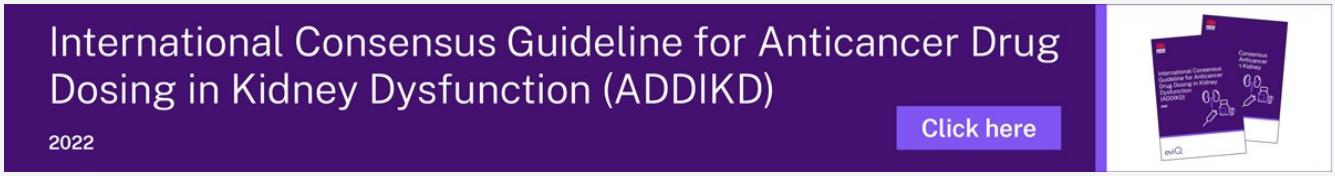
Breast adjuvant neratinib SUPERSEDED

ID: 3656 v.3 **Superseded**

This protocol has been superseded due to the availability of superior alternatives and no clinical need.

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.



Treatment schedule - Overview

Drug	Dose	Route
Neratinib	240 mg ONCE a day *	PO

*6 x 40 mg tablets

Continuous treatment for 1 year

Notes:
Antidiarrhoeal prophylaxis is recommended.

Commence within one year of completing trastuzumab.

Concurrent endocrine therapy for hormone receptor-positive patients is standard of care.

Drug status: Neratinib is TGA registered but not PBS listed for this indication

Neratinib is available as **40 mg** tablets

Cost: not available

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.*

Continuous treatment		
Neratinib	240 mg (PO)	ONCE a day (preferably in the morning) with food*

*6 x 40 mg tablets

Antidiarhhoeal prophylaxis is recommended.

Concurrent endocrine therapy for hormone receptor-positive patients is standard of care.

Continuous treatment for 1 year

Indications and patient population

Indications:

- Extended adjuvant treatment for stage I-III ER receptor positive HER-2 positive breast cancer following chemotherapy and one year of neoadjuvant or adjuvant trastuzumab therapy.

Cautions:

- Left ventricular ejection fraction (LVEF) of 45 % or less
- Any condition that increases the risk of serious dehydration or biochemical disturbance associated with severe diarrhoea e.g. elderly, frail or chronic gastrointestinal disorder with associated diarrhoea.

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Diarrhoea	Antidiarrhoeal prophylaxis is recommended during the first two months of treatment and should be initiated with the first dose. Antidiarrhoeals (e.g. loperamide) should be taken as directed in the table below, titrating to 1-2 bowel movements per day.

Time on treatment	Loperamide dose	Frequency
Weeks 1 - 2 (days 1 - 14)	4 mg	THREE times a day
Weeks 3 - 8 (days 15 - 56)	4 mg	TWICE a day
Weeks 9 - 52 (days 57 - 365)	4 mg	as required

	Additional anti-diarrhoeal medications may be required if diarrhoea is refractory. Dose interruption and reductions may also be required. For more information see dose modifications section. Patients at risk of serious dehydration or biochemical disturbance from severe diarrhoea e.g. elderly, frail or chronic gastrointestinal disorder with associated diarrhoea should be closely monitored. Read more about treatment induced diarrhoea
Blood tests	FBC, EUC and LFTs at baseline. Monitor LFTs at week 1, then monthly for the first 3 months and then every 6 weeks or as clinically indicated. Monitor FBC monthly for the first 6 months and EUCs every 3 months then as clinically indicated.
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).

The dose modifications are based on the neratinib product information

Neratinib dose reduction schedule	
Recommended starting dose	240 mg daily
First dose reduction	200 mg daily
Second dose reduction	160 mg daily
Third dose reduction	120 mg daily

*If further dose reduction below 120 mg daily is required, discontinue neratinib.

