Final results from the CLARITY trial

These results were presented at the American Society of Haematology conference in December 2022

This document is a plain English summary of the presentation.
A link to the summary presented at the conference is at the end of this document.

People whose CLL came back or stopped responding to treatment do well with ibrutinib plus venetoclax: Results 5 years after starting the CLARITY trial.

Why was the research needed?

In the past, people having their first treatment for chronic lymphocytic leukaemia (CLL) often had chemotherapy (usually the combination of fludarabine, cyclophosphamide and rituximab, called FCR). Some people do not need treatment again. For others, either their CLL comes back, or their treatment stops working. Ibrutinib and venetoclax are relatively new targeted cancer drugs (compared to chemotherapy). Both drugs work well for treatment of CLL, but this study was the first time they were used together for CLL.

What were the main questions studied?

The CLARITY trial studied whether taking ibrutinib with venetoclax cleared the CLL for people whose CLL had come back, or their treatment had not worked.

Who took part in the trial?

Participants joined the study between May 2016 and November 2017. Fifty-four adults who needed treatment for their CLL and who had had at least one previous treatment took part. Three quarters of those who took part were men, and the average age was 64 years. Most (82%) had had chemotherapy in the past, and of these for half their CLL had come back in less than three years.

What treatments did the participants receive?

Participants took ibrutinib and venetoclax. Ibrutinib was given as 3 capsules taken at the same time each day. After eight weeks of taking ibrutinib venetoclax was started. The dose of venetoclax was increased each week for five weeks. It then continued as 4 tablets taken at the same time each day.

Ibrutinib was taken until either the CLL was cleared based on a bone marrow test, or the CLL got worse. Venetoclax was taken for 3 years but could be stopped before that if the CLL cleared on a bone marrow test.

Four participants stopped ibrutinib in the first eight weeks because of side effects and did not start venetoclax. So, in total, 50 participants had the combination of ibrutinib and venetoclax.

What side effects and other problems did the participants have?

About a third of participants had problems with bruising and/or bleeding. Six (5%) had heart problems. Other problems included a low neutrophil count (a type of white blood cell) and abdominal pain.

Nine participants died. The cause of death was Richter's transformation for 3, another cancer for 3, complications of CLL for 1, and for 2 the cause is not known.

What were the results of the trial?

Five years after starting the study, for 78% participants their CLL had not got worse and 91% were alive. Some participants have been in the study for more than five years. So, overall, 9 participants (18%) have died, for 11 (22%) their CLL has got worse, and 9 (18%) have continued their ibrutinib for longer than five years.

People whose CLL responded more quickly to treatment were more likely to have their CLL cleared so they were then able to stop treatment. The CLL continued to improve after one to two years of combined ibrutinib and venetoclax.

How has this study helped people with CLL?

This study has shown that ibrutinib and venetoclax taken together can work for people whose CLL has come back, or their treatment stops working. This treatment is now being tested for people having their first treatment for CLL (in the FLAIR trial).

Who were the researchers who did this study?

The trial team was led by Professor Peter Hillmen and supported by the Cancer Research UK Clinical Trials Unit.

Summary of the conference presentation is available here:
https://ashpublications.org/blood/article/140/Supplement%201/222/488681/MRD4-Eradication-at-6-Months-and-Early-Clearance

Paper reporting results after one year is available here:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6879312/

Trial registration number: ISRCTN13751862