ALK Positive Lung Cancer (UK)

Lorlatinib Experiences

Some of our members set out below, in their own words, their experiences of taking Lorlatinib.

Patients who have just been prescribed Lorlatinib frequently ask what side effects they can expect. Patients who have been taking Lorlatinib for a while often ask whether other patients have experienced the side effects that they are experiencing. Patients often ask whether dose reductions are common.

Debbie

I took Alectinib for nearly 4 years and I moved onto Lorlatinib due to progression in my brain. I have now been taking Lorlatinib for 3 years and 8 months. I was initially prescribed the maximum dose of 100mg but within a couple of months the dosage was decreased to 75 mg.

Side effects

Neuropathy. I initially experienced extreme neuropathy in my arms, legs & hands. I used to wake in the mornings and my forearms and hands would feel completely numb and in the evenings I used to feel extreme tingling in my hands. I bought some ice pack gloves from Amazon and this seem to help the tingling and helped me to sleep. I still experience mild neuropathy but only in my finger tips and calfs which increases when I stand in one spot for too long.

Cholesterol. My cholesterol also rapidly increased within 3 weeks of taking Lorlatinib and so the dosage was decreased from 100mg to 75mg. I also take 40 mg Pravastatin and 10mg Ezitimbe.

Energy levels. I initially felt an increase of energy compared to Alectinib but after about six months, just as I had felt on Alectinib, I began to tire easily again.

Sun sensitivity. After experiencing sun sensitivity on Alectinib it was great being able to go out in the sun again and not suffer an intense burning feeling following any sun exposure.

Although, since last year I seem to have developed an intense prickly heat rash when I've been exposed to the sun. Difference being I seem to be able to prevent it by using a sun sensitive Factor 50 sun cream. My skin and scalp also feels a lot dryer than they used to but a good moisturiser is helpful.

Weight gain and low mood. Some people have reported weight gain and mood swings. I haven't particularly put on weight since taking either TKI although I have to be a bit more mindful of what I eat. I have a sweet tooth, particularly for chocolate and have found that I put weight on much easier than I used to. Swimming and regularly attending water aerobics has helped me to maintain a good weight and to feel more positive.

Cognitive and other mild side effects. I've not experienced speech or memory issues but I have found it more difficult to get off to sleep. I definitely feel that I have less patience and that I am less tolerant too. I occasionally suffer with mild nausea but I find Cyclizine really helps and I take several different medications for constipation.

It's difficult to know the exact cause of some side effects, particularly for women. I have to be mindful that some could be due to being perimenopausal.

The benefits of taking Lorlatinib compared to Alectinib

Lorlatinib only needs to be taken once a day as opposed to twice. It can be taken any time of the day. I take 3 x 25mg tablets every evening around 9pm.

Lorlatinib doesn't need to be taken with food.

Since taking Lorlatinib the neuropathy and muscular ache in my calfs can be uncomfortable at times but overall, given the choice, I would say that I prefer Lorlatinib to Alectinib.

Anon (male)

After 9 months of Alectinib post-diagnosis, I was switched to Lorlatinib.

I had never tolerated Alectinib very well due to the liver side effects and was on a 750mg dose as a result. I then developed multiple brain mets hence the switch to Lorlatinib. It almost immediately relieved the brain swelling and mets.

I have now been on Lorlatinib for 16 months and have tolerated it much better than Alectinib. My cholesterol readings are very high (when measurable!) and I have been taking Pravastatin and Ezetimibe from the start. A dose reduction of Lorlatinib (from 100mg to 75mg) after 13 months has reduced the cholesterol to measurable readings and alleviated most of the side effects.

Benefits of Lorlatinib (for me)

- 1 tablet per day (now 3 small ones) versus Alectinib
- high energy, can be busy all day now, no naps
- more stable blood tests, less monitoring required
- can now plan ahead much more due to more stability and less appointments
- body shape has improved and lost belly weight
- no longer have leg cramping
- bowels are much better
- can now walk distance, manage hills and non-impact gym, e-bike etc.

