SCAN Gynaecological Group

Clinical Management Protocols

Ovarian Cancer
(or primary peritoneal cancer of ovarian type or primary fallopian tube cancer)

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Introduction

The South East Scotland Cancer Network (SCAN) for Gynaecological Cancer was formally established over 10 years ago. Our first task was to develop a consensus document on management protocols. This year we have reviewed our protocols CT and MRI scanning are also becoming increasingly important in the management of patients with gynaecological malignancy and the update reflects this.

Patient pathways help patients, doctors, nurses and other members of the team to ensure that patients found to have gynaecological malignancy receive treatment in an appropriate and timely fashion. The clinical management protocols provide the evidence base on which to build these pathways. We are grateful for all the help that has been given by the members of SCAN in reviewing this document.

Melanie Mackean
Current chair of SCAN Gynaecological Group
August 2010

Membership – SCAN Gynae Group

See www.scan.scot.nhs.uk

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The Management of Ovarian Cancer or Primary Peritoneal Cancer of Ovarian Type

All patients with a diagnosis of ovarian cancer will be registered with the Edinburgh Gynaecological Oncology Group and have their management discussed at the multidisciplinary meeting at the Combined Gynaecological Oncology Clinic.

It is well recognised that women with ovarian cancer have a variety of psychosocial and informational needs. Patients will be provided with the opportunity to discuss their concerns and questions confidentially in a private area at all stages of the disease process. Written literature will be available to support verbal information. Referral to a Clinical Nurse Specialist will ensure continued support throughout the cancer journey.

Primary peritoneal cancer of ovarian type is diagnosed with widespread peritoneal disease, including possible surface involvement of the ovaries but no obvious ovarian primary. The immunohistochemistry needs to be in keeping with a gynaecological primary (e.g. CK7 +ve CK20 –ve). Throughout this document primary peritoneal cancer of ovarian type can be substituted for ovarian cancer as the management is the same. Primary cancer of the fallopian tube is also considered similar to ovarian cancer and is treated in the same fashion as ovarian cancer and again can be substituted for ovarian cancer in this management protocol.

Where ever possible patients will be seen in a rapid access clinic for suspected ovarian cancer with access to ultrasonography before or on the same day.

1. Diagnosis and Surgery

1.1a Diagnosis is usually made at staging laparotomy with adequate exposure through a vertical incision, and must include the following:

1. Peritoneal washings or collection of ascitic fluid for cytology.
2. Palpation of pelvic and abdominal contents including liver, diaphragm, paracolic gutters, intestine and para-aortic and pelvic nodes.
3. Biopsy of peritoneal surfaces, including atypical and ‘normal’ peritoneum.
4. Omentectomy.
5. Biopsy of palpable lymph nodes.

1.1b Other methods of diagnosis can include pathology from pleural biopsy, CT guided biopsy, cell block from ascitic drainage or laparoscopic biopsy. Diagnosis by CTScan and CA125 alone can be incorrect in up to 25% of cases and is to be discouraged. It particularly will incorrectly over diagnose borderline tumours as cancer.

1.2 Exirpative surgery is of prime importance in epithelial ovarian cancers. Removal of both adnexa, fallopian tubes, a total abdominal hysterectomy and omentectomy is indicated in Stage I epithelial ovarian cancer, and wherever possible, in Stages II to IV. A subtotal hysterectomy may be appropriate in advanced disease. Cytoreductive surgery (‘debulking’) improves chemotherapy response rates as well as increasing survival when tumour masses can be debulked to 1cm or less. Extended surgery (which may include bowel surgery) may be necessary to debulk the tumour adequately.
The role of lymphadenectomy is not routine but in early stage ovarian cancer should be discussed on a case by case basis preoperatively. In cases with no lymph node sampling found to be stage I A gd 1 or 2 ovarian cancers post operatively consideration should be given to adjuvant chemotherapy versus repeat operation for lymph node dissection in selected cases. Grade 1 mucinous ovarian cancers however are unlikely to respond to chemotherapy.

1.3 Neoadjuvant chemotherapy with interval debulking surgery after 3 cycles of chemotherapy may be of benefit in selected patients in whom primary cytoreductive surgery is unlikely to yield less than 2cm residual disease. A protocol has been developed for this approach and is attached as an appendix 2.

