Non small cell lung cancer metastatic gefitinib SUPERSEDED

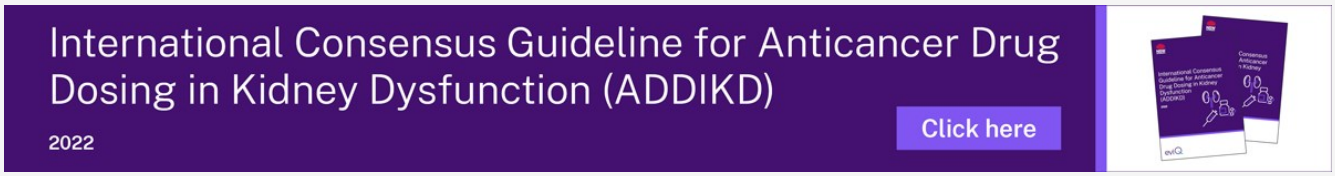
ID: 381 v.5 **Superseded**

This protocol has been superseded due to the availability of superior alternatives.

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

Link to Clinical practice guidelines for the treatment of lung cancer

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:

- Non small cell lung cancer metastatic erlotinib SUPERSEDED
- Non small cell lung cancer metastatic aFATinib
- Non small cell lung cancer locally advanced or metastatic osimertinib

Treatment schedule - Overview

Drug	Dose	Route
Gefitinib	250 mg ONCE a day	PO

Continuous until disease progression or unacceptable toxicity

Drug status: Gefitinib (PBS authority)

Cost: ~ $520 per month

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		
Gefitinib	250 mg (PO)	ONCE a day with or without food

Continuous until disease progression or unacceptable toxicity

Indications and patient population

- Locally advanced or metastatic non small cell lung cancer with epidermal growth factor receptor (EGFR) mutations known to confer sensitivity to treatment with EGFR tyrosine kinase inhibitors (TKIs) in tumour material, after failure of prior chemotherapy
- Initial treatment of metastatic non small cell lung cancer with EGFR mutations known to confer sensitivity to treatment with EGFR TKIs in tumour material

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
Acneiform rash	EGFR targeted therapies are commonly associated with acneiform rash. The rash may peak in the first 2 to 4 weeks. Ensure advice on skin care (i.e. moisturisers) and sunscreen is provided. Prophylactic or early therapy with a tetracycline antibiotic (e.g. doxycycline) and 1% hydrocortisone cream to affected areas may be considered. Patients developing skin rash should be monitored for infectious sequelae, dose reductions and/or delay or cessation of treatment may be required. Read more about acneiform rash associated with EGFR inhibitors
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Pulmonary toxicity	Interstitial lung disease (ILD) has been reported in patients treated with EGFR inhibitors. Read more about pulmonary toxicity associated with anti-cancer drugs.
Blood tests	FBC, EUC, eGFR and LFTs at baseline and throughout treatment as clinically indicated.
Hepatitis B screening and prophylaxis	The requirement for routine screening for HBsAg and anti-HBc for patients receiving this treatment is unknown. Clinical judgement and individual patient situations should be taken into consideration. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines should be used with caution in cancer patients. For cancer patients who are not receiving immunosuppressive therapy, there is currently no data as to the safety of giving live vaccines. 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 modification necessary

Hepatic impairment	
Hepatic dysfunction	
Due to liver metastases	No dose modification necessary
Secondary to treatment	Omit treatment if severe

Diarrhoea	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and restart gefitinib at 250 mg ONCE daily
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and consider restarting at 250 mg ONCE daily (1st occurrence) or alternate day dosing (2nd occurrence)

Rash acneiform	
Grade 1 or Grade 2	Treat rash; no delay in treatment is necessary
Grade 3	Treat rash; delay treatment until toxicity has resolved to Grade 1 or less and consider restarting at 250 mg ONCE daily (1st occurrence) or alternate day dosing (2nd occurrence)

