Understanding Results of the Ongoing **CARDINAL Trial**

A phase 1 study of TERN-701 for patients with previously treated chronic myeloid leukemia (CML) in chronic phase

What is the CARDINAL study?

The CARDINAL study is an ongoing Phase 1 study of the safety and effectiveness (how well it works) of TERN-701 in patients with chronic myeloid leukemia in chronic phase (CML-CP) who have previously been treated with one or more CML therapies.

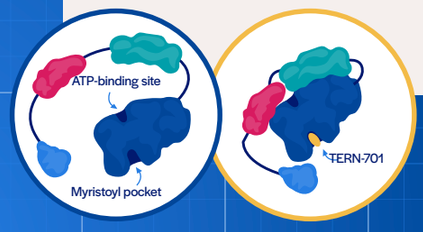
This is a summary of the first (preliminary) findings from the ongoing study, as of September 13, 2025. These results were presented to attendees at the American Society of Hematology conference in December 2025.

What is TERN-701?

TERN-701 is an investigational drug being developed to treat adults with CML-CP. *Investigational* means it is still being studied in clinical trials and hasn't yet been approved for use in patients with CML.

CML cells contain an abnormal protein called BCR::ABL1, which causes the cells to grow uncontrollably. Many current CML medicines, called tyrosine kinase inhibitors (TKIs), work by turning off the main "switch" of the BCR::ABL1 protein. This switch is called the ATP-binding site. Because this part exists on many proteins in the body, these medicines can affect several different proteins and may cause unintended or "off target" side effects.

TERN-701 attaches to a different and specific part of BCR::ABL1, called the myristoyl pocket, to switch off the protein. This is a different way of treating CML, known to doctors as "allosteric inhibition."



Why is the CARDINAL study being done?

CML is a cancer of the bone marrow and blood. Most people with CML are diagnosed in the chronic phase (CML-CP). This is the first phase of CML and the phase that usually responds best to treatment, because the cancer is still developing slowly.

TKIs are the main treatment for CML-CP. Many patients with CML-CP who are receiving TKIs still experience worsening (progression) of their CML or are unable to tolerate treatment because of side effects.

Since TERN-701 works differently to some existing treatments, study investigators want to understand if TERN-701 could have fewer side effects, be better tolerated, and work more effectively than other treatments.

How is the CARDINAL study being carried out?

CARDINAL is an open-label study. Both the investigators and their participants know which treatment and dose is being received. The study is running in many medical centers around the world.

The study has two parts.

Part 1 is testing four different doses of TERN-701

160 mg · 320 mg · 400 mg · 500 mg — 1x daily

At least **3** participants per group.

Up to **80** participants total.

The purpose of Part 1 is to find two doses of TERN-701 that have acceptable safety results and show some effect on CML.

Part 2 focuses on the two doses chosen in Part 1 and study them more closely.

320 mg · 500 mg — 1x daily

40 participants per group.

Approximately **80** participants total.

TERN-701 is given as a pill (orally) once daily with or without food. Participants stay on treatment until the study ends, or until they stop taking part.

Who can take part in the CARDINAL study?

Participants can take part in the study if they:

- are aged **18** years or over
- \+ Have a confirmed diagnosis of BCR::ABL1-positive CML-CP, with or without BCR::ABL1 mutations
- \+ Have previously been treated with one or more CML therapies and either stopped responding, or had an inadequate response; had no response; or were unable to tolerate these treatments because of side effects. Previous treatments include TKIs such as imatinib, dasatinib, nilotinib, bosutinib, ponatinib, and asciminib.

How will researchers evaluate safety and how well the treatment works?

To evaluate safety, researchers are monitoring what side effects participants experience, how often they occur, and how severe they are. They will also look at laboratory results and vital signs.

To understand how well the treatment works, researchers will look at how many participants have had a **major molecular response (MMR)**.

MMR means that the amount of BCR::ABL1 gene in the blood has dropped to a very low level, where fewer than 1 in every 1,000 cells (0.1%) has the BCR::ABL1 gene.

Achieving and staying in (maintaining) MMR is a standard way of measuring how well a drug works for CML.

Researchers will also look at how many participants have had a **deep molecular response** (DMR). This means BCR::ABL1 is almost undetectable in the body, and fewer than 1 in 10,000 cells (0.01%) has the BCR::ABL1 gene.

TERN-701 is investigational; the safety and efficacy of TERN-701 for CML-CP have not been established.

What are the initial results from the CARDINAL study?

Patient participants

As of 13 September 2025:

63 participants were enrolled

55 participants were still in the study and receiving TERN-701

Participants had received TERN-701 for a median of **6.1** months

At the start of the study (baseline):

64% (40 of 63) had stopped responding, had a limited response or no response to their most recent TKI, meaning it did not work effectively

29% (18 of 63) were unable to tolerate their most recent TKI because of side effects

Previous treatments:

60% (38 of 63) had been treated with 3 or more TKIs

38% (24 of 63) had previously received asciminib

22% (14 of 63) had previously received ponatinib

Safety results

Results were available for **63** participants

Study investigators did not observe severe side effects that would prevent participants moving to a higher dose. As a result, the study did not identify a maximum dose that participants could not tolerate.

In this study, investigators look at "treatment-emergent side effects." These are any unwanted effects that may emerge while a participant receives the study drug. These may or may not be caused by the treatment itself.

81% of patients had side effects

61% mild or moderate in severity and did not increase with higher doses of TERN-701.

The most common side effects of any cause, and any severity were

- **21%** Diarrhea
- **19%** Headache
- **19%** Nausea

2% (1 out of 63) participants stopped taking TERN-701 because of side effects

How well the treatment worked

Results were available for **38** participants

More participants reached MMR and DMR at higher dose levels (320 mg and above).

No participants had lost MMR at the time of the analysis.

74% **(28 of 38) participants were in MMR by 24 weeks of treatment.**

Achieved MMR during the study. 64% (18 of 28)

Already in MMR at the start of the study maintained it. 100% (10 of 10)

Achieved DMR. 29% (10 of 34)

MMR was achieved by participants who:

Stopped their most recent TKI treatment because it did not work effectively. 63% (12 of 19)

Were unable to tolerate their most recent TKI treatment because of side effects. 71% (5 of 7)

Had previous treatment with asciminib. 43% (3 of 7)

Had previous treatment with asciminib/ponatinib, and/or an investigational TKI. 50% (4 of 8)

What do these results mean?

In this study of participants who had previously received several CML treatments, the side effects seen so far were mostly mild or moderate. Side effects did not seem to increase with higher doses of TERN-701.

Early signs of response were seen in participants who had not responded well to previous treatments.

Most participants taking TERN-701 were able to reach or maintain MMR by 24 weeks. More participants reached MMR and DMR at higher dose levels (320 mg and above).

These are preliminary findings. Safety and effectiveness will continue to be assessed as the study progresses.

For more information about the CARDINAL study, please visit: **https://clinicaltrials.gov/study/NCT06163430**

If you would like to find out more about the results of this study, the full title of the abstract presented at the 2025 American Society of Hematology conference is: *"CARDINAL: A Phase 1 study of TERN-701, a novel investigational allosteric BCR::ABL1 inhibitor for patients with previously treated CML."*

TERN-701 is investigational; the safety and efficacy of TERN-701 for CML-CP have not been established. This study was organized and funded by Terns Pharmaceuticals, Inc.