SA Health

Cancer Chemotherapy Protocol Registration Form and Template

SA Health Cancer Drug Committee

July 2017

Applicant Details

Consultant Name: Nick Murray Position: Medical Oncologist	
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Supporting Tumour Stream Lead Details

Consultant Name: Position:	
Clinical Unit, Hospital/LHN:	
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Supporting Specialist Pharmacist Details

Name: Bronwen Body Position: Clinical Pharmacist – cancer services	
Clinical Unit, Hospital/LHN: Pharmacy / RAH / CALHN	
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Supporting Specialist Nurse Details

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SA Health Cancer Drug Committee Use only:

Application received (date): 22/6/22
Confirmation of costing confirmed* ☐
Approval Status APPROVED ☐ Conditions of approval (if any): REJECTED ☐ Reason(s) for rejection:
Treatment Risk Level allocated:
SAH-CDC comments (if any)
I acknowledge the application and to the best of my knowledge the information contained within is correct and confirm the decision made by the SA Health Cancer drug Committee in submitting this protocol to the SA Health Approved Cancer Chemotherapy Protocol Register: SAH-CDC Chair (or delegate): Position:
Signature: Date:

Protocol Name	
Protocol Number	

Breast Metastatic EPIrubicin weekly

Treatment Schedule - Summary

Drug	Dose	Route	Day
Epirubicin	25mg/m^2	IV	Day 1

Frequency: 7 days

Notes (e.g. *1st line treatment, alternate scheduling options):*

Number of Cycles: Continuous until disease progression or unacceptable toxicity

Protocol

Indications and Patient Population: Advanced or metastatic breast cancer

Indications for use: Advanced or metastatic breast cancer

Exclusions (e.g. *low* GFR):

Notes:

Drug Status (PBS status, formulation etc.):

PBS and SAFC listed

Clinical Information:

Venous access requirements	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment.
Supportive Care/ Premedication	**See schedule**
Hypersensitivity/infusion related reaction	Potential for flare reaction during administration of epirubicin (facial flushing and red streaking along the vein) stop infusion and exclude extravasation before continuing at a slower rate of infusion. Although rare, cardiac arrhythmias may occur during or immediately after epirubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.
Emetogenicity	**MINIMAL/LOW** Prochlorperazine 10mg pretreatment. Ensure that patients also have sufficient antiemetics for breakthrough emesis:

	Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO or 12.5 mg IV every 6 hours when necessary.
Blood tests	FBC, EUC and LFTs at baseline and prior to each treatment
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment.
Vaccinations	Live vaccines, including BCG, MMR, zoster and varicella vaccines, are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.
Effects of cancer treatment on fertility	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive age prior to commencing treatment.

Treatment Schedule - Detailed

Drug	Dose	Administration/frequency
Prochlorperazine	10 mg	Oral Day 1
Epirubicin	25mg/m^2	IV Day 1, 8, 15

Frequency: 21 days

Number of Cycles: Continuous until disease progression or unacceptable toxicity

Dose Modifications:

Haematological toxicity

ANC x 10^8/L (pre-treatment blood test)

1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well
0.5 to less than 1.0	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and reduce epirubicin by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and reduce epirubicin by 25% for subsequent cycles

Platelets x 10^8/L (pre-treatment blood test)

75 to less than 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local institutional guidelines
50 to less than 75	Delay treatment until recovery

Haematological toxicity

less than 50	Delay treatment until recovery and reduce epirubicin by 25% for subsequent cycles

Renal Impairment

No dose modifications necessary

Hepatic Impairment

Hepatic Impairment

Hepatic dysfunction

Mild	Reduce epirubicin by 25%
Moderate	Reduce epirubicin by 50%
Severe	Omit epirubicin

Mucositis and stomatitis

Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce epirubicin by 25% 3rd occurrence: Reduce epirubicin by 50% 4th occurrence: Omit epirubicin
Grade3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce epirubicin by 50% 2nd occurrence: Omit epirubicin

Interactions:

Drug	Interaction	Clinical management
Epirubicin		
Cardiotoxic drugs (e.g. bevacizumab, calcium channel blockers, propranolol, trastuzumab)	Increased risk of epirubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
Cimetidine	Increased toxicity of epirubicin possible due to reduced clearance and increased exposure	Combination contraindicated; use alternative gastric acid suppressant

General Interactions

	Interaction	Clinical management
Warfarin	Antineoplastic agents may alter the anticoagulant effect of warfarin	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant (e.g. LMWH or unfractionated heparin)
Digoxin	Antineoplastic agents can damage the lining of the intestine; affecting the absorption of digoxin	Monitor digoxin serum levels - adjust digoxin dosage as appropriate
Antiepileptics	Both altered antiepileptic and antineoplastic levels may occur, possibly leading to loss of efficacy or toxicity	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the antineoplastic therapy
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety: U[:)date
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated For more information, refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook 10th Edition (u[:)dated 2016}

Administration details

General patient assessment:

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access port or eve.

Safe handling and waste management

General Patient Assessment prior to each day of treatment

Pre-treatment medications:

Verify antiemetics taken or administer as prescribed.

Chemotherapy - © Time out checklist

Epirubicin

Administer epirubicin (vesicant):

- over 5 to 15 minutes
- via a minibag OR
- by IV bolus via a side port of a freely flowing IV infusion
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 ml of sodium chloride 0.9%
- potential for flare reaction during administration of epirubicin (facial flushing and red streaking along the vein) stop infusion and exclude extravasation before continuing at a slower rate of infusion.

Although rare, cardiac arrhythmias may occur during or immediately after epirubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

Discharge_Information

Antiemetics

- Antiemetics as prescribed.

Patient information

- Ensure patient receives patient information sheet.

Side-effects

Immediate (onset hours to days)	
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Nausea and vomiting	Read more about grevention of chemotherag induced nausea and vomitinq
Taste and smell alteration	Read more about taste and smell changes
Flare reaction	Anthracycline flare reaction is caused by a localised allergic reaction. It is characterised by erythematous vein streaking, urticaria and pruritus which may occur during drug administration and is often associated with too rapid an infusion. Extravasation must be ruled out if flare occurs.
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.

Early (onset days to.weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about neutro12enia
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocvtooenia
Oral Mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiotherapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Fatigue	Read more about fatique
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Radiation Recall	Erythematous or inflammatory skin reaction resembling severe sunburn at sites previously treated with radiotherapy can occur with certain antineoplastic drugs. Symptoms include vesiculation, desquamation and ulceration of the skin. Read more about radiation recall

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about aloQecia
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with antineoplastic treatment. Read more about nail toxicities

Delayed (onset months to years)	
Cardiotoxicity	Anthracyclines are the most frequently implicated antineoplastic agents associated with cardiotoxicity, which typically manifests as a reduction in left ventricular ejection fraction (LVEF), cardiomyopathy, or symptomatic CHF. Anthracycline induced cardiotoxicity has been categorised into acute, early-onset chronic progressive and late-onset chronic progressive and is usually not reversible. The risk of clinical cardiotoxicity increases with a number of risk factors including higher total cumulative doses. Read more about cardiac toxicity: associated with anthracyclines

Supporting Documents

Joensuu, H., K. Holli, M. Heikkinen, E. Suonio, A. R. Aro, P. Hietanen and R. Huovinen (1998). "Combination chemotherapy versus single-agent therapy as first- and second-line treatment in metastatic breast cancer: a prospective randomized trial." Journal of Clinical Oncology 16(12): 3720- 3730.

Twelves, C. J., S. M. O'Reilly, R. E. Coleman, M.A. Richards and R. D. Rubens (1989). "Weekly epirubicin for breast cancer with liver metastases and abnormal liver biochemistry." Br J Cancer 60(6): 938-941.

Yamaguchi, N., T. Fujii, S. Aoi, P. S. Kozuch, G. N. Hortobagyi and R. H. Blum (2015). "Comparison of cardiac events associated with liposomal doxorubicin, epirubicin and doxorubicin in breast cancer: a Bayesian Network meta-analysis." Eur J Cancer 51(16): 2314-2320.

For moreinformation

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