1.4 Primary chemotherapy may be considered in patients unfit for surgery due to Very advanced disease or comorbidities, e.g. pulmonary embolus. Again, a neoadjuvant approach with interval debulking may be considered in selected patients who improve with treatment.

1.5 Conservative surgery with conservation of uterus and contralateral ovary may be appropriate for germ-cell tumours, or those with Stage Ia borderline or well-differentiated carcinomas who wish to maintain fertility after surgery. Full staging laparotomy should be carried out, with consideration of contralateral ovarian biopsy.
2. **Staging (Figo System)**

**Stage I**  
**Tumour limited to the ovaries**
- Ia  
  Tumour limited to one ovary; capsule intact, no tumour on the ovarian surface, no ascites containing malignant cells.
- Ib  
  Tumour limited to both ovaries; capsule intact, no tumour on the ovarian surface, no ascites containing malignant cells.
- Ic  
  Tumour limited to one or both ovaries with any of the following: capsular rupture, tumour on the ovarian surface, malignant cells in ascites or peritoneal washings.

**Stage II**  
**Extension of tumour to true pelvis**
- IIa  
  Tumour involving one or both ovaries with extension and/or metastasis to uterus and/or tubes.
- IIb  
  Tumour involving one or both ovaries with extension and/or metastasis to other pelvic tissues.
- IIc  
  IIa or IIb with any of the following: capsular rupture, tumour on the ovarian surface, malignant cells in ascites or peritoneal washings.

**Stage III**  
**Peritoneal (including superficial liver capsule metastases), omental or retroperitoneal/inguinal node involvement**
- IIIa  
  Tumour grossly limited to true pelvis with negative nodes but with histologically confirmed microscopic involvement of omentum or peritoneal surfaces.
- IIIb  
  Histologically confirmed peritoneal or omental implants 2cm or less in greatest dimension with negative nodes.
- IIIc  
  Implants > 2 cm in greatest dimension and/or positive retroperitoneal or inguinal nodes.

**Stage IV**  
**Distant metastases or parenchymal liver metastases. Pleural effusion only if cytology positive.**
3. **Investigations**

3.1 **Pre-operative investigations**

Pre operative investigations should include chest imaging (CXR or CT Scan), Abdominal and pelvic USS and/or CT scan, CA125 and CEA.

AFP, HCG and LDH should be tested in young women suspected of having a germ cell tumour.

Consideration should be given to oestradiol and inhibin A+B testing in patients suspected of having a granulose cell tumour.

3.2 **Routine investigations before and during chemotherapy**

FBC, U&E, Creatinine, LFTs before each cycle.
Weekly FBC after first cycle only.
Tumour markers before each cycle (CA125 for epithelial tumours, LDH, AFP and bHCG in germ cell tumours, or oestradiol in granulosa cell tumours).
Baseline CT scan abdomen and pelvis in patients with residual disease, repeated after cycle 6.
ECG before paclitaxel.
Clinic review after cycles 3 and 6 (trial patients and those with residual disease) or 6 (those with no residual disease).
Oestradiol, inhibin A+B levels should be checked at the end of any chemotherapy for a granulosa cell tumour.

3.3 **Monitoring during follow-up after completion of chemotherapy**

CA125 monitoring is highly accurate in predicting relapse in patients with previous CA125 producing ovarian cancer. However, relapse is not curable and based on the OVO5 trial showing no survival benefit for early treatment of relapse on CA125 monitoring alone patients will be offered CA125 monitoring or not dependent upon their wishes. A rising CA125 may make them eligible for clinical trials and this will be discussed on an individual level. Patients will be offered palliative chemotherapy on the basis of symptoms not on the basis of scans or CA125 results.
If taken, tumour markers will be taken prior to clinic visit and the result available at clinic. Clinical history and appropriate examination to be undertaken when indicated.

No routine scans in marker-secreting tumours except for germ cell tumours (x-rays and scans as per testicular teratoma) or when required by trials. CT scans may be required for follow-up of marker negative epithelial cancer if symptoms suggestive of relapse.

3.4 **Investigations at suspected relapse**

CA125 (or other tumour marker if indicated)
Symptom monitoring
CT scan abdomen and pelvis (if symptoms of concern)
4. **Histopathology – please see Appendix 1**

5. **Adjuvant Chemotherapy of Epithelial Ovarian Cancer**

   All patients will have an opportunity to discuss their condition and will be given a full explanation of the aims and possible side effects of treatment, before giving their written informed consent to chemotherapy. All patients will be considered and offered clinical trials where available and appropriate.

