**West of Scotland Cancer Network**

**Gynaecological Cancer Managed Clinical Network**

# Gynaecological Cancer

# Regional Follow-up Guidelines

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| **Issue date** | September 2024 |
| **Review date** | September 2027 |
| **Version** | 3.0 |
| **Replaces** | Version 2.0 (June 2015) |

## Regional Follow-up Gynaecological Cancer Guidelines

The purpose of this regional follow-up guideline is to ensure consistency of practice across the West of Scotland. The principles of any update to the follow-up guidelines must continue to ensure that management of patients after initial treatment for gynaecological malignancy are:

- Patient-centred
- Aligned to recognised current best practice
- Equitable across the region
- Clinically safe and effective
- Efficiently delivered.

### Guideline Review

The guidelines have been reviewed on the basis that the key aims underpinning the purpose of follow-up are to:

- Manage and treat symptoms and complications
- Provide psychological and supportive care
- Detect and treat recurrent disease.

Follow-up practice should ideally be supported by empirical evidence of improved outcomes and survival. In the absence of good quality evidence, care should be tailored to patient needs. The construction of appropriate follow-up guidance requires balancing patient needs with effective and efficient utilisation of resources.

Effective shared care arrangements, between central and local oncology teams, can be beneficial to follow-up care and recommendations are made on the assumption that a named primary contact is identified to each patient.

***These regional guidelines are recommended by the Gynaecological Cancer MCN whose members also recognise that specific needs of individual patients may require to be met by an alternative approach and that this will be provided where necessary and documented in the patient notes.***

It should be noted that individual clinical trial protocols may also dictate a specific regimen of follow-up; intervals, tests and investigations.

This guideline is not intended to advise the management of patients with progressive or recurrent disease.

Appendix 1 of this document provides a quick-reference summary of the guidelines.

## 1. Borderline Ovarian Disease

### 1.1 Evidence Review

The overall outcomes of borderline ovarian tumours are favourable. Fertility conserving surgery of borderline ovarian tumours is associated with an increased risk of recurrence however it does not affect overall survival. Westerman et al reported a series of 507 patients who had been diagnosed with borderline ovarian tumours.[1] Among 153 patients (30.2%) who had fertility-sparing surgery, 21 (13.7%) experienced a recurrence (including one invasive relapse). The evidence supports follow up with ultrasound guidance in those who have had fertility conserving surgery as it is superior to CA125 and clinical examination.[2] No compelling evidence is identified for borderline follow-up after pelvic clearance.

### 1.2 Recommendations

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| **Pelvis Cleared** | *Low Risk Features* | No routine follow-up required |
| | *High Grade / High Risk Features (To be documented at MDT)* | 6 monthly intervals for 3 years |
| **Fertility sparing surgery** | *Ovary conserved* | 6 monthly intervals for 3 years<br>Annually years 4 and 5 |

Patients contact should be by the team providing original care. Ideally, routine follow-up contacts for these patients should be virtual (video-link or telephone). Prior arrangement should be made for tumour marker testing and ultrasound investigation as necessary:

- CA125 assessment to be discussed with patient
- Pelvic USS examinations (where fertility sparing surgery was undertaken only)

Nurse-led practice is recommended where local teams are agreed that the necessary expertise is available.

Scheduled appointment for clinical examination would only be required where there are concerning symptoms or results of testing and/or investigation indicate.

At discharge, provision of written patient information and service access contact details should be provided, as a small risk of recurrence for borderline disease remains over the long term.

*Note: Completion surgery for borderline tumours should be discussed when family is complete.*[2]

## 2. Epithelial Ovarian Cancer

### 2.1 Evidence Review

Follow up of patients with epithelial ovarian cancer is evolving. Historically, evidence shows no additional benefit in initiation of systemic anti-cancer treatment upon asymptomatic rise in CA125 compared to symptomatic progression, as such routine measurement of CA125 during follow up was not deemed mandatory.[3] However, the OVO5 trial was performed in a treatment era that did not include the use of first line maintenance PARP inhibitors. There is evidence to show that patients on PARP inhibitors who relapse can do so despite a normal CA125[4] Patients on adjuvant PARP inhibitors are therefore monitored with CA125 as well as 6 monthly CT scans at the Beatson West of Scotland Cancer Centre. There is thus some uncertainty as to whether similar patterns are observed in patients who have completed their course of PARP inhibitors and subsequently relapse. Furthermore, the DESKTOP III trial showed an overall survival benefit in patients who fulfil the AGO criteria for secondary

cytoreductive surgery in relapsed disease, therefore early detection of asymptomatic disease is relevant for a subset of patients.[5]

Patients receiving chemotherapy as part of their treatment for ovarian cancer may benefit from access to holistic needs assessment (HNA), provided by a suitably trained individual.

