This guideline is currently under review (commencing April 2023) and may not be fully reflective of all current practices.



Lead Group: North Cancer Gynaecology Pathway Board (NCGPB)

13TH November 2020

File Reference: NCA-CMG-OVA

Published: 16th December 2020

For symptoms of suspected Gynaecological cancer, please refer to the <u>Scottish Referral Guidelines for Suspected Cancer</u>

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Staging

All patients with a confirmed diagnosis of ovarian cancer will have their cancer staged using the FIGO system as documented on Page 6 of this CMG.

Cancer staging will allow a clinical decision on treatment options to be made in accordance with the guidance provided by this CMG in the management of patients aged 18 years and older with ovarian cancer.

General Principles

- Referrals should be vetted in accordance with the Scottish Referral Guidelines for Suspected Cancer.
- All patients must be discussed at MDT meetings throughout their patient journey as required.
- All patients referred for investigation of symptoms potentially indicative of ovarian cancer should receive an appointment to a specialist outpatient gynaecology clinic.
- All patients should be considered for surgery at MDT using the exclusions / inclusions on Page 4 to determine suitability.
- Where available, clinical trials should always be considered as the preferred option for all eligible patients and consideration given to national referral.
- Patients must be involved in all decision-making relating to their care with informed consent required for patients undergoing treatment.
- A list of SACT regimens is provided (page 8).
- Full regional SACT Protocols will be developed and linked to from this document.
- Patients in follow-up will have access to a clinical nurse specialist throughout their follow-up and post-discharge for any further symptoms relating to treatment for ovarian cancer.
- Patients will have a Holistic Needs Assessment undertaken as part of their pathway.



Diagnosis of Ovarian Cancer

All Patients: Initial Investigations

- Full medical history
- Physical examination including Pelvis
- Routine blood screen (Full Blood Count, biochemistry, CA125 and +/- CEA (other germ cell tumour markers if indicated for women under 40))
- If germ cell tumour, follow national guidelines for female germ cell tumour

All Patients: Further Investigations (if indicated)

- Paracentesis
- CT Chest, Abdomen & Pelvis*
- Image guided biopsy of disease
- Laparascopy if indicated
- Calculate RMI** score
- * as per guidelines on imaging of Gynaecological Malignancy
- ** RMI is a produce of the ultrasound scan score, the menopause status and the serum CA125 level (IU/ml)

All Patients: Other Considerations

Fertility expectations should be discussed.

All patients should be referred to identified Clinical Nurse Specialist (CNS) for assessment and ongoing support and advice. This is in addition to specialist referrals for clinical reasons.



North of Scotland Clinical Management Guideline (CMG): Ovarian Cancer Last Updated 27/04/2023 **Evaluation** Follow-Up **Treatment Debulking surgery** TAH **BSO** Omentectomy Suspected diagnosis of Pelvic washings ovarian cancer with ► Stage 1 Follow-up at Pelvic exenteration pathological / radiological Histopathology Gynaecology Pelvic and retroperitoneal evidence Yes - UFS report completed clinics for lymphadenectomy post-surgery physical Splenectomy All patients examination and Peritonectomy Stage 2 Registration at regional considered imaging as **Total Colectomy** Consider for surgery Gynaecology MDT required. Removal of superficial SACT according to hepatic lesions (see page 8) NCA Support Groin lymph nodes Guidelines available from for surgery CNS for any decision-If not already undertaken, symptomatic making CT or MRI staging imaging problems CT & MDT DECISION RE: (see page 3) → Stage 3 experienced **SURGERY AFTER 3 CYCLES** including post-Ensure Histological / discharge. NACT Yes - IDS Cytological diagnosis (see page 8) All patients discussed at obtained (See page 6 for MDT before treatment Stage 4 further decision information on follow-up) Consider SACT Consider No (see page 8) **IDS** Note: Patients to be considered for germline and somatic testing BRCA1+2. Ensure Histological / Cytological diagnosis obtained Page 3

North of Scotland Clinical Management Guideline (CMG): Inclusion & Exclusion Criteria Last Updated 27/04/2023