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	No dose modifications necessary
less than 30	No dose modification information available

Hepatic impairment	
Hepatic dysfunction at baseline	

Hepatic impairment	
Mild to moderate	No dose modifications necessary
Severe	Neratinib not recommended
Hepatoxicity during treatment (Hepatic impairment (elevated ALT and AST) +/- Bilirubin)	
Grade 3 ALT elevation or bilirubin	Withhold treatment 1st occurrence – if toxicity resolves to Grade ≤ 1 within 3 weeks, resume neratinib at the next lower dose level 2nd occurrence – permanently discontinue neratinib
Grade 4 ALT elevation or bilirubin	Permanently discontinue neratinib

Diarrhoea	
Grade 1, Grade 2 or Grade 3	Treat diarrhoea Once resolved to Grade 1 or less or baseline, start loperamide 4 mg with each subsequent treatment
Any grade with complicated features e.g. dehydration, fever, hypotension, renal failure or Grade 3 or Grade 4 neutropenia Or Grade 2 lasting 5 days or longer (despite optimal medical treatment) Or Grade 3 lasting longer than 2 days (despite optimal medical treatment)	Treat diarrhoea Withhold treatment If diarrhoea resolves to Grade 0 - 1 in one week or less, then resume treatment at the same dose. If diarrhoea resolves to Grade 0 - 1 in longer than one week, then resume treatment at next lower dose level Once resolved to Grade ≤ 1 or baseline, start loperamide 4 mg with each subsequent treatment
Grade 4	Permanently discontinue neratinib
Diarrhoea recurs to ≥Grade 2 at 120 mg per day	Permanently discontinue neratinib

All other adverse effects	
Grade 1 or 2	Treat symptoms. No dose modification necessary
Grade 3	Treat symptoms Withhold treatment until recovery to Grade ≤ 1 or baseline within 3 weeks of stopping treatment Resume neratinib at the next lower dose level
Grade 4	Permanently discontinue neratinib

Cease neratinib if any of the following occur
• failure to recover to Grade 0 or Grade 1 from treatment related toxicity • toxicities resulting in a treatment delay of greater than 3 weeks • if unable to tolerate dose of 120 mg daily

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*

Neratinib		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. amiodarone, aprepitant, azole antifungals, ritonavir, macrolides, grapefruit juice, Seville oranges etc.)	Increased toxicity of neratinib possible due to reduced clearance	Avoid combination or monitor for neratinib toxicity. If concomitant use of a CYP3A4 inhibitor cannot be avoided, reduce neratinib dose to 40 mg daily with a strong CYP3A4 inhibitor or 200 mg daily with a moderate CYP3A4 inhibitor. If the strong or moderate CYP3A4 inhibitor is ceased, increase neratinib dose to previous 240 mg dose.
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of neratinib due to increased clearance	Avoid combination or monitor for decreased effect of neratinib. If concomitant use of a strong or moderate CYP3A4 inducer cannot be avoided, increase neratinib dose to 320 mg daily. If the strong or moderate CYP3A4 inhibitor is ceased, reduce neratinib dose to previous 240 mg dose.
Drugs metabolised by CYP3A (e.g. hormonal contraceptives)	Reduced efficacy of CYP3A substrates possible due to increased clearance	Avoid combination. Consider alternative contraception to hormonal contraceptives
Drugs undergoing P-gp-mediated elimination (e.g. dabigatran, digoxin, loperamide, phenytoin etc.)	Increased effects/toxicity of these drugs possible due to inhibition of P-gp by neratinib resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity of the interacting drugs
H2 blockers (e.g. famotidine, ranitidine etc.) and proton pump inhibitors (e.g.omeprazole, pantoprazole, rabeprazole etc.) and antacids	Reduced efficacy of neratinib due to decreased absorption when gastric acid secretion suppressed (neratinib requires acidic environment for absorption)	Avoid combination H2 blockers may be used if taken at least 2 hours after or 10 hours before neratinib Antacids may be used if taken at least 3 hours before neratinib

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.

Administration

This is a continuous oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each treatment.

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

Treatment - Time out

Neratinib

- administer orally ONCE a day (preferably in the morning)
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken with food

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Discharge information

Neratinib tablets

- Neratinib tablets with written instructions on how to take them

Antiemetics

- Antiemetics if required or prescribed.

Antidiarrhoeals

- Antidiarrhoeals as 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)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

Early (onset days to weeks)	
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
Headache	

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
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

This protocol has been superseded due to the availability of superior alternatives and no clinical need.