My side effects (before dose reduction)

- very very high cholesterol
- stiff hands
- Xanthoma lumps on palms and knuckles
- tenderness around nipple area
- night sweats
- crawling feeling in scalp (wearing a hat?)
- some joint pain (knees, elbows)

None of these effects significantly impacted on my quality of life and I felt churlish bringing them up with my Oncologist, so usually didn't.

After dose reduction, I'm left (after 3 months) with

- less stiff hands
- some night sweats

Ronen

I have been taking Lorlatinib from 2023/12 to 2024/12.

Good results for 6 months, then only control some cancer spread, less and less toward end of 2024.

Main side effects for me, high cholesterol levels, high sugar levels, gain weight.

Robert

Lorlatinib has been a very good drug for me - the only side effect that bothered me sometimes was swelling but apart from that nothing else.

I also only had short weekly time off it.

Emmanuel

Taking Lorlatinib has been both a blessing and a challenge. I'm incredibly grateful for what it's done to keep my cancer under control. It has extended my life and given me time I might not otherwise have had. But the side effects have been tough.

The main issue for me has been neuropathy in my arms — it started as tingling and gradually got worse, making it hard to do everyday tasks. This side effect became so severe that I had to reduce my dosage. I'm now on half dosage. However, even with a lower dose, I still have to manage symptoms carefully.

I've not experienced the memory or speech issues that others sometimes report, and I've had no neuropathy in my feet — but fatigue, mood swings, and weight changes have been real and ongoing struggles.

It's not easy living with these side effects, but I try to stay focused on the fact that this treatment is working. I just wish more support was available for managing the impact it has on day-to-day life — especially when you're trying to keep going with work and personal projects.

Anon (male)

100mg

- Cognitive issues: aggressive, paranoia, argumentative, visual disturbances, split personality (Jekyll and Hyde) and out of body experience
- Weight gain
- Neuropathy in feet and hands
- Joint aches and pains

Dosage reduced to 75mg

- Reduced cognitive issues
- Still get weight gain
- Neuropathy issues
- Joint aches and pains

Sue

I have been on Lorlatinib for 3 months and feeling very fortunate not to have any side effects at this point, apart from a couple of days one-off vomiting which may or may not be attributed to Lorlatinib.

Elaine

I've been on 75mg lorlatinib as second line tki for 6 months, and my experience has been a mixture of benefits and challenges. I'm grateful for the time it gave me without needing chemotherapy.

The side effects have not been too significant for me. The most difficult has been increased weight gain and increased appetite, which have affected my body image and day-to-day comfort. I've also experienced fluid retention (including oedema), bladder irritation from the increased oedema, and bowel movement urgency.

Despite the side effects, I have tried to manage them as best I can and remain active where possible (including regular swimming). I also take 5mg rosuvastatin to keep cholesterol levels down.

Overall, while lorlatinib maybe helped to slow disease progression for a short time initially, the side effects (particularly oedema) and the loss of effectiveness in my case, have been difficult. I'm now preparing for the likelihood of starting chemotherapy in the coming weeks. That said, I remain thankful for the time lorlatinib gave me.

Debra

After 6 months on Crizotinib and 4.5 years on Alectinib, I switched to Lorlatinib.

Very soon, I was experiencing hallucinations and I was manic. I didn't realise I was manic and it took other people to tell me. It is important that carers are aware of this possibility as the patient will not notice.

The dose was reduced to 75mg and the hallucinations and mania disappeared. As with most patients, my cholesterol level rose and I take a statin.

I had a small area of progression in a lung and this was successfully treated by ablation.

Apart from occasional bouts of diarrhoea, especially if I have too many glasses of wine, I am tolerating Lorlatinib well. That said, I often struggle to find the right words and my memory has definitely deteriorated.

After over 4 years of hiding from the sun whilst on Alectinib, I now thoroughly enjoy sunbathing - just had a week in Morocco at 40C. Also, the fatigue of Alectinib has disappeared.