5.1 **Stage Ia or Ib, well differentiated, no risk factors for relapse**

   Completely debulked Stages Ia and Ib well differentiated tumours of all histological types except clear cell, have a 5 year survival of 80 - 90% without adjuvant treatment. Staging must be on the basis of a full staging laparotomy, including paraortic lymph node dissection, as this will ‘upstage’ 10 to 20% of Stage I tumours. Patients without paraortic lymph node dissection will be offered either further surgery, adjuvant chemotherapy or watch and wait policy after discussion of potential benefits and risks.

   **No adjuvant chemotherapy.**

5.2 **Stage I with risk factors for relapse**

   Adverse features increasing the risk of relapse to 30 - 40% in stage Ia and Ib patients include clear cell histology, moderate or poor differentiation, dense adherence and residual disease. These patients should be considered for adjuvant carboplatin at AUC 7 or be entered into the relevant clinical trial. Less fit patients should receive AUC 6. See section 5 for carboplatin dose calculations.

   Surface tumour, pre-operative capsule rupture, and malignant ascites confer additional risk and classify the stage as Ic. The significance of intraoperative capsule rupture is uncertain, but recent studies suggest that it carries a worse prognosis.

   **Carboplatin AUC7 over 30 mins, every 28 days for 6 cycles.**

5.3 **Stage II to IV**

   Patients should receive platinum-based chemotherapy, within a clinical trial wherever possible. A combination of a platinum drug and a taxane is standard treatment where age and general health allow; since carboplatin is not inferior to cisplatin in combination with paclitaxel, a combination of carboplatin and paclitaxel is now standard therapy for advanced disease in fit patients.

   **Paclitaxel 175mg/m² over 3 hours (give paclitaxel first)**  
   Carboplatin (6 x GFR)mg over 30 minutes  
   Repeated every 21 days for 6 cycles

   On the basis of results from ICON 3 patients may be offered single agent carboplatin, which may be as effective as carboplatin/paclitaxel, but uncertainty still exists. If a patient is not suitable for paclitaxel because of fitness, medical history or co-morbid conditions, she should receive carboplatin, at AUC7 if possible.
Patients deemed to be inoperable may be considered for Neoadjuvant chemotherapy with interval debulking after 3 cycles where appropriate. (see Appendix 2)

5.4 Borderline tumours (epithelial tumours of low malignant potential)

Most borderline tumours are Stage I at presentation and have an excellent prognosis. No adjuvant therapy is indicated for this group. The risk of relapse is around 5% for fully staged patients and around 15% for conservatively managed surgical patients. Relapse is best treated by further surgery with curative intent. The use of cytotoxic chemotherapy in more advanced stages is controversial, and no controlled trials have been done. While cases should be reviewed and discussed on an individual basis, adjuvant chemotherapy is not usually recommended.

No adjuvant chemotherapy.

6. Carboplatin Dose Calculations

Patients’ age, weight, and serum creatinine are required for the Chatelut calculation. Serum creatinine and weight should be rechecked and the dose recalculated before each cycle.

Carboplatin dose in mg =
(Desired AUC) x (calculated renal clearance) using the Chatelut calculation for renal clearance.

**AUC 7 every 28 days** for fitter patients (performance status 0 - 2) on first-line chemotherapy

**AUC 6 every 28 days** for less fit patients (performance status > 2) or those who have had prior chemotherapy

**AUC 6 every 21 days** when combined with paclitaxel

Chatelut formula:
Clearance (ml/min) = (0.134 x weight) + 
[(218 x weight) x (1 - 0.00457 x age) x (1 - 0.314 x sex)]
serum creatinine

weight in KG
age in years
sex: female = 1
creatinine in µM

Calculators pre-programmed with the Chatelut formula are available in Ward One.
Measuring GFR by EDTA:

Calculations by Chatelut may be inaccurate in the following situations:
- Estimated GFR is less than 60ml/min, and certainly less than 50ml/min
- Patients with significant effusions, ascites or oedema (isotope GFR may also be inaccurate in this situation)
- Patients with poor nutrition with a falsely low creatinine (often have a very low albumin as well)
- Extremes of age and weight (falsely high in obese young women and falsely low in thin elderly women)

In these situations GFR should be measured by EDTA but note the AUC is lowered by one

If estimated GFR is less than 50ml/min than an EDTA must be used. If GFR has been measured by EDTA clearance, the Calvert formula is then used:

\[
\text{Carboplatin dose in mg} = (\text{desired AUC}) \times (\text{measured GFR} + 25)
\]

If BMI \{(\text{height (in metres)}^2)/\text{weight (in kg)}\} is greater than 35 the mean of the ideal and actual body weight should be used for the Chatelut formula.

\[
\text{Ideal body weight} = 45.5 + (0.906 \times (\text{ht in cm} - 152.4))
\]

7. Management of Relapsed Epithelial Ovarian Cancer

All patients should be offered appropriate trials as available.

