

Chemotherapy protocol

Drug regimen

Weekly Carboplatin/paclitaxel concurrent with radiotherapy

Indications for use

Pre-operative neoadjuvant chemo-radiotherapy for Squamous cell or adenocarcinoma of the Oesophagus (T3, T4a or N1-3) - as per CROSS trial

Regimen

D1, 8, 15, 22, 29:

Carboplatin and Paclitaxel chemotherapy concomitantly with radiotherapy starting on D1

Week 1

Pre-medicate 30 mins pre chemo with:

Dexamethasone 10mg	IV in 100ml 0.9% sodium chloride
Chlorphenamine 10mg	I.V. bolus
Ranitidine 50mg	50mls 0.9% Sodium chloride

For subsequent weeks reduce dexamethasone dose as below. (If patient experiences any hypersensitivity reaction do not reduce the dose further, seek advice from consultant).

Week 2+

Dexamethasone 8mg	IV in 100mls 0.9% sodium chloride
Chlorphenamine 10mg	IV bolus
Ranitidine 50mg	IV 50ml 0.9% sodium chloride

DRUG	FLUID	TIME	ROUTE
Paclitaxel 50mg/m ² (maximum 90mg)	250mls 0.9% sodium chloride	1 hour	IV
Carboplatin AUC2 (maximum 200mg)	250-500mls 5% Glucose	1 hour	IV

Regimen to be given weekly for 5 weeks

Investigation prior to initiating treatment

FBC, U&Es, LFTs, calcium, random glucose

Investigations and consultations prior to each cycle

FBC U&Es and LFTs

Calcium, random glucose and Mg 3 weekly

Consultation needed every week in radiotherapy review clinic

Bloods to be checked ideally the day before (or Friday if treatment on a Monday) so that results are available pre-chemotherapy

Acceptable levels for treatment proceed

Neutrophils ≥ 1.0 and Platelets ≥ 75 (If outside these levels delay one week or contact consultant)

GCSF Is not usually administered during radiotherapy

BSA capped at 2.2m^2

For AUC calculations max GFR capped at 125mls/min

Side effects

Hypersensitivity reactions, myalgia, neuropathy, alopecia, nausea and vomiting, fatigue, bone marrow suppression, skin reaction, constipation

Dose Modification Criteria

Neutrophil count once weekly during CRT		Platelet count once weekly during CRT	Action
≥ 1.0	And	≥ 75	Full dose paclitaxel and carboplatin
< 1.0	Or	$\geq 25 - < 75$	Omit that week's chemotherapy and delay chemotherapy weekly until recovery. Dose reduce by 25% for subsequent cycles
Any	And	< 25	Omit that week's chemotherapy and delay weekly chemotherapy until recovery. Dose reduce by 50% for subsequent cycles

Renal Impairment

Carboplatin contraindicated (so should be stopped) if GFR $< 20\text{ml/min}$

Paclitaxel - no dose modification required

Hepatic impairment

Carboplatin - no dose modification required

For paclitaxel there is limited information available. If bilirubin $< 1.25\text{x ULN}$, and ALT $< 10\text{ ULN}$, continue full intended dose otherwise discuss with consultant.

Non-haematological toxicity

Due to overlapping toxicities for carboplatin and paclitaxel the instructions detailed below (interruption and potential dose reductions) should be applied to **both** drugs at each occurrence.

Incidence	Grade 2	Grade 3	Grade 4
1st occurrence	Interrupt until resolved to G0-1, then resume at original dose	Interrupt until resolved to G0-1, then resume at 75% of original dose	Discontinue treatment altogether unless consultant considers this in the best interest of the patient, in which case Interrupt until resolved to G0-1, then resume at 50% of original doses
2nd occurrence of same toxicity	Interrupt until resolved to G0-1, then resume at	Interrupt until resolved to G0-1, then resume at 50% of original dose	N/A

	75% of original dose		
3rd occurrence of same toxicity	Interrupt until resolved to G0-1, then resume at 50% of original dose	Discontinue treatment	N/A
4th occurrence of same toxicity	Discontinue treatment	N/A	N/A

Additional medications

Ondansetron 8mg bd 1 days
 Metoclopramide 10mg tds prn
 PPI (or ranitidine), mouth washes and laxatives as indicated

Specific Information on Administration

Use non PVC IV giving set with paclitaxel
 Give paclitaxel before carboplatin
 Treatment should be given before radiotherapy and on the same day

**THIS PROTOCOL HAS BEEN DIRECTED BY DR. MITCHELL, CONSULTANT ONCOLOGIST
 RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE**

Date	April 2018
Review	April 2020
Version	2

References

Shapiro, Joel et al. **Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial** The Lancet Oncology , Volume 16 , Issue 9 , 1090 - 1098

Somnath Mukherjee^{a1} et al (2017) **NEOSCOPE: A randomised phase II study of induction chemotherapy followed by oxaliplatin/capecitabine or carboplatin/paclitaxel based pre-operative chemoradiation for resectable oesophageal adenocarcinoma** European Journal of Cancer Volume 74, March 2017, Pages 38-46