In view of the results of the DESKTOP III trial, CA125 monitoring is therefore now routinely recommended. The follow up guidelines for cohorts of patients with epithelial ovarian cancer are thus revised as followed:

## 2.2 Recommendations

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| **Early stage/low grade tumours not treated with adjuvant chemotherapy** | 4 monthly intervals for 3 years followed by 6 monthly for 2 years. |

- Patients who have ***not*** had adjuvant therapy should have their follow up conducted by the team providing the original care.
- Routine CA125 monitoring is recommended. Patients diagnosed with mucinous ovarian carcinomas should have their CA125, CEA and CA19-9 monitored.

The team will inform patients of signs and symptoms of recurrent disease and provide contact details for access to services; patients will be advised to contact the team if these occur rather than waiting until their next appointment. This should be repeated at discharge.

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| **All epithelial ovarian cancer having surgery and chemotherapy and complete their course of adjuvant PARP inhibitors (3 years for niraparib, and 2 years for olaparib +/- bevacizumab)** | 5 years follow up is to commence after PARP inhibitor therapy has stopped. 4 monthly interval for 3 years followed by 6 monthly for 2 years. Annual CT scans are recommended. |

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| **All epithelial ovarian cancer having surgery and chemotherapy but do not receive adjuvant PARP inhibitors.** | 4 monthly interval for 3 years followed by 6 monthly for 2 years. |

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| **Patients with epithelial ovarian cancer who have had fertility conserving surgery and have had 1/both ovaries conserved.** | This requires individualised approach and discussion at the MDT / treating Medical Oncologist. Including a plan for any required imaging. |

Initial follow-up appointment, at 4 months following end of chemotherapy or PARP inhibitor therapy, will be with the Beatson oncology team. Thereafter appointments may be with the patient's local oncology team after discussion between the patient and their oncologist. Shared care may be considered and if agreed this needs to be clearly communicated to all parties and documented in patient notes. The follow-up appointments would usually involve:

- Assessment of symptoms and ongoing toxicity
- Clinical examination - imaging required as clinically indicated
- Routine CA125 monitoring is recommended
- Patients with stage 3 or 4 low grade serous ovarian carcinomas who have had surgery +/- chemotherapy are now commenced on adjuvant letrozole for at least 5 years although the optimal duration is currently unknown; these patients are at risk of accelerated osteoporosis and therefore require their bone health to be monitored. In pre-menopausal patients, DEXA scans are

recommended at baseline, and at 2 yearly intervals till patients complete the course of letrozole, or as dictated by the report.

The team will inform patients of signs and symptoms of recurrent disease and provide contact details for access to services; patients will be advised to contact the team if these occur rather than waiting until their next appointment. This advice should be repeated at discharge and the patient information leaflet used.

### 2.3 Germ Cell Tumours, Sex Cord and Stromal Tumours

These tumours are rare; individualised follow-up is recommended for all cases following MDT discussion.

## 3. Endometrial Cancer

### 3.1 Evidence Review

For patients who have completed primary therapy for endometrial cancer there is a lack of randomised controlled trial evidence to address follow-up. No impact on survival from routine follow-up has been demonstrated.

Studies have shown that 1 in 4 patients with recurrent disease are asymptomatic at diagnosis.[6,7,8] Most recurrences happen within the first three years (68 to 100%) and almost half of them occur locally (in the vagina).[7,8] Neither recurrence-free survival nor overall survival was improved in asymptomatic cases compared to those detected at clinical presentation.[7]

Two systematic reviews concluded that follow-up frequency may be reduced in low risk patients.[9,10]

Beaver *et al*. have provided randomised controlled evidence that telephone based follow up is not inferior to conventional hospital-based appointments for women with stage 1 endometrial carcinoma[11].