Link to more information on Acneiform rash associated with EGFR inhibitors

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*

Gefitinib		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of gefitinib possible due to reduced clearance	Avoid combination or monitor for gefitinib toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of gefitinib possible due to increased clearance	Avoid combination or monitor for decreased clinical response to gefitinib
Drugs metabolised by CYP2D6 (e.g. beta blockers, dextromethorphan etc.)	Increased effect/toxicity of these drugs possible due to inhibition of CYP2D6 by gefitinib resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity. (e.g. gefitinib)
H2 blockers (e.g. famotidine, ranitidine etc.) and Proton Pump Inhibitors (e.g. omeprazole, pantoprazole, rabeprazole etc.) and Antacids	Reduced efficacy of gefitinib due to decreased absorption when gastric acid secretion suppressed (gefitinib requires acidic environment for absorption)	Avoid combination Acid neutralising antacids, e.g. Gastrogel®, Mylanta® (which have a shorter duration of action), may be used if separated from gefitinib administration by several hours
Paracetamol	Risk of liver toxicity due to inhibition of metabolism of paracetamol by gefitinib	Avoid combination or monitor liver function

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 should be used with caution in cancer patients. For cancer patients who are not receiving immunosuppressive therapy, there is currently no data as to the safety of giving live vaccines. 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

Gefitinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food
- if difficulty is experienced swallowing the tablet advise patient to:
  - place the tablet in half a glass of plain drinking water (approximately 100 mL). No other liquids should be used
  - stir occasionally, for 10 to 15 minutes, until the tablet dissolves and the water becomes a cloudy pale orange solution
  - drink the liquid straight away
  - rinse the empty glass with half a glass of water and drink it.

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

Gefitinib tablets

- Gefitinib tablets with written instructions on how to take them.

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)	
Acneiform rash	A skin rash, characterised by papules and pustules affecting the face and upper body. This is commonly associated with small molecule EGFR inhibitors and some monoclonal antibodies (e.g. cetuximab, panitumumab). Read more about acneiform rash associated with EGFR inhibitors
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
Ocular changes	Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.

Late (onset weeks to months)	
Abnormal hair growth	Hair may become fine, brittle and curly. Eyelashes and eyebrows may grow more quickly and become unusually long.
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
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

Evidence

There are currently no randomised controlled trials that demonstrate a clinical benefit on overall survival with gefitinib.

First line setting:

The evidence supporting the use of gefitinib in the first line setting initially came from the IPASS study, a phase III, multicenter, randomised, study comparing gefitinib with carboplatin plus paclitaxel as first-line treatment in clinically selected patients in East Asia with advanced non-small cell lung cancer.

All patients had stage IIIB or IV NSCLC with histological features of adenocarcinoma, were nonsmokers (defined as patients who had smoked less than 100 cigarettes in their lifetime) or former light smokers (those who had stopped smoking at least 15 years previously and had a total of less than or equal to 10 pack-years of smoking), and had no previous chemotherapy or biologic or immunologic therapy.

Between March 2006 and October 2007, a total of 1217 patients were randomly assigned to receive gefitinib 250 mg/day (n=609) or carboplatin AUC=5 or 6 plus paclitaxel 200 mg/m^2 every 21 days for 6 cycles (n=608).

The primary end point was progression-free survival and secondary end-points included overall survival, objective response rate, quality of life, symptom reduction and safety.[1]

More recently two phase III, randomised studies have compared gefitinib with platin-based doublet regimens in Asian patients with NSCLC and activating EGFR mutations.

The WJTOG3405 study (cisplatin and docetaxel) recruited 177 patients between March 2006 and June 2009 from 36 centres in Japan. The primary endpoint was progression free survival. Data from 172 (86 in each group) were analysed and the gefitinib group had significantly longer progression-free survival than the chemotherapy group.[2]

In another study, NEJ002, 230 patients with EGFR mutation positive NSCLC were randomly assigned to receive either gefitinib or chemotherapy (carboplatin and paclitaxel). The primary endpoint was progression free survival, with secondary endpoints included overall survival, response rate and toxic effects. The study was terminated early after the interim analysis of the first 200 patients demonstrated significantly longer progression free survival in the gefitinib group.[3]

