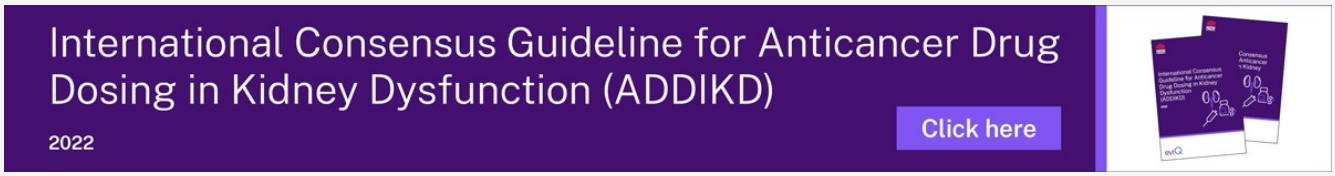
Breast adjuvant/neoadjuvant trastuzumab three weekly

ID: 4115 v.1 **Endorsed** Essential Medicine List

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 trastuzumab subcutaneous
- Anti-cancer therapy before breast cancer surgery (neoadjuvant therapy)

Treatment schedule - Overview

Cycle 1

Drug	Dose	Route	Day
Trastuzumab	8 mg/kg (loading dose only)	IV infusion *	1

Cycle 2 to 17

Drug	Dose	Route	Day
Trastuzumab	6 mg/kg (subsequent doses)	IV infusion *	1

*Trastuzumab is available as a subcutaneous formulation administered at a dose of 600 mg every three weeks. Subcutaneous trastuzumab has a similar safety profile to intravenous trastuzumab and is non-inferior in terms of pharmacokinetic profile and efficacy and therefore is a valid alternative route of administration compared to standard intravenous trastuzumab. Link to Breast trastuzumab subcutaneous protocol

Frequency: 21 days

Cycles: 17 (combined total adjuvant and neoadjuvant treatment)

Notes:

- Consider the Breast metastatic trastuzumab three weekly protocol for inflammatory breast cancers
- Commence trastuzumab sequentially after anthracyclines and concurrently with taxane chemotherapy. Concurrent trastuzumab and an anthracycline has a higher risk of cardiac toxicity and should only be considered in patients with LVEF of 55% or more

Drug status: Trastuzumab is PBS authority

Cost: ~ $420 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

Day 1		
Trastuzumab	8 mg/kg (IV infusion)	in 250 mL sodium chloride 0.9% over 90 minutes (loading dose; cycle 1 only)*

Cycle 2 to 17

Day 1		
Trastuzumab	6 mg/kg (IV infusion)	in 250 mL sodium chloride 0.9% over 30 minutes (if the initial loading dose was well tolerated)*

*Trastuzumab is available as a subcutaneous formulation administered at a dose of 600 mg every three weeks. Subcutaneous trastuzumab has a similar safety profile to intravenous trastuzumab and is non-inferior in terms of pharmacokinetic profile and efficacy and therefore is a valid alternative route of administration compared to standard intravenous trastuzumab. Link to Breast trastuzumab subcutaneous protocol

Frequency: 21 days

Cycles: 17 (combined total adjuvant and neoadjuvant treatment)

Indications and patient population - Adjuvant

Indications:

- continuing treatment for HER-2 positive early breast cancer following concurrent chemotherapy
  - HER-2 positive as demonstrated by in situ hybridisation (ISH).

Exclusion:

- left ventricular ejection fraction (LVEF) of 45% or less.

Indications and patient population - Neoadjuvant

Indications:

- neoadjuvant treatment for operable HER-2 positive breast cancer in combination with chemotherapy
  - HER-2 positive as demonstrated by in situ hybridisation (ISH).

Exclusion:

- left ventricular ejection fraction (LVEF) of 45% or less.

