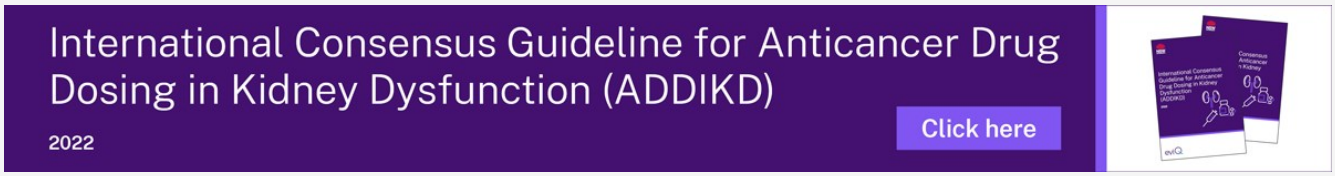
Non small cell lung cancer locally advanced or metastatic lorlatinib

ID: 3790 v.3 **Endorsed**

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 locally advanced or metastatic alectinib
- Non small cell lung cancer locally advanced or metastatic brigatinib
- Non small cell lung cancer locally advanced or metastatic entrectinib

Treatment schedule - Overview

Drug	Dose	Route
Lorlatinib	100 mg ONCE a day	PO

Continuous until disease progression or unacceptable toxicity.

Drug status: Lorlatinib is PBS Authority

Lorlatinib is available in **25 mg** and **100 mg** tablets

Cost: ~ $6,640 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		
Lorlatinib	100 mg (PO)	ONCE a day

Continuous until disease progression or unacceptable toxicity.

Indications and patient population

Indications:

- Treatment of anaplastic lymphoma kinase (ALK) positive, locally advanced or metastatic non small cell lung cancer (NSCLC)
- ECOG 0 to 2.

Cautions/Exclusions:

- Clinically significant uncontrolled cardiovascular disease e.g. PR interval prolongation/AV block
- Congenital long-QT syndrome
- Interstitial lung disease

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
Hyperlipidaemia	Hyperlipidaemia is a common adverse event. Dose adjustment or initiation of lipid-lowering agents may be required. Rosuvastatin or pravastatin are the preferred lipid lowering agents for use with lorlatinib.
Central nervous system (CNS) effects	A broad spectrum of CNS effects can occur in patients receiving this treatment. These reactions are generally mild in severity, intermittent and improved or resolved upon dose modifications. Mood effects include irritability, anxiety, depression and affect lability. It is important to note if a patient has a pre-existing psychiatric condition. Cognitive effects included memory impairment, cognitive disorder and amnesia. Speech effects included dysarthria, slow speech and speech disorder.
Peripheral neuropathy	Assess prior to each treatment and dose reduce if appropriate. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Prolongation of QT interval	This treatment may prolong the QT interval and increase the risk of cardiac arrhythmia. Use with caution in patients with a congenital long QT syndrome, patients treated with a high cumulative dose of anthracycline therapy, patients taking medications that may prolong the QT interval and those with electrolyte disturbances. Risk factors (e.g. electrolyte abnormalities) should be corrected, where possible, prior to commencement of treatment and the concurrent use of drugs that may prolong the QT interval should be avoided. Baseline and periodic monitoring of electrocardiogram (ECG) and electrolytes (potassium, magnesium, calcium) should be considered in patients at high risk of QT prolongation. Read more about drugs that may prolong QTc interval at crediblemeds.org (registration required).
Prolongation of PR interval/AV nodal block	PR interval prolongation and AV block events have been reported in patients receiving this treatment. Monitor electrocardiogram (ECG) prior to initiating treatment and monthly thereafter, particularly in patients at high risk of occurrence of clinically significant cardiac events.
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Oedema	Patients may experience an increased incidence of oedema, including peripheral oedema, with this treatment.

Pulmonary toxicity	This treatment has been associated with severe, life-threatening or fatal interstitial lung disease (ILD)/pneumonitis. Patients should be monitored for pulmonary symptoms indicative of ILD/pneumonitis. Treatment should be permanently discontinued in patients diagnosed with treatment-related ILD/pneumonitis. Read more about pulmonary toxicity associated with anti-cancer drugs.
Blood tests	FBC, EUC, eGFR, LFTs, fasting triglycerides, cholesterol and glucose at baseline, two weekly for the first month and then monthly throughout treatment or as clinically indicated. Lipase and amylase at baseline, not routinely monitored unless clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. 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. Non-hormonal methods of birth control should be used during this treatment. 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 below are based on a combination of the evidence,[1, 2, 3, 4] product information and reference committee consensus.