Second or third line setting:

The activity of gefitinib was evaluated in a randomised, double-blind, phase II, multicenter trial comparing two oral doses of gefitinib (250 mg/day versus 500 mg/day). A total of 216 patients received gefitinib. The 142 patients who were refractory to or intolerant of a platinum and docetaxel comprised the evaluable population for the efficacy analysis.[4]

The Iressa® Survival Evaluation in Lung Cancer (ISEL) trial investigated gefitinib compared with placebo, in the second or third line setting. That study included 1,692 patients who had progressed or could no longer tolerate chemotherapy. The results showed a statistically significant greater tumour shrinkage in the gefitinib arm, but the overall survival durations were similar in the two arms: 5.6 months in treated patients versus 5.1 months in patients receiving placebo.

Efficacy

First line setting:

IPASS

The 12-month rates of PFS were 24.9% with gefitinib and 6.7% with carboplatin/paclitaxel. In the subgroup of 261 patients who had EGFR mutations, PFS was significantly longer among those who received gefitinib than those who received carboplatin/paclitaxel. (HR=0.48; p<0.001).[1]

Mature data from the IPASS study, presented at the 2010 ESMO congress, showed that overall survival (OS) was similar, with no significant difference, between gefitinib and doublet chemotherapy in the overall population (median OS 18.8 vs. 17.4 months; p=0.11). Analysis by EGFR mutation status confirmed that patients with EGFR mutation-positive advanced non-small cell lung cancer (NSCLC) had better outcomes, regardless of which treatment arm they were in, compared to patients with EGFR mutation-negative disease. Median survival times were around 22 months for EGFR mutation-positive patients, but only 11 to 12 months for EGFR mutation-negative patients. The majority of EGFR mutation-positive patients in IPASS received an EGFR-TKI at some point as 64% of those randomised to carboplatin/paclitaxel later received an EGFR-TKI as subsequent therapy.[5]

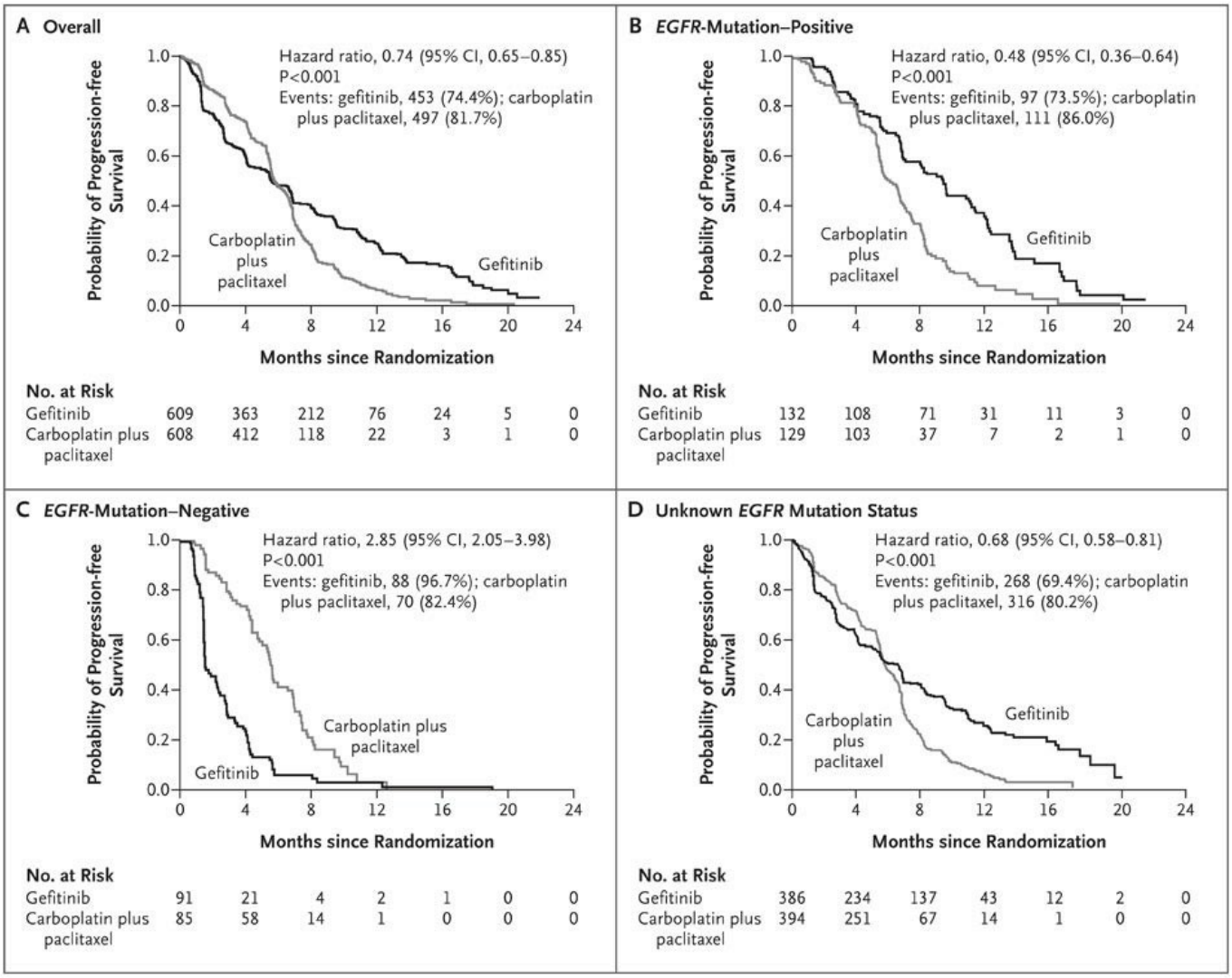
WJTOG3405 showed significantly longer progression free survival in the gefitinib group compared with the chemotherapy group. Median PFS of 9.2 months (95%CI 8.0-13.9)versus 6.3 months (5.8-7.8; HR 0.489 95% CI 0.336-0.710, log-rank p<0.0001).[2]