I find Lorlatinib at 75mg much easier to tolerate than Alectinib and have now been taking it for 3.5 years.

Nancy

I am a newbie, formally diagnosed in June, 2025, and started directly on Lorlatinib on 1st July (I am much luckier than my insurance company), so I haven't much experience to offer. I'm 78, with a good health baseline, on the full dose of one 100 mg pill a day.

The main side-effect so far is invisible: my cholesterol and lipids have shot up, so I am on a statin already.

The only other side-effect so far is paresthesia, more accurately disesthesia: a week ago I woke up late at night with severe pain in my hands, but after a few difficult episodes I have done away with it altogether by wearing wrist braces to sleep, meaning I must have an unknown carpal tunnel problem.

Otherwise I am just hoping I can stay like this. I'm keeping an eye on that long list of side effects and shall let you know if something interesting happens. I'll know more at the end of August, after the next follow-up and first scan.

I must say I was amazed at the speed of the effect: my cough stopped on day 1 of the treatment.

Lizzie

I started taking Lorlatinib as 1st line of defence in Nov 2024. I'm on 100mg dosage. Physically I feel really well and am very very grateful for that.

I am also very grateful that I was fortunate enough, by chance, to have private medical insurance and I really hope that Lorlatinib becomes available for 1st line treatment in NHS England ASAP!!!

I am also grateful that I can take this treatment in tablet form at home.

It pushed my cholesterol up so I've had to go onto Statins and Ezetimibe but am being monitored very closely and bar extra tablets to take, there's not any difference and cholesterol has come down.

Sometimes I get slightly stiff fingers in the morning which goes with a 'wiggle'.

I am aware it can alter moods so am keeping an eye on that...with a diagnosis there are so many factors to consider.

I know it can increase weight but am trying to stay fit and active to fight the good fight.

Looking forward to the day when I can take a tablet and it can be a cure.

James

I'm on the standard 100mg dose, I have been for 2 years. I have not yet experienced any dose reductions or pauses.

My side effects include:

- **High blood pressure.** Managed with drugs it is currently in or near the reference ranges.
- **Lethargy.** This might be linked to thyroid underactivity. I'm on Levothyroxine, which might be helping. It is very annoying.
- **Nausea.** I have occasional mild nausea, but it's not much of a problem.
- **Skin problems.** I've had skin problems since starting Lorlatinib. I have mild eczema on my face and blotches the rest of my body. I've been prescribed a steroid cream to manage the eczema. It's not much of a problem.
- **Sweating.** I have bouts of profuse sweating, alternating with shivering and goosebumps. I've asked many doctors and nurses about this, they don't know what is causing it. The only thing that helps is a handheld fan - drying and cooling.
- **Weight gain.** I have gained a lot of weight since starting Lorlatinib, perhaps linked to the lethargy. This has made my life a lot worse. People seem to be angry at me for being fat.
- **Liver function.** My liver function seems to have deteriorated since I started on Lorlatinib. My ALT is high and fluctuates a lot. It isn't causing me any problems but it is worrying.
- **Heart.** I have moderate heart failure. My heart function fell to about 35%. I am now on medicine for it, and it seems to be well managed, my heart function around normal.
- **Balance.** I am unsteady when walking. It makes me look drunk when I am sober. Ironically, I move more steadily after a couple of drinks.

Margo

I have been taking lorlatinib for over a year now. I take 3 x 25mg daily.

I started out on 100mg but found side effects to be very badly swollen feet, loss of taste, loss of smell, sore joints and swollen hands, so they reduced me down to 75mg which lessened the side effects mentioned.

I still don't have taste or smell but swelling has reduced a lot. Touch wood, it works fine for me with good results on my scans, the most recent being last month.

Gareth

I was on Alectinib for about 18 months, before it stopped working. I was moved to Lorlatinib with the highest start of dose of 100mg approximately 4 weeks ago.

There are many side effects that are similar to Alectinib - tiredness, lack of energy and strength, forgetfulness, brain fog, memory loss. Bone and muscle pain/ache. Breathlessness.