It is important to note that local recurrence may be salvageable in the low risk group.

Patients receiving adjuvant treatment for endometrial cancer should undergo holistic needs assessment (HNA) by a suitably trained individual.

At discharge, patients should be provided written patient information and local service access contact details. Earlier discharge at patient's request is appropriate as existing evidence has not demonstrated survival benefit in asymptomatic recurrence.

Follow up after definitive therapy for endometrial cancer is evolving from hospital-based schedules for all risk groups to a stratified approach. Patients with low risk endometrial cancer have a very low risk of recurrence, even in the absence of adjuvant treatment. Relapses typically occur early, within the first 2 years, and are predominantly located within the vagina[7,8]. Overall survival following salvage therapy for local recurrence is similar regardless of symptomatic presentation compared with asymptomatic detection at routine clinical assessment.[7]

The British Gynaecological Cancer Society (BGCS) supports PIFU for both low and intermediate risk endometrial cancer [BGCS], although the pattern of relapse is different with a higher proportion of systemic disease in the latter.[12] WOSCAN audit indicates that recurrence rates are very similar in intermediate risk patients who have vaginal brachytherapy and high-intermediate risk patients who undergo external beam radiotherapy to the pelvis. Providing patients have adequate information on red

flag symptoms suggestive of recurrence and awareness of late toxicity with a rapid means of accessing support and clinical assessment, PIFU is also suitable for the high-intermediate risk group.

High risk endometrial cancer encompasses a heterogeneous spectrum of disease and management is likely to include surgery, radiotherapy, and chemotherapy. The precise selection and scheduling of treatment modalities is individualised based on tumour bulk and distribution, resectability, and concomitant comorbidities, but is increasingly driven by molecular profile. As this patient cohort have a significant risk of recurrence despite adjuvant therapy and a higher preponderance for late toxicities, routine hospital based follow up (either clinic visit or telephone consultation) may be more appropriate, although there is no randomised evidence that hospital based protocols enhance survival outcomes in high risk endometrial cancer. Recent trials in the first line setting for advanced or relapsed endometrial cancer incorporating immunotherapy [RUBY, GY018] demonstrate significant response rates and prolonged duration of action;[13,14] it is currently unknown whether earlier detection of recurrence is of benefit, but as options increase and are more personalised based on molecular profile, there may be a drive towards more intensive surveillance in this population.

### 3.2 Recommendations

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| **Low Risk[15]** | No adjuvant therapy | No formal follow up advised. Patient initiated follow-up supported by provision of clear guidance on signs and symptoms and contact information to access the specialist clinical team for 3 years. |
| **Intermediate Risk[15]** | Vaginal cylinder brachytherapy | Single central follow up appointment at 2-3 months. Thereafter PIFU is recommended for up to 3 years. |
| **High-Intermediate Risk[15]** | External beam radiotherapy and/or vaginal cylinder brachytherapy | Single central follow up appointment at 2-3 months. Thereafter PIFU is recommended for up to 3 years. |
| **High Risk[15]** | SACTand/or radiotherapy | Central follow up appointment at 2-3 months. Ongoing 6-monthly follow up with oncology or gynaecology for up to 3 years. |

At Discharge patients should be provided written patient information and local service access contact details. Earlier discharge at patient's request is appropriate as existing evidence has not demonstrated survival benefit in asymptomatic recurrence.

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| **Leiomyosarcoma, Endometrial Stromal Cell tumours, High Grade Uterine Sarcomas, Smooth Muscle Tumours of Uncertain Potential (STUMP)** | Individualised follow-up for patients with these rarer uterine tumours should be endorsed by the MDT / Rare Tumour clinic. |

## 4. Cervical Cancer

### 4.1 Evidence Review

The SIGN guideline for cervical cancer (2008) highlights the lack of consistent evidence to demonstrate effectiveness of post treatment surveillance[16, 17, 18]

- Routine follow-up after radical hysterectomy and pelvic lymph node dissection is not a sensitive way of detecting recurrent disease
- Cervical cytology or vault smears are not indicated to detect asymptomatic recurrence of cervical cancer
- The BGCS Cervical cancer guideline does not suggest a specific follow up for early stage cervical cancer. The BSCCP guidance for the follow up of patients following a simple hysterectomy for CIN may be relevant in selected cases.[17]

Patients receiving treatment for cervical cancer (> Stage 1A1) should undergo a holistic needs assessment (HNA) by a suitably trained individual.