Maemondo et al demonstrated a significantly longer median progression free survival in the gefitinib group (10.8 months, vs. 5.4 months in the chemotherapy group; HR 0.30; 95% CI, 0.22 to 0.41; p<0.001) and a higher response rate 73.7 vs 30.7% p<0.001). Median OS was 30.5 months in the gefitinib group and 23.6 months in the chemotherapy group however this was not significant (p= 0.31).[3]

Second or third line setting:

Symptoms of NSCLC improved in 43% and 35% of patients receiving 250 mg/day and 500 mg/day of gefitinib respectively. Partial radiographic responses occurred in 12% and 9% of patients receiving 250 mg/day and 500 mg/day of gefitinib respectively. Responses were more frequent in females, Asians, adenocarcinomas and in non-smokers. The median duration of response was 7.0 months [4].

Kaplan-Meier Curves for Progression-free Survival[1]



A: PFS for the overall population
B: PFS for patients who were positive for EGFR mutations
C: PFS for patients who were negative for EGFR mutations
D: PFS for patients with unknown EGFR status

Toxicity

First line setting:

When compared with carboplatin/paclitaxel in the first line setting, the most common adverse events were rash or acne (66.2%) and diarrhoea (46.6%) in the gefitinib group and neurotoxic effects (69.9%), neutropenia (67.1%) and alopecia (58.4%) in the carboplatin/paclitaxel group.[1]

Second or third line setting:

The side effects of gefitinib were usually mild and mostly resolve within days after temporary cessation of gefitinib or improve despite ongoing treatment. Skin toxicity (62% in patients receiving 250mg/day) and diarrhoea (57% in patients receiving 250mg/day) were the 2 most common side effects with gefitinib. Other side effects included eye toxicities (19%), nausea (15%) and vomiting (10%). There were no cases of investigator-identified interstitial lung disease. There was one patient with grade 3 thrombocytopenia and one possible treatment-related death.[4]

Toxicity[1]

