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<th>Title:</th>
<th>Systemic Anti-Cancer therapy (SACT) guidelines for cervical, vaginal and vulvar cancer</th>
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<tr>
<td>Author(s):</td>
<td>Dr Jackie Clarke and Dr Anne Drake, Consultant Clinical Oncologists on behalf of the Gynae Clinical Oncology team</td>
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<td>Ownership:</td>
<td>NICaN</td>
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<td>Approval by:</td>
<td>NICaN Drugs &amp; Therapeutics Committee</td>
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<td>6.0 Supersedes 5.0</td>
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<td>Links to other policies</td>
<td>NICaN Cervical, Vaginal &amp; Vulvar SACT protocols</td>
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<td>Sept 09</td>
<td>V1.0</td>
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<td>Gynae clinical guidelines (radiotherapy and chemotherapy)</td>
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<td>2010</td>
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<td>J Clarke,</td>
<td>NICAN Gynae CMGs</td>
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<td>Sept 2011</td>
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<td>Updated gynae clinical guidelines (radiotherapy and chemotherapy)</td>
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<td>SACT gynae guidelines developed from radiotherapy gynae controlled document and NICAN gynae CMG</td>
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<td>Feb 2016</td>
<td>V6.0</td>
<td>J Clarke, A Drake</td>
<td>Updated SACT cervix vagina and vulva guidelines</td>
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Authorisation of Systemic Anti-Cancer Therapy (SACT) Guidelines for Cervical and Vulvar Cancer

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<tr>
<td>Written by Systemic Guidelines Author</td>
<td>Dr Jackie Clarke, Dr Anne Drake Consultant Clinical Oncologists</td>
<td>9/9/16</td>
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<tr>
<td>Approved by NICaN Drugs &amp; Therapeutics committee</td>
<td>Dr Martin Eatock, Consultant Medical Oncologist, Chair of the NICaN Drugs &amp; Therapeutics committee</td>
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These SACT guidelines are being submitted by the authors on behalf of the Gynae Clinical Oncology team.
1.0 INTRODUCTION / PURPOSE OF POLICY

1.1 Background
Systemic anti-cancer therapy (SACT) is a key treatment in managing cervical cancer. In this context chemotherapy is often delivered concurrently with radiotherapy and brachytherapy. Please refer to radiotherapy department clinical guidelines for gynae cancer for detailed information regarding radiotherapy and high dose rate brachytherapy. These guidelines describe the agreed management for patients’ cervical cancer.

1.2 Purpose
To ensure consistent use of SACT for patients with cervical cancer.

2.0 SCOPE OF THE POLICY
This document is aimed at all clinical staff involved in the management of patients receiving SACT for cervical cancer.

3.0 ROLES/RESPONSIBILITIES
It is the responsibility of all clinical staff involved in the management of patients receiving SACT for cervical cancer to familiarises themselves with these guidelines.

4.0 KEY POLICY PRINCIPLES

4.1 Carcinoma Cervix

4.1.1 Since the publication of five phase 3 clinical trials published in 1999 and two subsequent meta-analyses, concurrent chemoradiotherapy has been the standard of care for locally advanced cervical cancer as these studies have confirmed the survival benefit and improved pelvic control rates with the addition of cisplatin based chemotherapy. (3-8). Therefore, the combination of chemotherapy with radiotherapy should be regarded as the standard of care for the management of locally advanced disease.
Early stage disease (1B1 node negative, IIA) may be treated using radical surgery or radical chemo/ radiotherapy although the combination of both modalities should be avoided if possible as this leads to increased morbidity. Post-operative chemo/ radiotherapy is indicated for all node positive patients and node negative patients as per Sedlis criteria ie those patients who have poor prognostic factors which are indicated at surgery

- All Pelvic Node positive patients
- Two or more of the following risk factors
  - positive or close surgical margins
  - Extensive stromal invasion
  - tumour size > 4cm
  - extensive lymphovascular space involvement (4)

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<tr>
<th>LVSI</th>
<th>Stromal Invasion</th>
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<tbody>
<tr>
<td>+</td>
<td>Deep 1/3</td>
<td>any</td>
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<tr>
<td>+</td>
<td>Middle 1/3</td>
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<td>+</td>
<td>Superficial 1/3</td>
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<tr>
<td>-</td>
<td>Middle or deep 1/3</td>
<td>&gt;= 4 cm</td>
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**Patient selection**

