# SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

# Cisplatin
# Chemo-radiation regimen
# Cervical Cancer

PROTOCOL REF: **MPHAGYNCIX**
(Version No. 1.1)

## Approved for use in:

For use in combination with radiotherapy for the following tumour sites, for radical or adjuvant treatment.

- Locally advanced cervical cancer
- Locally advanced vulval cancer
- Locally advanced vaginal cancer
- ECOG performance status 0, 1 or 2

## Dosage:

| Drug | Dose | Route | Frequency |
|---|---|---|---|
| Cisplatin | **40mg/m$^2$ (max. 70mg)** | IV infusion | Repeat every 7 days<br>5 weeks concurrent with radiotherapy |

**For up to a maximum of 6 cycles**

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## Counselling Points:

Women of childbearing potential should use effective contraception throughout treatment and for at least 6 months following the last dose cisplatin

Contact the triage team for the following:

- New or worsening cough, chest pain or shortness of breath
- Diarrhoea or severe abdominal pain (with or without blood/mucous)
- Jaundice, severe nausea or vomiting, or easy bruising or bleeding
- Persistent or unusual headache, extreme weakness, dizziness or fainting, or vision changes
- Monitor for signs of infection / sepsis

## Emetogenic risk:

Highly emetogenic.

## Supportive treatments:

**Pre-Medication:**

Dexamethasone 8mg oral 30 minutes before chemotherapy

Ondansetron 16mg oral 30 minutes before chemotherapy

Aprepitant can be added if additional risk factors

**To take home medications**

Dexamethasone tablets 4mg oral, twice daily for three days

Metoclopramide tablets 10mg oral, up to 3 times a day as required for a maximum of 5 consecutive days

Ondansetron 8mg tablets oral, twice daily for 3 days

## Extravasation risk:

Cisplatin – IRRITANT

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

## Dosing in renal and hepatic impairment:

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| **Renal** | Ahead of each cycle of treatment calculate CrCl/GFR using C&G formula prior to treatment with cisplatin.<br><br>**GFR 50-59 ml/min**: 75% of the original dose<br><br>**GFR < 50 ml/min:** not recommended, discuss with a consultant and consider carboplatin |

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| **Hepatic** | No dose adjustment is expected |

## Interactions:

| **Cisplatin** |
|---|
| Nephrotoxic substances<br><br>Concomitant administration of nephrotoxic (e.g. cephalosporins, aminoglycosides, amphotericin B or contrast media) medicinal products will potentiate the toxic effect of cisplatin on the kidneys. During or after treatment with cisplatin caution is advised with predominantly renally eliminated substances, because of potentially reduced renal elimination.<br><br>Reduction of the blood's lithium values was noticed in a few cases after treatment with cisplatin combined with bleomycin and etoposide. It is therefore recommended to monitor the lithium values.<br><br>Ototoxic substances<br><br>Concomitant administration of ototoxic (e.g. aminoglycosides, loop diuretics) medicinal products will potentiate the toxic effect of cisplatin on auditory function. Except for patients receiving doses of cisplatin exceeding 60 mg/m$^2$, whose urine secretion is less than 1000 ml per 24 hours, no forced diuresis with loop diuretics should be applied in view of possible damage to the kidney tract and ototoxicity.<br><br>Attenuated live vaccines<br><br>Yellow fever vaccine is strictly contraindicated because of the risk of fatal systemic vaccinal disease. |

In view of the risk of generalized illness, it is advisable to use an inactivated vaccine if available.

Antihistamines, Phenothiazines and others

Simultaneous use of antihistamines, buclizine, cyclizine, loxapine, meclozine, phenothiazines, thioxanthenes or trimethobenzamides may mask ototoxicity symptoms (such as dizziness and tinnitus).

Anticonvulsive substances

Serum concentrations of anticonvulsive medicines may remain at sub-therapeutic levels during treatment with cisplatin.

Pyridoxine + altretamine combination

During a randomized study of the treatment of advanced ovarian cancer, the response time was unfavorably affected when pyridoxine in combination with altretamine (hexamethylmelamine) and cisplatin.

Paclitaxel

Treatment with cisplatin prior to an infusion with paclitaxel may reduce the clearance of paclitaxel and therefore can intensify neurotoxicity.