Table 2. Adverse Events.*

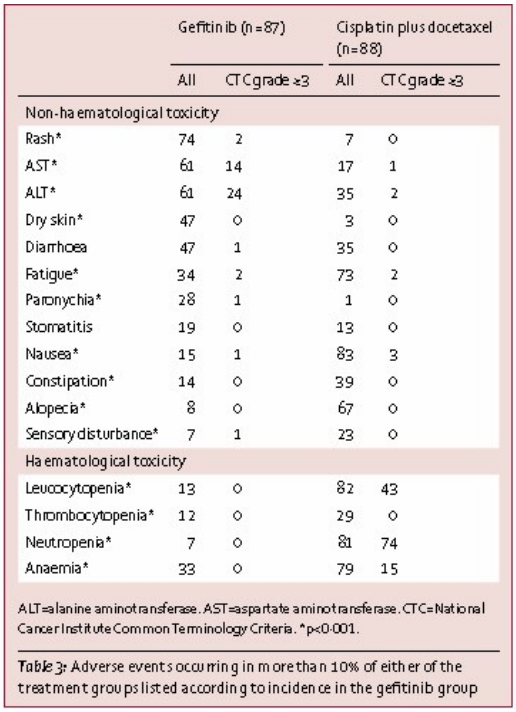
Adverse Event	Gefitinib (N=607)		Carboplatin–Paclitaxel (N=589)	
	All Adverse Events	CTC Grade 3, 4, or 5	All Adverse Events	CTC Grade 3, 4, or 5
	number (percent)			
Rash or acne†	402 (66.2)	19 (3.1)	132 (22.4)	5 (0.8)
Diarrhea	283 (46.6)	23 (3.8)	128 (21.7)	8 (1.4)
Dry skin	145 (23.9)	0	17 (2.9)	0
Anorexia†	133 (21.9)	9 (1.5)	251 (42.6)	16 (2.7)
Pruritus†	118 (19.4)	4 (0.7)	74 (12.6)	1 (0.2)
Stomatitis†	103 (17.0)	1 (0.2)	51 (8.7)	1 (0.2)
Asthenic conditions†	102 (16.8)	2 (0.3)	259 (44.0)	11 (1.9)
Nausea	101 (16.6)	2 (0.3)	261 (44.3)	9 (1.5)
Paronychia	82 (13.5)	2 (0.3)	0	0
Vomiting	78 (12.9)	1 (0.2)	196 (33.3)	16 (2.7)
Constipation	73 (12.0)	0	173 (29.4)	1 (0.2)
Alopecia	67 (11.0)	0	344 (58.4)	0
Neurotoxic effects†	66 (10.9)	2 (0.3)	412 (69.9)	29 (4.9)
Myalgia	47 (7.7)	3 (0.5)	186 (31.6)	10 (1.7)
Arthralgia	39 (6.4)	1 (0.2)	113 (19.2)	6 (1.0)
Neutropenia‡				
Any	NA	22 (3.7)	NA	387 (67.1)
Febrile	1 (0.2)	1 (0.2)	17 (2.9)	17 (2.9)
Anemia‡	NA	13 (2.2)	NA	61 (10.6)
Leukopenia‡	NA	9 (1.5)	NA	202 (35.0)

* Calculations were based on 1196 patients who received at least one dose of the study treatment. The Common Terminology Criteria (CTC) grade is defined on the basis of the National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0. Events are included if they occurred in at least 10% of patients in either treatment group, either while the patients were receiving treatment or during the 28-day follow-up, and if there was at least a 5% difference between groups. There were other adverse events that occurred in few patients and that may or may not have been related to the study drug. NA denotes not available.

† This is a group term (sum of high-level and preferred terms, according to the definitions in the *Medical Dictionary for Regulatory Activities*).

‡ Data are from the laboratory reports of 599 patients who were taking gefitinib and 577 who were taking carboplatin–paclitaxel. Events were included if there was a worsening in the laboratory value (absolute neutrophil count in the case of neutropenia, hemoglobin in the case of anemia, and white-cell count in the case of leukopenia) from baseline to CTC grade 3 or 4.