Lorlatinib dose reduction schedule	
Starting dose	100 mg once daily

Lorlatinib dose reduction schedule	
First dose reduction	75 mg once daily
Second dose reduction	50 mg once daily

If patient unable to tolerate 50 mg once daily consider permanent discontinuation

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well
0.5 to less than 1.0	Delay treatment until recovery, then rechallenge at the same dose level or reduce to next lower dose level
less than 0.5 or febrile neutropenia	Delay treatment until recovery and reduce the dose as follows: 1st occurrence: rechallenge at the same dose level or reduce to next lower dose level 2nd occurrence: reduce lorlatinib to next lower dose level 3rd occurrence: reduce lorlatinib to next lower dose level or consider permanent discontinuation
Platelets x 10^9/L (pre-treatment blood test)	
50 to less than 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local institutional guidelines
25 to less than 50	Delay treatment until recovery
less than 25	Delay treatment until recovery and rechallenge at the same dose level or reduce to next lower dose level

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	No dose modification necessary
less than 30	No data available, use with caution in patients with renal impairment

Hepatic impairment	
Hepatic dysfunction	
Mild	No dose modification necessary
Moderate	Delay treatment until toxicity has resolved to Grade 1 or baseline then rechallenge at the same dose level or reduce to next lower dose level
Severe	Delay treatment until toxicity has resolved to Grade 1 or baseline then reduce to next lower dose level. If recurs permanently discontinue lorlatinib

Lipid elevation toxicities	
Mild: - Cholesterol ULN-7.8 mmol/L OR - Triglycerides 1.7 mmol/L- 3.4 mmol/L Moderate: - Cholesterol >7.8 mmol/L-10.3 mmol/L OR - Triglycerides >3.4 mmol/L-5.7	Commence or modify lipid lowering therapy* Continue at same lorlatinib dose

Lipid elevation toxicities	
mmol/L	
Severe: - Cholesterol >10.3 mmol/L-12.9 mmol/L OR - Triglycerides >5.7 mmol/L-11.4 mmol/L	Commence lipid lowering therapy or increase dosage of ongoing lipid lowering therapy or change to new lipid lowering therapy* Continue at same lorlatinib dose without interruption
Urgent Intervention: - Cholesterol >12.9 mmol/L OR - Triglycerides >11.4 mmolL	Commence lipid lowering therapy or increase dosage of ongoing lipid lowering therapy or change to new lipid lowering therapy* Delay treatment until hyperlipidaemia has resolved to moderate or mild before rechallenging at the same dose while maximising lipid lowering therapy If severe hyperlipidaemia recurs despite maximal lipid lowering therapy, reduce lorlatinib to next lower dose level

*Rosuvastatin or pravastatin are the only high intensity statins recommended based on low their low involvement with the CYP 450 enzymes

Mood, speech and cognitive disturbance	
Grade 1	Continue lorlatinib at the same dose level and monitor closely Discuss supportive non-pharmacologic and pharmacologic intervention should symptoms persist or worsen
Grade 2	Reduce lorlatinib to next lower dose level Investigate reversible causes and consider mood stabilising supportive non-pharmacological and pharmacological intervention
Grade 3	Delay treatment until toxicity has resolved to ≤ Grade 1 or baseline and resume at next lower dose level Review supportive non-pharmacological and pharmacological intervention
Grade 4	Delay treatment until toxicity has resolved to ≤ Grade 1 or baseline and resume at two dose levels down If recurrent Grade 3 permanently discontinue lorlatinib Review supportive non-pharmacological and pharmacological intervention

Peripheral neuropathy	
Grade 1	Continue lorlatinib at same dose and monitor closely
Grade 2 which is present at the start of the next cycle	Delay treatment until until toxicity has resolved to Grade 1 or less and rechallenge at same dose or next lower dose level
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or baseline and resume at next lower dose level
Grade 4	Delay treatment until toxicity has resolved to Grade 1 or baseline and resume at next lower dose level or discontinue lorlatinib

Pneumonitis	
Grade 1	No dose modifications necessary
Grade 2	Delay treatment until toxicity has returned to baseline Rule out alternative causes Consider treatment with corticosteroids