7.1 Patients who previously responded to first-line chemotherapy and who relapse 6 months or more from primary treatment have a high probability of a further response to platinum-based therapy and should receive further carboplatin or enter Phase II new drug studies, if eligible. Evidence from ICON 4 study suggests that combination therapy can be considered in fit patients.

7.2 Patients with platinum resistant or refractory disease can be considered for dose dense therapy. Patients can also receive paclitaxel if they have not previously received this, or enter new drug trials. There is no benefit in re-treating with first-line drugs in this setting. Caelyx and topotecan are approved for use in this setting.

7.3 Further surgery may be of benefit in very selected patients where the disease recurs 6 months or more from primary treatment in a localised fashion.

7.4 Patients with marker relapse and low volume recurrence should be considered for endocrine therapy if immunohistochemistry is suggestive of sensitivity to such agents.

7.5 Localised recurrence, particularly isolated pelvic recurrence that is symptomatic, may benefit from radiotherapy.
8. Management of Non Epithelial Ovarian Cancer

8.1 Germ Cell Tumours

Germ cell tumours occur in young women and only 5% are malignant. Reproductive function can usually be preserved. Full staging laparotomy followed by unilateral ovariectomy, omentectomy, biopsy of contralateral ovary and peritoneal washings is the surgical treatment of choice.

All patients with Stages II to IV disease and some of those with Stage I malignant germ cell tumours will require adjuvant chemotherapy, usually with BEP. **All cases should be referred as early as possible to the Combined Gynaecological Oncology Clinic for discussion and review so that treatment can be planned on an individual basis.**

8.2 Stromal of sex-cord tumours

Granulosa cell tumours are the commonest in this group and occur in post-menopausal women. The natural history of the disease is long, and recurrences may occur late. Adjuvant chemotherapy is considered only where there are high-risk features or residual disease. Estradiol, inhibin A and B and FSH may be useful markers in follow up.

9. Follow Up

9.1 Epithelial ovarian cancer

3-monthly for 2 years, then 6-monthly to 5 years. Patients with no relapse at 5 years are discharged or as per trial protocol.

9.2 Germ cell tumours

Following chemotherapy and a normal post chemotherapy CTScan the follow up should be:
- Year 1 – 3 monthly
- Year 2 + 3 - 4 monthly
- Year 4 + 5 – 6 monthly
- Discharge at 5 years
- AFP, LDH, BHCG and CA125 at each visit

10. Screening

Family history of cancer should be collected from all patients, with particular reference to ovarian, breast and bowel cancers. The following definitions can be used to identify relatives of patients with ovarian cancer who might be at increased risk, and who should be referred to the Family Ovarian Cancer Clinic (see Table of Referral & Screening Guidelines for Ovarian Cancer)
10. Ovarian Risk Stratification and Counselling