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
Hypersensitivity/infusion related reaction	Although hypersensitivity with trastuzumab is common, severe hypersensitivity reactions are uncommon. Use with caution in patients with dyspnoea at rest from pulmonary/cardiac conditions as increased risk of infusion related symptoms.
Premedication	Premedication only required if patient has had a previous hypersensitivity reaction and should be based on clinical judgement.
Emetogenicity MINIMAL	No antiemetics should be routinely administered before treatment in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cardiac toxicity associated with HER-2 directed agents	Patients receiving HER-2 directed agents are at an increased risk of cardiotoxicity e.g. asymptomatic decrease in the left ventricular ejection fraction (LVEF) and congestive heart failure (CHF). In patients with a LVEF less than 45% and/or symptomatic heart failure HER-2 directed therapy should be avoided, except in the metastatic setting when breast cancer is life-threatening and where a cardiologist is also involved. Concurrent anthracycline and HER-2 directed therapy is not recommended for extended periods of time. Baseline and 3 monthly cardiac function tests are required during treatment. In the metastatic setting, after the first 12 months of therapy, if there are no cardiac complications, the frequency of cardiac assessments may be reduced at the discretion of the treating clinician unless there has been recent exposure to anthracyclines. Read more about cardiac toxicity associated with HER-2 targeted agents
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page
Blood tests	Routine blood tests are not required for trastuzumab monotherapy. If trastuzumab is given in combination with chemotherapy, refer to the blood tests required for that chemotherapy regimen.
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).

Renal impairment
No dose modifications necessary

Hepatic impairment
No dose modifications necessary

Cardiac toxicity	
Consider referral to a cardiologist if any of the following occur	
LVEF less than 45%	Delay trastuzumab. Repeat LVEF assessment within 3 weeks Consider discontinuing trastuzumab if LVEF less than 45% is confirmed
Symptomatic heart failure	Consider discontinuing trastuzumab

Missed doses of trastuzumab	
By 6 weeks or less	No dose modification necessary. Give trastuzumab as soon as possible, i.e. do not wait until the next planned cycle
By more than 6 weeks	Reload trastuzumab with a dose of 8 mg/kg Subsequent doses of 6 mg/kg should then be given every 3 weeks, according to the previous cycle However, if the delay was due to cardiac toxicity, clinician may choose not to reload the patient

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*

Trastuzumab		
	Interaction	**Clinical management**
Cardiotoxic drugs (e.g. anthracyclines cyclophosphamide)	Additive cardiotoxicity	Monitor cardiac function closely in patients who have previously been treated with cumulatively cardiotoxic drugs
Paclitaxel	Increased toxicity of trastuzumab possible due to reduced clearance	Monitor for trastuzumab toxicity (esp. cardiotoxicity)

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 (initial); 1 hour (subsequent)

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of treatment.

Any toxicity grade 2 or greater may require delay 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

Administer premedication only if previous hypersensitivity reaction.

Treatment - Time out

Trastuzumab

- Trastuzumab is incompatible with glucose solutions. Ensure IV administration sets are flushed with sodium chloride 0.9% pre and post administration.

Initial infusion - administer trastuzumab:

- via IV infusion over 90 minutes
- observe patient for fever and chills or other infusion-related symptoms
- flush with ~50 mL of sodium chloride 0.9%
- stop infusion at first sign of reaction:
  - if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate
  - for severe reactions seek medical assistance immediately and do not restart infusion
- educate the patient about the possibility of delayed infusion-related symptoms.

Subsequent infusions - administer trastuzumab:

- if no previous hypersensitivity reaction administer via IV infusion over 30 minutes
- observe patient for fever and chills or other infusion-related symptoms
- flush with ~ 50 mL of sodium chloride 0.9%
- stop infusion at first sign of reaction:
  - if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate
  - for severe reactions seek medical assistance immediately and do not restart infusion
- educate the patient about the possibility of delayed infusion-related symptoms.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Discharge information

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)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Flu-like symptoms	
Headache	

Early (onset days to weeks)	
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue

Late (onset weeks to months)	
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Delayed (onset months to years)	
Cardiotoxicity	Cardiotoxicity is a well recognised complication of HER-2 directed agents (e.g. trastuzumab, trastuzumab emtansine, pertuzumab). Mechanistically distinct from anthracycline-induced cardiotoxicity, it typically manifests as an asymptomatic decrease in the left ventricular ejection fraction (LVEF) and less commonly as congestive heart failure (CHF). Read more about cardiac toxicity associated with HER-2 targeted agents

