What the CROWN blood-test (ctDNA) study tells us about lorlatinib

A plain-English summary for people with ALK-positive lung cancer

Generated by artificial intelligence

The short version

Lorlatinib works very well for most people with ALK-positive advanced lung cancer, and many stay well for years. About **1 in 5** people have their cancer start growing again within the first year. Researchers looked at blood samples to understand why. They found some differences in the tumours of people whose cancer progressed early, but **these findings are early research and do not change how anyone is treated today.**

Background: how well does lorlatinib work?

The CROWN trial compared lorlatinib with an older ALK medicine, crizotinib, in 296 people who had not had treatment before. After seven years:

- About **55 in 100** people on lorlatinib were alive with their cancer not growing, compared with about **3 in 100** on crizotinib.
- The risk of the cancer growing or of death was about **81% lower** with lorlatinib.
- The risk of the cancer growing in the brain was about **94% lower**. After the first 2½ years, no new brain progression was reported.

What was studied?

Tumours shed tiny pieces of DNA into the blood. This is called **circulating tumour DNA, or ctDNA**. A blood test can read it, a bit like reading the tumour's "fingerprint" without a biopsy.

Researchers compared two groups who took lorlatinib:

- **Early progressors:** the cancer grew within 12 months.
- **Long-term responders:** still alive with no cancer growth at seven years.

Blood samples from the start of treatment were available for 120 people.

What did they find?

1. Early progressors had more complex tumours. Their tumours had changes in about 10 genes on average, compared with about 6 in long-term responders. A tumour that depends on only one main "driver" (ALK) seems easier for lorlatinib to control. A tumour with more going on may have other ways to survive.

2. A gene called TP53 was changed more often. About half of the early progressors had a TP53 change, compared with about 1 in 6 long-term responders. TP53 changes are linked to more aggressive cancers in general.

3. Genes linked to inflammation were changed more often. This was seen in about 1 in 3 early progressors, compared with about 1 in 14 long-term responders.

4. When lorlatinib stopped working, it was not because ALK changed. In people whose cancer grew, the team did not find new changes in the ALK gene. With older ALK medicines, the cancer often stops responding because ALK itself changes. Here, the cancer seemed to find other routes to keep growing. This is useful for researchers designing the next treatments. The number of samples was small, and blood tests can't catch every kind of resistance.

5. Lorlatinib worked across different ALK types. Some ALK changes ("variant 3" in particular) have been linked to a poorer outlook. Lorlatinib still worked well in these people. About 53 in 100 people with variants 1 or 2 and about 43 in 100 with variant 3 were free of cancer growth at seven years. Your ALK variant is not a reason to avoid lorlatinib.

6. The amount of tumour DNA in the blood was informative.

- People with **no detectable tumour DNA** in their blood at the start did especially well.
- People whose tumour DNA **cleared quickly during treatment**, in some cases within 4 weeks, also tended to do better.
- This suggests repeat blood tests might one day show how well treatment is working earlier than scans can.

What does this mean for me?

- **Nothing changes in your treatment because of this.** These tests are not used to decide who gets lorlatinib or whether to add other treatments, and the researchers say none of these results should be used that way yet.
- **This was an exploratory analysis,** looking back at blood samples to spot patterns. Patterns are not proof, and the numbers in some groups were small.
- **A pattern in a group doesn't predict what will happen to one person.** Some people with TP53 changes do very well, and some without them have early progression.
- **The hope is for the future.** Doctors may eventually combine blood tests and other information to find the few people who need extra treatment early, and to develop new medicines for the cancer routes that lorlatinib doesn't block.

Based on a report of research presented at the ESMO Congress 2026 (Solomon et al., CROWN trial, NCT03052608).