I am on a break at present.

Tiredness etc has been better than with Alectinib but memory function has been worse.

Clara

I have been on Lorlatinib as a first line treatment since I was diagnosed in October 2024. I started on 100 mg and after a month my liver function test results were poor so the oncologist paused the treatment for two weeks and then I returned to 100 mg until May 2025.

In May, I had a PET scan and the result was "complete metabolic response" so I was offered a dose reduction to 75 mg for quality of life improvement. (I have not had a scan result yet since then so cannot comment if the dose reduction has been equally as effective.)

When I was diagnosed, I made a point of increasing my daily exercise. To be fair, I was increasing from a very low base! However, I found this helped immensely with many of the side effects. 100 mg caused pain in the mornings particularly in my hands and knees but this was alleviated by walking on a treadmill and persevering even when the first few minutes were painful. I do 3km daily.

Other side effects for me included a complete loss of taste, the inevitable increase in cholesterol leading to statin requirements, an occasional out of body experience, and with hindsight since I have reduced to 75 milligrams, a sort of spacey sensation, what I imagine "stoned" must be like. I also had a very increased libido for about 2 months.

Since reducing to 75 milligrams, I still struggle to find the correct words at times, my memory is appalling, my hands can still be very stiff and on a day without exercise I do experience pain.

That all said, I'm extremely grateful to have Lorlatinib.

Jilly

I have been taking Lorlatinib for two years having previously taken Alectinib for 3½ years. Lorlatinib has helped reduce my brain mets and I think it's a very good drug. However there are, of course, side-effects. I will list them below:

- Weight gain - I have gained about two stone
- Burning soles of my feet
- Painful and swollen knee joints
- Diarrhoea
- My eyesight is affected
- Blurred vision
- Increased cholesterol, so I take statins

The Lorlatinib dose I take was reduced from 75mg down to 50mg per day 6 months ago as I was feeling a bit 'drugged' and I feel better for it.

Anon (male)

I switched to 100 mg Lorlatinib 15 months ago after 4 years on Alectinib. Within a few days I had complete relief from pain as the Lorlatinib got to work on my hip and pelvis mets.

I also was pleased to say goodbye to the sun intolerance, tiredness and constipation that Alectinib gave me.

In exchange, Lorlatinib gave me high cholesterol, oedema and peripheral neuropathy. The latter two are much improved now. This seems to be a gradual and natural improvement, while a statin controls my high cholesterol. I have not noticed any adverse psychological effects.

My last scan shows very small progression in my pelvis so the plan is to continue with Lorlatinib for now and review quarterly.

Karen

I started with Lorlatinib in July 2022. I had to stop taking Brigatinib in the May, due to a dramatic drop in my kidney function. I had a couple of months to give my kidneys time to recover.

With every TKI I have been on, my body reacts badly to any dose over 50%.

I started on Lorlatinib at the full dose of 100mg per day. That only lasted 2 weeks, and my blood results showed that my kidney function had dropped again. Between July and December 2022 I was 'on and off' my medication every 2 weeks.

In January 2023, my dose of Lorlatinib was reduced to 50mg (2 tablets a day). I have never looked back.

Most of my blood results came back with really bad readings, but I was sent to various specialists and each one recognised that the blood results were a side effect of the Lorlatinib rather than any other underlying health issues and prescribed the appropriate medication to control it.

Cholesterol was the worst, it shot up to 16 !!!! It is still high, wavering between 8 and 10, but stable.

Other than my blood results, I have no other side effects.

I have plenty of energy, still working full time and we are also building our own house, so I am managing stress very well. I can eat and taste my food. My CT Scan results show no disease progression.

Any problems that I have are not due to Lorlatinib. They have been caused by a change in my oncologist who prescribed Radiotherapy, for no reason at all, and that has scarred my lungs that has totally destroyed my quality of life.