<table>
<thead>
<tr>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk Stratification</strong></td>
<td><strong>Risk Stratification</strong></td>
<td><strong>Risk Stratification</strong></td>
</tr>
<tr>
<td>- Anyone not fulfilling medium or high risk criteria</td>
<td>- Two or more 1st or 1st and 2nd degree relatives with OvCa at any age;</td>
<td>- Women in a family where BRCA1, BRCA2, hMLH1, hMSH2 or other predisposing gene has been identified</td>
</tr>
<tr>
<td>- Individuals with a single 1st degree relative or 2nd degree relative by their father who have presented at any age, are not appropriate for screening</td>
<td>- Two 1st or 1st and 2nd degree relatives with OvCa at any age or BrCa diagnosis under 50yrs (i.e. one of each type of cancer);</td>
<td>- Untested 1st degree relatives of gene carriers</td>
</tr>
<tr>
<td></td>
<td>- One OvCa and two breast cancers diagnosed less than 60yrs on same side of family in 1st degree relatives or 2nd degree relatives via a male</td>
<td>- A woman with at least one 1st relative with breast and ovarian cancer</td>
</tr>
<tr>
<td></td>
<td>- Two 1st or 2nd degree relatives with CRC and an endometrial Ca and one OvCa</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- One affected relative with OvCa and HNPCC family history</td>
<td></td>
</tr>
<tr>
<td><strong>Counselling</strong></td>
<td><strong>Counselling</strong></td>
<td><strong>Counselling</strong></td>
</tr>
<tr>
<td>Individuals deemed at low risk will be informed either by:</td>
<td>Individuals deemed to be at medium risk will be counselled by the genetic counsellor, who will discuss with them information as recorded in Appendix 1.</td>
<td>Individuals deemed to be at high risk will be counselled by the clinical genetic physician.</td>
</tr>
<tr>
<td>- Telephone consultation with the genetic nurse associate, followed by letter with a copy to GP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Face to face consultation with the genetic nurse associate and then by letter to the patient and the GP</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Ovarian Management

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Medium Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reassurance</td>
<td>• Discussion of prophylactic oophorectomy</td>
<td>• Discussion of prophylactic oophorectomy</td>
</tr>
<tr>
<td>• Healthy lifestyle advice</td>
<td>In accordance with SIGN guidelines, ovarian cancer screening is currently</td>
<td>Depending on family history it may be appropriate to offer screening of</td>
</tr>
<tr>
<td>• Advise to report any changes</td>
<td>not available. This decision will be reviewed after UK Familial Ovarian</td>
<td>other organs. This decision will be reviewed after UK Familial Ovarian</td>
</tr>
<tr>
<td>in family history promptly</td>
<td>Cancer Screening Study (phase 2) results are reported in 2012.</td>
<td>Cancer Screening Study (phase 2) results are reported in 2012.</td>
</tr>
<tr>
<td>• Return to GP Care</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Surgical Management: High Risk Individuals

- In unaffected women, prophylactic surgery may be considered particularly in the high-risk cases.
- Affected women are treated along conventional lines as for best management of sporadic ovarian cancer.
  (It is anticipated that Cancer Managed Clinical Networks will include individuals with specific expertise in the surgical management of cancer in high-risk individuals.)

### Gene Testing

Following counselling by a clinical genetics physician, gene testing should be available to all high-risk families and predictive testing offered to at-risk individuals within these.
Appendix 1 - Histopathology

Introduction

All tissue specimens removed surgically are submitted for histopathological examination. Specimens are handled according to Standard Operating Procedures (SOPs) of the Department of Pathology, which cover fixation, dissection, block taking and reporting, and confirm to national guidelines and minimum data sets (where available).

All cases are reviewed by consultant pathologists with a special interest in gynaecological pathology, and presented at the Combined Gynaecological Oncology Multidisciplinary Meeting prior to decision making about post-surgical management.

Ovarian Cancer

Histopathology reports on ovarian cancer cases include the following:

- Summary of clinical history
- Macroscopic description of all specimens including dimensions of ovarian tumours, status of capsule, cyst contents
- Microscopic description (synoptic report available) including:
  - Histological tumour type (WHO classification)
  - Grade
  - Status of capsule
  - FIGO stage
Appendix 2 - Neoadjuvant chemotherapy protocol

Background
Optimal debulking at surgery to less than 1cm has been shown in many studies to be an independent predictor for long term survival from advanced ovarian cancer and remains the cornerstone of therapy. It has been controversial whether chemotherapy before surgery (neoadjuvant) improves the rates of debulking possible. The results of the EORTC/NCIC trial 55971 of primary surgery versus neoadjuvant chemotherapy (NACT) have been presented at international meetings although not yet in a peer reviewed journal. These show an improved rate of complete debulking from 21% with primary surgery to 53% with NACT followed by interval debulking. Sadly this has not translated into improved survival. However they did show an improvement in surgical mortality from 2.7% to 0.6%. The surgery at interval debulking was also associated with fewer complications such as post operative fever, bowel fistula, grade 3 or 4 haemorrhage and venous emboli. There was also a reduction in the number of women too unwell to start chemotherapy (7%) or complete 3 cycles of chemotherapy (22% to 12%). We therefore are proposing for selected women (estimated 25 patients per year for SCAN region) to undergo NACT as opposed to primary surgery for their advanced ovarian cancer.

