Plain-Language Summary of the CLL17 Interim Analysis

A phase 3 multicenter, randomized, prospective, open-label trial of ibrutinib monotherapy versus fixed-duration venetoclax plus obinutuzumab versus fixed-duration venetoclax plus ibrutinib in patients with previously untreated chronic lymphocytic leukemia (CLL)

Background of the study

Chronic lymphocytic leukemia (CLL) is a type of blood cancer in which certain white blood cells grow uncontrollably. In recent years, newer targeted therapies have significantly improved treatment options for patients with CLL. However, it is still unclear whether a time-limited combination treatment or continuous long-term therapy provides better results over time. The CLL17 study therefore compares 2 time-limited combination treatments with continuous long-term treatment. The study is sponsored by the University of Cologne and is conducted in collaboration with the German CLL Study Group (GCLLSG) and international partners. A total of 174 hospitals and clinics in 13 countries participated. The study was launched in February 2021 and will run until the end of 2027.

Purpose of the study

The study aims to compare:

- how well different treatments control the disease,
- how long patients remain free from disease worsening,
- how safe and tolerable the treatments are,
- and how treatment affects patients' quality of life.

Who participated?

A total of 909 adult patients with previously untreated CLL took part in the study. The study included patients with different health conditions and genetic risk factors.

Which treatments were studied?

Patients were randomly assigned to one of three treatment groups:

1. **Venetoclax plus Obinutuzumab:** a fixed-duration combination treatment
2. **Venetoclax plus Ibrutinib**: another fixed-duration combination treatment
3. **Ibrutinib alone**: a continuous long-term treatment

Patients underwent regular medical assessments during the study, including blood tests and imaging procedures (for example computer tomography).

Study results

After a median follow-up of about three years, the treatments showed broadly similar results:

- Around 80% of patients in each group remained free from disease progression after three years
- More than 90% of patients were still alive after three years

These findings suggest that a fixed-duration combination therapy of approximately one year (e.g., venetoclax plus obinutuzumab or venetoclax plus ibrutinib) is as effective as continuous long-term treatment with ibrutinib. This indicates that, for most patients with CLL, a time-limited, chemotherapy-free treatment regimen represents a valuable therapeutic option.

Side effects and safety

As with most cancer treatments, side effects occurred in all treatment groups. The most common side effects included infections, nausea and diarrhea as well as changes in blood cell counts. More serious side effects included severe infections, heart-related problems such as irregular heartbeat or high blood pressure, and, in rare cases, tumor lysis syndrome, a condition caused by the rapid breakdown of cancer

cells. Some patients stopped treatment because of side effects. Most deaths reported during the study were related to infections, including COVID-19.

What do the results mean?

The results so far suggest that both fixed-duration combination therapies and continuous treatment can effectively control CLL for several years.

The study provides important information about:

- which treatment strategies may offer long-term disease control,
- how well different therapies are tolerated,
- and which approaches may be most suitable for certain groups of patients.

Because the study is still ongoing, additional analyses will continue to evaluate long-term outcomes and possible differences between patient subgroups.

Summary

The CLL17 study compares modern treatment strategies for patients with previously untreated CLL. Based on the analyses available to date, all treatment approaches investigated have shown favorable outcomes in terms of disease control, with no apparent differences between fixed-duration combination therapy and prolonged continuous treatment. Therefore, for most patients with previously untreated CLL, a time-limited combination regimen can be considered a valuable therapeutic option.