**For more detailed interactions please refer to the SmPC**

## Treatment schedule:

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| | Dexamethasone | 8mg | PO | 30 minutes before chemotherapy |
| | Ondansetron | 16mg | PO | 30 minutes before chemotherapy |
| | Cisplatin | 40mg/m$^2$ | IV | 1000mL Sodium Chloride 0.9% over 60-90 minutes |

## Main toxicities/ Adverse Events:

| **Cisplatin** | |
|---|---|
| Cardiac disorders | Arrhythmia, bradycardia, tachycardia can occur |
| Gastrointestinal | anorexia, nausea, vomiting and diarrhoea |
| General disorders and administration site conditions | Alopecia, rash, pyrexia (very common), asthenia, malaise, injection site extravasation, dehydration, hypokalaemia, hypophosphataemia, hypocalcaemia, tetany, muscle spasms and/or electrocardiogram changes occur as a result of damage to the kidney caused by cisplatin. |
| Haematological | Neutropenia, anaemia, thrombocytopenia |
| Hepatobiliary | Hepatic enzymes and blood bilirubin increased |
| Nephrotoxicity | Cisplatin causes severe cumulative nephrotoxicity. A urine output of 100 mL/hour or greater will tend to minimize cisplatin nephrotoxicity. Hyperuricaemia and hyperalbuminaemia may predispose to cisplatin-induced nephrotoxicity. |
| Nervous system | Cisplatin can cause peripheral neuropathy. |
| Ototoxicity | Ototoxicity is common with cisplatin and is manifested by tinnitus and/or hearing loss in the high frequency range |

**For more detailed toxicities/adverse reactions please refer to the SmPC for each agent.**

## Investigations and treatment plan:

| | Pre | Day 1 | Day 8 | Day 15 | Day 22 | Day 29 |
|---|---|---|---|---|---|---|
| Informed Consent | X | | | | | |
| Clinical Assessment | X | | | | | |
| SACT Assessment (to include PS and toxicities) | X | X | X | X | X | X |
| On treatment review (floor clinic) | | | | X | | X |
| FBC | X | X | X | X | X | X |
| U&E & LFTs & Magnesium | X | X | X | X | X | X |
| CrCl (Cockcroft and Gault) and urine output | X | X | X | X | X | X |
| MR/PET-CT scan | X | | | | | |
| ECG | | | | | | |
| Blood pressure measurement | X | | | | | |
| Respiratory Rate | X | | | | | |
| Weight recorded | X | X | X | X | X | X |
| Blood glucose | X | | | | | |

Note: Bloods taken on a Friday are suitable to be used to assess if treatment on Monday is appropriate to go ahead.

## Dose Modifications and Toxicity Management:

If chemotherapy is deferred please liaise with radiotherapy team as radiotherapy should be continued where possible

## Haematological toxicity:

Proceed on treatment day if-

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| ANC ≥ 1.0 x $10^9$/L | Plt ≥ 100 x $10^9$/L |

Delay 1 week on day 1 if-

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|---|---|
| ANC ≤ 0.9 x $10^9$/L | Plt ≤ 99 x $10^9$/L |

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

## Non- Haematological toxicity:

**Grading and Management of Toxicity**

Toxicity should be grading according to the CTCAE criteria.

Following assessment treatment should be withheld for any toxicity until resolved to grade 0/1.

For dose modification, follow the general guidance below and discuss with treating clinician.

As patients are receiving concurrent radiotherapy, if there are any concerns related to potential radiotherapy toxicity, for example, grade 2 diarrhoea, abdominal pain or radiotherapy related skin toxicity, please contact the patient's consultant prior to delivering chemotherapy.

| | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|
| **1st appearance** | Interrupt treatment until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible | Interrupt treatment until resolved to grade 0/1, then continue at 75-80% of original dose with prophylaxis where possible | Discontinue treatment |
| **2nd appearance** | Interrupt treatment until resolved to grade 0/1, then continue at 75-80% of original dose | Interrupt treatment until resolved to grade0/1, then continue at 50% of original dose | |
| **3rd appearance** | Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose | Discontinue treatment | |
| **4th appearance** | Discontinue treatment | | |

## Peripheral Neuropathy

Severe cases of neuropathies have been reported. These neuropathies may be irreversible and may manifest by paresthesia, a proprioceptive loss and a sensation of vibrations. A loss of motor function has also been reported. A neurologic examination should be carried out if clinically indicated.

## Neurotoxicity/Ototoxicity

If patient develops Grade 2 neuropathy or ototoxicity, discuss with Consultant. Patients with functional hearing loss should have cisplatin omitted; weekly carboplatin AUC 2 can be substituted.

## References:

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4. Joint Formulary Committee. *British National Formulary (onlin*e) London: BMJ Group and Pharmaceutical Press
5. Keys HM et al NEJM 1999 340(15):1154-1161 Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma
6. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.
7. Northern Cancer Alliance (2018) *Anti-emetic Guidelines for Chemotherapy Induced Nausea and Vomiting (CINV)* Newcastle Upon Tyne: NHS England

## Circulation/Dissemination

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|---|---|
| Date added into Q-Pulse | For completion by DCM |
| Date document posted on the Intranet | For completion by DCM |

## Version History

| | | Author name and designation | Summary of main changes |
|---|---|---|---|

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|---|---|---|---|
| May 2023 | V1.1 | **Sarah Craig**<br>**Gynae SRG pharmacist** | **Routine protocol update** |
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