Positive outcomes possible from NACT
- Improved optimal debulking rates
- Reduction in ‘open and close’ unnecessary operations
- Reduction in surgical mortality (2.7% to 0.6%)
- Reduction in surgical morbidity (e.g. post op fever, bowel fistula, Gd 3 or 4 haemorrhage, gd 3 or 4 venous emboli)
- Reduction in patient stay for surgery as patients are fitter
- 10% reduction in patients completing 3 or less cycles of chemotherapy (22 to 12%)
- Less pressure on theatre lists to achieve 31 day target for start of therapy
- More time to liaise with bowel surgeons for optimal debulking
- Placement of intraperitoneal ports for chemotherapy (PETROC) study possible

Negative outcomes possible from NACT
- Increased bed utilization for laparoscopy
- Limited practitioners to do laparoscopy therefore may be increased travel for Fife and Borders General patients. Dumfries already come to Edinburgh.
- Increased complexity of pathway with more room for error
- Increased bed utilization for primary chemotherapy in unwell patients. Audit showed equivalent to 0.5 in patient bed in oncology per month per patient on NACT.
- Complications of laparoscopy including extra anaesthetic
- Wrong diagnosis (3% risk)
- 10% patients progress on initial 3 cycles of chemotherapy and do not proceed to interval debulking surgery
- Increased mortality from primary chemotherapy (not proven but a concern)
**Patient population for consideration**
- All patients with presumed stage IIIc and IV ovarian cancer should be discussed at the MDM and considered for NACT versus primary surgery
- Patients must be fit enough for tissue confirmation

**Inclusion Criteria**
- Unlikely to achieve optimal debulking (<1cm) at primary operation and/or
- Current temporary contraindication to surgery e.g. pulmonary emboli
- Tissue confirmation of ovarian cancer
- Stage IIIC or IV ovarian cancer

**Exclusion Criteria**
- Unsuitable for chemotherapy at full doses
- Unsuitable for surgery at any stage
- Malnutrition

**Unlikely to achieve optimal debulking**
- SMA/porta hepatis involvement
- Intra hepatic or extra abdominal mets
- Extensive serosal involvement e.g. diaphragmatic (usually assessed by laparoscopy)
- Extensive bowel involvement requiring multiple resections (usually assessed at laparoscopy)
- When unresectability assessed at laparoscopy this should be videotaped and played at MDM for confirmation

Some patients will be adequately assessed by CT scan alone but some will require laparoscopy to assess this criterion.

**Histology - Laparoscopy vs Biopsy**
- All patients require tissue confirmation of histology (not just ascites cytology)
- Either by CT or ultrasound guided biopsy or at laparoscopy
- Laparoscopy will also assess resectability (above) and has a higher +ve histological confirmation rate but at the expense of anaesthetic risks and risks of laparoscopy (e.g. bowel perforation) and needs to be considered on an individual basis.

The false +ve rate (i.e. patient does not have ovarian cancer) is 25% by CA125 and CT scan alone. False positives can include borderline tumours and bowel cancer. This improves to 3% if tissue histology is obtained.

**Tracking of patients**
- All patients deemed for NACT will be tracked from date of decision at MDM to date of completion of therapy
- Circulation of the list of patients will be weekly to chemotherapy/surgery
- Possible dates for surgery to be identified at decision for NACT MDM
- If patient deemed not suitable for interval surgery – surgical tracking to be alerted at first available opportunity
- Proposed pathway for tracking – see appendix

**Chemotherapy**
- Patients should receive full dose carboplatin/taxol wherever possible
- Initial chemotherapy to begin within 4 weeks of biopsy or laparoscopy to prevent seeding
- 3 cycles to be given 3 weekly
• CTscan after 3 cycles to be presented at MDM for discussion
• CA125 response to be tracked
• Around 10% of patients will progress through initial chemotherapy and be unsuitable for interval debulking and require a change of plan

Interval debulking surgery (IDB)
• Date of surgery to be set at start of NACT through liaison with theatre manager
• Bowel surgeon to be available in advance for difficult cases
• IDB to be as close as possible 3 weeks after 3rd cycle of chemotherapy
• Target 3-4 weeks after 3rd cycle of chemotherapy unless FBC not suitable
• All patients to proceed to IDB unless clear evidence of progression (not stable disease) on CTScan or CA125 prior to surgery