All patients with locally advanced disease confined to the pelvis (stage 1b2 to 4b) should be considered for concurrent chemoradiotherapy

- Biopsy proven squamous cell or adenocarcinoma (central pathology review at mdt to exclude neuroendocrine component)
- EUA to document local extent of disease
- MR Pelvis and paraaortic nodes
- CT PET or conventional CT chest and abdomen
- Laparoscopic Para aortic node dissection negative
- Category 1 patient definitive treatment within 62/31 day DOH targets thus urgent clinic slot and radiotherapy planning appointment

### 4.1.1 Treatment of Pelvic Confined Disease

#### 4.1.1.1 Radical Concurrent Chemoradiotherapy and Brachytherapy (Stage 1B2-4A)

**Background**

Patients who have locally advanced disease should be treated with concurrent chemoradiotherapy as 5 clinical trials and 2 meta analyses have confirmed improved pelvic control rates and lower risk of systemic relapse with addition of cisplatin based chemotherapy. The estimated benefit of chemotherapy is 13 % improvement in overall survival, thus all patients with adequate renal function who are fit to receive
Chemotherapy should be offered combined modality treatment. Carboplatin AUC 1.5-2.0 for 4 cycles can be considered in those with Cockroft GFR <40 or patients who would not tolerate hydration schedule due to cardiorespiratory disease.

Stage 1 B (2) to Stage 4A (para aortic node negative)
Pelvic radiotherapy dose /fractionation as per radiotherapy protocol (appendix 1)
Concurrent weekly cisplatin 40 mg/m²/week for 6 cycles (Ref 1)
HDR Brachytherapy 21 Gy to point A in 3 treatments starting week 5 of treatment.
MRI week 5 to assess response of primary cervical tumour
Refer to Radiotherapy protocol for details of radiotherapy planning and brachytherapy dose constraints.
Toxicity management – GI/Haem toxicity/ use of g-csf, enoxaparin

Follow up
- All patients should commence topical oestrogen to promote vaginal healing cycle 5/6 chemotherapy post brachytherapy. Premenopausal patients should be given systemic HRT unless contraindication at final chemotherapy assessment.
- All patients should be seen by brachytherapy nursing team pre and post brachytherapy and instructed in use of vaginal dilators to maintain vaginal patency post treatment (refer to cervix radiotherapy protocol ref 1)
- Review 2-3 weeks post chemoradiotherapy then 4 monthly for 2 years, then, 6 monthly years 3-5 and annually years 5-10 (for collection of follow-up data). If bulky disease still present on week 5 MRI, discuss at MDT, book EUA and MRI and assess for salvage surgery.
- All patients should have MRI 4 months’ post completion of treatment to confirm complete response. Serial MR may be necessary if incomplete response with prompt return to MDT for EUA as radical surgery may be curative in those with persistent or recurrent pelvic confined disease.
- Patients should be advised of risks of rectovaginal or vesicovaginal fistula if biopsy of anterior rectal wall or bladder is performed. Such procedures should be carried out by GI or GU team with experience of managing irradiated tissue.

4.1.1 2 Post-operative Adjuvant chemoradiotherapy and vaginal vault brachytherapy

Background
Long term results of GOG 92 (ref) pelvic radiotherapy or control, confirmed improved PFS favouring radiotherapy for those with negative pelvic nodes at radical surgery but 2 of bulky > 4cm tumours, lvsi, > 1/3 stromal invasion. Intergroup 0107 confirmed benefit of 4 cycles concurrent cisplatin /fluorouracil with pelvic radiotherapy for those with positive pelvic nodes, parametrial extension and/or positive margins at radical surgery.
Staging

Post-operative CT Chest, abdomen and pelvis

Treatment Regimen

1. High risk pelvic and paraaortic node negative (2 or more of Grade 3 histology, tumour 4 cm or more, lymphovascular invasion, close or involved surgical margins) and 1 pelvic node involved or older unfit patients

**concurrent weekly cisplatin 40mg/m²/week for 6 cycles**

Pelvic Radiotherapy 45 Gy in 25 fractions over 5 weeks and vaginal vault brachytherapy 8 Gy to 0.5 cm from applicator surface in 2 treatments

