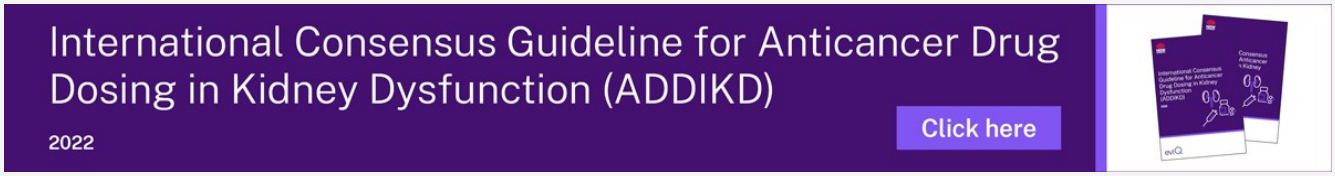
Breast adjuvant/neoadjuvant AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense

ID: 4102 v.1 **Endorsed** Essential Medicine List

Some indications in this protocol are based on limited evidence; please refer to the individual evidence sections for more information.

Check for clinical trials in this patient group. Link to Australian Clinical Trials website

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.



Related pages:

- Breast adjuvant/neoadjuvant AC (DOXOrubicin and CYCLOPHOSPHamide) three weekly
- Breast adjuvant AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense followed by PACLitaxel dose dense overview
- Breast adjuvant AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense followed by PACLitaxel weekly overview
- Breast neoadjuvant cARBOplatin three weekly and PACLitaxel weekly followed by AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense overview
- Breast neoadjuvant cARBOplatin weekly and PACLitaxel weekly followed by AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense overview
- Anti-cancer therapy before breast cancer surgery (neoadjuvant therapy)

Treatment schedule - Overview

Cycle 1 to 4

Drug	Dose	Route	Day
DOXOrubicin	60 mg/m^2	IV	1
CYCLOPHOSPHamide	600 mg/m^2	IV infusion	1
Pegfilgrastim	6 mg	Subcut	2

Frequency: 14 days

Cycles: 4

Notes:

- This is a potentially toxic regimen and should only be used in patients with a good ECOG performance status. Strategies to minimise toxicity include dose attenuation, thorough patient education and vigilant monitoring for any potential septic episodes.
  - Link to eviQ patient information sheet - Infection during cancer treatment

Drug status: Doxorubicin and cyclophosphamide are on the PBS general schedule

Pegfilgrastim is PBS authority

Cost: ~ $150 per cycle

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for **recommended doses of alternative antiemetics**.*

Cycle 1 to 4

Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	12 mg (PO)	60 minutes before chemotherapy. Note: the full dose of dexamethasone on Day 1 may not be required and may be reduced to 8mg at the clinicians discretion.
DOXOrubicin	60 mg/m^2 (IV)	over 5 to 15 minutes
CYCLOPHOSPHamide	600 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Day 2		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on Day 2, 3 and 4 may not be required and may be reduced or omitted at the clinicians discretion.*
Pegfilgrastim	6 mg (Subcut)	inject subcutaneously on day 2 at least 24 hours after chemotherapy
Day 3 and 4		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on Day 2, 3 and 4 may not be required and may be reduced or omitted at the clinicians discretion.*

* Link to ID 7 Prevention of anti-cancer therapy induced nausea and vomiting

Frequency: 14 days

Cycles: 4

Indications and patient population

- Adjuvant or neoadjuvant treatment of operable breast cancer.

Caution:

- Highly myelosuppressive regimen - consider only for patients with a good ECOG performance status.

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Emetogenicity HIGH	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. 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 every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cumulative lifetime dose of anthracyclines	Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone). Criteria for reducing the total anthracycline cumulative lifetime dose include: • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation. Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion. Read more about cardiac toxicity associated with anthracyclines
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC and LFTs at baseline and prior to each cycle.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).

Note: all dose reductions are calculated as a percentage of the starting dose.

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
0.5 to less than 1.0	Delay treatment until recovery and maintain the dose
less than 0.5	Delay treatment until recovery and reduce doxorubicin and cyclophosphamide by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and reduce doxorubicin and cyclophosphamide by 25% for subsequent cycles
Platelets x 10^9/L (pre-treatment blood test)	
75 to less than 100	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and consider reducing doxorubicin and cyclophosphamide by 25% for subsequent cycles

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	Reduce cyclophosphamide by 25%
less than 30	Reduce cyclophosphamide by 50%

Hepatic impairment	
Hepatic dysfunction	
Mild	Reduce doxorubicin by 25%
Moderate	Reduce doxorubicin by 50%
Severe	Omit doxorubicin

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 doxorubicin and cyclophosphamide by 25%

Mucositis and stomatitis	
	3rd occurrence: Reduce doxorubicin and cyclophosphamide by 50% 4th occurrence: Withhold chemotherapy
Grade 3 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 doxorubicin and cyclophosphamide by 50% 2nd occurrence: Withhold chemotherapy