Jerry

I began taking Lorlatinib at a daily dose of 100mg. After eight weeks, a routine blood test revealed elevated toxicity levels, and I was advised to pause treatment for a week. I then resumed on a reduced dose of 75mg, which I've now been on for five months. Since that adjustment, my blood tests have remained within a healthy range.

About six weeks into treatment, I started experiencing a fluttering sensation under my right rib cage, near the liver—almost like my liver was "dancing." My cholesterol levels were also elevated at the end of the first and second months. At the time, I was told that if the levels remained high, I might need to start statins. Fortunately, the readings improved on their own, and no additional medication was necessary.

Three months in, I noticed changes in my mood. I found myself becoming more easily upset, which added pressure at home—especially with a newborn baby and a three-year-old going through tantrums. It was a tough period for our family. Both my wife and I began weekly therapy sessions, and they've been incredibly helpful in giving us space to reflect and cope. For me, incorporating twice-daily breathwork and meditation has been especially grounding and supportive in day-to-day life.

Aside from these experiences, I haven't encountered any other issues I'm aware of. I'm 44 years old and generally fit and active when life allows. Just recently—after several long days of driving with poor sleep, too much coffee, and a fair amount of chocolate (I do have a terrible sweet tooth!)—I noticed the same "dancing" sensation in my liver return. I

recognise I haven't been looking after myself very well during this time, so I'm hoping a return to better habits will help ease that again.

I have my six-month scan and brain MRI scheduled next week. To anyone reading this—whether you're in the midst of your own treatment or supporting a loved one—I'm wishing you strength, peace, and good health on your journey.

Paul

I started Lorlatinib at 100mg dose, initially taking it after breakfast (same as when taking Brigatinib). I immediately started with two unusual side effects. One was a feeling that I was always wearing a hat and the other was that when I was in a room with people, whether holding conversations or not, I sometimes felt as though I was outside of the room looking in through a window.

After mentioning the two side effects I was experiencing to my oncologist, he suggested that I should try taking Lorlatinib an hour before going to bed to determine whether this would help resolve the side effects. This I did and I found that not only I was no longer experiencing the two side effects but I was also sleeping better and much deeper.

One side effect which I had carried through Crizotinib and Brigatinib and which was still being experienced with Lorlatinib but to a higher degree was constipation. After starting Lorlatinib, I found that I had to use Laxido once a day rather than once every other day as previously.

Other than the constipation, all was ok for 8 months but I then started to feel that my ability to concentrate was being negatively affected and that I was becoming confused when outside in windy conditions. Additionally the constipation was getting worse.

This coincided with me having a new oncologist, the first change in 8 years and a change from an oncologist whom I had a good relationship with and had a great deal of trust in. My new oncologist, who is very young and openly admitted that she knew nothing about ALK+ but was educating herself quickly, suggested a dose reduction to 75mg. I was initially sceptical because of her lack of expertise with ALK+ (my previous oncologist was an expert) and resisted but after a further 2 months I conceded and agreed to the dose reduction.

The side effects disappeared almost overnight. I was once again alert to everything. I could deal with being out in windy conditions and the constipation had eased back to "normal" levels.

After 18 months taking 75mg, scans show that the disease remains stable and I am back to living as I would without the diagnosis of ALK+ lung cancer with brain mets, apart from the daily routine of taking Lorlatinib and Laxido and the quarterly scans etc.

Ruth

I have been on Lorlatinib for 8 months after being on Alectinib for 18 months, at which point I experienced progression. I started on the full 100mg dose and am still on that dose.

Positives of Lorlatinib

1. Much more energy than when I was on Alectinib.
2. No sun sensitivity which I had with Alectinib.

Negatives of Lorlatinib

1. Increased weight gain despite many different diets / weight loss measures.
2. Swollen stomach and oedema in legs and hands.
3. Neuropathy in hands and arms, particularly the right side.
4. Sometimes speech is slurred.
5. Issues with memory from time to time - though perhaps this could be the result of aging / menopause!

Despite the side effects, I continue to work and generally can tolerate them. In recent weeks, neuropathy has been particularly bad at times, on occasion making it difficult to get to sleep.

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