**OR**

2. Pelvic Node Positive (2 or more pelvic nodes involved in younger fitter patients)

**cisplatin 70mg/m² day 1, fluorouracil 4000mg/m² 0ver 96 hours via infusor bottle**

for 4 cycles, starting day 1, 22, 43, 64 (ref 2). Weekly cisplatin may be substituted during radiotherapy if there have been concerns re 5-FU toxicity in previous cycles. Pelvic radiotherapy 50 Gy in 25 fractions over 5 weeks VMAT Plan commenced day 8 post cycle 2 to allow chemotherapy to commence while radiotherapy is being planned followed by vaginal vault brachytherapy 8 Gy to 0.5 cm from applicator surface in 2 treatments

3. Extensive para aortic or intraabdominal disease at radical surgery
   - Chemotherapy cisplatin 75mg/m² day1 / paclitaxel 175mg/m² day 1 (ref 3,4)
   - 3-week schedule
   - assess response after cycle 3 continue to 6 cycles if partial response with Pegfilgastrim cover day 4,
   - Monitor for PV bleeding, renal impairment, neurotoxicity
   - Radiotherapy to pelvis +/- PA nodes if residual post chemotherapy disease can be encompassed in radiation field

Followup

- All patients should commence topical oestrogen to promote vaginal healing cycle 5/6 chemotherapy post brachytherapy. Premenopausal patients should be given systemic HRT unless contraindication at final chemotherapy assessment.
• All patients should be seen by brachytherapy nursing team pre and post brachytherapy and instructed in use of vaginal dilators to maintain vaginal patency post treatment (refer to cervix radiotherapy protocol ref 1).
• Review 2-3 weeks post chemoradiotherapy then 3-4 monthly for 2 years, then, 6 monthly years 3-5 and annually years 5-10 (for collection of follow-up data).

4.1.2 Treatment of Stage 4 B Disease

4.1.2.1 Radical Primary Chemotherapy followed by Chemoradiotherapy and Brachytherapy (Stage 4 B Para aortic node positive and No Visceral Metastases)

Background
Patients who have positive pelvic nodes have 25-30% risk of positive para aortic nodes, thus these patients are offered laparoscopic para aortic node dissection (LA PAND). If the para aortic nodes are found to be involved, these patients require extended field radiotherapy which limits delivery of chemotherapy. They should thus be considered for primary chemotherapy with cisplatin / paclitaxel, unless local pelvic symptoms (severe transfusion dependant vaginal bleeding or sepsis) require urgent radiotherapy. To receive cisplatin / paclitaxel, patients should be
- Performance status ECOG 0-2
- Good renal, hepatic and bone marrow function
- Disease can be encompassed in radiotherapy field

Staging
If patients are being considered for radical therapy they require:
- CT Scan of Chest and Abdomen or CT PET Scan
- Baseline MRI of pelvis and para aortic nodes

Treatment Regimen

• Chemotherapy cisplatin 75mg/m² day1 / paclitaxel 175 mg/m² day 1 (ref 3,4)

• 3 week schedule for 2-3 cycles with Pegfilgrastim support (pelvic sepsis and post LAPAND)
• Monitor for PV bleeding, renal impairment
• Planning CT scan abdomen and pelvis 6 field arrangement to Para aortic nodes and pelvis, 50 Gy in 30 fractions to pelvic field, 45 Gy in 30 fractions to Para aortic fields. Cover with omeprazole and ondansetron
• Repeat CT after 2 cycles, if partial response or stable disease, proceed to cycle 3 chemotherapy
• Start radiotherapy D8 post cycle 3 chemotherapy. Monitor FBC/oncology profile.
• Commence weekly cisplatin 30mg/m² at Day 22 or as soon as ANC has reached 1.5 or more for 3-4 cycles
• HDR brachytherapy 21 Gy to point A in 3 fractions incorporated with external beam radiotherapy, MRI pelvis week 5 to assess response
• 2 Further cycles cisplatin /paclitaxel with 20% dose reduction and pegfilgastrim support starting 2-3 weeks post radiotherapy and brachytherapy when ANC has reached 1.5 and platelets 100.000