WJTOG3405[2]



	Gefitinib (n=87)		Cisplatin plus docetaxel (n=88)	
	All	CTC grade ≥3	All	CTC grade ≥3
Non-haematological toxicity				
Rash*	74	2	7	0
AST*	61	14	17	1
ALT*	61	24	35	2
Dry skin*	47	0	3	0
Diarrhoea	47	1	35	0
Fatigue*	34	2	73	2
Paronychia*	28	1	1	0
Stomatitis	19	0	13	0
Nausea*	15	1	83	3
Constipation*	14	0	39	0
Alopecia*	8	0	67	0
Sensory disturbance*	7	1	23	0
Haematological toxicity				
Leucocytopenia*	13	0	82	43
Thrombocytopenia*	12	0	29	0
Neutropenia*	7	0	81	74
Anaemia*	33	0	79	15

ALT=alanine aminotransferase. AST=aspartate aminotransferase. CTC=National Cancer Institute Common Terminology Criteria. *p<0·001.

Table 3: Adverse events occurring in more than 10% of either of the treatment groups listed according to incidence in the gefitinib group

Maemondo et al[3]

Toxicity	Gefitinib (n=114)			Carboplatin/Paclitaxel (n=113)			P Value for Grade ≥3
Grade	**3**	**4**	**≥3 (%)**	**3**	**4**	**≥3 (%)**	**P Value for Grade ≥ 3**
Diarrhoea	1	0	1(0.9)	0	0	0	<0.001
Appetite Loss	6	0	6(5.3)	7	0	7(6.2)	<0.001
Fatigue	3	0	3(2.6)	1	0	1(0.9)	0.002
Rash	6	0	6(5.3)	3	0	3(2.7)	<0.001
Neuropathy (sensory)	0	0	0	7	0	7(6.2)	<0.001
Arthralgia	1	0	1(0.9)	8	0	8(7.1)	<0.001
Pneumonitis	2	1	3(2.6)	0	0	0	0.02
Aminotransferase Elevation	29	1	30(26.3)	0	1	1(0.9)	<0.001
Neutropaenia	0	1	1(0.9)	37	37	74(65.5)	<0.001
Anaemia	0	0	0	6	0	6(5.3)	<0.001
Thrombocytopaenia	0	0	0	3	1	4(3.5)	<0.001
Any	43	4	47(41.2)	41	40	81(71.7)	<0.001

References

1 Mok, T. S., Y. L. Wu, S. Thongprasert, et al. 2009. "Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma." N Engl J Med 361(10):947-957.

2 Mitsudomi, T., Morita, S., Yatabe, Y. et al. 2010. "Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial." Lancet Oncol; 11 (2): 121-8.

3 Maemondo, M., Inoue, A., Kobayashi, K. et al. 2010. "Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR" N Engl J Med. 362(25): 2380-8.

4 Kris, Mark G., Ronald B. Natale, Roy S. Herbst, et al. 2003. "Efficacy of gefitinib, an inhibitor of the epidermal growth factor receptor tyrosine kinase, in symptomatic patients with non-small cell lung cancer: a randomized trial." JAMA 290(16):2149-2158.

5 Yang, CH, M. Fukuoka, T. S. Mok, et al. 2010. "Final overall survival (OS) results from a phase III: randomised, open-label, first-line study of gefitinib (G) v carboplatin/paclitaxel (C/P) in clinically selected patients with advanced non-small cell lung cancer (NSCLC) in Asia (IPASS). Presented at the European Society of Medical Oncology (ESMO) Congress, 2010."

History

Version 5

Date	Summary of changes
30/04/2021	Protocol reviewed by Medical Oncology Reference Committee. Protocol superseded due to superior alternatives being available. Version number increased to V.5. 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.
19/06/2023	Protocol reviewed at the Medical Oncology Reference Committee meeting on 19 May 2023. No changes. Next review in 4 years.