INCLUSIONS

1: Decision-making for Up Front Surgery (UFS)

EXCLUSIONS

- Patients of all stages considered (able to be resected to <1cm residual disease)Biopsy proven low grade or clear cell advanced ovarian cancer (chemo resistant) should have primary surgery where feasible
- All extra-abdominal metastases (stage IV) should be considered potential indications for NACT/IDS, not primary surgery, except for the following:
 - Resectable inguinal lymph nodes
 - Pleural fluid that contains cytologically malignant cells without proof of the presence of pleural tumours (IVA).
 - Where considering the clinical significance of cardiophrenic nodes

- Abdominal exclusion criteria:
 - Involvement of the root of the small bowel mesentery
 - Diffuse and confluent carcinomatosis of the stomach and/or small bowel that involves such large parts that resection would lead to a short bowel syndrome or a total gastrectomy
 - Intrahepatic metastases
 - Infiltration of the porta hepatis, duodenum and/or pancreas and/or the large vessels of the hepatoduodenal ligament or coeliac trunk
- Patient characteristics
 - Impaired performance status and comorbidity that does not allow a maximal surgical effort to achieve a complete resection;
 - Patients' nonacceptance of potential supportive measures, such as blood transfusions or temporary stoma
 - Significant recent arterial or venous clot <3months e.g. CVA, PE
- Disease requiring ultra-radical surgery (NICE guidance 470) i.e. multiple resections of the bowel, liver resection, partial gastrectomy, cholecystecomy, (currently assessed by radiology but may need laparoscopy).

INCLUSIONS

2: Decision-making for NACT before Interval Delayed Surgery (IDS) **EXCLUSIONS**

- 3 to 4 cycles of neoadjuvant platinum based chemotherapy (no published role after 6 cycles), or equivalent
- No progressive disease (poor prognosis)
- In the case of proven non-nodal extra-abdominal disease at diagnosis, the extra-abdominal disease should be resectable
- Performance status and comorbidity that allows a maximal surgical effort to no residual disease
- Able to have at least 2 cycles of chemotherapy after surgery

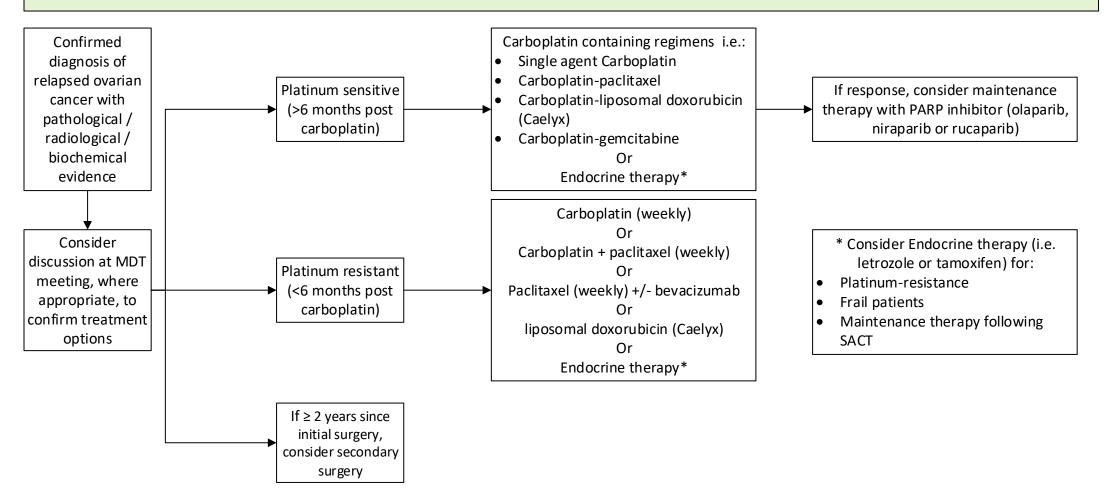
- Likely RD >2cm (which can be difficult to determine preoperatively and warrants attempt but to consider to stop surgery if at laparotomy becomes clear likely RD >2cm). Patients with symptomatic large masses may still benefit from surgery for symptom benefit.
- No / minimal response to neoadjuvant chemotherapy
- Patient characteristics (relative contraindication)
 - Impaired performance status & comorbidity that does not allow a maximal surgical effort to achieve a complete resection
 - Patients' nonacceptance of potential supportive measures, such as blood transfusions or stoma
 - Significant recent arterial or venous clot <3months e.g. CVA, PE
 - No increase in CA125
- Disease requiring ultra-radical surgery (NICE guidance 470) i.e. multiple resections of the bowel, liver resection, partial gastrectomy, cholecystectomy