Post IDB chemotherapy
• 3 further cycles of carboplatin/taxol to be given in all cases except progression
• To start within 4 weeks of surgery whenever possible
• CTScan and CA125 documentation of response at end of 6 cycles

Outcomes for audit
• Completion rates for surgery and chemotherapy
• Debulking rates
• Response rates on CTScan and CA125 @ 3 and 6 cycles
• Progression Free survival
• Overall survival
• Complications of treatment
  o Incorrect diagnosis
  o Progression on chemotherapy
  o Mortality within 30 days of either surgery or chemotherapy
  o % requiring bowel surgery
  o Admissions other than planned for treatment
  o Failed biopsy attempts
  o Seeding at laparoscopy site
  o Complications from laparoscopy e.g. perforation
  o Bed utilization for surgery and chemotherapy

Facilities utilisation

The use of neoadjuvant chemotherapy followed by interval debulking for ovarian cancer involves the use of laparoscopy in probably the majority of patients. Some patients will be assessed as unresectable on CTScan alone and a biopsy will be obtained by other means (CTGuided) but many will have an extra procedure in order to be assessed for NACT. This carries risks to the patient of an extra anaesthetic and known risks of laparoscopy (bowel perforation, etc). For services this also means extra theatre time, bed usage, and staff time.

Offset against this are the advantages for patients outlined above but savings for services in reduction of operative morbidity such as post operative fever, bowel fistula, haemorrhage and venous emboli for interval debulking compared to primary surgery. Also 10% of patients who progress on chemotherapy will be spared an unnecessary operation (debulking not possible and chemotherapy not effective) and palliative care/alternative treatments will be instigated at an earlier stage for such patients.
**Tracking of Neoadjuvant chemotherapy and interval debulking pathway**

The following will be tracked on an excel spread sheet and available from Ashley Saladen (gynaecology cancer tracker) once a week by e-mail.

- Name
- CHI number
- Dates (P = provisional) for the following:
  - Initial discussion at MDM (may occur at same time as ‘decision’ MDM)
  - Biopsy or laparoscopy
  - MDM ‘decision’ definitely for NACT
  - 1st chemotherapy
  - 2nd chemotherapy
  - 3rd chemotherapy
  - Interval CT Scan
  - Interval MDM discussion
  - Interval debulking surgery preadmissions
  - Interval debulking surgery theatre date
  - MDM discussion for results of surgery
  - 4th chemotherapy
  - 5th chemotherapy
  - 6th chemotherapy

Circulation list to include the following:

- Medical oncology team (Drs Gourley, Mackean, Nussey and registrar)
- Ward 1 scheduler for chemotherapy
- Gynaecology oncology surgical team (Drs Farquaharson, BusbyEarle, Martin, Walker, Pinion, McNab, Fegan)
- Preadmissions at RIE (Marion Robertson)
- Ashley Saladen for MDM appointments
- Trials team (ECMC for tissue collection)
Possible pathway for neoadjuvant chemotherapy (Sept 2009)

GP Assessment
Examination / Ultra sound
CA125, CEA, FBc, U+Es, LFTs

RMI
> 200
Refer to Gynaecology Oncology Service via Rapid Access Clinic or MDT

RMI
< 200
Refer to General Gynaecologist.

Full History + Exam
Review Blood and Imaging Results
Suspicion of Inoperable stage IIC or IV disease or primary tumour still unclear

Diagnostic Laparoscopy and/or Biopsy (Video)
Prediction of Inoperable Disease. MDT / Video Bx
Three cycles of NACT chemotherapy
Prediction of Operable disease (CT and CA125)
Laparotomy
TAH BSO Omentectomy Washings

Prediction of Operable disease

Laparotomy
TAH BSO Omentectomy Washings
Six cycles of chemotherapy

Medically Unfit Refer to Med Onc for primary chemotherapy +/- Pall

Three cycles of chemotherapy

Five years of Follow up Appointments

Scan Gynae Group – Clinical Management Protocol, Last updated August 2010
Appendix 3 – Other sources of information

SIGN guideline &5: Epithelial ovarian cancer - www.sign.ac.uk/guidelines/fulltext/75/index.html

NICE website - www.nice.org.uk

Macmillan Cancer Support website - www.macmillan.org.uk


Ovacome website - www.Ovacome.org.uk

SCAN website – www.scan.scot.nhs.uk

Target Ovarian Cancer website – www.targetovarian.org.uk