Two studies make breakthroughs in treating some cancers in women

Hope for clear cell ovarian cancer, triple negative breast cancer patients

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Associate Professor David Tan and Dr Natalie Ngoi of the National University Cancer Institute, Singapore are part of the team involved in the Lara trial, which found that combining two drugs – pembrolizumab and lenvatinib – showed promise in treating patients with recurrent clear cell endometrial and ovarian cancers resistant to standard treatments. ST PHOTO: JASON QUAH

Two recent studies led by Singapore researchers have uncovered new treatments for certain cancers affecting women, such as clear cell ovarian cancer and triple negative breast cancer.

One study found that combining two drugs – pembrolizumab and lenvatinib – showed promise in treating patients with recurrent clear cell endometrial and ovarian cancers resistant to standard treatments.

The Lara trial, as the study was called, was spearheaded by the Asia-Pacific Gynecologic Oncology Trials Group – a collaborative research network founded by Associate Professor David Tan, a senior consultant at the National University Cancer Institute, Singapore's (NCIS) haematology-oncology department.

Many patients with clear cell cancers of the ovary and endometrium respond poorly to standard chemotherapy.

These cancers have been difficult to treat, partly because of the tumours' unusual cell features, abnormal blood vessel growth and a tumour environment – referring to the cancer cells surrounding a tumour – which allow them to evade the immune system.

Such clear cell cancers disproportionately affect Asian populations, making up almost 30 per cent of ovarian cancers in Japan, compared with about 12 per cent in Western countries.

The reasons for this are unclear, said Prof Tan, who is also principal investigator at the Cancer Science Institute of Singapore.

One possibility, he said, is the cancer's link to endometriosis – where uterine tissue grows outside the uterus – which is more prevalent in Asian women.

Lenvatinib blocks signals that support tumour growth, while making the tumour environment more accessible to immune cells.

Pembrolizumab then boosts the body's immune response to recognise and attack cancer cells.

While this combination is already approved here for use in patients with recurrent clear cell endometrial cancer, it has not been cleared for use on patients with clear cell ovarian cancers.

Clear cell ovarian cancers make up 30 per cent of all new ovarian cancer cases here.

Of the 25 patients undergoing the trial, 40 per cent saw their tumours shrink by 30 per cent or more within the first 24 weeks of treatment, with 50 per cent of patients showing no disease progression for more than six months.

Conducted between 2021 and 2023 in Singapore and South Korea, the clinical trial involved clinicians and scientists from both countries, and the findings were published in The Lancet Oncology in February.

NCIS consultant Natalie Ngoi, the study's first author, said: "Trials like ours are small but mean a lot for patients with rare cancer subtypes who are often excluded from larger randomised trials that focus on the common cancer subtypes."

One of the patients, who wanted to be known as Michelle, joined the trial after two lines of standard chemotherapy were unsuccessful, but could not continue with the trial after a month due to her liver enzymes increasing beyond the acceptable range. However, the benefits persisted even after treatment had stopped, with tumours in her neck and pelvic lymph nodes continuing to shrink.

"I'm very grateful to experience the magic of this pembrolizumab and lenvatinib," said the 49-year-old, adding that she hopes the treatment could be added to the Health Ministry's cancer drug list.

Prof Tan noted that a recent study in the United States showed similar results, further validating the results of the Lara trial.

"We are currently working to try to get this combination into the US National Comprehensive Cancer Network guidelines, which would then guide our subsequent efforts to make this treatment available for patients in Singapore," he said.

Separately, another trial involving patients with untreated, advanced triple negative breast cancer has shown significant improvements in their survival.

Triple negative breast cancer is an aggressive subtype that disproportionately affects women under the age of 40, and is associated with early recurrence and shorter survival.

It accounts for some 15 per cent of all breast cancer cases in Singapore, said Professor Rebecca Dent, deputy clinical chief executive officer at the National Cancer Centre Singapore.

Trial patients were treated with datopotamab deruxtecan (Dato-DXd), an antibody-drug conjugate that targets and kills tumour cells while sparing healthy ones.

It is currently approved for another type of breast cancer, but not the triple negative variety.

The study, which was published in the journal Annals of Oncology in April, recruited 644 triple negative breast cancer patients across multiple countries, including the United States, China and Singapore.

It found that progression-free survival – the duration one lives with a disease without it worsening – doubled to a median 10.8 months using Dato-DXd compared with chemotherapy, while overall survival also improved with the new drug.

Some 63 per cent of patients experienced a sustained shrinking of their tumours using Dato-DXd, compared with 29 per cent under chemotherapy.

The drug is currently under review as a first-line treatment for triple negative breast cancer by both the US Food and Drug Administration and Singapore's Health Sciences Authority, with Prof Dent hopeful that it receives approval within a year.

While tumours reduce in size using conventional treatments, they can often grow back, said Prof Dent, who is the study's lead investigator.

"One thing that's very consistent for all of these antibody-drug conjugates is that you can see a sustained response," she said.

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