• Follow up

All patients should commence topical oestrogen to promote vaginal healing post brachytherapy. Premenopausal patients should be given systemic HRT unless contraindication at final chemotherapy assessment.
All patients should be seen by brachytherapy nursing team pre and post brachytherapy and instructed in use of vaginal dilators to maintain vaginal patency post treatment (refer to cervix radiotherapy protocol ref 1)
Review 2-3 weeks post chemoradiotherapy then 3-4 monthly for 2 years, then, 6 monthly years 3-5 and annually years 5-10 (for collection of follow-up data).
If bulky disease still present on week 5 MRI, discuss at MDT, book EUA and MRI and assess for salvage surgery
All patients should have MRI 4 months post completion of treatment to confirm complete response. CT of chest, abdomen and pelvis should be performed post treatment and thereafter as clinically indicated if systemic relapse or post treatment toxicity is suspected.
Patients should be advised of risks of rectovaginal or vesicovaginal fistula if biopsy of anterior rectal wall or bladder is performed. Such procedures should be carried out be GI or GU team with experience of managing irradiated tissue.

4.1.2. 2 Primary Chemotherapy (Stage 4 B Visceral Metastases at diagnosis)

Background

Rarely patients may present with metastatic disease outside pelvis and para aortic region. Neuroendocrine tumours should be excluded by central pathology review. If squamous / adenocarcinoma is confirmed, patients should proceed with palliative chemotherapy with cisplatin /paclitaxel, patients should be
• Performance status ECOG 0-2
• Good renal, hepatic and bone marrow function

Treatment Regimen

• Primary Chemotherapy cisplatin 75mg/m² / paclitaxel 175 mg/m² (Ref 3,4)
• 21 day schedule assess response after cycle 3 ie CT chest, abdomen and pelvis continue to 6 cycles with Pegfilgastrim if pelvic sepsis,
• Monitor for PV bleeding, renal impairment, neurotoxicity
• Radiotherapy to pelvis +/- PA nodes if residual post chemotherapy disease can be encompassed in radiation field
• HDR Brachytherapy 2 fractions 14 Gy to point A incorporated towards end of radiotherapy if controlled systemic disease and significant pelvic disease at presentation

4.1.3. Recurrent Disease Post Radical Hysterectomy

Background

4.1.3.1 Recurrent Disease Post Radical Hysterectomy Confined to Pelvis

Staging

• MRI pelvis/ PA nodes
• CT PET to document extent recurrent disease

Patient Selection

Performance status 0-2
Adequate renal, hepatic, bone marrow function
In older, unfit patients with significant co morbidity concurrent weekly cisplatin at 30-40mg/m² for 4-6 cycles should be considered

Treatment Regimen

Week 1,4,7 - cisplatin 75mg/m² / paclitaxel 175mg/m² every 21 days for 3 cycles
Week 8-13 - Commence radiotherapy day 8 – 10 post cycle 3
Week 10,11,12, 13 cisplatin 40mg/m²/ week for 3-4 cycles during radiotherapy
Week 15 Cisplatin 60mg/m² Paclitaxel 140mg/m² (20% dose reduction) with pegfilgrastim day 2

• assess response with CT/ MR after cycle 3 Monitor for PV bleeding, renal impairment, neurotoxicity
• Serial MR of PA nodes and Pelvis should be considered to reduce radiation portals as disease responds during treatment
• Vaginal vault brachytherapy
• Carboplatin should be substituted for cisplatin if e GFR <40 mls/min

Follow up
Discuss at Gynae MDT if small volume residual disease post treatment to consider salvage surgery
All patients should commence topical oestrogen to promote vaginal healing post brachytherapy. Premenopausal patients should be given systemic HRT unless contraindication at final chemotherapy assessment
4.1.3.2 Recurrent Disease Post Radical Hysterectomy or radical chemoradiotherapy – Visceral Metastatic / Extra pelvic Disease

Staging
Baseline CT chest abdomen and pelvis, repeat after cycle 3 and only continue if stable disease or partial response and manageable toxicity

Patient Selection
Patients with metastatic disease should be considered for systemic therapy providing they demonstrate:

- Adequate performance status (ECOG PS 0/1, but to be considered in those of ECOG PS 2)
- Adequate renal function, liver and bone marrow function

Treatment Regimen
Chemotherapy cisplatin 75mg/m\(^2\)/ paclitaxel 175mg/m\(^2\) 3 week after cycle 3 continue to 6 cycles if Partial response. Cover with Pegfilgrastim if pelvic sepsis, or previous XRT. Consider dose reduction if toxicity problems encountered during previous chemoradiation.

