

PALLET Trial

A phase II randomised study evaluating the biological and clinical effects of the combination of palbociclib with letrozole as neoadjuvant therapy in post-menopausal women with ER+ primary breast cancer

Summary of Results

Some time ago you kindly agreed to take part in a clinical trial called PALLET. The aim of the trial was to find out if adding a new drug called palbociclib to standard hormone therapy with letrozole is better than using letrozole alone at treating breast cancer before surgery. The trial also aimed to find out who will be helped the most by the combination treatment by looking at the way the cancer reacted to the drugs given prior to surgery to remove the cancer.

You were one of 307 postmenopausal women with early stage breast cancer who joined the study between February 2015 and March 2018. The study was conducted at 38 hospitals and treatment centres in the UK, United States and Canada.

The main results of the trial are now available and have been explained in this leaflet.

More about this trial

Doctors sometimes treat breast cancer with hormone therapy before surgery. This is called neo-adjuvant therapy. It can help to shrink the cancer before surgery so that the operation is easier and the surgeon may not need to remove as much breast tissue.

In this situation, doctors often give a hormone therapy called letrozole (Femara). In this trial the researchers wanted to find out if another drug called palbociclib was beneficial if given alongside letrozole. Palbociclib (Ibrance) is a type of biological therapy. It targets and blocks the proteins that help cancer cells to divide and grow. If the cancer cells can't divide, the cancer can't get bigger.

When you consented to take part in the PALLET Trial you were allocated at random to one of 4 treatment groups:

- A. Letrozole alone
- B. Letrozole for 2 weeks followed by letrozole + palbociclib for the next 12 weeks
- C. Palbociclib for 2 weeks followed by letrozole + palbociclib for the next 12 weeks
- D. Letrozole + palbociclib for 14 weeks

During the trial, blood and tumour tissue biopsy samples were collected just before the start of treatment, after 2 weeks of treatment and when the trial treatment was finished. The investigators used these samples to assess the following before and after treatment:

- how quickly cancer cells are dividing (this is called cell proliferation)
- the number of cancer cells which die (this is called apoptosis) and are no longer able to divide
- changes in the size of the breast cancer using ultrasound scans
- the number of women who had no signs of remaining cancer at the time of surgery

- the proportion of women whose intended surgery at the time of diagnosis changed from the removal of the whole breast (mastectomy) to removal of the cancer area only (called breast conservation) after treatment

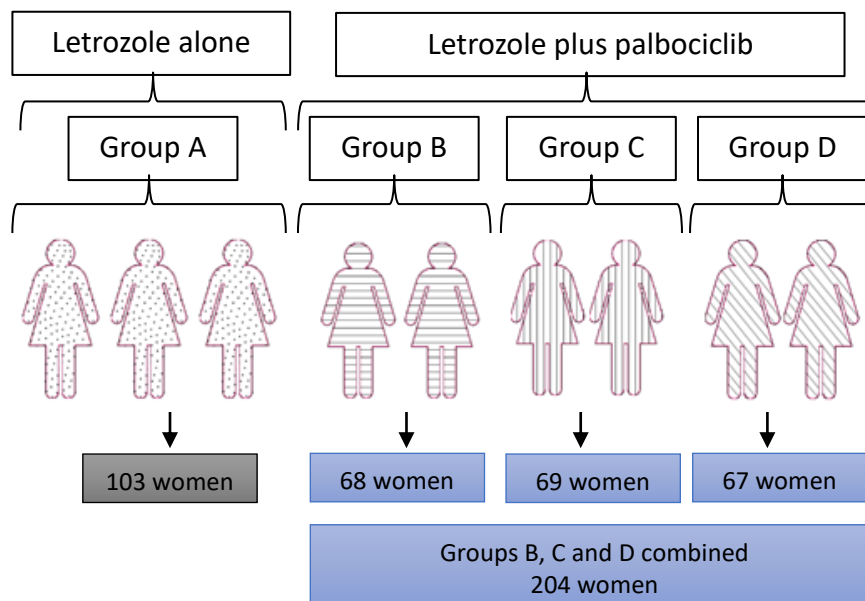
The researchers also assessed the side effects of the trial treatments.

The above results, along with information from the clinic appointments you kindly attended over the 12 months you participated in the trial, were collected and analysed at the Clinical Trials and Statistics Unit at The Institute of Cancer Research (ICR-CTSU). The results were published in a leading medical journal (Journal of Clinical Oncology, 2019, free to view) so that doctors from around the world can be made aware of the findings. The results included were for groups of patients and so you cannot be identified in this or any future publication.

Summary of Results

A total of 307 postmenopausal women took part in the study – 166 from the UK and 141 from the United States and Canada combined. The average age of the participants was 65 years.

For every 9 women who took part in the trial, 3 were allocated to Group A and took letrozole alone, and 6 women were allocated to a treatment group that included letrozole plus palbociclib, as shown below:



Overall 253 patients completed 14 weeks of treatment prior to planned surgery.

The trial team found that treatment with palbociclib plus letrozole **worked better** than treatment with letrozole on its own at slowing down how quickly the cancer cells divided (cell proliferation). When the researchers explored this further they also found that a greater proportion of women treated with palbociclib plus letrozole had cancer cells that were no longer able to divide compared to those treated with letrozole alone.

The researchers **did not see any difference** in the number of women whose cancer had shrunk in size by at least half or had disappeared completely after 14 weeks treatment with palbociclib plus letrozole compared with letrozole alone. Nor did they see any difference between the treatment groups in the proportion of women

whose intended surgery prior to treatment changed from whole breast removal (mastectomy) to the removal of the cancer area only (breast conservation) after treatment.

Side effects of treatment

The proportion of women who reported any side effect was similar between those treated with both palbociclib and letrozole and those treated with letrozole alone. The majority of side effects were considered mild or moderate. However women who received letrozole plus palbociclib were more likely to have a reduced number of white blood cells in their blood during treatment compared to those who received letrozole alone.

Results from the PALLET trial did not identify any unexpected side effects or risks of treatment in patients who received palbociclib and letrozole at the same time.

Conclusions

This study showed that 14 weeks of treatment with both palbociclib and letrozole was much better at slowing down how quickly the cancer cells divided compared to letrozole alone.

There was no difference in the size of the cancer between the groups at the end of 14 weeks of treatment. However the researchers think that this is because it may take much longer than 14 weeks for the cancer to decrease in size with treatment. This is why it was important in the PALLET trial to look closely at what was happening to the actual cancer cells with treatment.

Ongoing research

All patients who took part in the PALLET trial have now completed the trial and the main results have already been published as described above. However further research is being done on the samples that were collected during the trial. This work will provide more information about the effects of the combination treatment of letrozole and palbociclib on cancer cells. It may also help researchers identify new genes or proteins (called biomarkers) in the tumour samples that could be used to evaluate new treatments for early breast cancer in the future.

Thank you for taking part in the PALLET trial. Without the contribution of people like you, this trial would not have been possible. If you have any questions about the result of PALLET, please discuss this with your doctor who will be happy to help you.

Local Investigator:

Telephone number:

This trial was supported by Cancer Research UK, the National Surgical Adjuvant Breast and Bowel Project Foundation in North America and the drug company Pfizer. Support was also provided by the National Institute for Health Research funding to the Royal Marsden and Institute of Cancer Research Biomedical Research Centre.