NHS
North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
Ifosfamide & doxorubicin

Indications for use
Alternative palliative chemotherapy to Carboplatin/Paclitaxel in Ovarian Carcinosarcoma when sarcoma elements predominate

Regimen

The regimen below is to be repeated DAILY on days 1-3:

1 litre Sodium Chloride 0.9% IV over 2 hours, on **Day 1 ONLY**
Furosemide 20 mg orally
Doxorubicin 20mg/m^2 IV bolus via fast running infusion
Mesna IV 400mg/m^2 bolus prior to starting ifosfamide infusion
Ifosfamide IV 2000mg/m^2 with mesna IV 2000mg/m^2 in 1 litre Sodium Chloride 0.9% over 4 hours
Mesna IV 600mg/m^2 in 1 litre Sodium Chloride 0.9% over 6 hours
Mesna IV 600mg/m^2 in 1 litre Sodium Chloride 0.9% over 6 hours

Regimen to be given every 3 weeks for 6 cycles

Investigation prior to initiating treatment
FBC, U&Es, creatinine clearance, LFTs
MUGA scan /echo
Appropriate imaging (i.e. CXR and CT scan) to measure metastatic sites of tumour

Cautions
Pre-existing cardiac morbidity
MUGA scan - LVEF < 50% or >20% decrease from baseline, Doxorubicin may have to be discontinued

Hepatic impairment: bilirubin >21µmol / litre dose modification must be considered.

The following is a guideline: -
If bilirubin 21-50µmol / litre – 50% dose reduction

Cumulative dose of doxorubicin should not exceed 450mg/m^2

Investigations and consultations prior to each cycle
Consultation each cycle
FBC, U&Es, LFTS, Calcium, Phosphate, Magnesium and Glucose
MUGA scan may be repeated if clinically indicated
A urine specimen should be examined before and after each dose of Ifosfamide for haematuria

Acceptable limits for treatment to proceed (if outside these delay one week or contact consultant)
Acceptable blood levels= Neutrophil > 1.5 and plts > 100 Hb >90
Otherwise delay treatment by 1 week until patient recovers
Creatinine clearance should be >60ml/min – See renal dose adjustment.
If neutrophils 1.2 – 1.5 contact **consultant**

Side Effects
Nausea and vomiting, alopecia, mucositis, possible diarrhoea, myelosuppression, cardiac side effects, amenorrhoea/infertility, fatigue, skin changes, nail changes, confusion, hepatotoxicity, encephalopathy, haemorrhagic cystitis.

Dose Modification Criteria
Hepatic impairment: bilirubin >21µmol / litre dose modification must be considered.

The following is a guideline: -
If bilirubin 21-50µmol / litre – 50% dose reduction

Renal Impairment: GFR (ml/min) - Ifosfamide Dose
> 60 100%
50 – 59 70%
< 50 Omit Ifosfamide

Specific Information on Administration
Doxorubicin is a vesicant and should be administered via the side port of a fast running infusion.

Hydration / Fluid balance – Ifosfamide
Weight should be recorded prior to and at the end of Ifosfamide treatment, and a strict fluid balance chart should be maintained. For low urine output, consider increasing the pre-hydration and diuretic regimen. Consider adding diuretics in weight-gain of 1.5 - 2 kg, or symptoms of fluid overload or if there is an excessive positive fluid balance (> 1.5 L/Kg from the start of treatment)

Encephalopathy – Ifosfamide
Ifosfamide encephalopathy is a serious neurotoxic condition that can develop on any treatment cycle. In the early stages, it can present with a variety of symptoms such as somnolence, confusion and hallucinations. Any reports of patients being excessively drowsy or confused should be regarded as indicators of Ifosfamide encephalopathy. As this is a progressive condition, discuss with Consultant, discontinue Ifosfamide and institute treatment with methylthioninium (methylene blue) 50mg IV four hourly immediately. Seek consultant advice
Three factors that have also been demonstrated to predispose individuals to this problem are renal impairment, low albumin and large pelvic tumour mass. If a patient has two of the three risk factors, consider discontinue Ifosfamide and institute appropriate supportive therapy. Future treatment needs to be reviewed by the consultant.
If the patient is at high risk of developing Ifosfamide induced encephalopathy, methylthioninium (methylene blue) can be given prophylactically at 50mg IV TDS.

Methylthioninium should be given over 5 minutes (can be diluted to 50ml with 5% glucose)

Nephrotoxicity – Ifosfamide
Renal function should be assessed at the start of the treatment using the Cockcroft & Gault equation so long as the patient has a stable creatinine concentration and no confounding factors (e.g. catabolic states).

Haemorrhagic cystitis – Ifosfamide
A urine specimen should be examined before and after each dose of Ifosfamide because of the possibility of Ifosfamide – induced haemorrhagic cystitis. To decrease the incidence and severity of bladder toxicity, adequate hydration, maintenance of fluid balance and a uroprotective agent, Mesna, should be used.
In patients who develop microscopic haematuria, an additional bolus dose of Mesna 1000-2000mg IV should be given. The consultant or on-call Registrar needs to be informed.
In the presence of macroscopic haematuria or worsening microscopic haematuria then the Ifosfamide infusion must be stopped.

THIS PROTOCOL HAS BEEN DIRECTED BY DR YIANNAKIS, DESIGNATED LEAD CLINICIAN FOR GYNAE CANCERS

RESPONSIBILITY FOR THIS TEMPLATE LIES WITH THE HEAD OF SERVICE

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