Diarrhoea	
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 doxorubicin and cyclophosphamide by 25% 3rd occurrence: Reduce doxorubicin and cyclophosphamide by 50% 4th occurrence: Withhold chemotherapy
Grade 3 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 doxorubicin and cyclophosphamide by 50% 2nd occurrence: Withhold chemotherapy

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. ***References & Disclaimer***

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

Cyclophosphamide		
	Interaction	**Clinical management**
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Increased toxicity of cyclophosphamide possible due to increased conversion to active (and inactive) metabolites	Avoid combination or monitor for cyclophosphamide toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Reduced efficacy of cyclophosphamide possible due to decreased conversion to active (and inactive) metabolites	Avoid combination or monitor for decreased clinical response to cyclophosphamide
Amiodarone	Possible additive pulmonary toxicity with high-dose cyclophosphamide (i.e. doses used prior to stem cell transplant; 60 mg/kg daily or 120 to 270 mg/kg over a few days)	Avoid combination or monitor closely for pulmonary toxicity
Allopurinol, hydrochlorothiazide, indapamide	Delayed effect. Increased risk of bone marrow depression; probably due to reduced clearance of active metabolites of cyclophosphamide	Avoid combination, consider alternative antihypertensive therapy or monitor for myelosuppression
Ciclosporin	Reduced efficacy of ciclosporin due to reduced serum concentration	Monitor ciclosporin levels; adjust dosage as appropriate; monitor response to ciclosporin
Suxamethonium	Prolonged apnoea due to marked and persistent inhibition of cholinesterase by cyclophosphamide	Alert the anaesthetist if a patient has been treated with cyclophosphamide within ten days of planned general anaesthesia

Doxorubicin		
	Interaction	**Clinical management**
Cardiotoxic drugs (eg. bevacizumab, calcium channel blockers, propranolol, trastuzumab)	Increased risk of doxorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
Cyclophosphamide	Sensitises the heart to the cardiotoxic effects of doxorubicin; also, doxorubicin may exacerbate cyclophosphamide induced cystitis	Monitor closely for cardiotoxicity and ensure adequate prophylaxis for haemorrhagic cystitis when combination is used
Glucosamine	Reduced efficacy of doxorubicin (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II *in vitro*)	The clinical effect of glucosamine taken orally is unknown. Avoid combination or monitor for decreased clinical response to doxorubicin
CYP2D6 inhibitors (e.g. SSRIs (esp. paroxetine), perhexiline, cinacalcet, doxepin, flecainide, quinine, terbinafine)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of doxorubicin possible due to increased clearance	Monitor for decreased clinical response to doxorubicin

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	**Clinical management**
Dexamethasone	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of **antiemetic dexamethasone** by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of **antiemetic dexamethasone** has already been taken into account. If **dexamethasone is part of the chemotherapy protocol**, dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
Warfarin	Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant	INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant
Combined oral contraceptive	Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant	Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of NK-1 antagonist possible due to increased clearance	Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of NK-1 antagonist possible due to reduced clearance	Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation)
Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist	Avoid combination or monitor for increased toxicity especially with orally administered drugs

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs 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 anti-cancer drug 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 anti-cancer 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 Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 2 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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 TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Chemotherapy - Time out

Doxorubicin

Administer doxorubicin (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 doxorubicin (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 doxorubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 30 to 60 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- rapid infusion can cause dizziness, rhinitis, nausea and perioral numbness. If symptoms develop, slow infusion rate.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Continue safe handling precautions until 7 days after completion of drug(s)

Discharge information

Antiemetics

- Antiemetics as prescribed.

Growth factor support

- Arrangements for administration if prescribed.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

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
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.
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
Taste and smell alteration	Read more about taste and smell changes
Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.

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 immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
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 radiation therapy can occur with certain anti-cancer 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 alopecia
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about nail toxicities

Delayed (onset months to years)	
Menopausal symptoms	Irregular or absent periods, hot flushes, mood swings, sleep disturbance, night sweats, vaginal dryness, decreased libido and dyspareunia. This is caused by ovarian failure and may be temporary or permanent.
Cardiotoxicity	Anthracyclines are the most frequently implicated anti-cancer drugs 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

Evidence - Adjuvant

The evidence for this protocol comes from the trial CALGB 9741 by Citron et al, 2003. The study used a 2 X 2 factorial experimental design to assess the 2 factors of dose density (administering the drug every 2 weeks versus 3 weeks) and treatment sequence (concurrent vs sequential) and the possible interaction between them.[1]

A total of 2005 women were randomly assigned to receive one of the following 4 arms:

1. Sequential doxorubicin x 4 -> paclitaxel x 4 -> cyclophosphamide x 4 with every 3 weeks
2. Sequential doxorubicin x 4 -> paclitaxel x 4 -> cyclophosphamide x 4 every 2 weeks with filgrastim
3. Concurrent doxorubicin and cyclophosphamide x 4 -> paclitaxel x 4 every 3 weeks
4. Concurrent doxorubicin and cyclophosphamide x 4 -> paclitaxel x 4 every 2 weeks with filgrastim

The primary end point was disease-free survival (DFS) and overall survival (OS) was a secondary endpoint.