Evidence - Adjuvant

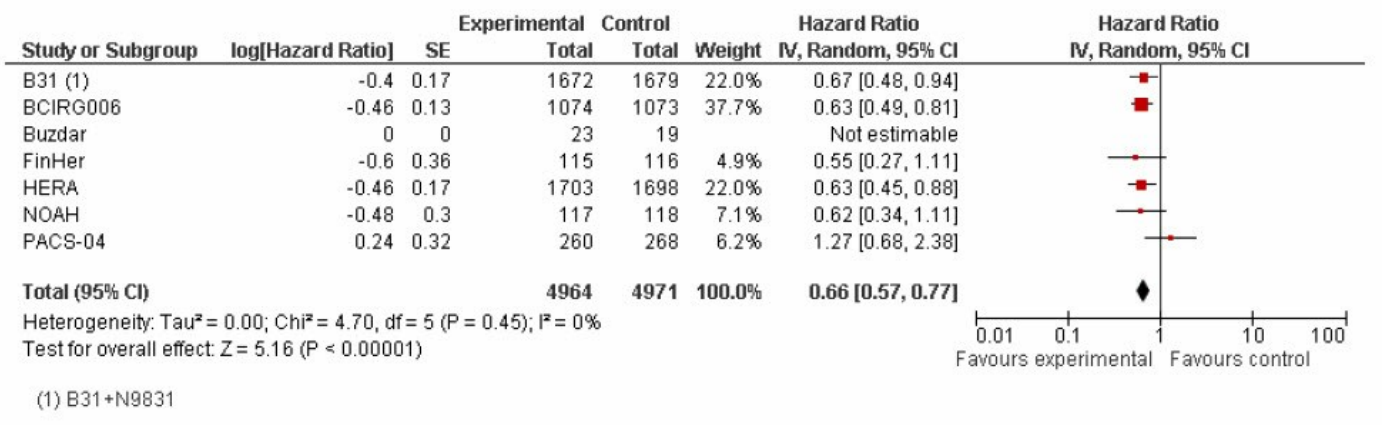
The evidence supporting the use of this regimen comes from a number of large phase III randomised trials comparing the addition of trastuzumab to standard adjuvant chemotherapy (and/or neoadjuvant chemotherapy) to the same chemotherapy regimen without trastuzumab. The Cochrane Breast Cancer Group have published a systematic review summarising the efficacy and safety data from eight randomised controlled trials enrolling 11991 women with HER-2 positive early breast cancer.[1] 7020 women were randomised to a trastuzumab-containing arm and 4971 to a treatment without trastuzumab. The primary endpoints for the review were disease-free survival (DFS) and overall survival (OS) using intention to treat (ITT) analysis. Secondary endpoints included cardiac toxicity, other toxicities, treatment-related deaths and brain metastases as first site of relapse.

Efficacy

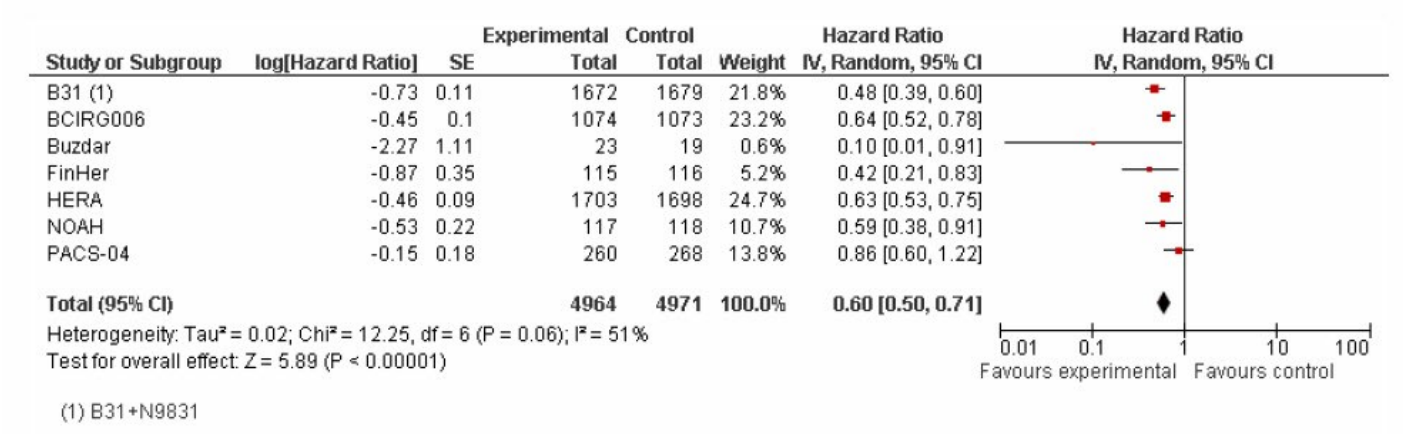
The addition of trastuzumab to standard chemotherapy significantly improved OS and DFS. The combined hazard ratio (HR) for OS was 0.66 (95% confidence interval (CI) 0.57 to 0.77, P < 0.00001). The combined HR for DFS was 0.60 (95% CI 0.50 to 0.71, P < 0.00001). Studies that administered trastuzumab concurrently or sequentially did not differ significantly in efficacy.[1]