The evidence supporting this protocol is provided by a large phase III multicentre international randomised trial (ExteNET) involving 2840 patients comparing extended adjuvant therapy with neratinib vs placebo after completion of neoadjuvant or adjuvant trastuzumab in patients with stage 1-3 HER-2 positive early breast cancer.[1]

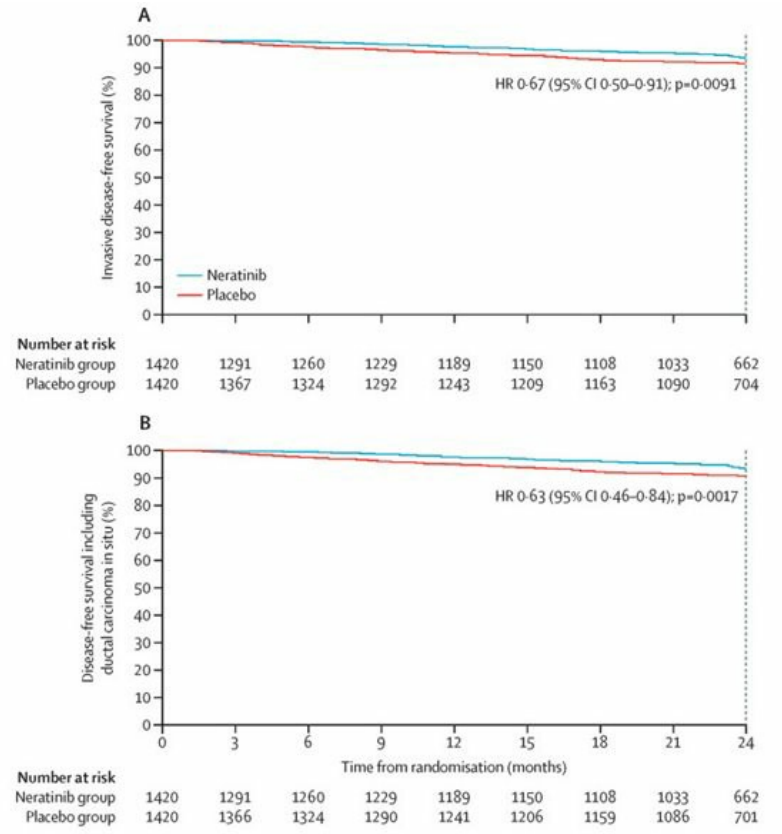
Between July 2009 and October 2011, 1420 patients were randomised to receive neratinib at 240 mg daily for 12 months and 1420 patients were randomised to receive placebo for 12 months.

The primary end point was invasive disease-free survival at 2 years, and secondary end points were disease free survival including ductal carcinoma in situ (DCIS), distant disease free survival, time to distant recurrence, cumulative incidence of CNS recurrences, overall survival and safety.

Efficacy

The 2-year invasive disease-free survival rate was 93.9% in the neratinib group and 91.6% in the placebo group (HR 0.67, 95% CI 0.50 – 0.91, p=0.0091).[1]

Kaplan-Meier curves for 2-year invasive disease-free survival (A) and disease-free survival including ductal carcinoma in situ (B) in the intention-to-treat population[1]