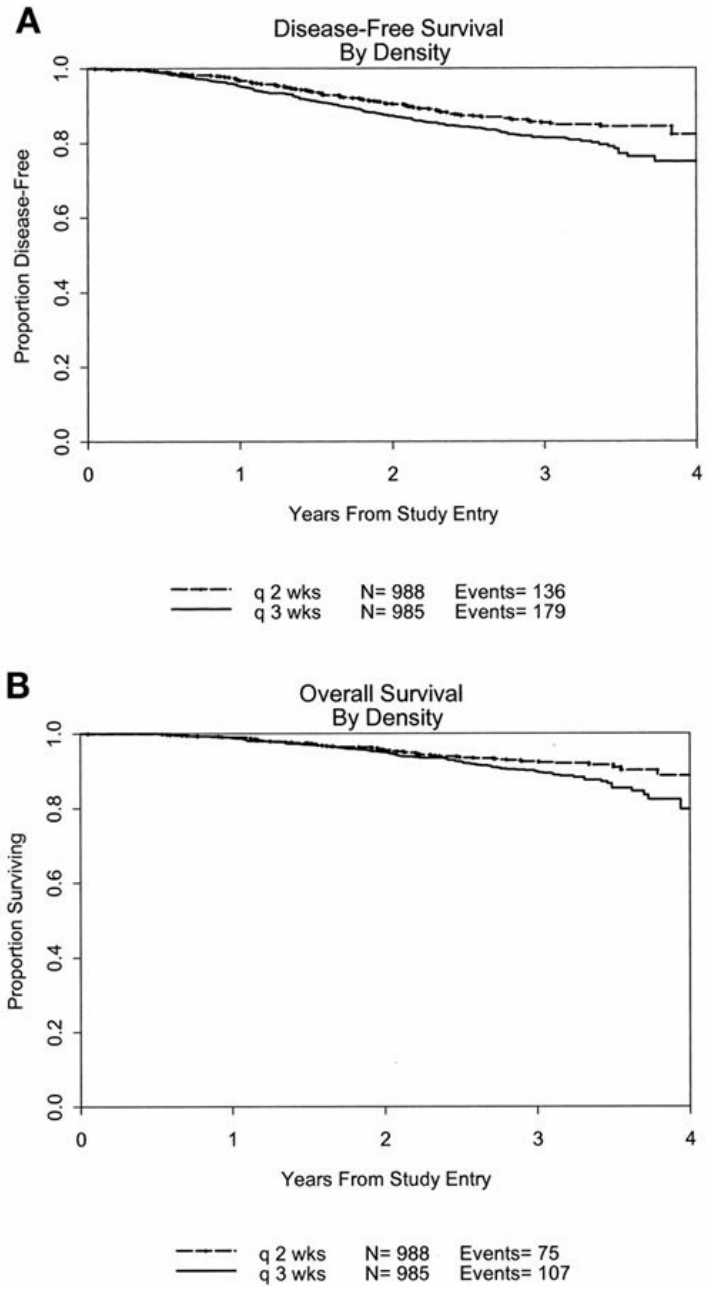
Efficacy

CALGB 9741 trial

After a median follow-up of 36 months, the dose dense treatment improved DFS (risk ratio (RR) =0.74; *p*=0.01) and OS (RR=0.69; *p*=0.013).

4 year DFS was 82% for the dose dense regimens and 75% for the others.