- Monitor for PV bleeding, renal impairment, neurotoxicity
- Radiotherapy to pelvis +/- PA nodes if residual post chemotherapy disease can be encompassed in radiation field

4.1.3.3 Metastatic Disease – 2nd and 3rd Line Chemotherapy

Patient selection
Younger fitter women with aggressive metastatic disease who have previously responded to cisplatin based chemotherapy may be considered for further palliative chemotherapy if they are performance status 2 or better, have adequate renal, bone marrow and hepatic function

1. Relapse more than 6 months post cisplatin based treatment
2. Treatment Regimen

   Carboplatin AUC 4/Paclitaxel 175mg/m\(^2\) day 1 21 day cycle for 3-4 cycles,
   Or
Cisplatin 50mg/m² Topotecan 0.75mg/m² day 1,2,3
or
single agent Carboplatin AUC 6 21 DAY CYCLE FOR 3-4 CYCLES

Bevacizumab is accepted for restricted use within NHS Scotland in combination with paclitaxel and cisplatin for the treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix. This advice is contingent on the availability of the Patient Access Scheme.

In young fit patients with metastatic relapse, funding should be sought via cost per case for Bevacizumab in combination with Cisplatin, Paclitaxel.

Bevacizumab 15mg per kg with Cisplatin 50 mg/m² and paclitaxel 135mg/m² every 21 days for 6 cycles
- Contraindicated in those at risk of GI fistula, monitor for hypertension, thromboembolic events and proteinuria

Relapse within 6 months of platinum based chemotherapy

Treatment Regimen

Gemcitabine 1,000 mg/m² day 1 and 8 Docetaxel 60 mg/m² day 8
Or
Paclitaxel 80mg/m²/week, assess response at week 10
Or

Gemcitabine 1000mg/m² day 1,8,15 22 day cycle
Pulmonary function tests & chest x ray required.

4.2 Neuroendocrine Small or Large Cell Cancer

4.2.1 Background

Neuroendocrine tumours account for less than 10 % cervical cancer, they should be suspected in patients with extensive nodal disease associated with smaller primary tumours. All patients should have pathology checked by specialist gynae pathologist to confirm neuroendocrine component before treatment commences. These tumours follow similar biological behaviour as in other sites with rapid tumour doubling time, aggressive clinical behaviour and propensity for systemic metastases. It is essential to treat occult metastatic disease with chemotherapy, but best results are achieved with combined modality approach and commencing radiotherapy as soon as possible, ie day 8 post cycle 2 chemotherapy for pelvic confined disease and day 8 of cycle 3 if paraaortic nodes also require treatment. With this approach longterm survival > 50% 5 year can be achieved (ref 12) Prophylactic cranial irradiation (PCI) significantly improves survival and reduces incidence of brain metastases in LS and ES patients who achieve at least a partial response to treatment [17, 18].
Staging
CT or CT PET Scan of chest and abdomen
CT Brain scan if clinically indicated
Bone scan if clinically indicated
MRI Pelvis and para aortic nodes

4.2.2 Primary Treatment
In lung cancer, several studies have compared two commonly used regimens: cisplatin/etoposide and vincristine/doxorubicin/cyclophosphamide. Early studies suggested that the two regimens have equal efficacy, however, a meta-analysis of 4054 patients from 19 trials showed that platinum containing regimens are superior in terms of response rates and survival [19]. Platinum/etoposide regimens are now the treatment of choice for patients who can tolerate platinum with anthracyclines based regimens reserved for those who cannot.

Most of the trial evidence is for cisplatin based regimens rather than carboplatin and in the UK the pragmatic view is generally taken that cisplatin is used when survival is the main aim (limited stage, good prognosis), and carboplatin when the treatment is palliative. This approach is supported by a recent meta-analysis showing no difference in efficacy between cisplatin and carboplatin but differences in the toxicity profile [20].

Given the rarity of small and large cell carcinoma cervix, no randomised trial data exists, best reported outcomes are from single institution series (ref) using cisplatin/etoposide chemotherapy in conjunction with pelvic radiotherapy and brachytherapy.