Pneumonitis	
	If recurs or fails to recover after 6 weeks of withheld treatment and steroid treatment: permanently discontinue lorlatinib
Grade 3 or 4	Permanently discontinue lorlatinib

QT prolongation	
Grade 1 or Grade 2	No dose modification necessary Assess electrolytes and concomitant medications. Correct as appropriate.
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and resume at next lower dose level
Grade 4	Permanently discontinue lorlatinib

PR interval prolongation/ atrioventricular (AV) block	
First degree Heart Block (PR >200ms)	Consider effects of concomitant medicinal products and correct electrolyte imbalances (if present) 1st occurrence and asymptomatic: no dose modification necessary 2nd occurrence and/or symptomatic: delay treatment until recovery and recommence at same dose or reduce to next lower dose level
Second degree heart block	Consider effects of concomitant medicinal products and correct electrolyte imbalances (if present) 1st occurrence and asymptomatic: delay treatment until recovery Repeat ECG in 48 hours, if resolution recommence at same dose or reduce to next lower dose level 2nd occurrence and/or symptomatic: delay treatment until recovery or PR interval < 200 msec. Refer for cardiac investigation Recommence at next lower dose level
Complete heart block	Permanently discontinue lorlatinib if confounding aetiology excluded Consider effects of concomitant medicinal products and correct electrolyte imbalances (if present) Refer for cardiac investigation, pacemaker may be indicated for severe symptoms associated with AV block Delay treatment until recovery If pacemaker placed, resume at same dose If no pacemaker, resume at next lower dose level when symptoms resolve and PR interval < 200 msec

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*

Lorlatinib		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. amiodarone, aprepitant, azole antifungals, ritonavir, macrolides, grapefruit juice etc.)	Increased toxicity of lorlatinib possible due to reduced clearance	Avoid combination or monitor for lorlatinib toxicity. If concomitant use of strong CYP3A4 inhibitors cannot be avoided, reduce lorlatinib starting dose to 75 mg once a day. After discontinuation of a strong CYP3A4 inhibitor, lorlatinib should be resumed at the dose that was tolerated prior to the initiation of the strong CYP3A4 inhibitor and after a washout period of 3 to 5 half lives of the strong CYP3A4 inhibitor.
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of lorlatinib possible due to increased clearance	Combination with strong CYP3A inducers is contraindicated. Discontinue strong CYP3A4 inducers for at least 3 half lives before initiating lorlatinib treatment. Avoid combination with moderate CYP3A4 inducers
CYP3A substrates (e.g. hormonal contraceptives, ciclosporin, fentanyl, quinidine, ergotamine, pimozide, sirolimus, tacrolimus etc.) with narrow therapeutic indices	Reduced efficacy of substrate possible due to increased clearance	Avoid combination with CYP3A substrates with a narrow therapeutic index. For hormonal contraceptives, non-hormonal methods should be used during and up to at least 21 days after stopping lorlatinib. If concomitant use of statins is required, rosuvastatin or pravastatin are preferred.
P-gp substrates (e.g. dabigatran, digoxin, loperamide, phenytoin etc.) with narrow therapeutic indices	Reduced efficacy of substrate possible due to increased clearance	Monitor for reduced efficacy of interacting drug.
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 day of treatment.

Peripheral neuropathy assessment tool

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

Treatment - Time out

Lorlatinib

- 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.

Note: If a dose is missed it should be taken as soon as possible unless it is less than 4 hours before the next dose. 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

Discharge information

Lorlatinib tablets

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

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)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
CNS effects	Mood effects include irritability, anxiety, depression and affect lability. Cognitive effects include memory impairment, cognitive disorder and amnesia. Speech effects included dysarthria, slow speech and speech disorder.
Hyperlipidaemia and hypercholesterolaemia	Abnormally elevated levels of lipids and cholesterol in the blood.
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
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.
QT prolongation	This treatment can cause QTc interval prolongation. QTc prolongation can lead to ventricular arrhythmias that may be fatal.
PR prolongation/AV nodal block	Rarely, this treatment can cause PR interval prolongation and/or atrioventricular nodal block.

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
Weight gain	

Evidence

First line setting[1]

The evidence to support the use of lorlatinib in the first line setting is provided by results from a double-blind, multicentre phase III trial (CROWN).