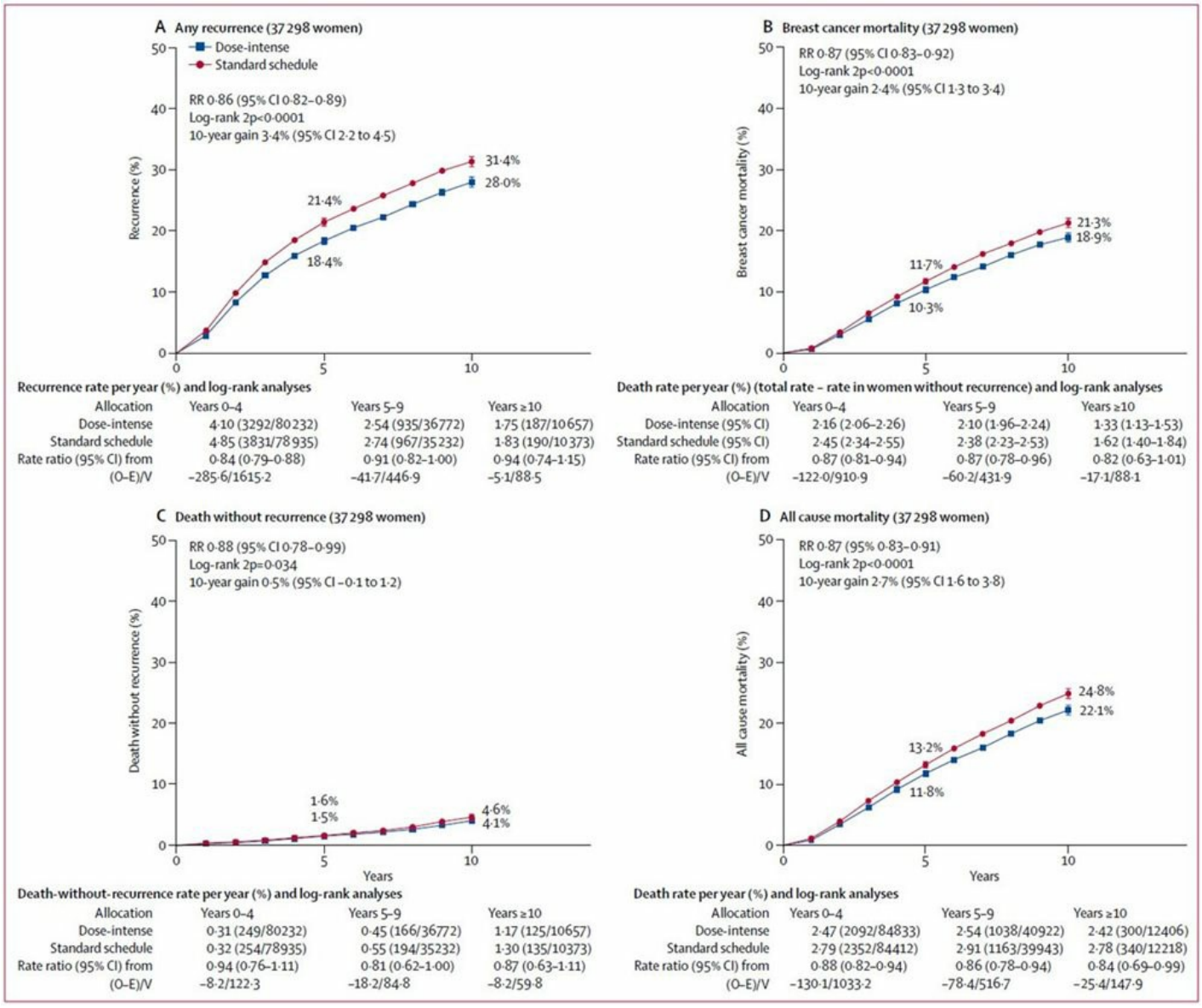
There was no difference in DFS or OS between concurrent and sequential regimens.[1]



EBCTCG meta-analysis

A meta-analysis by the EBCTCG demonstrated a lower 10 year risk of recurrence with dose-intense chemotherapy compared with standard-schedule chemotherapy (28.0% vs 31.4%, RR 0.86, 95% CI 0.82 to 0.89; p<0.0001). Dose-intense chemotherapy was also associated with lower 10 year breast cancer mortality rates (18.9% vs 21.3% respectively; RR 0.87, 95% CI 0.83 to 0.92; p<0·0001) and all-cause mortality (22.1% vs 24.8% respectively; RR 0.87, 95% CI 0.83 to 0.91; p<0·0001). The proportional reductions in recurrence with dose-intense chemotherapy were similar in oestrogen receptor (ER)-positive and ER-negative disease (p<0·0001) and did not differ significantly by other patient or tumour characteristics.[2]

Pooled analysis of all dose-intensification trials for 10 year cumulative risk of any recurrence (A), breast cancer mortality (B), death without recurrence (C), and all-cause mortality (D) for dose-intense vs standard-schedule chemotherapy groups[2]



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Toxicity

The DFS and OS advantages of dose density were not accompanied by an increase in haematological toxicity because of the use of filgrastim in the dose dense regimens.[1]

Grade 3/4 toxicity [1]	AC followed by paclitaxel (dose dense) (%)	AC followed by paclitaxel (3 weekly) (%)
Neutropenia	9*	43
Vomiting	6	8
Diarrhoea	1	2
Stomatitis	3	3
Cardiac	<1	<1
Sensory	4	5
Pain	9	7
Myalgia/Arthralgia	5	5

** Patients received filgrastim*

Evidence - Neoadjuvant

Note: Limited evidence is specific to the neoadjuvant setting.

A search of the literature did not find strong phase III evidence for use this regimen in the neoadjuvant setting. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The reference committee was most strongly influenced by the phase II CALGB 40603 trial and the phase III BrighTness trial.[3, 4]

Source	Study & year published	Supports use	Is the dose and regimen consistent with the protocol?	Comments
Phase III trial	Loibl et al.[4]	**Yes**		-
Phase II trials	Sikov et al. [3]	**No**	Yes	-
Observational studies	-	**N/A**	-	-
Case series	-	**N/A**	-	-
Guidelines	**Date published/revised**	**Supports use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	v.5 2021	**Yes**	-	-
BCCA	-	**N/A**	-	-
CCO	-	**N/A**	-	-
ESMO	2015[5]	**Yes**	No doses stated	Increased pCR in triple negative tumours, particularly those carrying BRCA 1/2 or RAD mutations

The CALGB 40603 trial was a randomised, open-label phase II study used a 2 x 2 factorial experimental design to evaluate the impact of adding carboplatin and/or bevacizumab to standard neoadjuvant chemotherapy on achieving pathological complete response (pCR) in patients with triple-negative breast cancer (TNBC).[3, 6]

Between May 2009 and August 2012, a total of 443 patients with stage II to III TNBC were randomly assigned to receive one of the following 4 arms:

1. Sequential weekly paclitaxel x 12 -> dose dense doxorubicin and cyclophosphamide x 4, every 2 weeks with filgrastim (N=115).

