NHS
North West Coast
Strategic Clinical Networks

Chemotherapy Protocol

DRUG REGIMEN
Concurrent bladder chemoradiation with mitomycin C and 5-Fluorouracil
(BC2001 trial protocol. Ref New England Journal of Medicine 366;16 April 19 2012 :1477-1541, James et al)

Indication for use
Histologically proven muscle invasive bladder carcinoma predominant TCC component.
Pure Adenocarcinoma or squamous cell tumours may also be treated.
T2-T4aNoMo on CT and MRI
WHO performance status 0-2
Patients suitable for radical radiotherapy to pelvis with adequate bladder capacity
Undergone maximal TURBT
WHO performance status 0-2

Patients can have previously received neo-adjuvant chemotherapy

Regimen
Day 1 Fraction 1 of radical radiotherapy mitomycin C 12 mg/m^2 IV stat
Days 1-5: 5-fluorouracil 500mg/m^2/24 hours continuous infusion, corresponding to fractions 1-5 of radiotherapy
Week four: corresponding to fractions 16-20 of radical radiotherapy, 5-fluorouracil 500mg/m^2/day,
Mitomycin C is ONLY given on day 1 of radiotherapy.

PICC or Hickman line required for administration

Investigation prior to initiating treatment
WHO performance status 0-2
WBC > 4
Platelets > 100
GFR > 25 ml.min (Cockcroft Gault)
Serum bilirubin < 1.5 ULN, Alt or AST < 1.5 ULN
Hickman line or PICC line insertion
Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle). Patients require DPD testing prior to administration. Dose adjustments should be made in accordance with local DPD policy.

Cautions
Patients should not be prescribed metronidazole while receiving 5FU

Investigations and consultations prior to each cycle
Review weekly during chemoradiation in radiotherapy
Weekly U&E, FBC, LFTs

Acceptable levels for treatment to proceed (if outside these levels contact consultant.)
WBC > 3
Neutrophils > 1.5
Platelets > 100
Hb > 10
GFR > 25 ml/min (cockroft Gault)
Bili < 1.5 ULN, ALT or AST < 1.5 ULN
Please see modification table below re acceptable levels of diarrhoea or mucositis to proceed with treatment

Side Effects
Diarrhoea
Mucositis
Plantar palmar syndrome is unlikely given short duration of therapy, may be managed with pyridoxine 50 mg tds
Myelosuppression (rare with 5FU, more common with mitomycin C)
Nausea and vomiting
Pulmonary toxicity with mitomycin C
Haemolytic ureaemic syndrome (rare)
Angina may be precipitated by 5-FU (rare)

Dose Modification Criteria

Diarrhoea
Grade 1(increase of < 4 stools/day over pre-treatment)
Manage with loperamide, low residue diet

Grade 2 (increase of 4-6 stools per day or nocturnal stools)
Reduce 5-FU infusion dose by 125mg/m2 per day and continue radiotherapy

Grade 3 diarrhoea (increase of >/+ 7 stools per day or incontinence, or need for parenteral support for dehydration.
Discontinue 5FU permanently
Consider interrupting radiotherapy (until symptoms resolve to grade 1)

Grade 4 diarrhoea (physiological consequences requiring intensive care; or haemodynamic collapse)
Stop all therapy

Mucositis

Grade 2 (painful erythema, oedema or ulcers but can eat or swallow)
Reduce infusion dose by 125mg/m2 per day

Grade 3 (preventing swallowing or requiring IV hydration)
Discontinue infusion permanently
Continue radiotherapy unless diarrhoea also present

Grade 4 (severe ulceration or requires hydration or parenteral nutritional support)
Stop all therapy

Specific Information on Administration
Metoclopramide 10 mg tds PRN
Loperamide PRN

THIS PROTOCOL HAS BEEN DIRECTED BY DR BIRTLE, DESIGNATED LEAD CLINICIAN FOR BLADDER CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

DATE **June 2017**
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VERSION **3**