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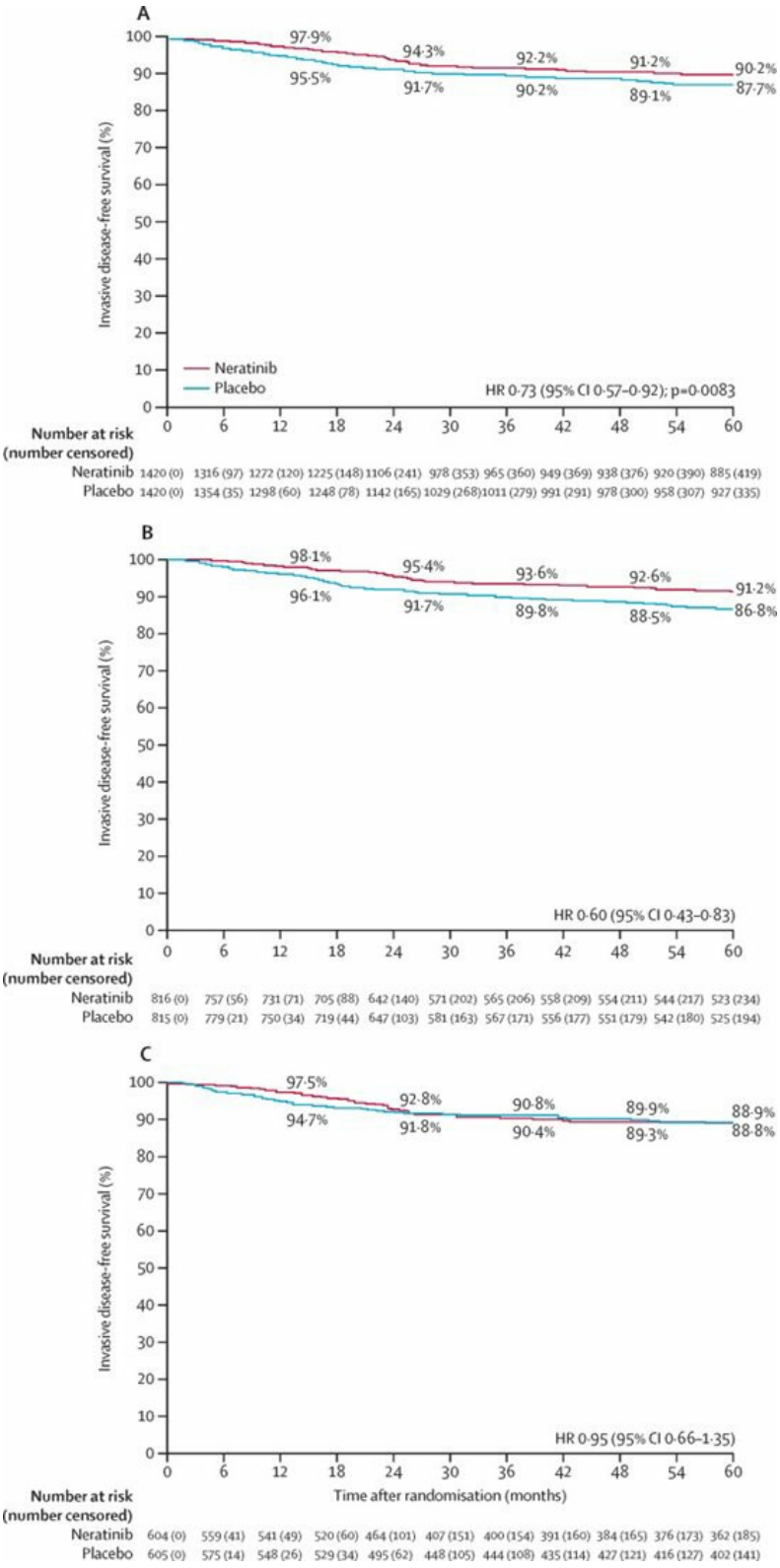
The 5-year invasive disease-free survival rates were 90.2% in the neratinib group compared with 87.7% in the placebo group (HR 0.73, 95% CI, 0.57 – 0.92, p = 0.0083). Secondary endpoints, such as distant disease-free survival and time to distant recurrence were not met.[2]

In the updated analysis, for the subgroup of patients with hormone receptor-positive disease, the HR for invasive disease-free survival in the neratinib group compared with the placebo group was 0.60 (95% CI, 0.43 – 0.83), whereas for the patients with hormone receptor-negative disease, the HR for invasive disease-free survival was 0.95 (95% CI, 0.66 – 1.35).

Kaplan-Meier curves for 5-year invasive disease-free survival for A) ITT population, B) patients with hormone receptor-positive breast cancer and C) hormone receptor-negative breast cancer[2]



For the subgroup of patients with hormone-receptor positive disease who initiated treatment ≤ 1 year post-trastuzumab, the 8-year overall survival rate in the neratinib group was 91.5% (95% CI, 88.9 - 93.5) vs 89.4% (95% CI, 86.6 - 91.6) in the placebo group (HR=0.79, 95% CI, 0.55 – 1.13).[3]

Toxicity

Diarrhoea was the most common adverse event, commonly occurring early (after a median of 8 days). Grade 3 diarrhoea occurred in 561 (40%) of patients treated with neratinib and 23 (2%) of patients treated with placebo. Diarrhoea led to dose reductions in 372 (26%) of patients in the neratinib group, with 20 (1%) patients requiring hospital admission and 237 (17%) requiring drug discontinuation. Prophylactic antidiarrhoeal medication was not stipulated in the protocol.[1]

Toxicity[1]

	Neratinib group (n=1408)			Placebo group (n=1408)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Diarrhoea	781 (55%)	561 (40%)	1 (<1%)	476 (34%)	23 (2%)	0
Nausea	579 (41%)	26 (2%)	0	301 (21%)	2 (<1%)	0
Fatigue	359 (25%)	23 (2%)	0	276 (20%)	6 (<1%)	0
Vomiting	322 (23%)	47 (3%)	0	107 (8%)	5 (<1%)	0
Abdominal pain	314 (22%)	24 (2%)	0	141 (10%)	3 (<1%)	0
Headache	269 (19%)	8 (1%)	0	269 (19%)	6 (<1%)	0
Upper abdominal pain	201 (14%)	11 (1%)	0	93 (7%)	3 (<1%)	0
Rash	205 (15%)	5 (<1%)	0	100 (7%)	0	0
Decreased appetite	166 (12%)	3 (<1%)	0	40 (3%)	0	0
Muscle spasms	157 (11%)	1 (<1%)	0	44 (3%)	1 (<1%)	0
Dizziness	143 (10%)	3 (<1%)	0	125 (9%)	3 (<1%)	0
Arthralgia	84 (6%)	2 (<1%)	0	158 (11%)	4 (<1%)	0

Data are n (%). Full adverse events are presented in the appendix (p 16).