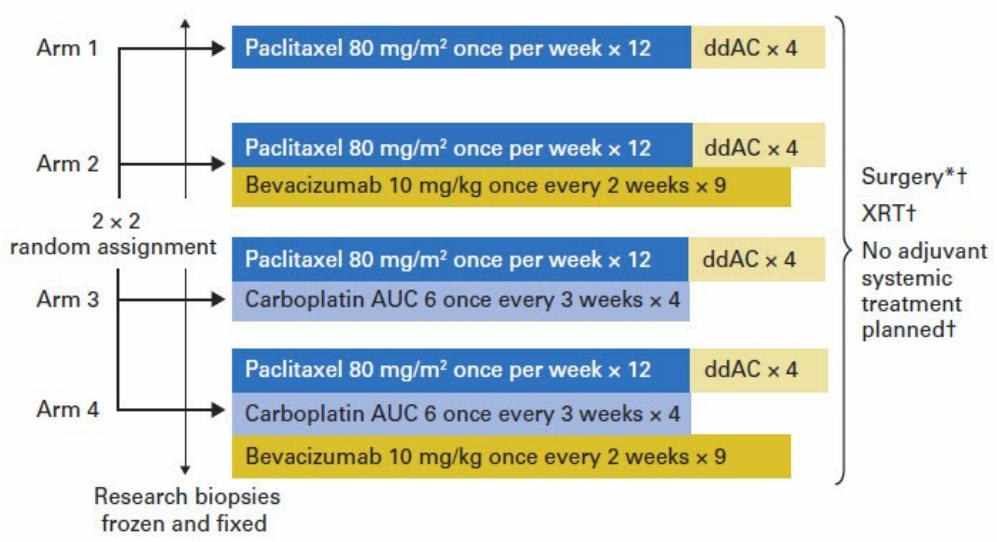
2. Weekly paclitaxel x 12 -> dose dense doxorubicin and cyclophosphamide x 4 every 2 weeks with filgrastim; with concurrent bevacizumab x 9 every 2 weeks (N=113).

3. Concurrent weekly paclitaxel x 12 and carboplatin x 4 every 3 weeks -> dose dense doxorubicin and cyclophosphamide x 4 every 2 weeks with filgrastim (N=113).

4. Concurrent weekly paclitaxel x 12 and carboplatin x 4 every 3 weeks -> dose dense doxorubicin and cyclophosphamide x 4 every 2 weeks with filgrastim; with concurrent bevacizumab x 9 every 2 weeks (N=113).

Triple negative was defined in the CALGB 40603 trial by ER and PR expression 10% or less, AND HER-2 negativity (i.e. IHC 0 to 1+ OR FISH ratio less than 2.0 if IHC 2+ or IHC not performed).

Schema of CALGB 40603[3]



The primary end point was pCR in the breast. (NB: pCR as a valid surrogate endpoint for long-term clinical benefit, such as disease-free survival and overall survival, is still an area of contention).

Secondary end points were pCR breast/axilla, treatment delivery, treatment-related toxicities, residual cancer burden, conversion from clinically node-positive to pathologically node-negative status, and conversion from breast conserving surgery (BCS)-ineligible to BCS-eligible status after treatment.

BrighTness[4]

The BrighTNess study, a phase III trial evaluating the benefit of veliparib plus carboplatin in the neoadjuvant setting in stage II and III triple negative breast cancer. In this study, 55.6% of patients received dose dense AC, with G-CSF support given at the discretion of the clinician.

The study had 3 arms which included:

1. Carboplatin (AUC 6 q3weekly) x 4 + paclitaxel (80 mg/m^2 q1weekly) x 12 + veliparib (50 mg orally twice daily) followed by doxorubicin (60 mg/m^2) + cyclophosphamide (600 mg/m^2) q2weekly or q3weekly based on clinician discretion.
2. Carboplatin (AUC 6 q3weekly) x 4 + paclitaxel (80 mg/m^2 q1weekly) x 12 followed by doxorubicin (60 mg/m^2) + cyclophosphamide (600 mg/m^2) q2weekly or q3weekly based on clinician discretion.
3. Paclitaxel (80 mg/m^2 q1weekly) x 12 followed by doxorubicin (60 mg/m^2) + cyclophosphamide (600 mg/m^2) q2weekly or q3weekly based on clinician discretion.

