New drug combination for aggressive breast cancer could save thousands of lives

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An immunotherapy drug called pembrolizumab has been shown to significantly reduce disease recurrence in patients with the most aggressive type of breast cancer, according to results from a phase III

clinical trial led by Queen Mary University of London and Barts Health NHS Trust.

The trial, named KEYNOTE-522, is the first phase III trial to demonstrate the benefit of adding immunotherapy to chemotherapy before patients receive surgery to remove their tumour. The results were published in the *New England Journal of Medicine*.

Patients with early triple-negative breast cancer (TNBC), where the disease had not yet spread beyond the breast and lymph nodes (stage II and III), were treated with pembrolizumab in addition to standard chemotherapy prior to surgery, followed by pembrolizumab after surgery.

In the most recent assessment, conducted over three years after the trial began, the risk of disease recurrence was 37% lower in patients treated with pembrolizumab in combination with chemotherapy than in patients treated with chemotherapy alone.

The findings from the trial represent a significant step forward for the treatment of TNBC, and indicate that the addition of pembrolizumab to preoperative standard chemotherapy can prevent breast cancer recurrence and result in higher long-term cure rates.

Study lead, Professor Peter Schmid from Queen Mary University of London and Clinical director at St Bartholomew's Hospital said: "We had previously demonstrated that the addition of immunotherapy to preoperative chemotherapy increases the treatment response in patients with triple-negative breast cancer at the time of surgery. We now have long-term results demonstrating that the combination therapy significantly reduces recurrences by approximately 37%, including reduction of secondary breast cancer by 39%.

"This means that the cure rate for these cancers is significantly increased. The estimates are that, just in the US where this treatment was recently approved by the Food and Drug Administration, this new treatment may save as many as 10,000 lives per year."

A total of 1,174 patients across 21 countries with previously untreated stage II or III TNBC were recruited to the trial, with some coming from St Bartholomew's Hospital. The trial was funded by Merck Sharp and Dohme. Patients were randomly allocated to receive pembrolizumab in combination with chemotherapy (784 patients) or placebo in combination with chemotherapy (390 patients). Following surgery, patients continued to receive either pembrolizumab alone or the placebo.

TNBC is an aggressive and hard-to-treat subtype of breast cancer, with a shorter survival time than other breast cancer subtypes. The cancer cells do not have oestrogen receptors, progesterone receptors, nor receptors for the HER2 protein; therefore, hormone therapies and drugs that target these receptors (commonly used to treat other breast cancer subtypes) are ineffective against TNBC.

Approximately 15% of all breast cancers (over 8,000 cases per year in the UK) are TNBC. The current standard of care for patients with early stage TNBC is chemotherapy, which is typically used to shrink the tumour ahead of surgery. Patients who have no detectable disease following surgery have an increased chance of survival; however, the risk of the disease returning remains high.

Pembrolizumab is a type of immunotherapy known as an immune checkpoint inhibitor, which works by binding to a protein called PD-1 on the surface of immune cells. Cancer cells can use the PD-1 pathway to hide from the immune system so, by blocking PD-1, pembrolizumab triggers the immune system to identify and kill cancer cells.

More information: Peter Schmid et al, Event-free Survival with Pembrolizumab in Early Triple-Negative Breast Cancer, *New England Journal of Medicine* (2022). DOI: 10.1056/NEJMoa2112651