Version 4

Date	Summary of changes
25/08/2009	Reviewed, new dose modifications and transferred to eviQ.
18/10/2010	Link to safe administration or oral antineoplastic agents corrected.
08/02/2011	Gefitinib first line indication added to protocol as per Medical Oncology Reference Committee meeting 23/10/2010.
14/02/2011	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 PHC view.
30/11/2012	Reviewed at Medical Oncology Reference Committee meeting. Indications to include first line setting. Evidence update. Next review in 2 years.
15/03/2013	Links to EGFR screening removed.
02/09/2014	PHC view removed.
12/09/2014	Reviewed by Medical Oncology Reference Committee. Indications wording consistent across all EGFR TKI's.
18/02/2016	Discussed with Medical Oncology Reference Committee Chairs, for review every 5 years. Next review 3 years.
31/05/2017	Transferred to new eviQ website. Version number change to V.3.
06/12/2018	Links to erlotinib and afatinib related pages added. Patient information updated as per Medical Oncology Reference Committee consensus- your treatment, when to get help and blood tests changed to less chemotherapy focused information.
15/05/2020	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes. Review 2 years.

First approved: 9 January 2007
Last reviewed: 19 May 2023
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Patient information - Lung cancer metastatic - Gefitinib

Patient's name:

Your treatment

It is important to understand that gefitinib 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. The treatment schedule below explains how the drug for this treatment is given.

Gefitinib		
This treatment is continuous. Your doctor will advise you how long to take the treatment for.		
Day	**Treatment**	**How it is given**
Continuous	**Gefitinib** (*geh-FIT-in-ib)*	Take orally ONCE a day, at the same time each day, with or without food. Swallow whole with a glass of water, do not break, crush or chew. If you are taking an antacid, do not take within two hours as this may interfere with its absorption. If you are unable to swallow the tablets whole they may be dissolved in water and the solution swallowed (see directions in *Other information about your treatment*). If you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.

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.

Emergency contact details

Ask your doctor or nurse from your treating team when you should get help and who to contact if you have a problem

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

- **Antidiarrhoeals:** you may be given some medication to treat diarrhoea. Your doctor or nurse will tell you how and when to take your antidiarrhoeal medication.
- **Medication for skin rash:** you may be given some medication (which may include a steroid cream, an antibiotic cream and/or oral antibiotics) to prevent or treat skin rash. Your doctor or nurse will tell you how to take or use these medications.

Instructions for dissolving gefitinib tablets:

- Gefitinib tablets should not be crushed, cut or chewed. For patients with swallowing difficulties gefitinib tablets can be dissolved.
- You (or whoever is dissolving the tablets) should wear disposable gloves and try to minimise touching the tablets.
- Place the gefitinib tablet in half a glass of plain drinking water (approximately 100 mL). No other liquids should be used.
- Stir occasionally, for 10 to 15 minutes, until the tablet dissolves and the water becomes a cloudy pale orange solution
- Drink the liquid straight away.
- Rinse the empty glass with half a glass of water and drink it.

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)	
Skin rash (acneiform rash)	• You may get an acne-like skin rash. • Your skin may become red and dry. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Do not use over-the-counter acne treatments as these can make the rash worse. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • You may be given medications to prevent the rash. • **Tell your doctor or nurse as soon as possible if you notice any changes to the rash like itching, pain or pus forming**
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.
Eye problems	• You may get: ◦ eye pain ◦ red, sore or swollen eyes ◦ blurred vision ◦ watery or gritty eyes ◦ changes in your eyesight ◦ sensitivity to sunlight. • Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes. • **Tell your doctor or nurse if you get any of the symptoms listed above. Eye drops may help with your symptoms.**

Late (onset weeks to months)	
Hair changes	• Your hair may become fine or curly and may break easily. • Your eyelashes and eyebrows may grow more than normal. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au).
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.**
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.

General advice for patients 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.

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.

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
- Call the Lung Foundation Australia on 1800 654 301

Lung cancer information

- Lung Foundation Australia – lungfoundation.com.au
- Lungevity – lungevity.org

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
- Carer Help - carerhelp.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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