### 4.2 Recommendations

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| **Stage IA1** | No Hysterectomy | 6 monthly intervals for 5 years with annual cytology |
| | Following Hysterectomy | At 6 months for a vault smear and if hrHPV negative can be discharged to PIFU for up to 2 years. |
| **Stage IA2/IB1** | No Hysterectomy (Fertility Sparing) | Central follow up, 6 monthly intervals for 5 years with annual cytology at colposcopy clinic. |
| | Following Hysterectomy with nodes | 6 monthly for 2 years**, *no*** routine cytology required |

The follow-up appointments would usually involve:

- Vaginal examination
- Rectal examination

At discharge (local oncology team), provision of written patient information and local service access contact details.

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| **Primary Radiotherapy/ Chemoradiotherapy based treatment** | Central follow up at 6-8 weeks with MRI arranged for 3 to 4 months post treatment.<br>If complete response on MRI, offer shared follow up 6 monthly for 3 years.<br>(oncology or gynaecology, preferably at a centralised dedicated clinic). PIFU may be appropriate in individual cases<br><br>If incomplete response on MRI, serial MRI imaging and/or PET-CT is recommended, especially if there is a radical salvage option |

At discharge (local oncology team), provision of written patient information and local service access contact details.

## 5. Vulval Cancer

All patients receiving treatment for high risk vulval cancer should undergo a holistic needs assessment (HNA) by a suitably trained individual. It is anticipated that the local CNS should undertake these HNAs.

### 5.1 Evidence Review

Up to a third of vulval cancers will recur even after satisfactory primary treatment. As salvage is dependent on further excision or radiotherapy, recognition of recurrence as early as possible seems logical.[18,19,20] Loco-regional recurrence most commonly occurs in the first two years and follow-up regimes should reflect this.[19,20]

**Recommendations**

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| **Low Risk** | Early disease - no adjuvant therapy | 6 monthly intervals for 3 years |
| **High Risk** | Patients who had adjuvant therapy or surgery after NACT | Central follow up at 2 months with ongoing gynaecological follow up at 6 monthly intervals for 3 years. |

The follow-up appointments would usually involve:

- Clinical examination including assessing groins and legs (imaging arranged where clinically indicated).
- Assessing for physical and psychological sequelae of treatment.

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## Appendix 1

## Follow-up Guidelines – Quick Reference

| Primary Site | Stage/ Grade | Qualifier | Year 1 | | | | Year 2 | | | | Year 3 | | | | Year 4 | | Year 5 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 4 | 6 | 8 | 12 | 16 | 18 | 20 | 24 | 28 | 30 | 32 | 36 | 42 | 48 | 54 | 60 |
| **Ovary** | Borderline | Pelvis Cleared Low Risk | Patient Initiated Follow-up | | | | | | | | | | | | | | | |
| | Borderline | Pelvis Cleared High Risk | | L[1] | | L[1] | | L[1] | | L[1] | | L[1] | | L[1] | | | | |
| | Borderline | Fertility Saving Surgery | | L[3] | | L[3] | | L[3] | | L[3] | | L[3] | | L[3] | L[3] | | L[3] | |
| | Early stage/ low grade | No Adjuvant Treatment | L[1] | | L[1] | L[1] | L[1] | | L[1] | L[1] | | | L[1] | L[1] | L[1] | L[1] | L[1] | L[1] |
| | All (others) | Epithelial Type - Surgery, chemo, PARPi[4] | C[1] | | L[2] | L[2,5] | L[2] | | L[2] | L[2,5] | L[2] | | L[2] | L[2,5] | L[2] | L[2,5] | L[2] | L[2,5] |
| | | Epithelial Type - Surgery CHEMO No PARPi[6] | C[1] | | L[2] | L[2,5] | L[2] | | L[2] | L[2,5] | L[2] | | L[2] | L[2,5] | L[2] | L[2,5] | L[2] | L[2,5] |
| | All (others) | Germ Cell/Sex Cord/ Stromal Fertlity conservation | Individualised patient follow-up agreed by the regional MDT | | | | | | | | | | | | | | | |