Consider concurrent chemoradiotherapy in patients who have:
- limited stage disease
- good performance status
- adequate lung function
- adequate bone marrow, liver and renal function

4.2.2.1 Pelvic Confined Disease

Treatment Regimen

Concurrent chemoradiotherapy
Week 1,4 Cisplatin 80 mg/m² day 1 & etoposide 120mg/m² day 1-3
21 day cycle 2-3 cycles
Week 5 Commence radiotherapy day 8-10 cycle 2 or 3
Radiotherapy and brachytherapy as per protocol [21]

Week 7,8,9,10 Cisplatin 40mg/m² per week from week 3 radiotherapy for 3-4 cycles

Week 14 and 17 Cisplatin 65mg/m² day 1 & etoposide 100mg/m² day 1-3. Pegfilgrastim day 4
Management
- CT scan chest and abdomen
  - at baseline
  - after cycle 3 (even if planning to go to 6 cycles as this allows time for XRT planning)
- Consider consolidation thoracic radiotherapy and prophylactic cranial irradiation (PCI) in patients with at least partial response

4.2.2.1 Extra Pelvic Disease – Para aortic Node Positive Treatment
Regimen
Concurrent chemoradiotherapy
Week 1, 4, 7, Cisplatin 80 mg/m² day 1 & etoposide 120mg/m² day 1-3
21 day cycle 2-3 cycles
Week 8 Commence radiotherapy day 8-10 cycle 2 or 3
Radiotherapy and brachytherapy as per protocol [21].
Confirm platelets>100,000 (x10⁹/L) before radiotherapy.

Week 10, 11, 12, Cisplatin 30mg/m² per week from week 3 radiotherapy for 3-4 cycles

Week 17 and 20 Cisplatin 65 mg/m² day 1 & etoposide 100mg/m² day 1-3.
Pegfilgrastim day 4

Management
- CT scan chest and abdomen
  - at baseline
  - after cycle 3 (even if planning to go to 6 cycles as this allows time for XRT planning)
- Consider prophylactic cranial irradiation (PCI) in patients with at least partial response

Follow up – all patients
All patients should commence topical oestrogen to promote vaginal healing post brachytherapy. Premenopausal patients should be given systemic HRT unless contraindication at final chemotherapy assessment.
All patients should be seen by brachytherapy nursing team pre and post brachytherapy and instructed in use of vaginal dilators to maintain vaginal patency post treatment (refer to cervix radiotherapy protocol ref 1)
Review 2-3 weeks post chemoradiotherapy then 3-4 monthly for 2 years, then, 6 monthly years 3-5 and annually years 5-10 (for collection of follow-up data).

If bulky disease still present on week 5 MRI, discuss at MDT, book EUA and MRI and assess for salvage surgery

All patients should have MRI 4 months post completion of treatment to confirm complete response. CT of chest, abdomen and pelvis should be performed post treatment and thereafter as clinically indicated if systemic relapse or post treatment toxicity is suspected.

Patients should be advised of risks of rectovaginal or vesicovaginal fistula if biopsy of anterior rectal wall or bladder is performed. Such procedures should be carried out by GI or GU team with experience of managing irradiated tissue.

4.2.3 Second and Subsequent Line Therapy

In fit patients (PS 0 or 1) who have had a good response to first and second line chemotherapy for SCLC, third line treatment with CAV can be considered in selected patients. In practice these tend to be patients who received re-challenge platinum/etoposide in the second line setting and who have had a progression-free interval of greater than 6 months.

**Treatment Regimen**

Vincristine 1.4mg/m², max 2mg, doxorubicin 50mg/m² and cyclophosphamide 800g/m² [26]

21 day cycle, no more than 4 cycles

**Management**

- CT scan chest and abdomen
  - at baseline
  - after every 2 cycles

4.3 Vaginal Cancer

**Background**

Vaginal cancer is a rare tumour presenting in elderly women with locally advanced usually inoperable disease, the treatment schedule follows that of cervical cancer, but groin nodes are included in the treatment field and brachytherapy may be confined to vaginal cylinder or ovoid treatment.

**Patient Selection**

All patients fit to receive concurrent chemotherapy should receive treatment if adequate renal, bone marrow and hepatic function.
Consider dose reduction to 30mg/m$^2$ in patients > 70 or if calculated GFR is 50-59ml/min. See SACT protocol for further details of dose reduction recommendations in renal impairment.