Five trials reported on brain metastases as the site of first relapse. The risk of brain metastases was significantly higher in patients receiving trastuzumab (2.3% of 3120 patients) compared with patients receiving chemotherapy alone (1.3% of 3761 patients); RR 1.75; 90% CI 1.29 to 2.38, *p*=0.002). [1]

OS for all studies[1]



DFS for all studies[1]



Toxicity

Congestive heart failure was reported in 2.5% of 5471 patients in the trastuzumab group and 0.4% in the control group (Risk Ratio (RR) 5.11; 90% CI 3.00 to 8.72; $p < 0.00001$). Decline in left ventricular ejection fraction (LVEF) occurred in 11.2% of 4147 patients in the trastuzumab group and 5.6% of 3792 patients in the control group (RR 1.83; 90% CI 1.36 to 2.47, $p = 0.0008$). Trastuzumab was not associated with a higher risk of neutropenia, neutropenic fever or anaemia.[1]

Evidence - Neoadjuvant

The evidence for this protocol comes from a series of phase II and III trials demonstrating that the addition of trastuzumab to neoadjuvant chemotherapy improves pathologic complete response (pCR) rates. The phase III trials have demonstrated that adding trastuzumab to neoadjuvant chemotherapy improves event free survival but an OS benefit has not been established. In the 3 trials listed below anthracyclines were given concurrently with trastuzumab but eligible patients in each trial had a baseline LVEF $\geq$ 55%.

Efficacy

In the **GeparQuinto** trial, 307 patients with HER-2 positive operable or locally advanced breast cancer received neoadjuvant chemotherapy with 4 cycles of EC (epirubicin plus cyclophosphamide) every 3 weeks followed by 4 cycles of docetaxel every 3 weeks. Patients received concurrent trastuzumab (8 mg/kg IV loading dose followed by 6 mg/kg) every 3 weeks from cycle 1 of EC. Following surgery all patients completed trastuzumab treatment for 1 year. The pathological complete response rate (pCR) was 30.3% and 63.6% had breast conserving surgery.[2]

In the **NOAH** trial, 228 patients with HER-2 positive locally advanced or inflammatory breast cancer were randomly assigned to neoadjuvant trastuzumab concurrent with chemotherapy followed by adjuvant trastuzumab (to complete one year of treatment) or neoadjuvant chemotherapy alone. The neoadjuvant chemotherapy regimen consisted of 3 cycles of AT (doxorubicin plus paclitaxel) every 3 weeks, followed by 4 cycles of paclitaxel every 3 weeks, and then 3 cycles of CMF (cyclophosphamide, methotrexate, and fluorouracil) every 4 weeks. Patients receiving neoadjuvant trastuzumab compared to chemotherapy alone had a significantly improved pCR rate (43% v 23%) and three-year event-free survival (71% v 56%). With median follow-up of 3.2 years, there was no significant difference in OS (87% v 79%).[3]