INCLUSIONS

3: Decision-making for Secondary Surgery post-SACT

EXCLUSIONS

- Only one line of previous chemotherapy
- complete resection at first surgery
- Performance status zero
- Ascites < or = 500mls OR any clear cell histology ovarian cancer relapse resectable to zero
- Under 6 months since last platinum chemotherapy (platinum resistant)
- Symptomatic from relapse (not PS 0)
- Comorbidity precluding maximal surgical effort
- Radiological evidence of metastases not accessible to surgical removal (i.e. complete resection not deemed possible)



Multiple lines of treatment may be required. Choice will depend on a number of factors including previous response, duration of response, previous toxicities and patient preference.

The follow-up schedules for Ovarian Cancer patients in the North of Scotland are indicative-only. Clinical judgement will determine the requirement for follow-up including any further imaging required depending upon patient factors and treatments undertaken.

Ovarian Cancer (Stage 1-4)	Borderline Ovarian Cancer	
Years 1 & 2 Every 3 months at Gynae-oncology Clinic Year 3 Every 6 months at Gynae-oncology Clinic	Note – all cases of Borderline Ovarian Cancer to be discussed at Gynae Oncology MDT, with review of surgical staging and pathology and determination of follow-up schedule.	
Consider discharge at 36 months if no evidence of disease recurrence.		
Ongoing access to Gynaecology Clinical Nurse Specialist for	Stage 1	No follow-up required (regardless if one Ovary remains in-situ)
symptomatic problems experienced ongoing post-discharge in each North of Scotland board.	Stage 2-4 as below	
Follow-Up to consist of physical exam at Gynae-Oncology Clinic and imaging as clinically indicated.	Years 1-3	Every 6 months at Gynae Clinic
CA125 should not be performed routinely unless evidence of disease recurrence.	Discharge at 36 months if no evidence of disease recurrence	

Where there is a recurrence in Ovarian disease, patient follow-up returns to Year 1 after subsequent treatment.

Where appropriate, consider patient initiated follow-up or extended follow-up.

North of Scotland Clinical Management Guideline (CMG): FIGO staging Last Updated 27/04/2023

The International Federation of Gynaecology and Obestrics (FIGO) staging (January 2014)

	FIGO Staging					
1A	Tumo	nour limited to 1 ovary, capsule intact, no tumour on surface, negative washings.				
1B	Tumo	umour involves both ovaries otherwise like IA.				
	[Tumo	[Tumour limited to 1 or both ovaries]				
1C	1Ci	1Ci Surgical spill				
	1Cii	i Capsule rupture before surgery or tumour on ovarian surface				
	1Ciii	1Ciii Malignant cells in the ascites or peritoneal washings				
2A	Extens	ension and/or implant on uterus and/or Fallopian tubes				
2B	Extens	ension to other pelvic intraperitoneal tissues				
	[Posit	[Positive retroperitoneal lymph nodes and /or microscopic metastasis beyond the pelvis]				
24		Positive retroperitoneal lymph nodes only				
3A	3A1	3A1(i)	Metastasis ≤ 10 mm			
		3A1(ii)	Metastasis > 10 mm			
3A2	Micro	Microscopic, extrapelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes				
3B	Macro	Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen				
3C	Macro	Macroscopic, extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.				
4A	Pleura	Pleural effusion with positive cytology				
4B		Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)				