4.3.1 First line therapy

Treatment Regimen

Cisplatin 40mg/m$^2$ for 4-6 cycles

Refer to radiotherapy treatment protocol for details of dose /fractionation and toxicity management

Management

- CT Scan of chest and abdomen
  - at baseline
  - after 3 and 6 cycles

Follow up

3 monthly

4.4 Vulval Cancer

Background

Vulval cancer is rare 1.7/100,000 women, prognosis falls from > 80% to less than 50% 5 year survival if groin nodes are involved. Post operative radiotherapy +/- cisplatin based chemotherapy should be considered if 2 microscopic nodes are involved or 1 macroscopic node and surgical margin < 8mm.

Concurrent chemoradiotherapy may be considered as primary treatment of locally advanced disease for sphincter preservation or to downstage disease to allow radical surgery to proceed.

4.4.1 Adjuvant Post operative Chemotherapy and Radiotherapy

Patient Selection

Patients should be of good performance status 0/1
Adequate renal, hepatic, bone marrow function

Treatment Regimen

Cisplatin 40mg/m$^2$ per week for 4 cycles
Concurrent with Radiotherapy to vulva, groins and lower pelvis

Toxicity Management
4.4.2 Primary Treatment of Locally Advanced Inoperable disease

Cisplatin 40mg/m\(^2\)/week for 4-6 cycles with radiotherapy refer to radiotherapy treatment protocol for dose fractionation and toxicity management

or

Cisplatin 70mg/m\(^2\) Fluorouracil 4000mg/m\(^2\)over 96 hours via infusor bottle for 1-2 cycles followed by radiotherapy. If severe (g3) mucositis/gi toxicity/skin reaction switch to weekly cisplatin

For 4-6 cycles

4.4.3 Treatment of Locally Advanced/recurrent /metastatic disease

Fluorouracil and Mitomycin can be considered or cisplatin /paclitaxel or weekly paclitaxel in patients fit to undergo SACT ie performance status 2 or better.

4.5 Supportive Therapies

Prophylatic antibiotics are not routinely used with concurrent chemoradiotherapy. Ciprofloxacin and other broad spectrum antibiotics should be avoided to reduce risk of clostridium difficile diarrhoea during radiotherapy. Metronidazole should be used as first line treatment of vaginal discharge and trimethoprim for urinary tract infections if sensitive organisms. Gentamycin is given perioperatively with urinary catheterisation during brachytherapy. Consider peg filgrastim for patients at risk of pelvic sepsis ie uncontrolled pelvic disease, recent laparotomy/LAPAND, PREVIOUS RADIOTHERAPY OR CHEMOTHERAPY. During radiotherapy filgrastim may be given to support WCC to reduce risk of infection at spinal anaesthetic and uterine cannulation for safe delivery of brachytherapy.

Blood transfusions should be used to maintain Hb >100g/L in patients receiving concurrent chemoradiotherapy only

5.0 IMPLEMENTATION OF POLICY

5.1 Dissemination

This policy will be agreed by all consultant oncologists treating patients with SACT for gynae malignancies. The guideline will form the basis for development of the SACT regimen specific protocols. It will be available on the intranet for use by all doctors, nurses and pharmacists involved in all stages of SACT assessment and delivery in patients with gynaemalignancies.

6.0 MONITORING

Use of these guidelines will be monitored using audit
7.0 EVIDENCE BASE / REFERENCES

1. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma.


10. Improved survival with Bevacizumab in advanced cervical cancer NEJM 2014 Feb 20, 370 (8) 734-43 Tewarki , Sill , Long et al


13. Small-Cell Carcinoma of the Cervix: Fourteen Years of Experience at a Single Institution Using a Combined-Modality Regimen of Involved-Field Irradiation and Platinum-Based Based Combination Chemotherapy

P.J. Hoskins, K.D. Swenerton,J.A. Pike, P. Lim, C. Aquino-Parsons, F. Wong and N. Lee JCO September 15, 2003 vol. 21 no. 18 3495-3501


8.0 CONSULTATION PROCESS
Gynae oncologists group.

9.0 APPENDICES / ATTACHMENTS
Authorisation signature sheet.
10.0 **EQUALITY STATEMENT**

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out. The outcome of the Equality screening for this policy is:

- Major impact □
- Minor impact □
- No impact. ☒