In the **GeparQuattro** trial, the subset of 445 HER-2 positive patients with operable or locally advanced breast cancer received neoadjuvant trastuzumab concurrent with one of three randomly assigned neoadjuvant chemotherapy regimens, followed by adjuvant trastuzumab to complete one year of therapy. All patients received 4 cycles of epirubicin and cyclophosphamide then were randomized to either 4 cycles of docetaxel, 4 cycles of docetaxel concomitantly with capecitabine, or 4 cycles of docetaxel followed by 4 cycles of capecitabine. The pCR rate was 31.7% and the breast conserving surgery rate was 63%.[4]

A meta-analysis including 5 trials and 515 patients randomised to trastuzumab plus neoadjuvant chemotherapy or neoadjuvant chemotherapy alone found probability of achieving pCR was higher for the trastuzumab plus chemotherapy arm (RR 1.85, 95% CI 1.39-2.46; $p<0.001$) but there was no significant difference in rates of breast conserving surgery.[5]

Toxicity

Cardiotoxicity rates were low in these trials but all patients had LVEF ≥ 55% at baseline. Of the 307 patients receiving trastuzumab in the GeparQuinto trial, there was 1 case of CHF (0.3%) and 4 patients (1.4%) had an LVEF < 50% and a decline in LVEF of > 10 points from baseline.[2] In the NOAH trial, 2 patients receiving trastuzumab developed NYHA class III CHF (1.7%) and 2 had asymptomatic grade 2 declines in LVEF.[3] In the trastuzumab treated patients in GeparQuattro, CHF was reported in 1 patient and LVEF decline >10% in 2 patients.[4]

The meta-analysis concluded that the addition of trastuzumab to neoadjuvant chemotherapy did not increase the incidence of neutropenia, neutropenic fever or cardiac adverse events. Two out of 217 patients (0.9%) in the trastuzumab arms developed congestive heart failure (CHF) compared to none in the chemotherapy alone arms.[5]

References

1 Moja, L., L. Tagliabue, S. Balduzzi, et al. 2012. "Trastuzumab containing regimens for early breast cancer." Cochrane Database Syst Rev 4:CD006243.

2 Untch, M., S. Loibl, J. Bischoff, et al. 2012. "Lapatinib versus trastuzumab in combination with neoadjuvant anthracycline-taxane-based chemotherapy (GeparQuinto, GBG 44): a randomised phase 3 trial." Lancet Oncol 13(2):135-144.

3 Gianni, L., W. Eiermann, V. Semiglazov, et al. 2010. "Neoadjuvant chemotherapy with trastuzumab followed by adjuvant trastuzumab versus neoadjuvant chemotherapy alone, in patients with HER2-positive locally advanced breast cancer (the NOAH trial): a randomised controlled superiority trial with a parallel HER2-negative cohort." Lancet 375(9712):377-384.

4 Untch, M., M. Rezai, S. Loibl, et al. 2010. "Neoadjuvant treatment with trastuzumab in HER2-positive breast cancer: results from the GeparQuattro study." J Clin Oncol 28(12):2024-2031.

5 Valachis, A., D. Mauri, N. P. Polyzos, et al. 2011. "Trastuzumab combined to neoadjuvant chemotherapy in patients with HER2-positive breast cancer: a systematic review and meta-analysis." Breast 20(6):485-490.

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 2 years.

As ID 4115 Breast adjuvant/neoadjuvant trastuzumab three weekly replaces two existing approved protocols, their individual History sections are included below for consistency in documentation.

ID 127 Breast adjuvant trastuzumab three weekly version 6	
Date	**Summary of changes**
28/03/2007	Dose vial recommendations added.
07/12/2007	Option of rapid administration added.
04/08/2009	Reviewed and transferred 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.
08/03/2011	Febrile neutropenia alert removed from the PHC view.
27/04/2012	Protocol reviewed at Medical Oncology Reference Committee meeting.