**L** – Seen by the local Board team **C** – Seen by the Central Oncology Team

[1] Clinical examination and CA125 assessment offered
[2] Symptoms and signs of ongoing toxicity assessed, Clinical examination, CA125 assessment discussed
[3] Clinical examination, CA125 assessment offered and pelvic USS examination
[4] Commences afrer PARPi has stopped
[5] Offer CT CAP scan
[6] Includes low grade serous ovarian cancer

| Primary Site | Risk | Qualifier | Year 1 | | | | | Year 2 | | Year 3 | | Year 4 | | Year 5 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 2 | 4 | 6 | 8 | 12 | 18 | 24 | 30 | 36 | 42 | 48 | 54 | 60 |
| **Endometrium** | Low | No Adjuvant Therapy | | L | No formal routine follow-up schedule advised | | | | | | | | | | |
| | Intermediate | Receiving Adjuvant VBT | | C | Patient Initiated Follow-up | | | | | | | | | | |
| | High-Intermediate | EBRT and / or VBT | C | Patient Initiated Follow-up | | | | | | | | | | | |
| | High | Adjuvant therapy other | C | | 6 monthly Local / Central | | | | | | | | | | |
| | | Leiomyosarcoma, Endometrial Stromal Cell tumours, High Grade Uterine Sarcomas, Smooth Muscle Tumours of Uncertain Potential, others | | This rarer collection of uterine tumours should be referred centrally to the oncology team after MDT discussion. Follow-up will depend on original pathology and findings. | | | | | | | | | | | |

**L** – Seen by the local Board team **C** – Seen by the Central Oncology Team

Clinical examination – no routine vault smears, blood analysis and imaging only if clinically indicated
Discuss treatment effects, clinical examination – no routine vault smears, blood analysis and imaging only if clinically indicated

| Primary Site | Stage/Grade | Qualifier | Year 1 | | | | | Year 2 | | Year 3 | | Year 4 | | Year 5 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 2 | 4 | 6 | 8 | 12 | 18 | 24 | 30 | 36 | 42 | 48 | 54 | 60 |
| **Cervix** | Stage IA1 | No Hysterectomy | | | L[1] | | L[1] | L | L[1] | L | L[1] | L | L[1] | L | L[1] |
| | Stage IA1 | Hysterectomy | | | L[1] | | L | L[1] | | | | | | | |
| | Stage IA2/IB1 | No Hysterectomy | | | C[1] | | C[1] | C | C[1] | C | C[1] | C | C[1] | C | C[1] |
| | Stage IA2/IB1 | Hysterectomy and Nodes | | | C[2] | | L[2] | L[2] | L[2] | | | | | | |
| | All (others) | Primary Radiotherapy | C[2] | C[3] | | | L/C[2] | L/C[2] | L/C[2] | | | | | | |

**L** – Seen by the local Board team **C** – Seen by the Central Oncology Team

[1] Clinical examination with cervical (or vault) cytology annually
[2] Vaginal examination
[3] MRI Scan

| Primary Site | Stage/ Grade | Qualifier | Year 1 | | | | Year 2 | | Year 3 | | Year 4 | | Year 5 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 2 | 6 | 8 | 12 | 18 | 24 | 30 | 36 | 42 | 48 | 54 | 60 |
| **Vulva** | All | Surgically Treated (only) | | L[1] | | L[1] | L[1] | L[1] | L[1] | L[1] | | | | |
| | All | Adj Radiotherapy (node +ve/margins close) | C[1] | | L/C[1] | L/C[1] | L/C[1] | L/C[1] | L/C[1] | L/C[1] | | | | |

**L** – Seen by the local Board team **C** – Seen by the Central Oncology Team

[1] Clinical examination including groins - imaging required only as clinically indicated. Imaging is likely to involve groin ultrasound +/- FNA of groin nodes combined with MRI pelvis to detect local recurrence. Suspicion of distant recurrence should be assessed by CT chest, abdomen and pelvic.