AME Publishing Company.