	Evidence and cardiac toxicity clinical information updated with Cochrane. Review 2012 Next review in 2 years.
08/05/2014	Safe handling precautions (waste) removed.
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.
24/03/2017	Consensus of the Medical Oncology Reference Committee (via email discussion) to remove observation time frames from all trastuzumab protocols and replace with the statement "Observe patient for fever and chills or other infusion-related symptoms" as per current trastuzumab product information. Individual institutions may still implement/maintain local policies on monitoring time frames if they choose to do so.
28/03/2017	Per consensus at the 2016 eviQ Breast Reference Committee meeting, retrospectively added "Caution: left ventricular ejection fraction (LVEF) of 45% or less" to the Indications and patient population section in all trastuzumab protocols.
31/05/2017	Transferred to new eviQ website. Version number changed to V.3.
30/01/2019	Link to ID 1875 Breast subcutaneous trastuzumab protocol added in related pages and treatment schedule sections.
08/10/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 30/08/2019. LVEF of 45% or less changed from caution to exclusion. Dose modification missed dose cutoff changed to 6 weeks, cardiac toxicity dose modification added. Version number changed to V.4. Next review in 5 years.
04/05/2020	Treatment cycles updated to '17 (up to a total of 17 cycles including any prior neoadjuvant or adjuvant treatment)'. Biosimilar trastuzumab added to clinical information. Approximate treatment time changed to 2 hours (initial), 1 hour (subsequent). Version number changed to V.5
16/11/2021	Pulmonary toxicity added to side effects. Version number changed to V.6.

ID 1323 Breast neoadjuvant trastuzumab three weekly version 5

Date	Summary of changes
27/04/2012	New protocol taken to Medical Oncology Reference Committee meeting. Next review in 1 year.
25/03/2013	Approved and published on eviQ.
30/06/2013	Protocol reviewed by committee via email survey. No changes and next review in 2 years.
08/05/2014	Safe handling precautions (waste) removed.
22/06/2015	Protocol reviewed electronically by Medical Oncology Reference committee. No changes and next review in 2 years.
24/03/2017	Consensus of the Medical Oncology Reference Committee (via email discussion) to remove observation time frames from all trastuzumab protocols and replace with the statement "Observe patient for fever and chills or other infusion-related symptoms" as per current trastuzumab product information. Individual institutions may still implement/maintain local policies on monitoring time frames if they choose to do so.
28/03/2017	Per consensus at the 2016 eviQ Breast Reference Committee meeting, retrospectively added "Caution: left ventricular ejection fraction (LVEF) of 45% or less" to the Indications and patient population section in all trastuzumab protocols.
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.2.
03/11/2017	Reviewed by Medical Oncology Reference Committee. No changes. Review in 5 years.
30/01/2019	Link to ID 1875 Breast subcutaneous trastuzumab protocol added in related pages and treatment schedule sections.
08/10/2019	Treatment schedule total duration changed from 52 weeks to 17 cycles. LVEF of 45% or less changed from caution to exclusion. Dose modification missed dose cutoff changed to 6 weeks, cardiac toxicity dose modification added. Version number changed to V.3.
04/05/2020	Biosimilar trastuzumab added to clinical information. Approximate treatment time changed to 2 hours (initial), 1 hour (subsequent). Version number changed to V.4.

16/11/2021	Pulmonary toxicity added to side effects. Version number changed to V.5.

First approved: 25 August 2022
Review due: 31 December 2024

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/4115
08 Jun 2023

Patient information - Breast cancer adjuvant/neoadjuvant - Trastuzumab three weekly

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 drug for this treatment is given.

Trastuzumab

This treatment cycle is repeated every 21 days. You will have 17 cycles (including in combination with chemotherapy). Your doctor will discuss your treatment plan with you.

Day	Treatment	How it is given	How long it takes
1	**Trastuzumab** (*tras-TOOZ-ue-mab*)	By a drip into a vein	About 2 hours for the first treatment. If no reactions, subsequent treatment may be given over a shorter amount of time e.g. 1 hour

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

You may need to have blood tests while you are receiving this treatment. Your doctor or nurse will tell you when to have these blood tests.

Treatment before surgery (neoadjuvant therapy)

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

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)	
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • Tell your doctor or nurse if you get any of the symptoms listed above. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**

Early (onset days to weeks)	
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.**

Late (onset weeks to months)	
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

Delayed (onset months to years)	
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

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.
- 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.

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

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