Targeted therapy promising for HER2-positive metastatic breast cancer

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A new type of breast cancer treatment has shown encouraging activity as a first-line therapy in HER2-positive metastatic disease, researchers reported at the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy.

Principal investigator Edith Perez, MD, Mayo Clinic in Florida, presented the results of the first ever randomized trial of trastuzumab-DM1 (T-DM1) as a first-line treatment for metastatic breast cancer.

T-DM1 is the first of a new type of cancer medicine known as an antibody-drug conjugate. It binds together two existing cancer drugs with the aim of delivering both drugs specifically to cancer cells: trastuzumab, a monoclonal antibody that targets cells that overproduce the protein HER2; and DM1, a chemotherapy agent that targets microtubules.

"This is the first ever presentation of an anti-HER2 antibody-drug conjugate used as first-line therapy for patients with advanced breast cancer," said Professor Perez. "We are encouraged by the results. The study demonstrated that T-DM1 has very good anti-tumor activity as well as much lower toxicity when evaluated side by side to the older 'standard'."

T-DM1 has shown promising activity in preclinical studies. Other clinical trials have also shown it to be effective in patients whose advanced cancer has not responded to other treatments. "This trial represents the logical step --moving the drug up to patients with newly diagnosed HER2-positive metastases," Prof Perez said.

In the trial, researchers randomly assigned 137 women to treatment with either trastuzumab plus the chemotherapy drug docetaxel, or T-DM1. All participants had HER2-positive metastatic cancer, with no prior chemotherapy for their metastatic disease.

After a median of approximately 6 months of follow-up, the researchers found an overall response rate of 48% in patients administered T-DM1, compared to 41% in the trastuzumab plus docetaxel arm. Importantly, the rates of clinically relevant adverse events were significantly lower in the T-DM1 arm (37%) compared to the rate in women given traztuzumab plus docetaxel (75%).

This trial is ongoing and the positive outcomes are generating enthusiasm for a larger Phase-III trial which is now underway. "This trial is named MARIANNE, and it evaluates taxane plus trastuzumab against T-DM1 as administered in this study, with a third option being T-DM1 plus pertuzumab, another novel anti-HER2 agent," said Prof Perez. "I feel privileged to continue our collaborative work to help bring new and better therapeutic options for patients."

The results are important for two reasons, commented Dr Fabrice André from Institut Gustave Roussy in Villejuif, France.

"Firstly, they confirm that in coming years chemotherapy could be replaced by a less toxic compound. Indeed, in the present study, the rates of serious adverse events were much lower in patients given T-DM1 compared to the chemotherapy arm. These results suggest that, with the same efficacy, T-DM1 could dramatically reduce the toxicities related to chemotherapy."

The second important implication of this study is that it proves the concept that linking a monoclonal antibody to a cytotoxic drug leads to an anticancer effect. "This could have several implications beyond drugs that target HER2," Dr André said.

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