EBCTCG meta-analysis[2]

A meta-analysis by the EBCTCG demonstrated a lower 10 year risk of recurrence with dose-intense chemotherapy compared with standard-schedule chemotherapy (28.0% vs 31.4%, relative risk (RR) 0.86, 95% CI 0.82 to 0.89; p<0.0001). Dose-intense chemotherapy was also associated with lower 10 year breast cancer mortality rates (18.9% vs 21.3%; RR 0.87, 95% CI 0.83 to 0.92; p<0·0001) and all-cause mortality (22.1% vs 24.8%; RR 0.87, 95% CI 0.83 to 0.91; p<0·0001).

Efficacy

CALGB 40603[3]

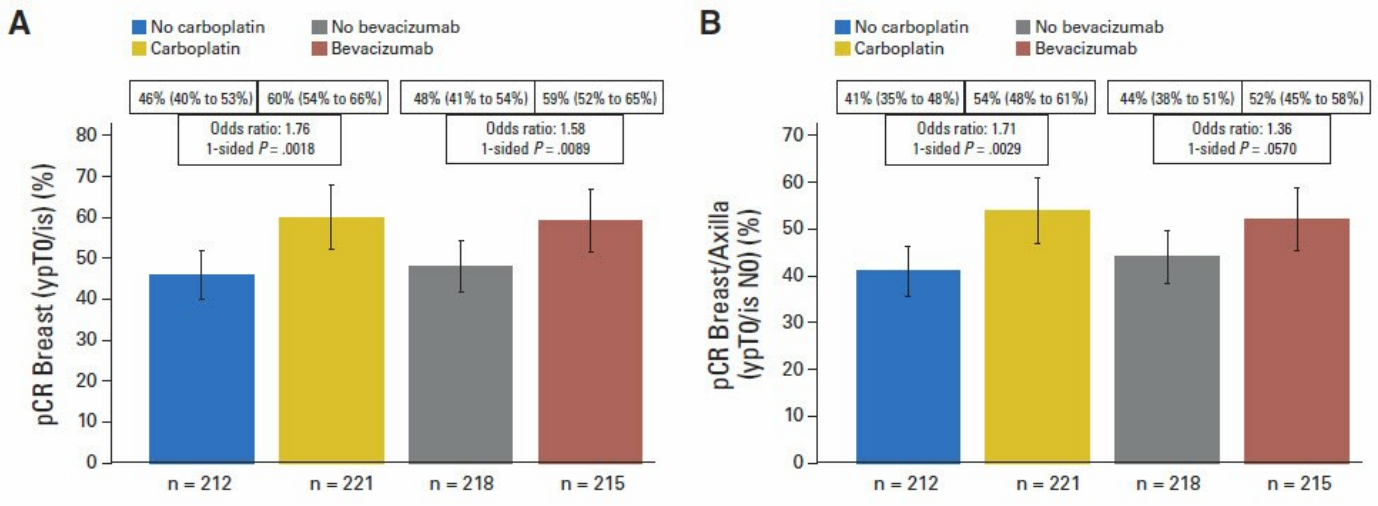
Specifically addressing carboplatin, efficacy was reported in two forms:

- Carboplatin-containing regimens (arms 3 and 4) vs non-carboplatin regimens (arms 1 and 2)
- Individual pCR rates for each arm

The addition of carboplatin significantly increased the pCR breast rate (60% vs 46%, OR 1.76; *p*=0.018) as well as pCR breast/axilla (54% vs 41%, OR 1.71; *p*=0.0029).

Individually, Arm 3 (chemotherapy backbone + carboplatin) had a pCR rate of 53% compared with 42% in Arm 1 (chemotherapy backbone alone), though statistical analysis was not performed on this comparison.

(A) Pathologic complete response (pCR) breast (ypT0/is); (B) pCR breast/axilla (ypT0/is N0)[3]



BrighTness[4]

In the subgroup analysis of BrighTNess, the comparison of dose dense AC (q2weekly) vs standard schedule AC (q3weekly) found pathological complete response rates to be similar between both groups.

	pathological complete response (pCR)[4]		
	Paclitaxel + carboplatin + veliparib	Paclitaxel + carboplatin	Paclitaxel
Dose dense AC	56%	56%	31%
Standard schedule AC	50%	59%	31%

Toxicity

In the CALGB 40603 trial carboplatin-containing regimens (Arm 3 and Arm 4) were associated with a significantly greater incidence of grade 3 to 4 neutropenia (56% and 67% respectively) compared to non-carboplatin regimens (Arm 1 and Arm 2, 22% and 27% respectively).[3] Growth factor support was used only during the ddAC cycles of the study protocol.

Thrombocytopenia was also more frequent in the carboplatin arms (Arm 3: 20%, Arm 4: 26% vs Arm 1: 4%, Arm 2: 3%).[3]

Other toxicities were relatively evenly matched.