The CROWN trial enrolled 296 patients with locally advanced or metastatic non-small cell lung cancer, with ALK rearrangement. Between May 2017 and February 2019, 149 patients were randomised to lorlatinib 100 mg daily and 147 patients to crizotinib 250 mg twice daily. Treatment in both arms was continued until disease progression, unacceptable toxicity, death or withdrawal.

The primary end point was progression-free survival (PFS) [as determined by blinded independent central review]. Secondary end points included investigator assessed progression free survival, overall survival (OS), objective response rate (ORR), objective intracranial response (OIR), and safety.[1]

Second line setting[2]

There is a lack of strong evidence to support the use of lorlatinib in the second line setting the reference panel was most strongly influenced by Solomon et al. in supporting publication of this protocol. Solomon et al, was a phase II single arm study, which included 276 patients recruited from September 2015 to October 2016 with advanced non- small cell lung cancer who were either ALK-positive or ROS-1 positive, and were enrolled into different cohorts based on ALK and ROS1 status and prior treatment. In the ALK-positive cohort, 59 patients had received previous crizotinib (EXP2 and EXP3A), 28 patients had received non-crizotinib ALK TKI (EXP3B), 112 had received two or three previous ALK TKI's (EXP4-5). Other cohorts included treatment naive ALK positive (EXP1) and ROS1 positive (EXP6).[2]