Neoadjuvant Carboplatin-paclitaxel (+/- bevacizumab if stage 4 disease) Carboplatin (if not suitable for/intolerant of taxanes)	Primary SACT Carboplatin-paclitaxel + bevacizumab (6 cycles) then bevacizumab (maintenance) Carboplatin-paclitaxel Carboplatin
Adjuvant Carboplatin-paclitaxel Carboplatin (if not suitable for/intolerant of taxanes) Carboplatin-liposomal doxorubicin	Additional treatment options for advanced disease Topotecan (weekly) Topotecan (days 1-5) Cisplatin Cisplatin-etoposide (Rotterdam) Liposomal doxorubicin (Caelyx)
Maintenance therapy after response to platinum based treatment Olaparib (platinum-sensitive relapsed disease and after complete or partial response to 1 st line platinum-based treatment) Rucaparib or Niraparib (platinum-sensitive relapsed disease)	Relapsed disease (Platinum sensitive i.e. > 6 months post carboplatin) Carboplatin Carboplatin-paclitaxel Carboplatin-liposomal doxorubicin Carboplatin-gemcitabine
Relapsed disease (Platinum resistant i.e. < 6 months post carboplatin) Carboplatin (weekly) Carboplatin – paclitaxel (weekly) Liposomal doxorubicin (Caelyx) Paclitaxel (weekly) Paclitaxel (weekly) + bevacizumab	For carboplatin allergy, consider a cisplatin-containing regimen. For paclitaxel allergy or intolerance, options include docetaxel containing regimen, e.g. carboplatin-docetaxel.

Endocrine therapy can be considered at all stages if ER positive

North of Scotland Clinical Management Guideline (CMG): Definitions Last Updated 27/04/2023

Definitions

BSO Bilateral Salpingo Oophorectomy

CT Computerised Tomography

IDS Interval Delayed Surgery

MDT Multidisciplinary Team Meeting

MRI Magnetic Resonance Imaging

NACT Neo-adjuvant Systemic Anti-Cancer Therapy

NCA North Cancer Alliance

RMI Risk of Malignancy Index

SACT Systemic Anti-Cancer Therapy

TAH Total Abdominal Hysterectomy

UFS Up Front Surgery

National Cancer Medicines Advisory Group (NCMAG)

COVID-19 NCMAG advice expired on 31/3/23.

The following advice is no longer valid and has been withdrawn:-

- NCMAG006 olaparib in combination with bevacizumab, as maintenance treatment of patients with stage IV BRCA mutant and wild type tubo-ovarian and primary peritoneal cancer following cessation of neoadjuvant. (Originally supported then withdrawn superseded by SMC2368)
- NCMAG011 olaprib, as treatment without preceding chemotherapy in patients with high grade epithelial tubo-ovarian cancer who have a deleterious somatic or germline BRCA mutation who have a recent relapse of platinum sensitive disease.
- NCMAG012 Niraparib, as treatment without preceding chemotherapy in patients with high grade epithelial tubo-ovarian cancer who have a deleterious somatic or germline BRCA mutation who have a recent relapse of platinum sensitive disease. (NOT SUPPORTED by NCMAG)
- NCMAG013 Rucaparib, as treatment without preceding chemotherapy in patients with high grade epithelial tubo-ovarian cancer who have a deleterious somatic or germline BRCA mutation who have a recent relapse of platinum sensitive disease.(NOT SUPPORTED by NCMAG)
- NCMAG014 Niraparib, as maintenance treatment for patients with advanced BRCA wild-type high grade epithelial tubo-ovarian cancer who are in response (complete or partial) following completion of first-line neo-adjuvant chemotherapy in the time prior to undergoing delayed primary surgery. Originally supported then withdrawn superseded by SMC2338)
- NCMAG028 trametinib, for treatment of patients with advanced low grade serous ovarian cancer (LGSOC), who have: inoperable disease or residual disease following primary debulking surgery (first line), or relapsed disease (NOT SUPPORTED by NCMAG)

Requests for treatment for new patients must be made on an individual patient basis via local Board approval processes.

For further information, including access to a full list of expired advice, please see the section relating to the National Cancer Medicines Advisory Group (NCMAG) on the home page of the NCA website. https://www.nhsscotlandnorth.scot/nca