Treatment-related toxcity[3] (Grade 3/4)	Arm 1: Sequential weekly paclitaxel + ddAC (%)	Arm 3: Concurrent weekly paclitaxel and carboplatin + ddAC (%)
Leukopenia	12	13
Neutropenia	22	**56**
Thrombocytopenia	4	**20**
Anaemia	0	4
Febrile neutropenia	7	12
Nausea	4	3
Vomiting	2	2
Mucositis	2	1
Diarrhoea	0	2
ALT elevation	0	0
Hypokalaemia	3	6
Peripheral neuropathy	2	7
Fatigue	10	10

Treatment-related toxcity[3] (Grade 3/4)	Arm 1: Sequential weekly paclitaxel + ddAC (%)	Arm 3: Concurrent weekly paclitaxel and carboplatin + ddAC (%)
Pain	3	3

*Note: **Bold** font indicates significant difference in incidence compared with other treatment arms.*

Patients assigned to carboplatin were more likely to miss ≥ 2 doses of weekly paclitaxel (36% vs 16%).

Because of treatment delays and toxicities, only 80% of patients assigned to carboplatin received all four planned doses.[3]

References

1 Citron, M. L., D. A. Berry, C. Cirrincione, et al. 2003. "Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment. J.Clin Oncol. 21(8):1431-1439.

2 Gray, R., R. Bradley, J. Braybrooke, et al. 2019. "Increasing the dose intensity of chemotherapy by more frequent administration or sequential scheduling: a patient-level meta-analysis of 37 298 women with early breast cancer in 26 randomised trials." The Lancet 393(10179):1440-1452.

3 Sikov, W. M., D. A. Berry, C. M. Perou, et al. 2015. "Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 (Alliance)." J Clin Oncol 33(1):13-21.

4 Loibl, S., J. O'Shaughnessy, M. Untch, et al. 2018. "Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): a randomised, phase 3 trial." The Lancet Oncology 19(4):497-509.

5 Senkus, E., S. Kyriakides, S. Ohno, et al. 2015. "Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up." Ann Oncol 26 Suppl 5:v8-30.

6 Sparano, J. A. 2015. "Defining a role and predicting benefit from platinum-based therapy in breast cancer: an evolving story." J Clin Oncol 33(1):1-3.

History

Version 1

Date	Summary of changes
25/08/2022	New multi-indication protocol approved electronically by Medical Oncology reference committee.
30/08/2022	Protocol published on eviQ. Next review in 1 year.

As ID 4102 Breast adjuvant/neoadjuvant AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense replaces two existing approved protocols, their individual History sections are included below for consistency in documentation.

ID 134 Breast adjuvant AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense version 8	
Date	**Summary of changes**
01/09/2006	Patient sheet updated Hepatitis B guidelines added
05/04/2007	Independent evaluation added
09/08/2009	Full review, new dose modifications, transfer to eviQ
10/12/2010	New format to allow for export of protocol information Protocol version number changed to V.2

	Antiemetics and premedications added to the treatment schedule Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations Drug specific information placed behind the drug name link
07/04/2011	Monitoring - Test/Assessments added to Primary Health Care
27/04/2012	Protocol reviewed at Medical Oncology Reference Committee meeting. No changes and next review in 2 years.
30/01/2013	PHC/OMIS transfer completed
09/05/2014	Protocol reviewed by email survey. No change and next review in 2 years. PHC view removed.
18/02/2016	Discussion with Medical Oncology Reference Committee Chairs and protocol to be reviewed every 5 years. Next review due in 3 years.
31/05/2017	Transferred to new eviQ website. Protocol version number increased to V.3. Link to the independent evaluation of the evidence completed in 2006/7 removed from the evidence section as no longer relevant. Antiemetic change: Netupitant/palonosetron combination has replaced aprepitant and a $5HT_3$ receptor antagonist in combination with dexamethasone for all highly emetogenic regimens.
10/05/2018	Haematological dose modifications updated per consensus of the expert clinician group. Version number increased to V.4.
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
08/10/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 30/08/2019. Clinical information updated with PBS expanded indications for GCSF. Next review in 5 years.
04/05/2020	Clinical information updated- FBC nadir cycle 1 removed from blood tests, wording changed from 'each treatment' to 'each cycle'. Version number changed to V.6.
04/09/2020	Biosimilar drug added to clinical information. Version number changed to V.7.
22/01/2021	Evidence updated to include EBCTCG meta-analysis data. Version number changed to V.8.

ID 1869 Breast neoadjuvant AC (DOXOrubicin and CYCLOPHOSPHamide) dose dense version 6	
Date	**Summary of changes**
08/04/2016	New protocol taken to Medical Oncology Reference Committee meeting.
27/07/2016	Approved and published on eviQ.
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.2. Antiemetic change: Netupitant/palonosetron combination has replaced aprepitant and a $5HT_3$ receptor antagonist in combination with dexamethasone for all highly emetogenic regimens.
03/11/2017	Protocol reviewed at Medical Oncology Reference Committee meeting on 3/11/2017. ESMO guidelines added to the evidence. Nil other changes Review protocol in 2 years.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version increase to V.3.
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
08/10/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 30/08/2019. Drug status and clinical information updated with PBS expanded indications for GCSF. Next review in 5 years.
04/09/2020	Biosimilar drug added to clinical information. Version number changed to V.5.
13/08/2021	Protocol reviewed at Medical Oncology Reference Committee meeting. Changed to standalone protocol. "Part 2" removed from title. Annotations to "part 2" removed from treatment schedule. Patient information updated to remove information about "first part" and "second part" of regimen. Note added that this regimen can be used in the adjuvant setting. Indications updated to remove patient population section. Evidence updated. Version increased to V.6.