Table 3: **Treatment-emergent adverse events occurring in at least 10% of patients in the safety population**

References

1 Chan, A., S. Delaloge, F. A. Holmes, et al. 2016. "Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial." Lancet Oncol 17(3):367-377.

2 Martin, M., F. A. Holmes, B. Ejlertsen, et al. 2017. "Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial." Lancet Oncol 18(12):1688-1700.

3 Chan, A., B. Moy, J. Mansi, et al. 2020. "Final efficacy results of neratinib in HER2-positive hormone receptor-positive early-stage breast cancer from the phase III ExteNET trial." Clinical Breast Cancer.

History

Version 3

Date	Summary of changes
05/08/2022	Protocol reviewed at Medical Oncology Reference Committee meeting. Protocol superseded due to the availability of superior alternatives and no clinical need. Version number changed to V.3. Next review in 2 years.

Version 2

Date	Summary of changes
19/11/2020	Protocol reviewed electronically by Medical Oncology Reference Committee. Updated overall survival results added. Version number changed to V.2. Next review in 2 years.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.

Version 1

Date	Summary of changes
30/08/2019	New protocol taken to Medical Oncology Reference Committee
17/10/2019	Protocol approved and published. Review 1 year.

First approved: 30 August 2019
Last reviewed: 5 August 2022
Review due: 31 December 2026

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/3656
19 Jun 2023

Patient information - Breast cancer adjuvant - Neratinib

Patient's name:

Your treatment

It is important to understand that neratinib is not a traditional chemotherapy drug and has a different way of working. It works by targeting the cancer cells to stop them growing and spreading.

Neratinib

The treatment schedule below explains how the drug for this treatment is given.This treatment is continuous. Your doctor will advise you how long to take the treatment for.

Day	Treatment	How it is given
Continuous	**Neratinib** (*ne-RA-ti-nib*)	Take orally (6 x 40 mg tablets) ONCE a day, at about the same time each day with food, preferably in the morning. Swallow whole with a glass of water, do not break, crush or chew. If you forget to take your tablets, do not make up that dose. Do not take two doses at the same time to make up for a missed dose. If you vomit your tablets, you can take the next dose at the scheduled time.

At the start of your treatment you will need to take some medication to prevent diarrhoea

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 suddenly 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
• uncontrolled diarrhoea despite taking antidiarrhoeal medicine • yellowing of the skin or eyes • darkening of the urine • severe abdominal pain • nausea or vomiting • shortness of breath	Daytime:..... Night/weekend:..... Other instructions:..... ....

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 will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

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.
- **Antidiarrhoeal medication:** diarrhoea is common when starting this treatment. Your doctor will prescribe some loperamide tablets or capsules to help control the diarrhoea (called "prophylaxis"). You need to take them regularly for the first 8 weeks. You should aim to have 1-2 bowel movements (poos) a day. The following table may be used to remind you how to take your medication.

Week of neratinib	Dose	How to take
1 - 2	4 mg	Two loperamide tablets or capsules three times a day
3 - 8	4 mg	Two loperamide tablets or capsules twice a day
9 - 52	4 mg	Two loperamide tablets or capsules as needed

Tell your doctor or nurse if you don't think the tablets are working.

Superseded treatments

This treatment is superseded meaning that better treatments have taken its place. Uncommonly superseded treatments are still used. Your doctor will explain why this treatment has been selected for you.

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)	
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.**

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.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.

Liver problems	• You may get:
	  ◦ yellowing of your skin or eyes
	  ◦ itchy skin
	  ◦ pain or tenderness in your stomach
	  ◦ nausea and vomiting
	  ◦ loss of appetite
	• You will have regular blood tests to check how well your liver is working.
	• **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**
Stomach pain	• You may get: ◦ dull aches ◦ cramping or pain ◦ bloating or flatulence (gas). • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control.**
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.**

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.**
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.
- Seville oranges, 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.

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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