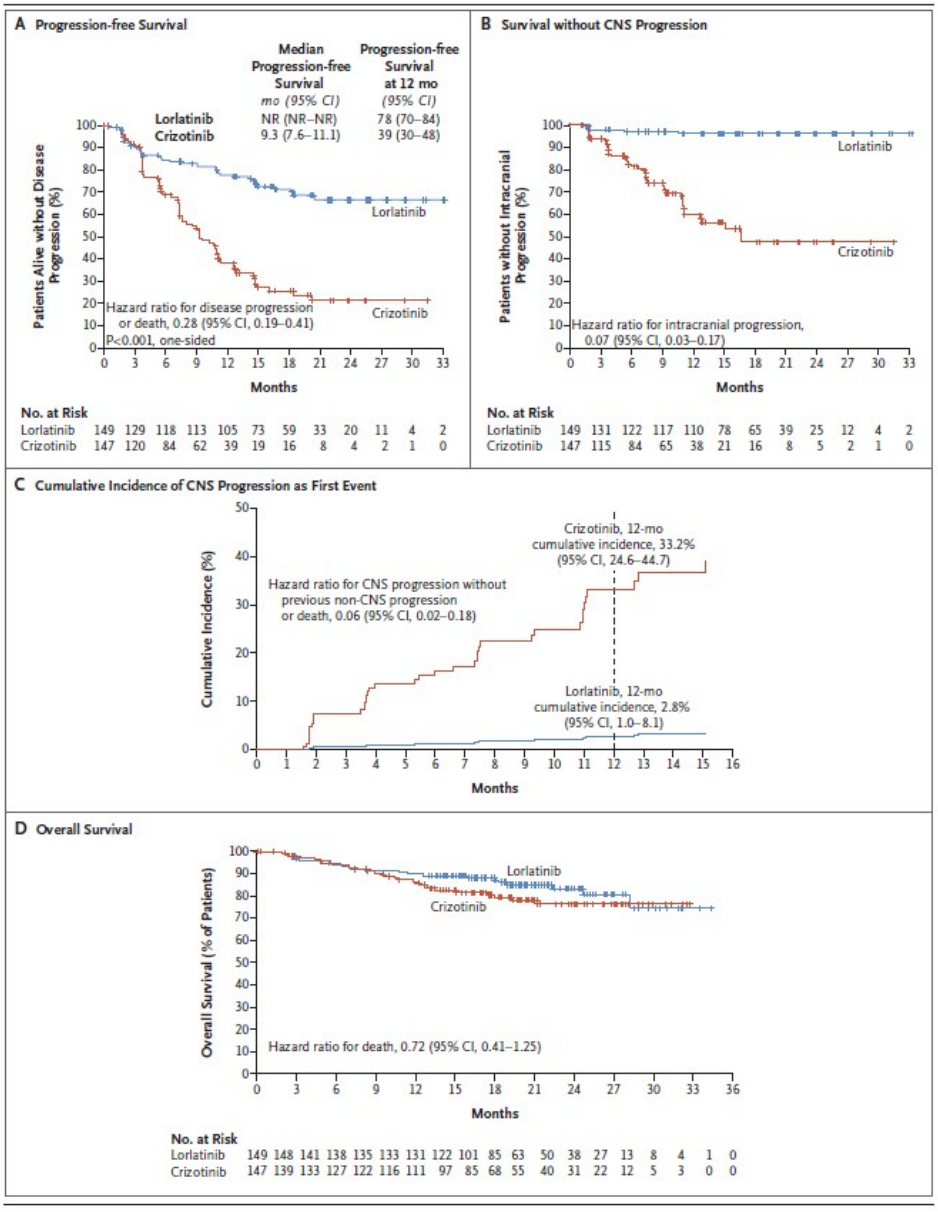
Efficacy

First line setting[1]

At data cut-off median duration of follow up was 19.3 months in the lorlatinib group and 14.8 months in the crizotinib group. With regards to primary outcome, the median progression free survival (PFS) was not reached (NR) in the lorlatinib arm and 9.3 months (95% CI 7.6-11.1) in the crizotinib arm [HR 0.28; 95% CI 0.19-0.41 p<0.001]. The 12 month PFS was 78% in the lorlatinib group and 39% in the crizotinib group.[1]

Secondary outcomes showed a higher overall response rate (ORR) for lorlatinib in comparison to crizotinib [76 v 58%]. Lorlatinib also exhibited higher CNS penetration with higher CNS response rates in comparison to crizotinib [66 v 20%]. Patients alive, and without CNS progression at 12 months was higher in the lorlatinib arm [96 v 60%; HR 0.07; 95% CI 0.03 to 0.17]. Lorlatinib also had a lower cumulative incidence of CNS progression as first event [3 v 33%; HR 0.06; 95% CI 0.02-0.18]. Overall survival data is still immature.[1]

Kaplan-Meier estimates for Progression-free Survival (A), Survival without CNS progression (B), CNS progression as first event (C) and Overall survival (D)[1]



Second line setting[2]

Response rates to lorlatinib in the second line setting in different expansion cohorts are highlighted in the table below[2]

Outcome	EXP2 and 3A (n=59)*	EXP 3B (n=28)**	EXP 4-5 (n=111)***
Median PFS (months)	Not reached	5.5	6.9
ORR	41 (69.5%) CR - 1 (2% PR - 8 (29%)	9 (32%) CR - 1 (4%) PR - 8 (29%)	43 (39%) CR - 2 (2%) PR - 41 (37%)
Intracranial ORR	20 (87%) CR - 5 (22%) PR - 15 (65%)	5 (55.6%) CR - 1 (11%) PR 4 (44%)	26 (53/1%) CR - 10 (20%) PR - 16 (33%)

CR: Complete Response, PR: Partial Response

* EXP 2 and 3A: previous crizotinib with or without chemotherapy

** EXP3B: Expansion Cohort 3B - previous non-crizotinib ALK TKI with or without chemotherapy

*** EXP4-5: Expansion Cohorts 4-5 - ≥2 previous ALK TKIs with or without chemotherapy

Toxicity

A summary of the toxicities associated with this protocol are included in the table below. The most clinically significant toxicities for this treatment are hypercholesterolaemia and hypertriglyceridaemia. Cognitive and mood effects related to lorlatinib were typically grade 1 and reversible with dose interruption. [3]

Adverse events[3]

Adverse drug reactions, *n* (%)	Pooled lorlatinib 100 mg once daily (*N* = 295)		
	All grades	Grade 3	Grade 4
Hypercholesterolemia[a]	243 (82.4)	41 (13.9)	5 (1.7)
Hypertriglyceridemia[a]	179 (60.7)	39 (13.2)	7 (2.4)
Edema[a]	151 (51.2)	7 (2.4)	0 (0.0)
Peripheral neuropathy[a]	129 (43.7)	7 (2.4)	0 (0.0)
Cognitive effects[a]	68 (23.1)	5 (1.7)	0 (0.0)
Fatigue[a]	68 (23.1)	1 (0.3)	0 (0.0)
Mood effects[a]	62 (21.0)	4 (1.4)	0 (0.0)
Weight increase	61 (20.7)	7 (2.4)	0 (0.0)
Arthralgia	58 (19.7)	0 (0.0)	0 (0.0)
Diarrhea	52 (17.6)	2 (0.7)	0 (0.0)
Constipation	42 (14.2)	0 (0.0)	0 (0.0)
Vision disorder[a]	39 (13.2)	1 (0.3)	0 (0.0)
Speech effects[a]	28 (9.5)	1 (0.3)	0 (0.0)

[a]Clustered term comprising adverse events that represent similar clinical symptoms/syndromes.