First approved: 25 August 2022
Review due: 31 December 2023

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/4102
07 Jun 2023

Patient information - Breast cancer adjuvant/neoadjuvant - AC (doxorubicin and cyclophosphamide) dose dense

Patient's name:

Your treatment

This treatment can be given either before or after surgery. The aim of neoadjuvant (before surgery) treatment is to shrink the tumour to make it easier to remove. Your doctor will advise which treatment plan is recommended for you.

The treatment schedule below explains how the drugs for this treatment are given.

AC (doxorubicin and cyclophosphamide) dose dense			
This treatment cycle is repeated every 14 days. You will have 4 cycles. Your doctor will discuss your treatment plan with you.			
Day	**Treatment**	**How it is given**	**How long it takes**
1	**Doxorubicin** (*dox-oh-roo-bi-sin)* **Cyclophosphamide** *(SYE-kloe-FOS-fa-mide)*	By a drip into a vein	About 2 hours
2	**Pegfilgrastim** *(peg-fil-GRA-stim)*	By injection under the skin	About 5 minutes

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime: Night/weekend: Other instructions:

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Treatment with cyclophosphamide

You should drink at least 8 to 10 glasses of fluid (unless you are fluid restricted) for 2 days after treatment with cyclophosphamide. You should also empty your bladder often.

Treatment before surgery (neoadjuvant therapy)

For more information see the eviQ patient information sheet on Anti-cancer therapy before breast cancer surgery (neoadjuvant therapy).

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **G-CSF:** your chemotherapy regimen is called dose dense, which means that you will be having your treatments closer together than usual. To allow the chemotherapy to be given this way you will be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. G-CSF helps to boost your white blood cell count after the chemotherapy. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.**
Redness and itching along vein	• You may get redness and itching along the vein where your chemotherapy is being infused. • This will usually go away within 30 minutes of stopping the injection. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above. Your nurse will check to make sure the drug has not leaked out of the vein.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Urine turning orange or red	• Your urine will turn an orange or red colour. • This is not harmful and should only last for up to 48 hours after treatment.
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.
Bone pain after G-CSF injection	• You may have discomfort or a dull ache in your pelvis, back, arms or legs. • To reduce the pain, take paracetamol before each injection. • **Tell your doctor or nurse as soon as possible if your pain is not controlled.**

Early (onset days to weeks)

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Skin reaction in an area previously treated with radiation therapy (radiation recall)	• In the area that was treated with radiation therapy, your skin may become:
	  ◦ dry, red and itchy
	  ◦ tender and swollen
	• It may also:
	  ◦ peel or blister
	  ◦ form ulcers
	• This usually happens weeks or months after chemotherapy treatment.
	• Avoid wearing tight clothing.
	• Avoid direct sunlight and very hot or cold temperatures.
	• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.

Nail changes	• Your nails may:
	  ◦ grow more slowly
	  ◦ become darker
	  ◦ develop ridges or white lines
	  ◦ become brittle and flaky
	• In some cases, you may lose your nails completely.
	• Keep your nails clean and short.
	• Avoid things like biting your fingernails, getting a manicure, pedicure or false nails.
	• Wear gloves when you wash the dishes, work in the garden, or clean the house.

Delayed (onset months to years)	
Menopausal symptoms	• You may get: ◦ hot flushes or night sweats ◦ mood changes ◦ vaginal dryness ◦ irregular or no periods. • You may also: ◦ have trouble sleeping ◦ find sex painful or lose interest in sex • These symptoms may go away after treatment, or the menopause may be permanent. • If you have sex you should use contraception as there is still a risk of pregnancy. Talk to your doctor about what form of contraception is right for you. • Talk to your doctor or nurse about ways to manage these symptoms.
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems can occur months to years after treatment. • Tell your doctor if you have a history of heart problems or high blood pressure. • Before or during treatment, you may be asked to have a test to see how well your heart is working. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

General advice for people having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - Chemotherapy safety at home.

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support.

Breast cancer information

- Australasian Lymphology Association – lymphoedema.org.au
- Australasian Menopause Society – menopause.org.au
- Breast Cancer Network Australia – bcna.org.au
- National Breast Cancer Foundation – nbcf.org.au
- YWCA Encore breast cancer exercise program – ywcaencore.org.au

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au

- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- CHILL Cancer related hair loss – scalpcooling.org
- eviQ Cancer Treatments Online – eviQ.org.au
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information – patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer – targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

Additional notes:

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The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/4102
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