References

1 Shaw, A. T., T. M. Bauer, F. de Marinis, et al. 2020. "First-Line Lorlatinib or Crizotinib in Advanced ALK-Positive Lung Cancer." N Engl J Med 383(21):2018-2029.

2 Solomon, B. J., B. Besse, T. M. Bauer, et al. 2018. "Lorlatinib in patients with ALK-positive non-small-cell lung cancer: results from a global phase 2 study." Lancet Oncol 19(12):1654-1667.

3 Bauer, T. M., E. Felip, B. J. Solomon, et al. 2019. "Clinical Management of Adverse Events Associated with Lorlatinib." Oncologist 24(8):1103-1110.

4 Reed, M., A. S. Rosales, M. D. Chioda, et al. 2020. "Consensus Recommendations for Management and Counseling of Adverse Events Associated With Lorlatinib: A Guide for Healthcare Practitioners." Adv Ther 37(6):3019-3030.

History

Version 3

Date	Summary of changes
10/01/2023	Indications updated. "after progression on previous second generation ALK inhibitor" removed. No change to review date. Version number increased to V.3.

Version 2

Date	Summary of changes
20/05/2022	Protocol reviewed at Medical Oncology Reference Committee meeting. Indications updated. Evidence section- updated with first line setting data. Version number increased to V.2. Review in 2 years.

Version 1

Date	Summary of changes
30/04/2021	Protocol reviewed and approved by Medical oncology Reference Committee
21/05/2021	Protocol published on eviQ. Review in 1 year.
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.

First approved: 21 May 2021
Last reviewed: 20 May 2022
Review due: 30 June 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/3790
09 Aug 2023

Patient information - Lung cancer locally advanced or metastatic - Lorlatinib

Patient's name:

Your treatment

It is important to understand that lorlatinib 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.

Lorlatinib		
This treatment is continuous. Your doctor will advise you how long to take the treatment for.		
Day	**Treatment**	**How it is given**
Continuous	**Lorlatinib** (*lor-lat-i-nib)*	Take orally ONCE a day at the same time each day. Swallow the tablet whole with a glass of water with or without food. Do not break, crush or chew. If you forget to take a tablet, and it is more than 4 hours before your next dose, take it as soon as you remember. If it is less than 4 hours until your next dose, skip the missed dose and take your normal dose the next time it is due. Do not take a double dose for a missed dose or if a dose is vomited.

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.

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)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Mood, memory and speech changes	• You may have changes in your mood such as: ◦ irritability ◦ anxiety ◦ depression ◦ euphoria ◦ mood swings ◦ aggression ◦ agitation ◦ personality changes • You may also have changes in your memory such as ◦ forgetfulness ◦ memory loss ◦ confusion • You may have some difficulty speaking such as ◦ slurred speech ◦ slow speech **It is very important to tell your doctor or nurse if you get any of the symptoms above as these symptoms generally settle with a dose reduction.**
High blood cholesterol levels	• This treatment may increase your blood cholesterol levels. This is not a side effect you will notice. • Your cholesterol levels will be checked during your treatment.

Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including:
	  ◦ tingling or pins and needles
	  ◦ numbness or loss of feeling
	  ◦ pain.
	• You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects.
	• Test water temperature with your elbow when bathing to avoid burns.
	• Use rubber gloves, pot holders and oven mitts in the kitchen.
	• Wear rubber shoes or boots when working in the garden or garage.
	• Keep rooms well lit and uncluttered.
	• Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**

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.**

Heart changes	• You may get chest pain, shortness of breath, an abnormal heartbeat or swelling in your arms or legs. • Before, during or after treatment you may be asked to have tests to see how well your heart is working. • You will also have other blood tests to check your electrolyte levels. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department, 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.**
Weight gain	• You may have weight gain due to an increase in appetite (feeling hungrier). • Regular exercise and a balanced diet may help. • If you are worried about gaining weight or you gain a large amount of weight over a short period of time please talk to your doctor or nurse.

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.
- 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. Hormonal contraception (such as pills, injections or patches) may not work as well in women having this treatment, and non-hormonal methods of contraception should be used. 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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https://www.eviq.org.au/pi/3790
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